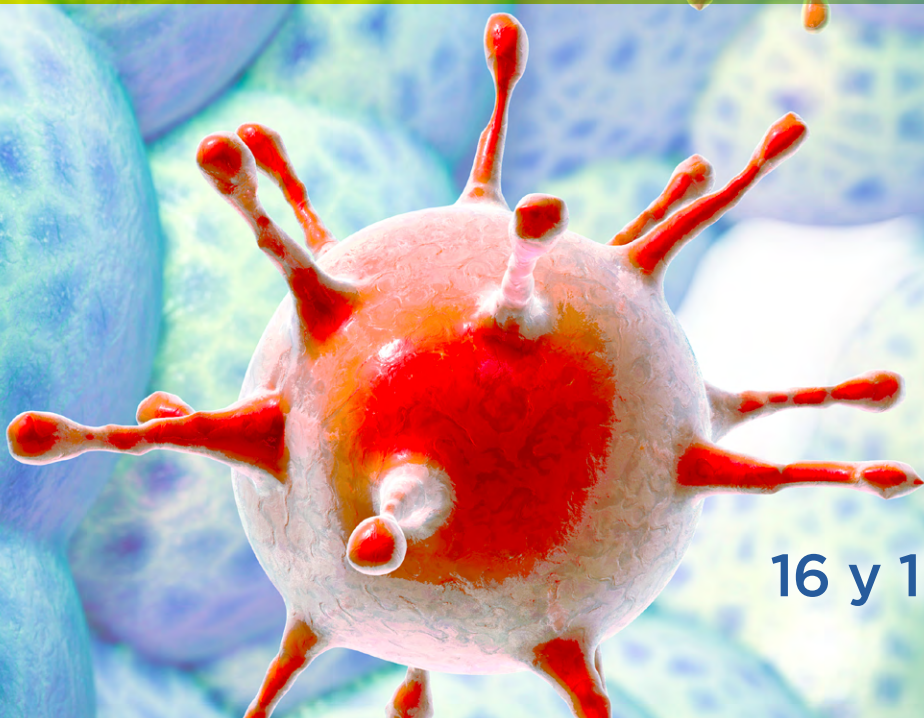


Organizado por:



**3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA**

INFECTHEMA



**16 y 17 de abril de 2026
Valencia**

LIBRO DE PONENCIAS

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Dr. Pau Montesinos Fernández

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INTERPRETACIÓN DEL ANTIBIOGRAMA Y GÉNESIS DE LAS RESISTENCIAS	
Dr. Juan Carlos Rodríguez Díaz	3
¿CÓMO SELECCIONAR A LOS PACIENTES CANDIDATOS PARA PROFILAXIS ANTIFÚNGICA?	
Dr. Francisco Manuel Martín Domínguez	21
INTERACCIONES DE LOS ANTIMICROBIANOS Y LAS NUEVAS TERAPIAS EN ONCOHEMATOLOGÍA	
Dr. José Ramón Azanza Perea	41
TALLER. INFECCIONES EN LEUCEMIAS AGUDAS	
Dr. José Francisco Tomás Martínez	60
TALLER. CASO CLÍNICO REAL EN PACIENTE CON MIELOMA MÚLTIPL	
Dra. Estrella Carrillo Cruz	97
TALLER. DIAGNÓSTICO Y TRATAMIENTO DE PATOLOGÍA INFECCIOSA EN PACIENTE HEMATOLÓGICO	
Ignacio Márquez Gómez	114
CC-ESCENARIO CLÍNICO DESAFIANTE: FIEBRE Y NEUTROPENIA	
Dra. Bianca Mendoza Zambrano	144
CC-FIEBRE EN EL PRIMER MES POST-INFUSIÓN DE CAR-T	
Dr. Miguel Soler Pérez	151
CC-INFILTRADOS PULMONARES EXTENSOS Y RÁPIDO DETERIORO RESPIRATORIO EN UN PACIENTE CON LMA	
Dra. Uxia Taboada Rodríguez	156
CC-RETINITIS EN PACIENTE CON MIELOMA MÚLTIPLE EN TRATAMIENTO CON ANTICUERPO BIESPECÍFICO ANTIBICMA	
Dra. Diana Casares Aguiar	166
TRATAMIENTO ANTIFÚNGICO ANTICIPADO (PRE-EMPTIVE) EN PACIENTES DE ALTO RIESGO: UNA ESTRATEGIA GUIADA POR DIAGNÓSTICO	
Dra. Isabel Izquierdo García	171
ABORDAJE INTEGRAL DEL PACIENTE CON NEOPLASIAS HEMATOLÓGICAS EN LAS UNIDADES DE CUIDADOS INTENSIVOS	
Dr. Pedro Castro Rebollo	182

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INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Interpretación del antibiograma y génesis de las resistencias

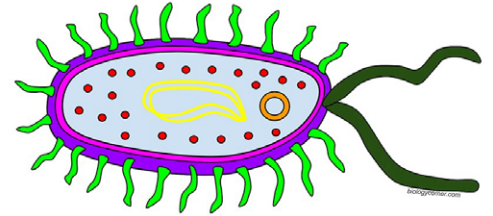
Juan Carlos Rodríguez Díaz

S. Microbiología. Hospital General Universitario Dr Balmis, Alicante
Instituto Sanitario y Biomédico de Alicante (ISABIAL)
Universidad Miguel Hernández



INDICE

- Microbiología del siglo XXI
- Interpretación del antibiograma
 - Genotípico
 - Fenotípico
- Generación de resistencias
 - Causas
 - Resistencias con mayor importancia clínica
- Conclusiones



Microbiología del siglo XXI



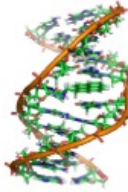





Microbiología 24/7



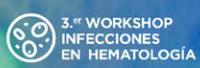
Adoption of new technologies in laboratory workflow practices for positive blood culture bottles: a cross-sectional survey among hospitals in the Autonomous Community of Valencia, Spain



Diagnostic Accuracy in Clinical Microbiology: An Unpredictable Component of Patient Care






¿Qué necesitamos saber?

Cartera de servicios de Microbiología

Etiología más frecuente y epidemiología local de resistencias

Guía local de tratamientos empíricos

Sistemas de comunicación rápida

Imprescindible:
 Información al grupo PROA y a la Comisión de infecciones
Recomendable:
 Página web/APP



OPINIÓN PERSONAL

Prueba correcta

Momento oportuno

Paciente seleccionado

Interpretación correcta

Tratamiento adecuado

➔

OBJETIVOS

Disminuir los falsos positivos

Sobretratamiento

Sobreutilización de recursos

Diagnostic Stewardship
Appropriate Testing and Judicious Treatments

Yasaman Fatemi, MD^{a,*}, Paul A. Bergl, MD^{b,c}

Crit Care Clin 38 (2022) 69–87

<https://doi.org/10.1016/j.ccc.2021.09.002>

RECOMENDACIONES SEIMC 2023

1. Debe aplicarse en todos los grupos PROA
2. Toma y transporte de la muestra
3. Cartera de servicios adecuada
4. Aplicar pruebas rápidas en hemocultivos:
 1. Etiología
 2. Mecanismos de resistencia
5. Detección rápida de virus asociados a IRA
6. Diagnóstico de infecciones fúngicas por métodos diferentes al cultivo
7. Procesamiento de muestras urgentes
8. Seleccionar los antibióticos a informar
9. Informes periódicos sobre epidemiología local de resistencias
10. Programa de vigilancia de bacterias multirresistentes

Consensus document

Antimicrobial stewardship in hospitals: Expert recommendation guidance document for activities in specific populations, syndromes and other aspects (PROA-2) from SEIMC, SEFH, SEMSPSCS, SEMICYUC and SEIP

Enrique Coronado¹, Jesús Rodríguez-Baño^{2,3,*}, José Luis Albarrán⁴, Esther Ciller⁵, Luis Escobar⁶, Aurora Fernández-Pérez⁷, Julio García-Rodríguez⁸, José Garrucha⁹, María Victoria Gil-Razcano¹⁰, Santiago Grau¹¹, Carlota Guzmán¹², Juan Pablo Hernández¹³, Norven Llanusa¹⁴, Carmen Martínez¹⁵, José Muñoz¹⁶, Xavier Novales¹⁷, Antonio Olivera¹⁸, José Ramón Palao-Pardo¹⁹, María Teresa Pérez-Rodríguez²⁰, Paula Ramírez²¹, Pedro Rey-Bell²², Pablo Vidal²³, Pilar Benítez-García²⁴



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Comunicación bidireccional

- ✓ Sistemas expertos de comunicación con el clínico
- ✓ Automatización total del Laboratorio
- ✓ Telemedicina
- ✓ Bases de datos multicéntricas: REDMIVA



Revista Iberoamericana
de Microbiología



Isolation of *Candida* spp. in large hospitals in the Antimicrobial Community of Valencia: population-based study (2013-2017)
Lara Ruiz-Alcaraz^{1,2}, Miguel Sanz-Balboa^{1,2}, Francisco Javier Roca^{1,2}, Manuel de la Voz, Juan Carlos Ruiz-Vizcaino^{1,2}, Vicente Balle^{1,2}, Sergio Perillo-Suñer^{1,2}, José Andrés Páez^{1,2}, Esperanza Menéndez^{1,2} (see also Rodríguez)

Use of Electronic Health Records and Clinical Decision Support Systems for Antimicrobial Stewardship

Steven B. Green¹, Tessa E. De la Motte², Kevin S. Gell³, Kevin T. Gell⁴, Ben Rong⁵ and Michael Ruppel⁶

¹Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; ²Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; ³Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; ⁴Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; ⁵Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA; ⁶Department of Medicine, University of Michigan, Ann Arbor, Michigan, USA



Clinical Microbiology Informatics

David D. Rhoads¹, Vikki Sirodzenko^{2,3}, Carol A. Rosick⁴, Ulan Parfenovitch⁵

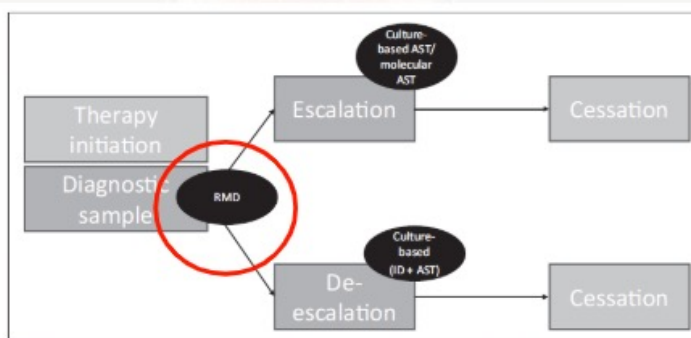
Table 1. Electronic Health Records and Clinical Decision Support Systems Commonly Available in the United States

	CDSS		CDSS				Smart? (Pharmacist OneSource)	MediAlert (SafeLinx)
Feature	Epix	Cerner	Therapy Advisor	Safety Surveillance	CC (Pharmacist)	CC (Pharmacist)	Yes	Yes
Drug Interactions	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Treatment guidelines	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baseline data	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug utilization	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Customizable alerts	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Clinical information	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Medication reconciliation	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prescription monitoring	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Reporting capabilities	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Product cost	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Mini Review: Clinical Routine Microbiology in the Era of Automation and Digital Health

Stefano Leo¹, Aleksandr Cherkasov², Geanilo Renda³ and Jacques Schrenzel^{1,2*}

Abbreviations: CDSS, Clinical Decision Support System; EHR, Electronic Health Record; EMR, Electronic Medical Record; LIMS, Laboratory Information Management System; POC, Point-of-Care; RPA, Robotic Process Automation; SaaS, Software as a Service; TDM, Therapeutic Drug Monitoring; UH, Ultra-High Performance Liquid Chromatography; WMS, Warehouse Management System; YTD, Year-to-Date.



npj | antimicrobials & resistance

Review article

Limitations of current techniques in clinical antimicrobial resistance diagnosis: examples and future prospects

Just Henzel¹, Carmen Gomez², Vincent C. Pithers³, Bruce E. Colebourne⁴ & Cheryl Beggs^{1*}



Antimicrobial stewardship and molecular diagnostics: a symbiotic approach to combating resistance in the ED and ICU

Jan J. De Waele^{1,2} and Jorina Boonstra^{1,2*}

Critical Care

Critical Care

The role of rapid multiplex molecular syndromic panels in the clinical management of infections in critically ill patients: an experts-opinion document

Thomas J. Evans¹, David J. Nisbet², Miguel Salazar³, Miguel Salazar⁴, Juan Luis del Real⁵, Thomas J. Evans⁶, David J. Nisbet⁷, Miguel Salazar⁸, Miguel Salazar⁹, Juan Luis del Real¹⁰, Thomas J. Evans¹¹, David J. Nisbet¹², Miguel Salazar¹³, Miguel Salazar¹⁴, Juan Luis del Real¹⁵, Thomas J. Evans¹⁶, David J. Nisbet¹⁷, Miguel Salazar¹⁸, Miguel Salazar¹⁹, Juan Luis del Real²⁰, Thomas J. Evans²¹, David J. Nisbet²², Miguel Salazar²³, Miguel Salazar²⁴, Juan Luis del Real²⁵, Thomas J. Evans²⁶, David J. Nisbet²⁷, Miguel Salazar²⁸, Miguel Salazar²⁹, Juan Luis del Real³⁰, Thomas J. Evans³¹, David J. Nisbet³², Miguel Salazar³³, Miguel Salazar³⁴, Juan Luis del Real³⁵, Thomas J. Evans³⁶, David J. Nisbet³⁷, Miguel Salazar³⁸, Miguel Salazar³⁹, Juan Luis del Real⁴⁰, Thomas J. Evans⁴¹, David J. Nisbet⁴², Miguel Salazar⁴³, Miguel Salazar⁴⁴, Juan Luis del Real⁴⁵, Thomas J. Evans⁴⁶, David J. Nisbet⁴⁷, Miguel Salazar⁴⁸, Miguel Salazar⁴⁹, Juan Luis del Real⁵⁰, Thomas J. Evans⁵¹, David J. 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Medicina personalizada
Detección precoz de brotes
Política de antibióticos
Diagnóstico procesos complejos

Table 1. Cont.

AI Applications for AMR	Concepts	Advantages	Drawbacks
AI, infectious diseases, and pediatric practices			
Appropriate antibiotic prescription	Appropriate therapy selection, dose, and correct administration route	- Automatic support for decisions and review of antimicrobial prescriptions - Automatic feedback input and relevant improvement - Directed operation	- Blissness in operation - Little labor - Need for health funds
Prediction of antibiotic resistance	ML techniques to predict early AMR or the probability of a microbial agent becoming resistant	- Genomic exploitation to predict the phenotype - Ability to support clinician's decision	- Lack of genotypes and genome data in NCBI or other databases - Challenge of large data integration
The severity of infection prediction	Machine/deep learning tools for infectious pathology recognition and appropriate management	- The efficiency of distinguishing infectious and noninfectious diseases - Decision support provision - Mortality reduction	- Challenge of accurate data collection - Insufficient relevant laboratory information

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.elsevier.com/locate/jcm

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Review
Machine learning in the clinical microbiology laboratory: has the time come for routine practice?
N. Peiffer-Smadja^{1,2}, S. Delliere¹, C. Rodriguez¹, G. Bigand¹, F.-X. Lescure¹, S. Fourati¹, E. Kuper^{1,2}

Clin Infect Microbiol. 2020 Oct;26(10):1300-1309

Interpretación del antibiograma



3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

MALDITOF

Características

- Identifica la especie desde cultivo positivo (sólido o hemocultivo)
- Resultado en 15 minutos

Inconvenientes:

- No se puede hacer de muestra directa
- No sirve en infecciones polimicrobianas
- No aporta datos de sensibilidad antibiótica

Conocimiento
epidemiología local
de resistencias



Original

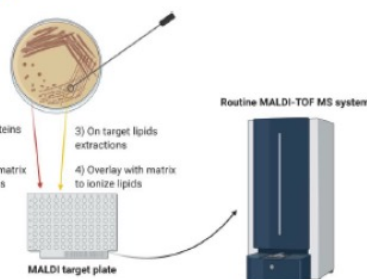
Revista Española de Quimioterapia
doi:10.37201/req/109.2020

Esperanza Merino¹
Adelina Gimeno²
Mar Alcalde³
Javier Cay⁴
Vicente Boia⁵
Carmen Molina-Pardines⁶
Maria Paz Ventero⁷
Antonio Galiana⁸
Elena Caro⁹
Juan Carlos Rodríguez²

Impact of Sepsis Flow Chip, a novelty fast microbiology method, in the treatment of bacteremia caused by Gram-negative bacilli

¹Department of Infectious Diseases, General University Hospital of Alicante (ISABIAL), Spain.
²Department of Microbiology, General University Hospital of Alicante (ISABIAL), Spain.
³Department of Infectious Diseases, Hospital Universitario Santa Lucía, Cartagena, Murcia.
⁴Department of Microbiology, FISABIO, General University Hospital of Elche, Elche, Spain.

Rev Esp Quimioter. 2021 Jun;34(3):193-199.



Enterobacterias

Escherichia coli

- BLEE/carbapenemasa (< 1 h)
- Rara a carbapenems

Proteus spp.

- BLEE (< 1 h)
- Poco frecuente
- No resistencia a carbapenems

Klebsiella spp.

- BLEE/carbapenemas (< 1 h)
- Mayor resistencia que *E. coli*

Resistencia a cef 3^{ra}:

95% BLEE
5% AmpC

Resistencia carbapenems:

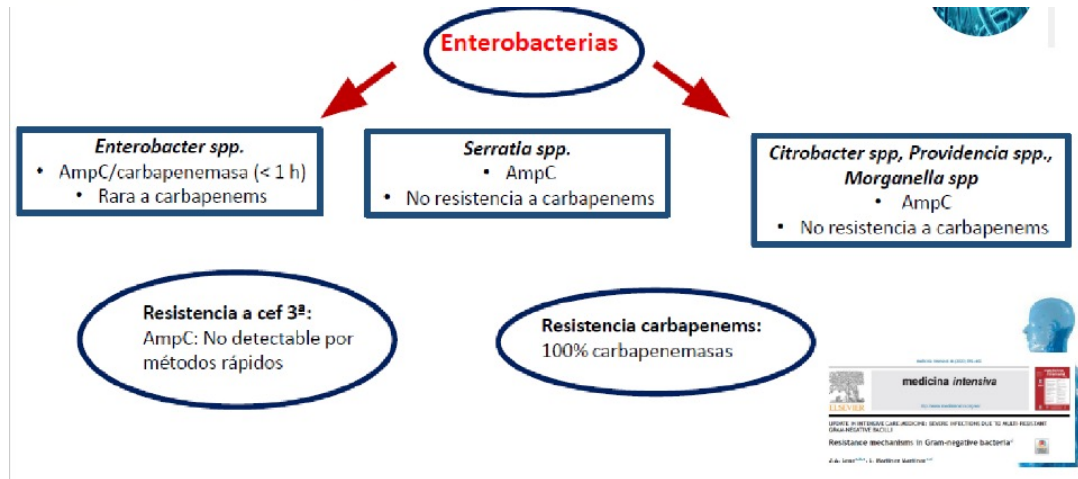
100% carbapenemasas





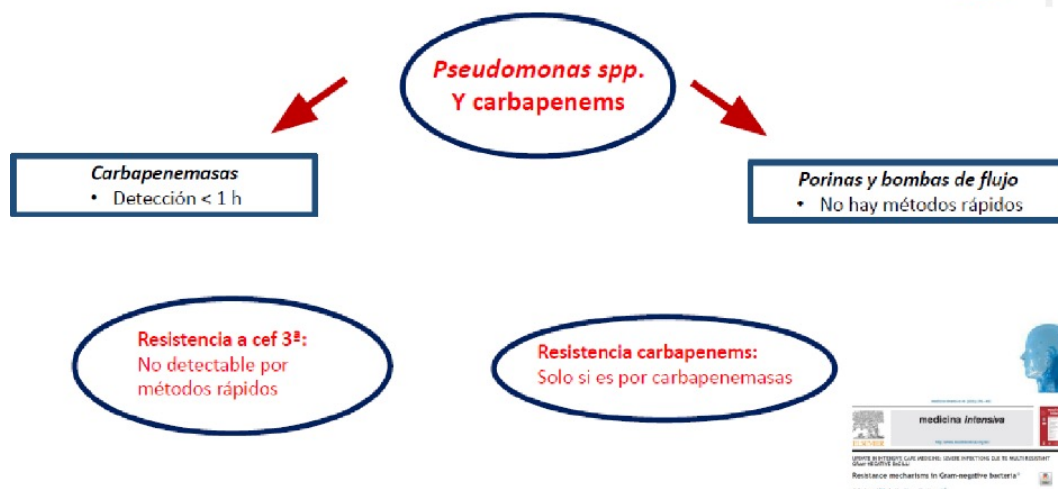
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INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA



3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA





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EN HEMATOLOGÍA

INFECTHEMA

TIPO DE CARBAPENEMASA	CARACTERÍSTICAS
Clase A	KPC Y GES No se inhiben por clavulánico ni tazobactam Es activo vaborbactam y avibactam
Clase B	IMP, VIM, NDM, GIM No hidrolizan aztreonam No son activos los inhibidores Aztreonam/avibactam
Clase D	OXA-23, OXA-40 Y OXA-48 Es activo avibactam
Algunas no son detectadas por los métodos habituales	



Expert Review of Anti-Infective Therapy

Carbapenemase producing *Klebsiella pneumoniae*: Implication on future therapeutic strategies

Alio-Hartwig, Ines-Gabriela, Voss-Braun, Laura, et al. (2015) *Journal of Antimicrobial Chemotherapy*



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INFECTHEMA

ESPECIE	CARACTERÍSTICAS
<i>Pseudomonas aeruginosa</i>	- Entre el 4 y el 30% - Metalobetalactamasas (VIM e IMP), GES - Otros mecanismos de resistencia a carbapenems: Betalactamasas tipo C, porinas y bombas de flujo
<i>Enterobacterias</i>	> 95% - KPC, metalobetalactamasas y OXA-48 - BLEE, AMPc, porinas y bombas de flujo
<i>Acinetobacter baumannii</i>	- Entre el 80 y el 100% - OXA-23, OXA-56 - AMPc, porinas y bombas de flujo

No son detectadas por los métodos habituales



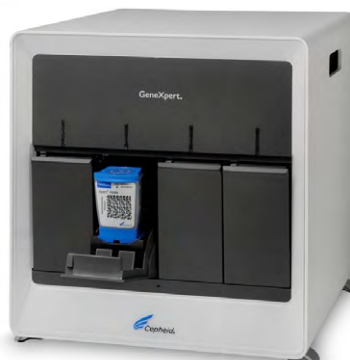
Métodos rápidos disponibles para detectar resistencias a fármacos betalactámicos

- | | |
|--|----------------------------------|
| a.- <i>Escherichia coli</i> , <i>Proteus spp</i> | Muy raramente |
| b.- <i>Klebsiella spp</i> | Carbapenemasas KPC, OXA-48 y MBL |
| c.- <i>Pseudomonas aeruginosa</i> : | Carbapenemasas MBL |
| e.- <i>Acinetobacter baumannii</i> | Otras carbapenemasas |
| f.- <i>Stenotrophomonas maltophilia</i> | Otros mecanismos |



Staphylococcus aureus

- SARM: Adquisición del gen *mecA*
- Baja afinidad a todos los betalactámicos excepto ceftarolina y ceftobiprol





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EN HEMATOLOGÍA

INFECTHEMA

Enterococcus

- Es importante conocer la especie:
 - *E. gallinarum*: Siempre resistente a glicopéptidos
 - *E. faecalis*: Siempre sensible a ampicilina y a glicopéptidos
 - *E. faecium*: Frecuentemente resistente a ampicilina y ha cepas resistentes a glicopéptidos
 - Fenotipo vanA:
 - El más frecuente
 - Resistencia a vancomicina y teicoplanina
 - Fenotipo vanB:
 - Resistencia a vancomicina



EUCAST rapid disc diffusion

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Acinetobacter baumannii*

- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Enterococcus spp.*



Lectura en 6-8 horas



J Antimicrob Chemother 2020; 75: 968-978
doi:10.1093/jac/dkz548 Advance Access publication 4 February 2020

**Journal of
Antimicrobial
Chemotherapy**

The EUCAST rapid disc diffusion method for antimicrobial susceptibility testing directly from positive blood culture bottles

Emma Jonasson¹*, Erika Matuschek² and Gunner Kahlmeter^{1,2}



[illegible]

 Clinical Microbiology and Infection (2006) 52, 320–321
 © 2005 The Authors
 Journal compilation © 2005 Blackwell Publishing Ltd
Clinical Microbiology and Infection
 Journal of Hospital Infection (2005) 60, 320–321
 doi:10.1016/j.cmi.2005.07.011

Correspondence: Dr J. A. Archer, Department of Microbiology, St James's Hospital, Dublin 8, Ireland.
 E-mail: jay@stjames.ie

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INFECTHEMA

CATEGORÍAS CLÍNICAS

Predicen el resultado del tratamiento

SENSIBLE

Alta probabilidad de **éxito** terapéutico

INTERMEDIO

Efecto terapéutico **incierto**

¿Probabilidad?

RESISTENTE

Alta probabilidad de **fracaso** terapéutico



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INFECTHEMA

REDEFINICIÓN CATEGORÍAS CLÍNICAS

SENSIBLE

Alta probabilidad de **éxito** terapéutico **usando dosis estándar**

**SENSIBLE
alta dosis**

Alta probabilidad de **éxito** terapéutico **cuando se incrementa la exposición**

RESISTENTE

Alta probabilidad de **fracaso** terapéutico **incluso cuando se incrementa la exposición**






Pseudomonas aeruginosa

- Piperacilina/tazobactam
- Ceftazidima
- Cefepime
- Imipenem
- Aztreonam
- Ciprofloxacino
- Levofloxacino

Stenotrophomonas maltophilia

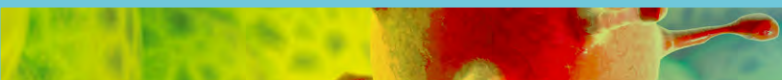
- Cotrimoxazol

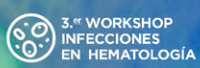
Acinetobacter baumannii

- Ciprofloxacino

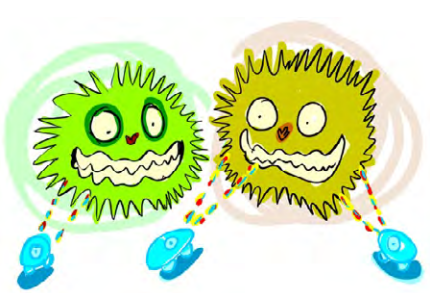
¡¡¡Todas las cepas son I!!!!

Mantienen S:
Meropenem
Cefta-avi
Ceftoloz/taz






Generación de resistencias



2019 ----- **2050**

Category	Value
Cancer	82,000,000
Cholera	15,000,000
AMR	7,000,000
Tetanus	12,000,000
Road Traffic	14,000,000
Measles	1,300,000
Diarrhoeal disease	1,200,000
Diabetes	60,000

2050 Data (Projected)

AMR (10,000,000)

International Journal of Biological Macromolecules 201 (2015) 15020

Contents lists available at ScienceDirect

International Journal of Biological Macromolecules

Journal homepage: www.elsevier.com/locate/ijbiomac

Review

An escape from ESKAPE pathogens: A comprehensive review on current and emerging therapeutics against antibiotic resistance

Anamika Singh, Mani Tamwar, T.P. Singh, Sujata Sharma, Prashant Sharma

ESKAPE

MRSA aggregate worldwide

CR-PA

CRAB

VRE

CRE

ESKAPE pathogens: antimicrobial resistance, epidemiology, clinical impact and therapeutics

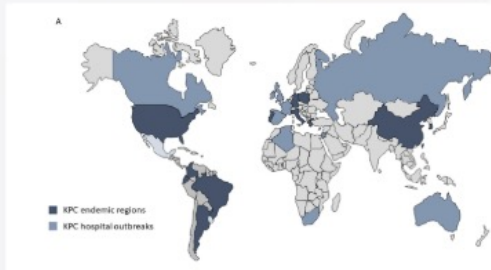
William H. Miller, D. J. B. Cook, A. K. Singh, P. Sharma



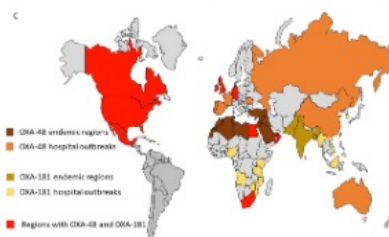
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INFECTHEMA

Carbapenemasas



Brotos frecuentes pero no
hay endemia



Clinical Microbiology Reviews
Laboratory detection of carbapenemases among Gram-negative organisms
Pankaj J. Sarma¹, J. J. Liaw², D. B. Naser³, S. C. Duggan⁴

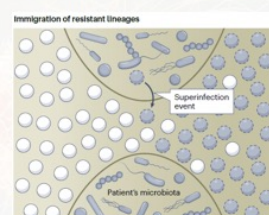
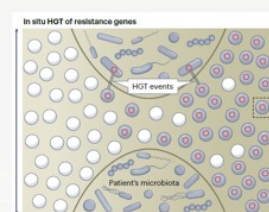
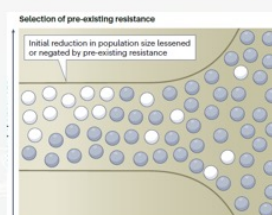
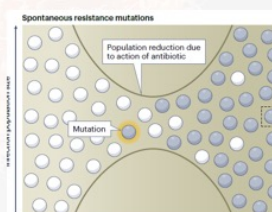
Generación de la Resistencia antibiótica

CAUSAS

- Mutaciones aparecidas de forma espontánea
- Transmisión horizontal de genes de resistencias de otras bacterias
- Selección de subpoblación previamente resistente
- Colonización por una cepa resistente

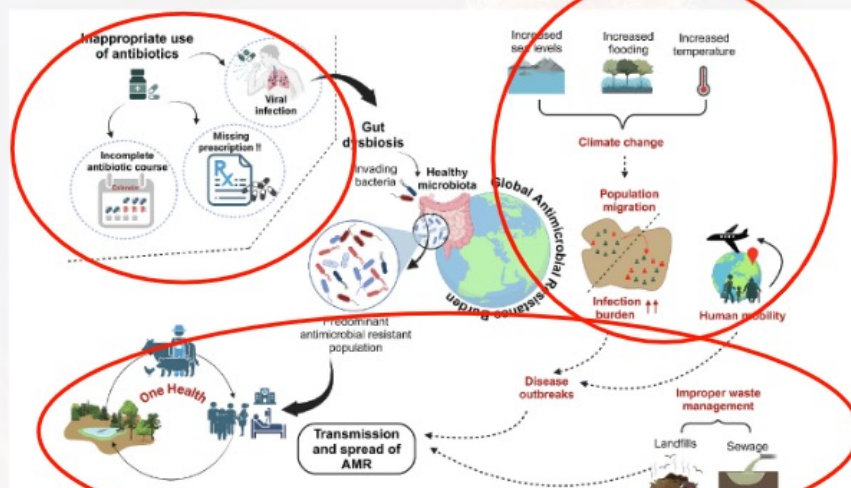
Review article
Ecological and evolutionary mechanisms driving within-patient emergence of antimicrobial resistance

Matthew J. Shephard¹, Aaron Fu², Naveed E. Harrington³, Annette Kottar⁴, Randall Cogney⁵, James D. Chalmers⁶, Steve Paterson⁷, Joanne L. Fothergill⁸ & Michael A. Brockhurst⁹





Generación de la Resistencia antibiótica



PARÁMETROS

- Virulencia
- Resistencia
- Fitness



Conclusiones





Conclusiones

- La Microbiología del siglo XXI permite:
 - Diagnóstico etiológico rápido
 - Detectar genotípicamente los principales mecanismos de resistencia
- El manejo de las infecciones por microorganismos multirresistentes exige un manejo multidisciplinar: equipos PROA
- Debe haber una comunicación fluida y constante con Microbiología

Organizado por:



3.^{er} WORKSHOP
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EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

¿CÓMO SELECCIONAR A LOS PACIENTES CANDIDATOS PARA PROFILAXIS ANTIFÚNGICA?

Francisco Manuel Martín Domínguez

Servicio de Hematología y Hemoterapia
Hospital Universitario Virgen del Rocío
Instituto de Biomedicina de Sevilla





CONFLICTO DE INTERESES

He recibido honorarios por simposios, charlas o consultoría científica por parte de Abbvie, Kite-Gilead, Abbvie, GSK y AstraZeneca.



ÍNDICE

1. STATE OF THE ART: INVASIVE FUNGAL DISEASE

2. ANTIFUNGAL PROPHYLAXIS

3. DIFFERENT SCENARIOS IN ANTIFUNGAL PROPHYLAXIS

4. HOW TO SELECT AN APPROPRIATE POPULATION FOR ANTIFUNGAL PROPHYLAXIS

5. CONCLUSIONS

ÍNDICE

1. STATE OF THE ART: INVASIVE FUNGAL DISEASE

Invasive fungal disease

Invasive fungal disease (IFD)

- **Molds**
 - *Aspergillus spp.*
 - *Fusarium spp.*
 - *Scedosporium spp.*
- **Yeasts**
 - *Candida spp.*
 - *Cryptococcus spp.*
 - *Trichosporia spp.*
- **Pneumocystis**
- **Dimorphic**
 - *Histoplasma.*
 - *Coccidioides spp.*
 - *Blastomyces.*

Definition EORTC / MSGERC

Proven

Probable

Possible

Clinical Infectious Diseases
MAJOR ARTICLE

Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium

Proven Invasive Fungal Disease

Invasive fungal disease (IFD)

- **Molds**
- **Yeasts**
- **Pneumocystis**

	Microscopic analyses	Culture	Blood	Serology	Tissue Nucleic Acid Diagnosis
Molds	👍	👍	👍	👎	👍
Yeasts	👍	👍	👍	👍	👍
Pneumocystis	👍	👎	👎	👎	👎

Probable Invasive Fungal Disease

Invasive fungal disease (IFD)

- **Host factors**
- **Clinical features**
- **Mycological evidence**

+

+

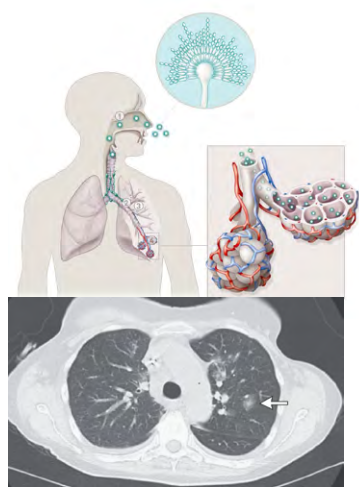




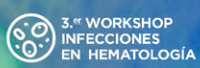

Probable Invasive Fungal Disease

Mold fungi

- **Host factors**
 - Neutropenia
 - Hematological malignancy
 - Allogeneic SCT
 - Solid organ transplant
 - Corticosteroids ≥ 0.3 mg/kg for ≥ 3 weeks
 - Treatment with T-cell immunosuppressants
 - Immunodeficiency
 - aGvHD grade III-IV refractory to steroids
- **Clinical features**
 - Radiological patterns
 - Signs and symptoms
- **Mycological evidence**
 - Non-sterile culture
 - Galactomannan antigen
 - *Aspergillus* PCR



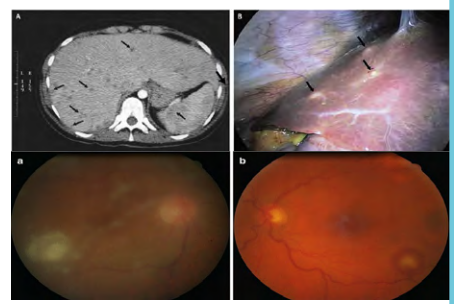


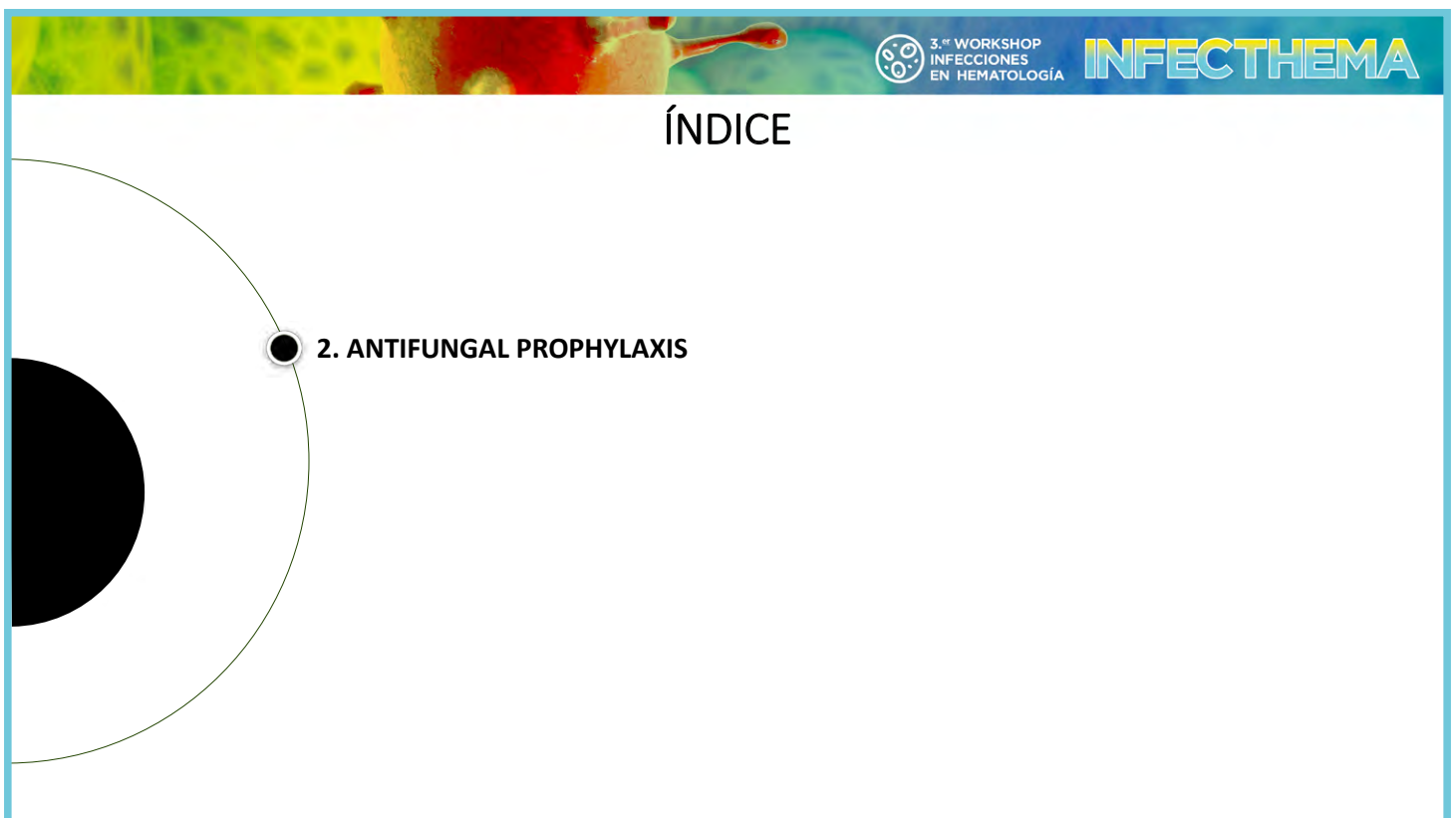
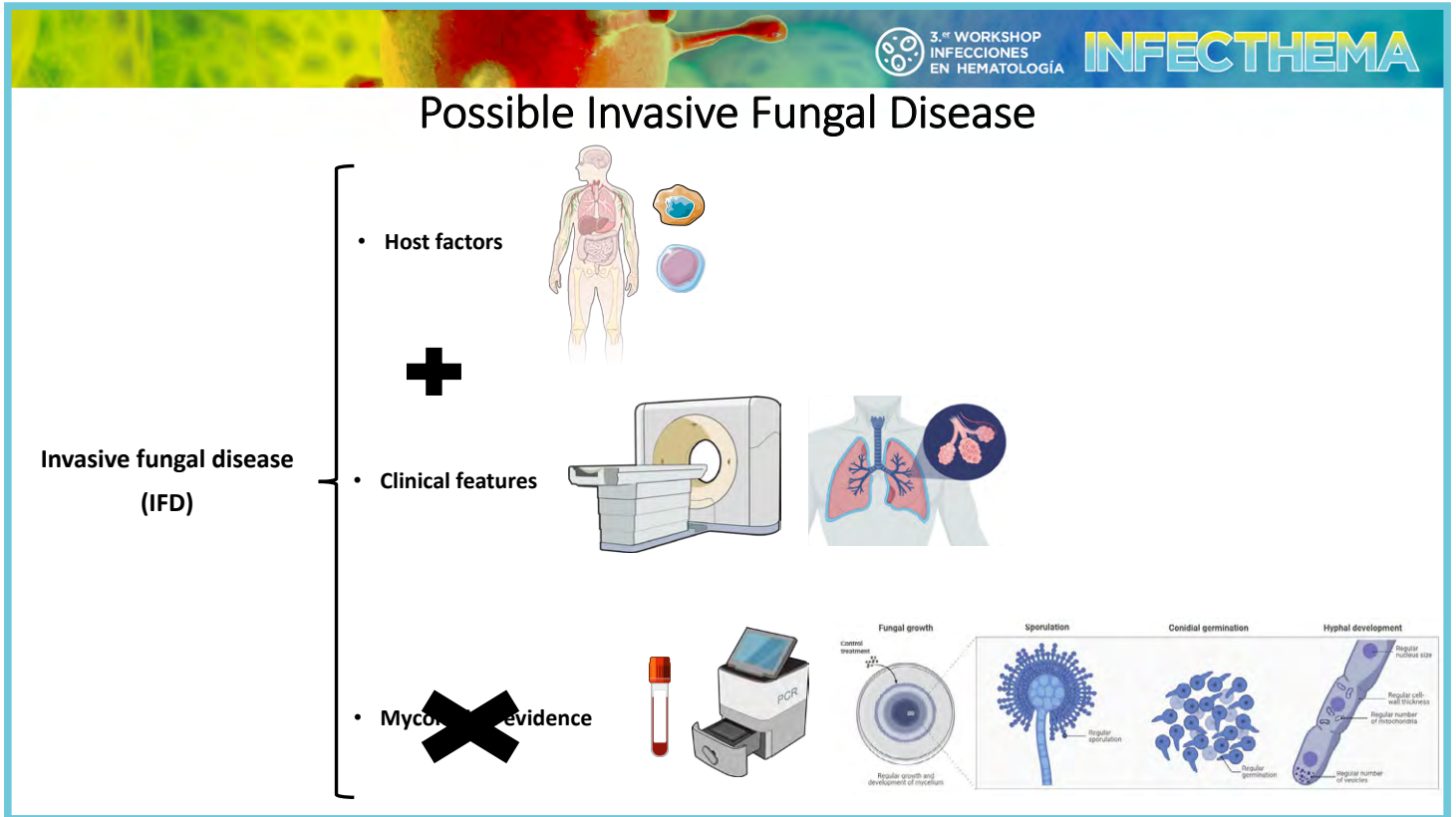



Probable Invasive Fungal Disease

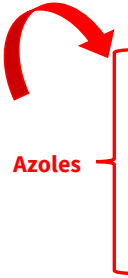
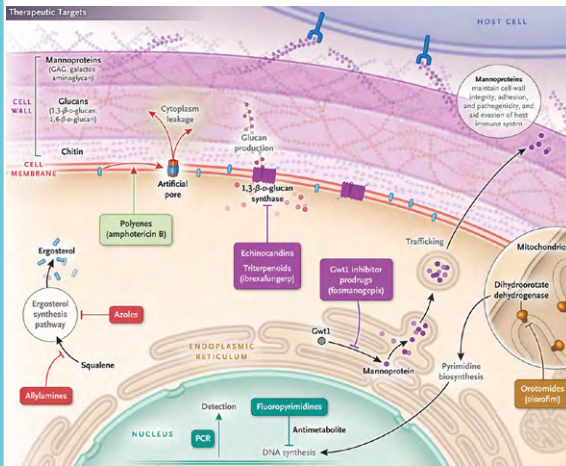
Candidiasis

- **Host factors**
 - Neutropenia
 - Hematological malignancy
 - Allogeneic SCT
 - Solid organ transplant
 - Corticosteroids ≥ 0.3 mg/kg for ≥ 3 weeks
 - Treatment with T-cell immunosuppressants
 - Immunodeficiency
 - aGvHD grade III-IV refractory to steroids
- **Clinical features**
 - Small, target-like abscesses in liver or spleen (bull's-eye lesions) or in the brain, or, meningeal enhancement
 - Progressive retinal exudates or vitreal opacities on ophthalmologic examination
- **Mycological evidence**
 - β -D-glucan (Fungitell) ≥ 80 ng/L (pg/mL) detected in at least 2 consecutive serum samples provided that other etiologies have been excluded
 - Positive T2Candida





Pharmacological agents used in fungal infections



Azoles

- Posaconazole → *Aspergillus spp, Candida spp, Mucor spp*
- Fluconazole → *Candida spp*
- Voriconazole → *Aspergillus spp, Candida spp, Mucor spp*
- Isavuconazole → *Aspergillus spp, Mucor spp*
- Itraconazole

Echinocandins

- Micafungin
- Caspofungin → *Aspergillus spp, Candida spp*
- Anidulafungin

Polyenes

- Liposomal amphotericin B → *Aspergillus spp, Mucor spp > Candida spp*

Hossain CM, Ryan LK, Gera M, Choudhuri S, Lyle N, Ali KA, Diamond G. Antifungals and Drug Resistance. *Encyclopedia*. 2022; 2(4):1722-1737. <https://doi.org/10.3390/encyclopedia2040118>

ÍNDICE

3. DIFFERENT SCENARIOS IN ANTIFUNGAL PROPHYLAXIS

Antifungal prophylaxis

Clinical setting

- AML
- MDS
- ALL
- MPNs
- CLL
- Multiple myeloma
- Non-Hodgkin lymphoma
- Hodgkin lymphoma
- Allo-HSCT
- CAR T
- Autologous HSCT

Drug interactions

- Venetoclax interactions
- Vinca Alkaloid interactions
- Calcineurin Inhibitors
- QTc prolonging agents
- Corticosteroids
- Cyclophosphamide

Pagano L, Maschmeyer G, Lamoth F, Blennow O, Xhaard A, Spadea M, Busca A, Cordonnier C, Maertens J; ECIL. Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). Leukemia. 2025 Jul;39(7):1547-1557. doi: 10.1038/s41375-025-02586-7. Epub 2025 Apr 9. PMID: 4020079; PMCID: PMC12208874.

Antifungal prophylaxis

National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2026

Prevention and Treatment of Cancer-Related Infections

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

PREVENTION OF FUNGAL INFECTIONS
See [Antifungal Agents \(FEV-B\)](#) for dosing, spectrum, and specific comments/cautions

Overall Infection Risk in Patients with Cancer ^a	Disease/Therapy Examples	Consider Antifungal Prophylaxis Based on Patient- and Center-Specific Risk Factors See Antipneumocystis Prophylaxis (INF-6)	Duration
Intermediate to high	Acute lymphoblastic leukemia (ALL)	• Fluconazole^f or an echinocandin^g • Amphotericin B products^h (category 2B)	Typically until resolution of neutropenia
	Myelodysplastic syndromes (MDS) (neutropenic)	• Posaconazole^f (category 1) • Voriconazole,^f isavuconazole,^f an echinocandin,^g amphotericin B products,^h or fluconazole (if mold activity not needed)ⁱ (all category 2B)	
	Acute myeloid leukemia (AML) (neutropenic)	• Fluconazole ^f or an echinocandin ^g (both category 1)	
	Autologous HCT with mucositis ^g	No prophylaxis (category 2B)	N/A
	Allogeneic HCT (neutropenic) ^a	• Fluconazole^f or an echinocandin^g (both category 1) • Voriconazole,^f posaconazole,^f isavuconazole,^f or amphotericin B products^h (all category 2B)	Continue during neutropenia ⁱ
	Immune and targeted treatments	See Immune and Targeted Treatments (INF-A)	Depends on nature and duration of treatment
	Significant acute GVHD (especially grade 3/4) receiving IST	• Posaconazole^f (category 1) • Voriconazole,^f echinocandin,^g amphotericin B products,^h or isavuconazole,^f (all category 2B)	Until resolution of significant GVHD



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EN HEMATOLOGÍA

INFECTHEMA

Antifungal prophylaxis: AML

Agent	Dosage	ECIL 5-6
Posaconazole	Tablet 300 mg q24h p.o (q12h on day 1)	A-I
Amphotericin B liposomal	inhalation 10 mg twice weekly	B-I
Fluconazole	400 mg q24h, p.o or i.v	B-I
Voriconazole	6 mg/Kg q12 h first day then 4 mg/Kg q12h, i.v or p.o	B-II
Isavuconazole	200 mg q8h p.o first 2 days then 200 mg q24h	?

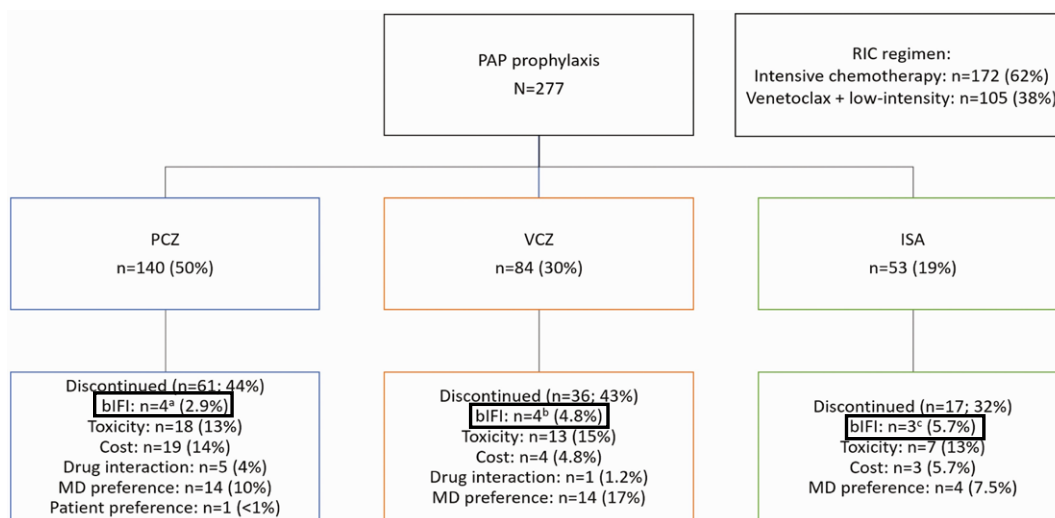
Pagano L, Maschmeyer G, Lamoth F, Blennow O, Xhaard A, Spadea M, Busca A, Cordonnier C, Maertens J; ECIL Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). Leukemia. 2025 Jul;39(7):1547-1557. doi: 10.1038/s41375-025-02586-7. Epub 2025 Apr 9. PMID: 40200079; PMCID: PMC12208874.



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INFECTHEMA

Antifungal prophylaxis: AML



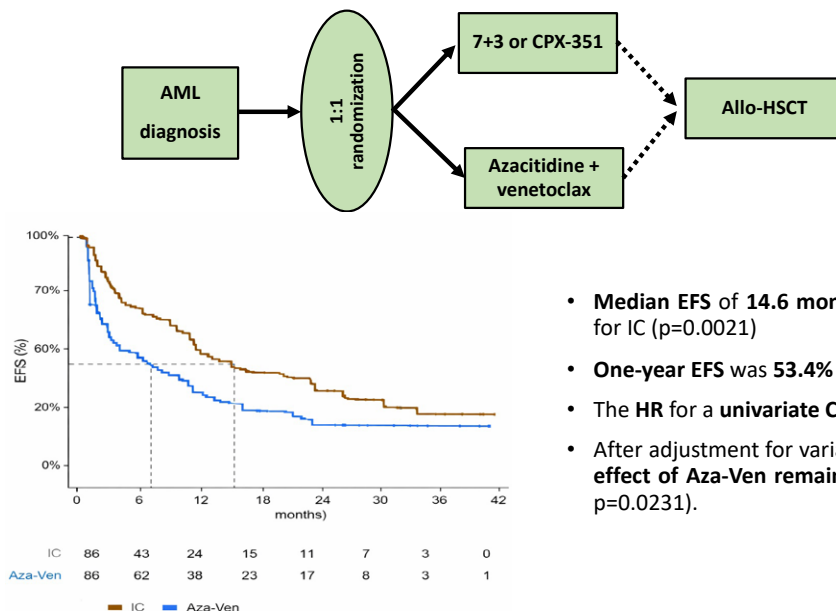
Rausch CR, DiPippo AJ, Jiang Y, DiNardo CD, Kadia T, Maiti A, et al. Comparison of mold active triazoles as primary antifungal prophylaxis in patients with newly diagnosed acute myeloid leukemia in the era of molecularly targeted therapies. Clin Infect Dis. 2022 Oct 29;75(9):1503-1510. doi:10.1093/cid/ciac230.



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INFECTHEMA

Changing PARADIGM: azacitidine and venetoclax



- Median EFS of 14.6 months for Aza-Ven vs 6.15 months for IC (p=0.0021)
- One-year EFS was 53.4% for Aza-Ven vs 36% for IC.
- The HR for a univariate Cox model was 0.57 (p=0.0022).
- After adjustment for variables in multivariable model, the effect of Aza-Ven remained protective for EFS (HR 0.66; p=0.0231).

Fathi AT. ASH. 2025



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Antifungal prophylaxis: AML

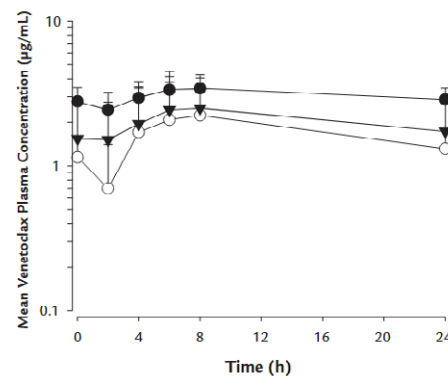
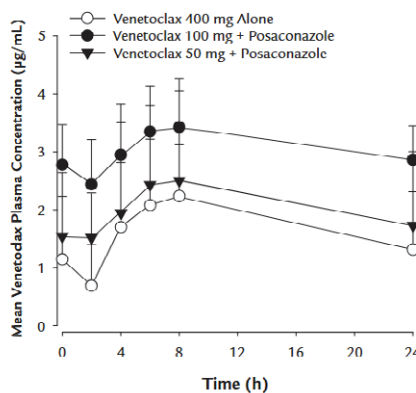
ASCO Annual Meeting

Abstract #: 6530

Poster Session

Comparable efficacy of venetoclax 50mg with posaconazole versus venetoclax 400mg in newly diagnosed AML patients: A prospective study of pharmacokinetics, toxicity, and clinical outcomes.

Authors: Gaurav Prakash, Rudra N. Swain, Anu Kumari, Smriti Pattanaik, Charanpreet Singh, Anilant Jain, Alka Khadwal, Pankaj Malhotra



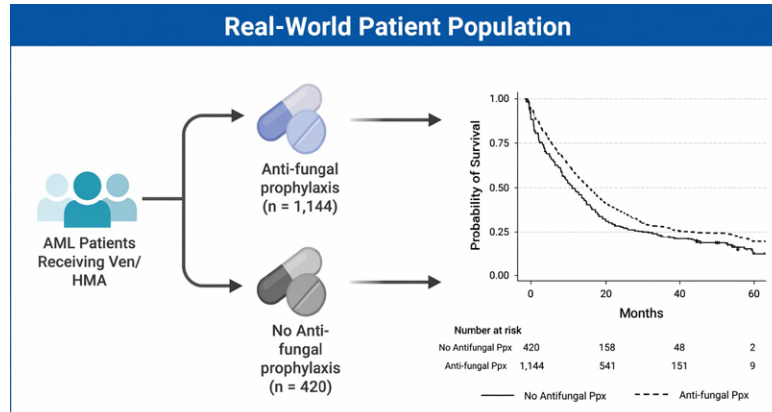
- In the context of azacitidine-venetoclax therapy, the **standard dose** of **venetoclax** is **400 mg daily** (after ramp-up: 100 mg on day 1, 200 mg on day 2, and 400 mg from day 3 onward).
- When **posaconazole 300 mg daily** is **added**, the **venetoclax dose should be reduced to 70 mg daily** according to official recommendations.



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Antifungal prophylaxis: AML



- A **variety of azoles** are **commonly used** as AFP in **patients receiving first-line Ven/HMA**.
- In a large real-world population, **azole use does not improve overall survival** in patients with newly diagnosed AML receiving Ven/HMA.
- Only **60%** of patients on azole AFP had **appropriate venetoclax dose reductions**, risking DDIs that offset potential benefit.

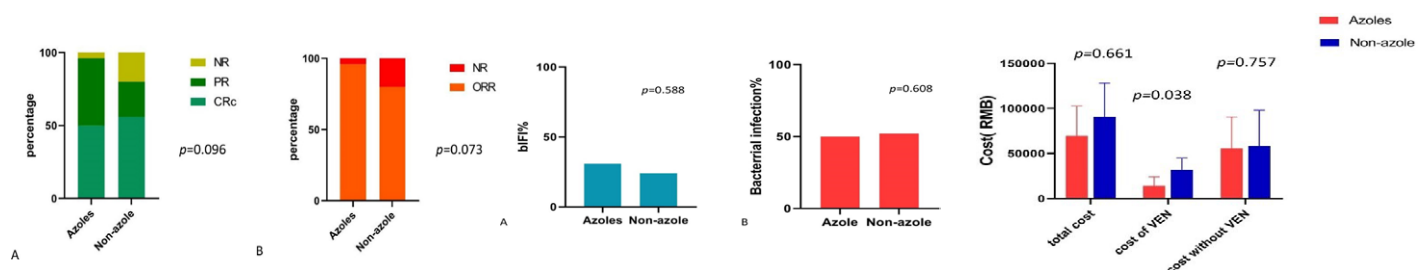
Ambinder A, Levis M, Wang X, Pratz K, Matthews A. A real-world analysis of the impact of azole antifungal prophylaxis on outcomes in patients with newly diagnosed acute myeloid leukemia treated with venetoclax-based therapy. Leuk Res. 2026 Mar 15;164:108204. doi: 10.1016/j.leukres.2026.108204. Epub ahead of print. PMID: 41855751.



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EN HEMATOLOGÍA

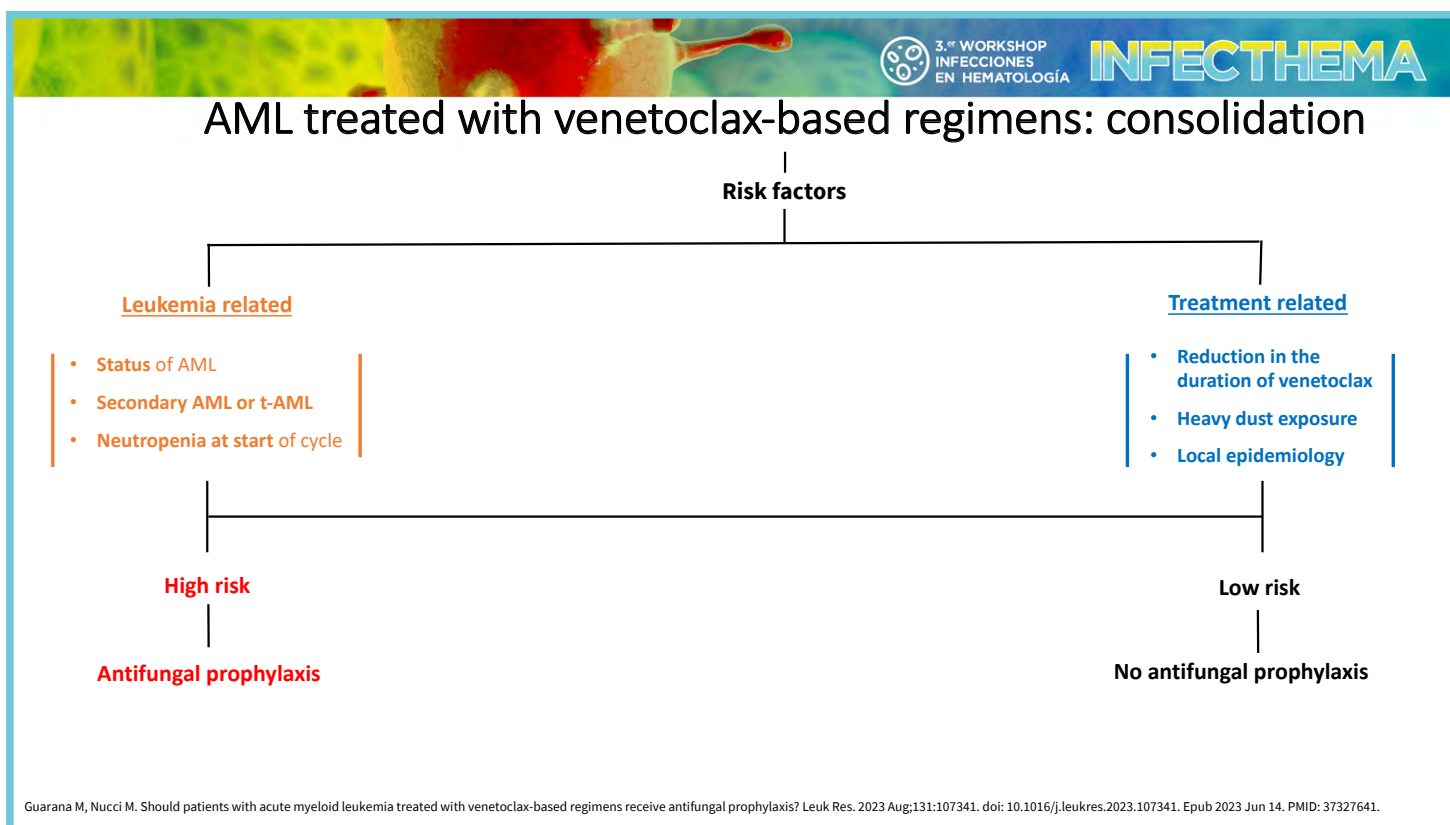
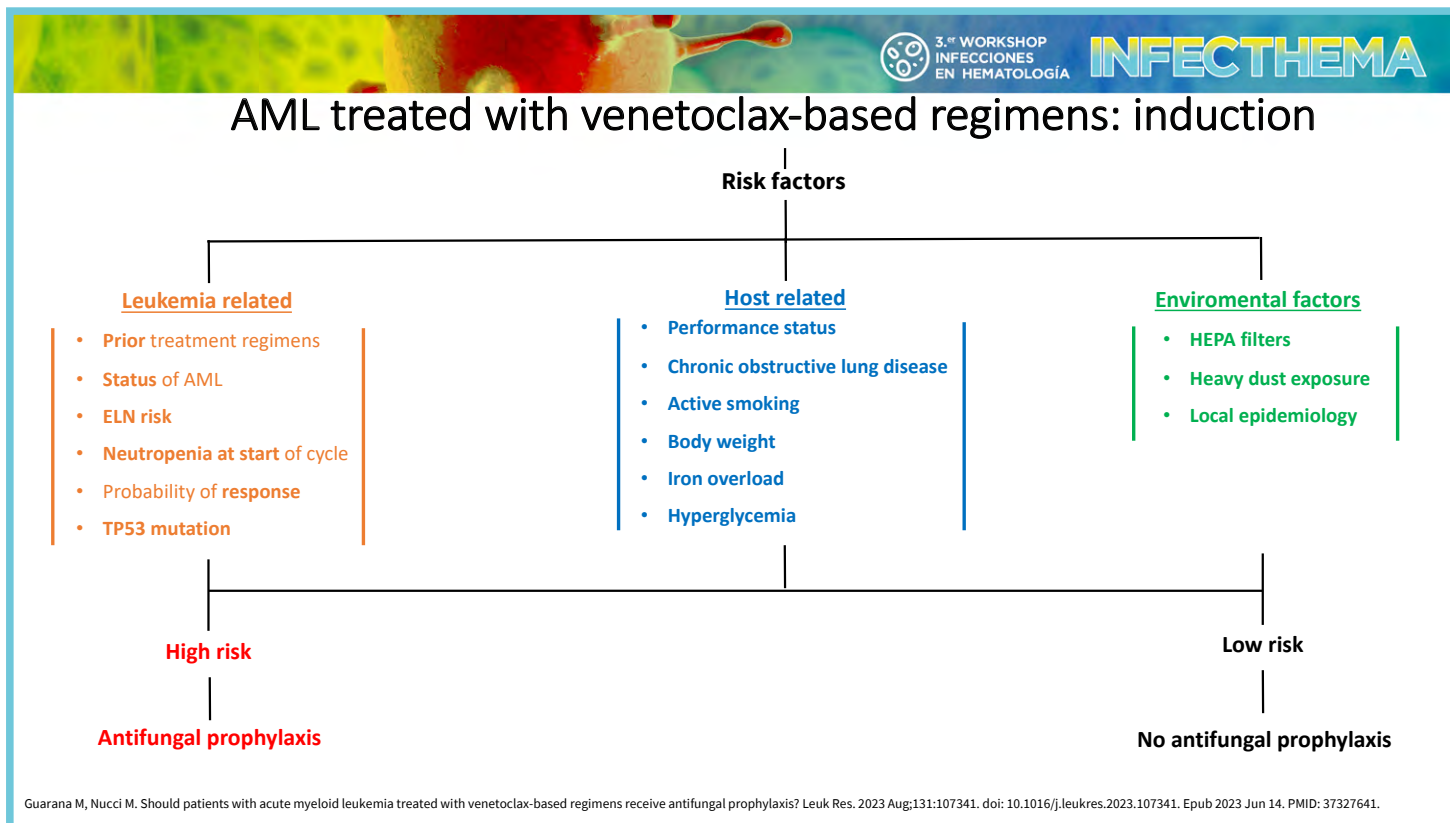
INFECTHEMA

Antifungal prophylaxis: AML



- There was **no significant difference in CRc rates** between the azole and nonazole groups (50% vs 56%, $p = 0.096$). There was **no significant difference in ORR** between the azole and nonazole groups (96.2% vs 80.0%, $p = 0.073$).
- There was **no significant difference of breakthrough fungal infection** in the azole group and nonazole group (30.8% vs 24%, $p = 0.588$). There was **no significant difference of bacterial infection** in the azole group and nonazole group (50% vs 52%, $p = 0.608$).
- For the mean total cost and cost without VEN, **no difference was observed** between the azole group and the nonazole group ($p = 0.661$ and $p = 0.757$, respectively). **The mean VEN costs in the azole group and nonazole group were significantly different** ($p = 0.038$).

Zhong X, Wang J, Dai Y, Huang X, Liu J, Xiang B, Ma H. Combining azole antifungals with venetoclax plus azacitidine in patients with newly diagnosed acute myeloid leukemia. Hematology. 2024 Dec;29(1):2433172. doi: 10.1080/16078454.2024.2433172. Epub 2024 Nov 25. PMID: 39585800.



Antifungal prophylaxis: AML

FLT3 inhibitor

Midostaurin

- Induction therapy
- Consolidacion only if risk factors
- No dose adjustment.

Gilteritinib

- No dose adjustment.
- Controversial in R/R setting

Quizartinib

- Dose adjustment if concomitant posaconazole

Agarwal SK, DiNardo CD, Potluri J, Dunbar M, Kantarjian HM, Humerickhouse RA, et al. Management of venetoclax-posaconazole interaction in acute myeloid leukemia patients: evaluation of dose adjustments. Clin Ther. 2017 Feb;39(2):359-367. doi:10.1016/j.clinthera.2017.01.003.

Antifungal prophylaxis: isavuconazole in AML

Isavuconazole

NCNN 2026 (2b)

- AML / MDS with concurrent neutropenia
- Allo-HSCT with neutropenia
- GvHD with systemic treatment

ECIL-10 (BII)

- AML / MDS with induction therapy
- Allo-HSCT in post-engraftment period

AGIHO 2022

Moderate recommendation

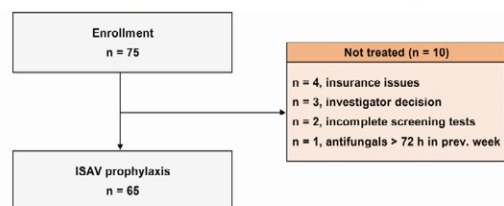
Bose P, McCue D, Wurster S, Wiederhold NP, Konopleva M, Kadia TM, et al. Isavuconazole as primary antifungal prophylaxis in patients with acute myeloid leukemia or myelodysplastic syndrome: an open-label, prospective, phase 2 study. Clin Infect Dis. 2021;72(10):1755-1763. doi:10.1093/cid/ciaa358.



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EN HEMATOLOGÍA

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Antifungal prophylaxis: isavuconazole in AML / MDS



Characteristic	No. (%)
Age, y, median (range)	67 (21–86)
Sex, No. (%)	
Male	36 (55)
Female	29 (45)
Diagnosis, No. (%)	
AML	62 (95)
MDS	3 (5)
Absolute neutrophil count at enrollment, median (range)	0.72 (0.00–23.18)
RIC received	
High-intensity RIC, ^a no. (%)	30 (46%)
Without FLT3 TKI or venetoclax	22
With FLT3 TKI	5
With venetoclax	2
With FLT3 TKI + venetoclax	1
Hypomethylating agents, ^b no. (%)	25 (38)
Without FLT3 TKI or venetoclax	1
With venetoclax	23
With FLT3 TKI + venetoclax	1
Low-intensity chemotherapy, ^c no. (%)	10 (15)

- **Isavuconazole** is a **safe and effective** alternative.
- **Breakthrough IFI** rate was **15%.**
- Short-term survival with **b-IFIs** was **excellent.**
- **Isavuconazole** may be **less effective** in patients with **prolonged neutropenia and delayed neutrophil recovery.**
- **Isavuconazole** may increase **venetoclax serum concentrations.**
- **Isavuconazole toxicity** is **less toxic** and **good-alternative** in patients with posaconazole-associated toxicities

Reason for Discontinuation of ISAV	Total No. (%)	IFI Outcome 30 d After the Last Dose of ISAV			
		No IFI	Possible IFI	Probable IFI	Proven IFI
Completed 12 wk of ISAV	9 (14)	9	0	0	0
Achieved CR/CRi + ANC > 0.5	37 (57)	36	0	0	1
Investigator decision	7 (11)	6	1	0	0
Death, not IFI-related	2 (3)	NA (2)	NA	NA	NA
Possible IFI	8 (12)	0	7	1	0
Probable IFI	2 (3)	0	0	2	0
All patients, no. (%)	...	53 (82)	8 (12)	3 (5)	1 (2)

Bose P, McCue D, Wurster S, Wiederhold NP, Konopleva M, Kadia TM, et al. Isavuconazole as primary antifungal prophylaxis in patients with acute myeloid leukemia or myelodysplastic syndrome: an open-label, prospective, phase 2 study. Clin Infect Dis. 2021;72(10):1755-1763. doi:10.1093/cid/ciaa358.

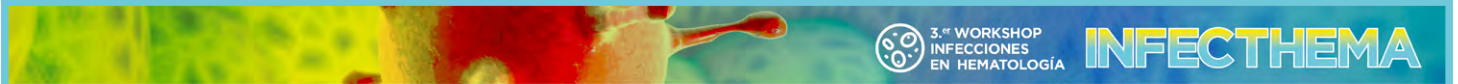


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Antifungal prophylaxis: MDS and MPNs

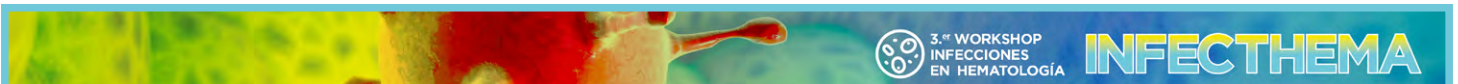
Scenario	Agent	ECIL 5-6
MDS Intermediate/High treated as AML with intensive chemotherapy	Posaconazole	A-I
MDS Intermediate/High Treated with Azacytidine	Posaconazole	?



Antifungal prophylaxis: ALL, CLL, NHL, HL and MM

Nothing

Pagano L, Maschmeyer G, Lamoth F, Blennow O, Xhaard A, Spadea M, Busca A, Cordonnier C, Maertens J; ECIL. Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). *Leukemia*. 2025 Jul;39(7):1547-1557. doi: 10.1038/s41375-025-02586-7. Epub 2025 Apr 9. PMID: 40200079; PMCID: PMC12208874.



Antifungal prophylaxis: allo-HSCT

Engraftment?

Pre-engraftment

Risk of mold infection

Low risk

- Fluconazol
- **Micafungin**
- Voriconazole
- Posaconazole
- Isavuconazole

High risk

- Voriconazole
- **Posaconazole**
- Isavuconazole

Girmenia et al, BBMT 2014

- Active leukemia
- Cord blood
- Unrelated donor

Post-engraftment

Steroids?

Non-steroids

- Posaconazole
- Voriconazole

Steroids

- **Posaconazole**
- Voriconazole
- Isavuconazole

Pagano L, Maschmeyer G, Lamoth F, Blennow O, Xhaard A, Spadea M, Busca A, Cordonnier C, Maertens J; ECIL. Primary antifungal prophylaxis in hematological malignancies. Updated clinical practice guidelines by the European Conference on Infections in Leukemia (ECIL). *Leukemia*. 2025 Jul;39(7):1547-1557. doi: 10.1038/s41375-025-02586-7. Epub 2025 Apr 9. PMID: 40200079; PMCID: PMC12208874.

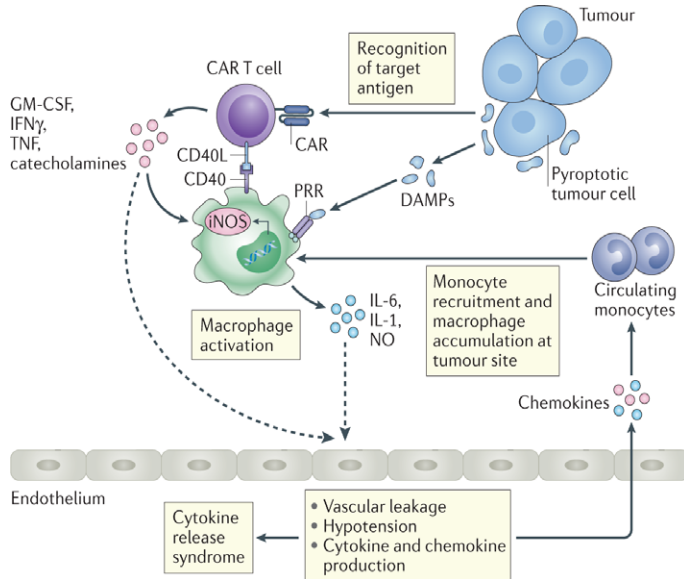
Rausch CR, DiPippo AJ, Jiang Y, DiNardo CD, Kadia T, Maiti A, et al. Comparison of mold active triazoles as primary antifungal prophylaxis in patients with newly diagnosed acute myeloid leukemia in the era of molecularly targeted therapies. *Clin Infect Dis*. 2022 Oct 29;75(9):1503-1510. doi:10.1093/cid/ciac230.



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EN HEMATOLOGÍA

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Antifungal prophylaxis: CART



Fungal infection rate: 3-15%

Risk factors

- Prior treatment regimens
- Prolonged cytopenias
- Anti-inflammatory drugs

¿Prophylactic strategy?

- Fungal resistance
- Drug interactions
- Toxicity

Individualized approach

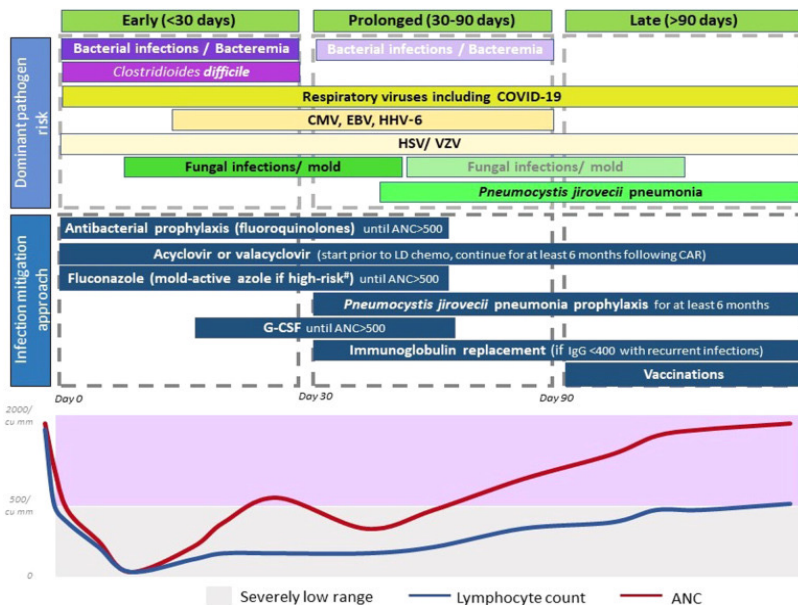
Melica G, Luna de Abia A, Shah GL, Devlin S, Corona M, Fein J, et al. Shift from widespread to tailored antifungal prophylaxis in lymphoma patients treated with CD19 CAR T cell therapy: results from a large retrospective cohort. Transplant Cell Ther. 2025 Jan;31(1):36-44. doi:10.1016/j.jtct.2024.10.010.



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INFECCIONES
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Antifungal prophylaxis: CART



Early post-CART
< 30 days

Risk factors

- Prior BMT
- Steroids > 3 days
- Prolonged cytopenia

Posaconazole

No risk factors

Fluconazole

Melica G, Luna de Abia A, Shah GL, Devlin S, Corona M, Fein J, et al. Shift from widespread to tailored antifungal prophylaxis in lymphoma patients treated with CD19 CAR T cell therapy: results from a large retrospective cohort. Transplant Cell Ther. 2025 Jan;31(1):36-44. doi:10.1016/j.jtct.2024.10.010.



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ÍNDICE

4. HOW TO SELECT AN APPROPRIATE POPULATION FOR ANTIFUNGAL PROPHYLAXIS

How to select an appropriate population of patients with hematologic malignancies for antifungal prophylaxis

Risk factors

High risk

- AML with **intensive chemotherapy**
- AML with **Aza-Ven** and **neutropenia**
- t-AML or secondary AML
- MDS Intermediate/High **treated** as AML with **intensive chemotherapy**
- **High-risk allo-HSCT**
- Allo-HSCT on **steroids**
- CART with **high-risk factors**

Posaconazole

Moderate risk

- **Low-risk allo-HSCT**
- **CART** with isolated **neutropenia** as risk factor
- AML with FLT3i and QTc

Fluconazole

Mild risk

- AML with **Aza-Ven** and non-high risk factors
- CART with **no high-risk factors**
- ALL, HL, NHL, MM, CLL with **no high-risk factors**

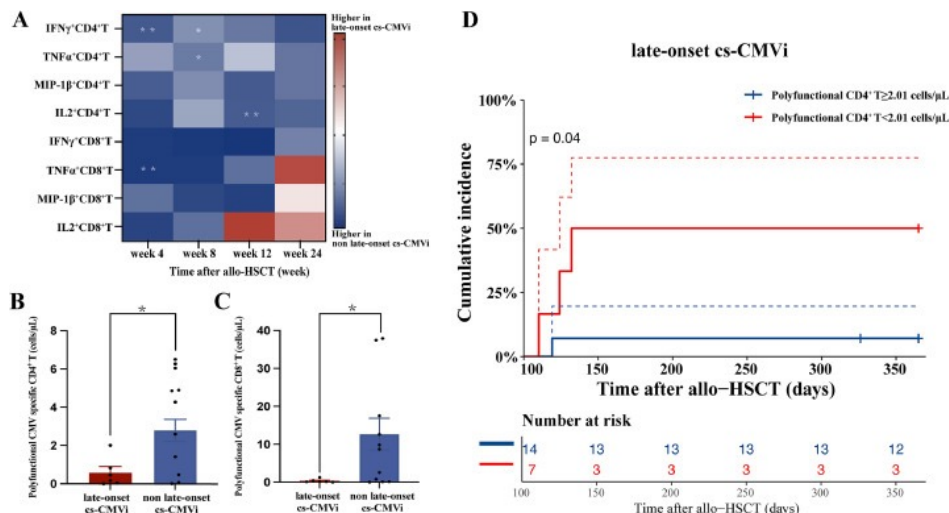
No antifungal prophylaxis



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How to select an appropriate population of patients with hematologic malignancies for antifungal prophylaxis



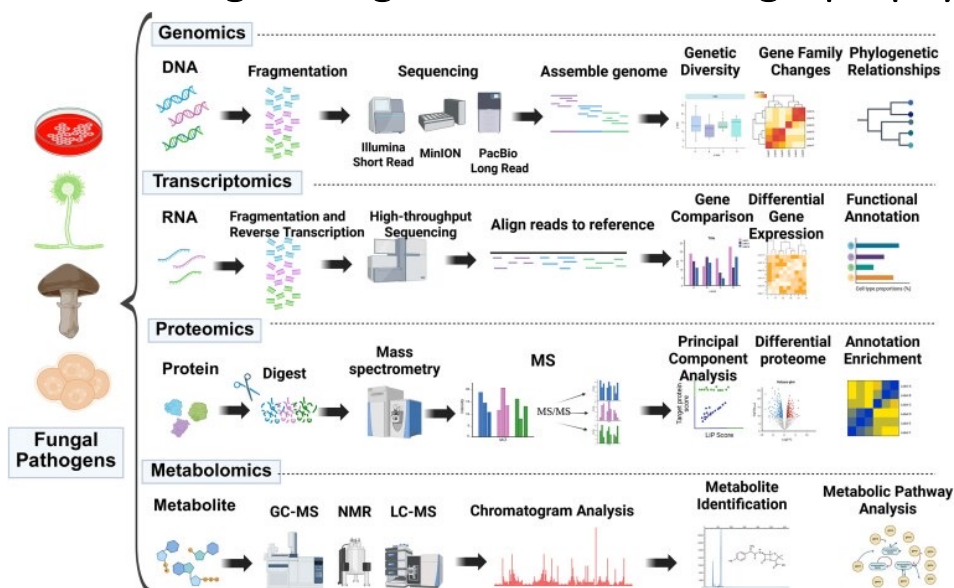
Wang L, Li S, Huang J, Zhang Z, Pan Z, Jiang C, Lu H, Zhang S, Cao Y, Cai X, Cai G, Hu X. Impaired CMV-specific CD4⁺T-cell reconstitution is associated with CMV infection after letermovir cessation. *Exp Hematol*. 2025 Oct;150:104859. doi: 10.1016/j.exphem.2025.104859. Epub 2025 Jul 16. PMID: 40680812.



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INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

How to select an appropriate population of patients with hematologic malignancies for antifungal prophylaxis



Scott J, Machado A, Carvalho A, Cunha C. Harnessing host-derived biomarkers for personalized diagnosis of invasive fungal infections. *Expert Rev Mol Diagn*. 2025 Dec;25(12):847-858. doi: 10.1080/14737159.2025.2587613. Epub 2025 Nov 12. PMID: 41208553.



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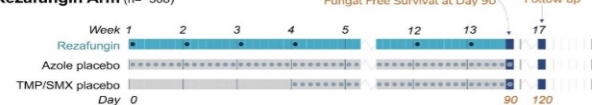
INFECTHEMA

The future of prophylaxis: new agents

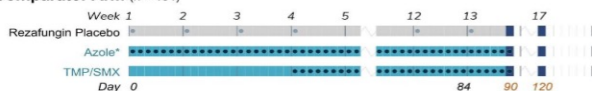
Rezafungin

- Mechanism:** echinocandin (β -glucan synthase inhibitor).
- Spectrum:** *Candida* spp., *Aspergillus* spp., and *Pneumocystis jirovecii*.
- Prophylaxis potential:** preclinical studies demonstrate efficacy in prophylactic mouse models of invasive candidiasis, aspergillosis, and *Pneumocystis pneumonia*.
- Current status:** Phase 3 trials for prevention of invasive fungal disease in **blood and marrow transplant recipients** are ongoing.
- Advantages:** Once-weekly dosing facilitates outpatient management. Low drug-drug interaction.

Rezafungin Arm (n=308)



Comparator Arm (n=154)



*Fluconazole to start in all patients. Posaconazole optional in patients who develop GVHD per label.

Miesel L, Cushion MT, Ashbaugh A, Lopez SR, Ong V. Efficacy of Rezafungin in Prophylactic Mouse Models of Invasive Candidiasis, Aspergillosis, and *Pneumocystis Pneumonia*. *Antimicrob Agents Chemother*. 2021 Feb 17;65(3):e01992-20.

Ibrexafungerp

- Mechanism:** triterpenoid (β -glucan synthase inhibitor).
- Spectrum:** *Candida* spp., *Aspergillus* spp., and *Pneumocystis jirovecii*.
- Prophylaxis potential:** no.
- Current status:** FDA-approved (June 2021) for vulvovaginal candidiasis; granted orphan drug status by EMA for invasive candidiasis. Phase 3 trials for invasive aspergillosis are ongoing.
- Advantages:** Oral bioavailability, novel mechanism avoiding cross-resistance with azoles, and potential for combination therapy with echinocandins.

Olorofim

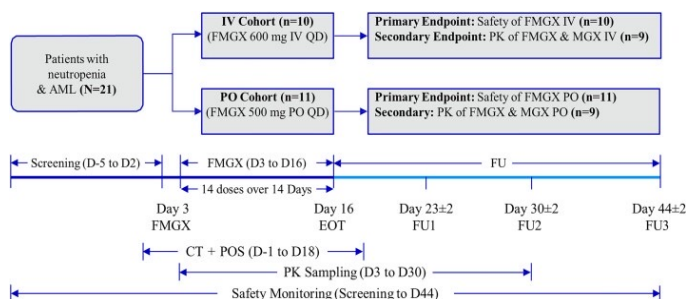
- Mechanism:** orotomide (DHODH inhibitor).
- Spectrum:** *Aspergillus* spp. (including azole-resistant strains), *Lomentospora prolificans*, *Scedosporium* spp., *Coccidioides*, and other difficult-to-treat molds.
- Prophylaxis potential:** no.
- Current status:** Phase 2b study showed successful global and clinical responses in patients with invasive fungal disease who had few or no treatment options, including infections due to highly resistant organisms and difficult-to-treat sites (brain, bone).

Opelconazole

- Mechanism:** Triazole (inhaled).
- Spectrum:** *Aspergillus* spp.
- Prophylaxis potential:** yes.
- Current status:** Phase 3 studies.

Fosmanogepix

- Mechanism:** Gwt1 inhibitor.
- Spectrum:** Broad activity against *Candida* spp. (including *C. auris*), *Aspergillus* spp., *Fusarium*, *Scedosporium*, *Lomentospora*, and *Cryptococcus*. Limited activity against *Mucorales*.
- Prophylaxis potential:** Phase 1b in AML and neutropenia.
- Current status:** Granted orphan drug status by EMA (July 2022); phase 3 studies ongoing for invasive candidiasis and aspergillosis.



Cornely OA, Ostermann H, Koehler P, Teschner D, Limburg E, Kramer WG, et al. Phase 1b safety and pharmacokinetics of intravenous and oral fosmanogepix in patients with acute myeloid leukaemia and neutropenia. *J Antimicrob Chemother*. 2023;78(11):2645-2652.

ÍNDICE

5. CONCLUSIONS

Conclusions

- Invasive fungal disease (IFD) remains a major cause of morbidity and mortality in patients with hematologic malignancies, particularly in those with prolonged neutropenia and intense immunosuppression.
- Primary antifungal prophylaxis should be risk-adapted, based on disease characteristics, treatment type, host factors and local epidemiology rather than applied universally.
- Patients with highest benefit from mold-active prophylaxis include those with AML receiving intensive chemotherapy, AML treated with azacitidine-venetoclax and prolonged neutropenia, high-risk allo-HSCT recipients, and selected CAR-T patients with additional risk factors.
- Drug-drug interactions are a key determinant of prophylaxis choice, especially with targeted therapies such as venetoclax, FLT3 inhibitors, calcineurin inhibitors or other QT-prolonging drugs.
- Posaconazole remains the preferred agent in many high-risk scenarios, while fluconazole or no prophylaxis may be appropriate in lower-risk settings.
- Future strategies will likely involve more individualized prophylaxis, incorporating clinical risk stratification and emerging antifungal agents with broader spectrum and fewer drug interactions.



Instituto de Biomedicina de Sevilla
Servicio de Hematología
Hospital Universitario Virgen del Rocío



Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Interacciones de los antimicrobianos y las nuevas terapias en oncohematología

José Ramón Azanza Perea

Clínica Universidad de Navarra

Interacciones de los antimicrobianos y las nuevas terapias en oncohematología

Conflicto de intereses. José Ramón Azanza

Ha participado en sesiones, reuniones, asesorías de las siguientes empresas:

Andrómaco, Angelini, Astellas, Astra Zeneca, Baxter, Boehringer, Bial, Biogen, Bioibérica, Cassen, Cinfa, Eisai, Esteve, Ferrer, Geiser, GSK, Gilead, Idifarma, Leo, Menarini, MSD, Merck, Norgine, Novartis, Nycomed, Ojer, Pfizer, Recordati, Robi, Roche, Sanofi, Seagen, Shionogi, UCB, Zambon

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Interacciones de los antimicrobianos y las nuevas terapias en oncohematología

Índice

- Interacciones: Fisiología y Farmacología.
- Efectos sobre CYP450 y proteínas de transporte:
 - Antifúngicos azoles.
 - Fármacos oncohematológicos.
 - Otros antiinfecciosos.
- Efectos sobre el QT.
- Interacciones CYP450 y proteínas de transporte: ejemplos.
- Resumen/Recomendaciones.
- Nuevos medicamentos oncohematológicos.

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Review

Recommendations on the use of azole antifungals in hematology-oncology patients

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Farmacocinética

Azanza JR. Datos personales. Marzo 2026

• Absorción

• **Alteración pH gástrico**

• **Alteración velocidad vaciado**

• **Quelación**

• **Efecto de primer paso (CYP3A4, P-gp, BCRP,)**

• Distribución

• **Desplazamiento de fijación a proteínas**

• **Inducción /inhibición de transportadores (P-gp, BCRP,)**

• Metabolismo

• **Inducción/inhibición de CYP450, UGT, ...**

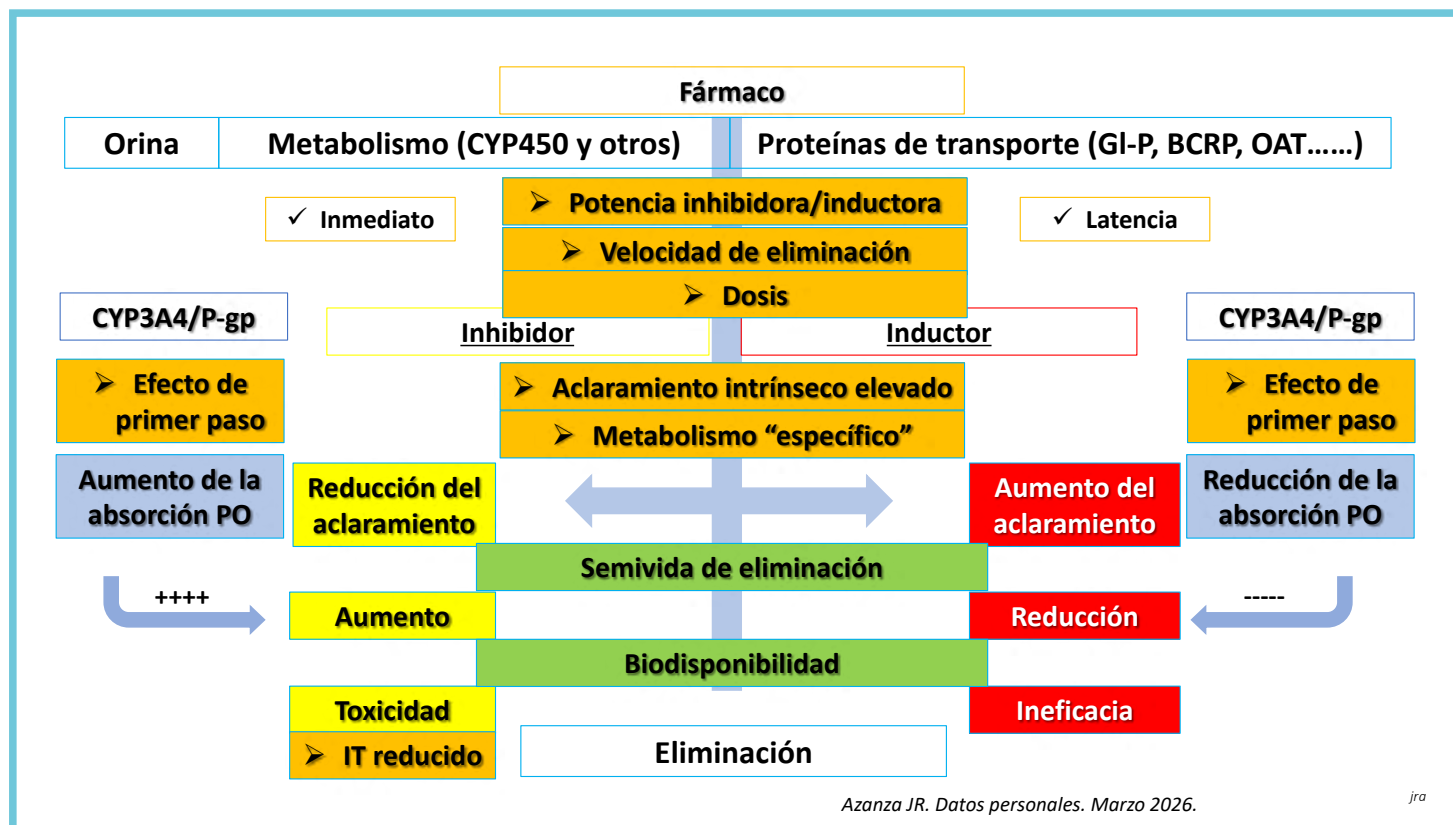
• Eliminación

• **Inducción /inhibición de transportadores (p-GP, bcrp, OAT, OAT1B,)**

• **Alteración pH orina**

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Oncohematológicos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

(I/II)	3A4	1A2	2B6	2A6	2C8	2C9	2C19	2D6	P-gp	BCRP	MATE	OCT1	OTROS	QT
Acalabrutinib	S	ID							S-IH	S-IH	S-IH			
Ascinimib	S/IH D					IH			IH					SI
Avapritinib														
Belumosudil	S													
Bortezomid	S													
Bosutinib	S									Intest.		OCT1: IH		SI
Brentuximab vedotina	S								S					
Busulfano	S													
Carfilzomib									S				IH: OAPT1B1, UGT1A1	SI
Ciclofosfamida	S		S	S		S	S							
Crizotinib	S/ID		ID		ID	ID			IH			OCT1: IH	UGT1A1:ID. 2E1, 1A1:	
Dacarbazina		S												
Dasatinib	S/IH													SI
Doxorubicina	S								S					
Duvelisib	S/IH													
Fedratinib	S/IH								S/IH	IH	IH		IH: OAPT1B1-1B3, OCT2	
Gilteritinib	S								S/IH	S/IH			OCT1: IH	SI
Glasdegig	S				S				IH		IH		UGT1A9	
Ibrutinib	S								S/IH	S/IH				
Idelalisib	S/IH		ID			ID	ID		S	S			UGT1A4	
Imatinib	S/IH							IH						SI
Inotuzumab ozogamicina														SI
Ivosidenib	S/ID		ID		ID	ID	ID						UGT:ID	SI
Lenalidomida									S					

S: sustrato. ID: inductor. IH: inhibidor. SI: riesgo de prolongación del QT. Intest.: intestinal.

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Oncohematológicos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

(II/II)	3A4	1A2	2B6	2A6	2C8	2C9	2C19	2D6	P-gp	BCRP	MATE	OCT1	OTROS	QT
Midostaurina	S	ID	ID										2E1: ID	SI
Mitoxantrona										S				
Momelotinib	S	S:ID	ID		S	S	S			IH	IH		OATP: S	
Nilotinib	S/IH				S/IH	S/IH		S/IH	S					SI
Oxaliplatino														SI
Pirtobrutinib	S/IH				IH	IH			IH	IH			UGT: S	
Pixantrona					IH				S	S/IH		OCT1: S		
Polatuzumab ved	S								S					
Pomalidomida	S	S							S					
Ponatinib	S								IH	IH				SI
Prednisona	S													
Quizartinib	S								IH	IH				SI
Ruxolitinib	S					S			IH	IH				
Sirolimus	S								S					
Tacrolimus	S								S					SI
Tazemetostat	S													
Transretinoico														SI
Treosulfano	S						S							
Trióxido de Arsenio	S/IH													SI
Venetoclax	S/IH						S/IH		S/IH	S/IH			OATP1B1: IH	
Vincristina	S													
Zanabrutinib	S/id						S/id		IH					

S: sustrato. ID: inductor. IH: inhibidor. SI: riesgo de prolongación del QT. Intest.: intestinal.

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Antibacterianos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

	<u>Sustrato</u>	<u>Inductores</u>	<u>Inhibidores</u>
CYP1A2		Meropenem (débil), Rifampicina	Norfloxacin Ciprofloxacino
CYP2B6		Rifampicina	
CYP2C8		Rifampicina	Metronidazol
CYP2C9		Rifampicina	Oritavancina (débil) Metronidazol
CYP2C19		Rifampicina	Oritavancina (débil)
CYP2E1		Isoniazida	
CYP3A4		Oritavancina	
	Clindamicina, Delamanid, Eritromicina, Claritromicina, Cloroquina, Ivermectina, Retapamulina, Roxitromicina, Rifaximina	Meropenem Vaborbactam Rifabutina Rifampicina Oritavancina (débil)	Eritromicina Claritromicina Metronidazol Diacetilmidexamicina Roxitromicina Fluoroquinolonas
UGT		Rifampicina	
OAT1B1			Ceftobiprole
OAT3	Amoxicilina, ampicilina, aztreonam, cefalexina, cefazolina, cefiderocol, cefixima, cefonicid, cefpodoxima, cloxacilina, doripenem, etambutol, ertapenem, meropenem, imipenem, penicilina G, sulbactam, vaborbactam.		

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Antiviricos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

(1/3)	Sustrato	Inductor	Inhibidor
Abacavir	UGT		
Aciclovir	OAT1/3		
Adefovir			
Boceprevir	3A4, P-gp, BCRP		3A4
Brivudina	Fluopirimidina deshidrogenasa		F. deshidrogenasa
Bulerviritiva			OATP1B1, 3A4
Cabotegravir	UGT1A1, UGT1A9, P-gp, BCRP		
Cobicistat	3A4		3A4, 2D6 (débil), -P-gp, BCRP, MATE1, OATP1B1, OATP1B3
Darunavir	3A4		
Dolutegravir	UGT1A2, 1A3, 1A9, 3A4, P-gp, BCRP		OCT2, MATE1
Efavirenz		3A4, 2B6, UGT1A1, 2C9, 2C19	3A4, QT
Elbasvir	3A4, P-gp		BCRP
Elvitegravir	3A4	2C9, UGT	
Entecavir	OCT		
Entreltinib		Débil: 3A4, P-gp, BCRP	

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Antiviricos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

(2/3)	Sustrato	Inductor	Inhibidor
Etravirina	3A4, 2C9, 2C19	Débil: 3A4	2C9, 2C19, P-gp
Famciclovir	OAT3		
Fampiridina	OCT2		
Fosamprenavir	3A4		
Foscarnet			Nefrotoxicidad
Fostemsavir	3A4, P-gp, BCRP		OATP1B, BCRP
Ganciclovir	OAT3		
Glecaprevir			P-gp, BCRP, OATP1B1, BSEP, 3A4
Grazoprevir	OATP1B, CYP3A y P-gp		BCRP
Indinavir	3A4	Débil: 3A4	
Lamivudina	OCT		
Ledipasvir	P-gp	P-gp, BCRP	
Letermovir	P-gp, BCRP, UGT		OATP1B1
Lopinavir	3A4	3A4, 2C9, 2C19, UGT	
Maraviroc	3A4, P-gp		
Maribavir	3A4	1A2	
Nevirapina		3A4, 2B6	
Nirmaltrevir	3A4, BCRP	1A2, 2B6, 2C8, 2C19, UGT3A4	
Oseltamivir	OAT		

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Antivíricos. CYP450 y Proteínas de transporte (Fuentes: Fichas Técnicas. AEMPS. Marzo 2026)

(3/3)	Sustrato	Inductor	Inhibidor
Pibrentasvir	3A4, P-gp	P-gp, BCRP, OATP1B BSEP	
Raltegravir	UGT1A1		
Remdesivir	2C8, 2D6, 3A4, OATP1B1, P-gp	1A2, 3A4	3A4, OATP1B1
Rilpivirina	3A4		P-gp, MATE2K
Ritonavir		1A2, 2C8, 2C9, 2C19	3A4, P-gp
Simeprevir	3A4, OATP1B3		OATP1B3, P-gp, BCRP
Sofosbuvir	P-gp, BCRP		
Telaprevir	3A4, P-gp		3A4, P-gp
Telbivudina	OCT		
Tenofovir	OCT, OATP1B1		
Tipranavir	3A4		3A4
Valganciclovir	OAT1/3		
Velpatasvir	P-gp, BCRP, OATP1B, 3A4, 2C8		P-gp, BCRP, OATP1B
Zidovudina	OAT1/3		

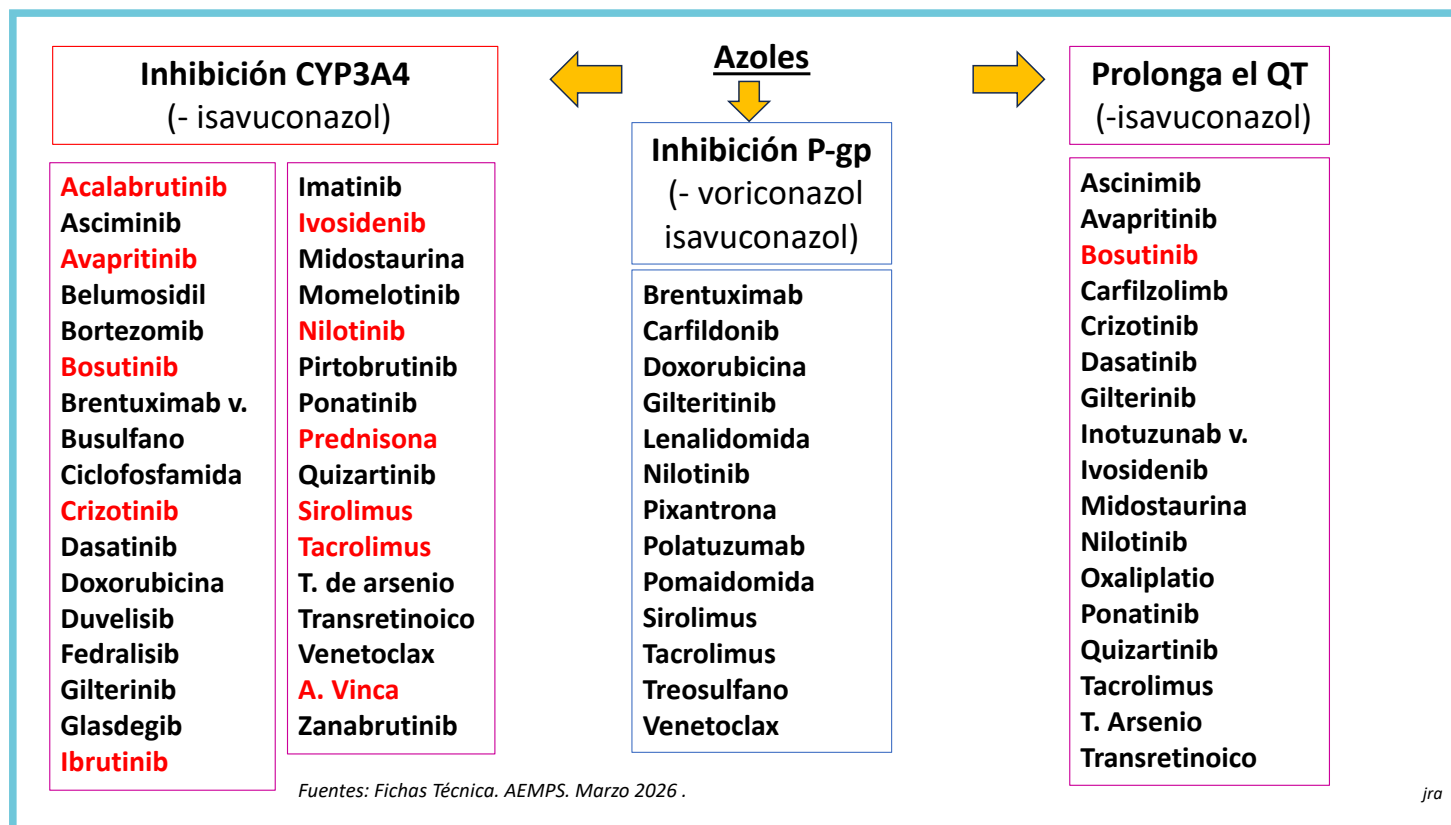
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Efectos de los azoles sobre las isoenzimas de la CYP450 y sobre las proteínas de transporte. (Fichas técnicas. Agencia Española de Medicamentos y Productos Sanitarios. Marzo 2026)

Itraconazol	Potente inhibidor de la CYP3A4, inhibidor de la P-gp y de la proteína de resistencia al cáncer de mama (BCRP).
Posaconazol	Sustrato UDP y P-gp. Potente inhibidor de la CYP3A4 y P-gp.
Voriconazol	Sustrato e Inhibidor (potente) de CYP2C19, CYP2C9 y CYP3A4.
Isavuconazol	Inhibidor moderado de la CYP3A4/5. Inductor ligero de: CYP2B6, P-gp, OCT2 y de la UGT.

P-gp: glicoproteína P. *OCT2*: transportador de cationes orgánicos 2. *UGT*: uridin glucuronil transferasa.

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Efectos de los azoles sobre el QTc. (Fichas técnicas. Agencia Española de Medicamentos y Productos Sanitarios. Marzo 2026)

Itraconazol	El aumento de las concentraciones plasmáticas de algunos de medicamentos puede conducir a una prolongación del intervalo QT y a taquiarritmias ventriculares. Está contraindicado.
Posaconazol	Posaconazol no se debe administrar con medicamentos que sean sustratos del CYP3A4 y que prolonguen el intervalo QTc.
Voriconazol	Voriconazol deberá ser administrado con precaución a pacientes en situaciones potencialmente proarrítmicas tales como medicación concomitante de la que se conoce que prolongue el intervalo QTc.
Isavuconazol	En un estudio sobre el síndrome de QT en sujetos humanos sanos, el isavuconazol acortó el intervalo QTc de manera dependiente de la concentración.

Fármacos oncohematológicos que producen prolongación del QTc. (Fichas técnicas. AEMPS. Marzo 2026)

Asciminib Avacitinib Bosutinib Carfilzomib	Crizotinib Dasatinib Gilterinib Inotuzumab	Ivosidenib Midostaurina Nilotinib Oxaliplatino	Ponatinib Quizartinib Tacrolimus T. arsénio	Transretinoico
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Definido	Posible			Condicional		
Amiodarona	Inotuzumab v.	Adenosina	Gadobutrol	Prucaloprida	Amantadina	Posaconazol
Anagrelida	Ivosidenib	Agomelatonina	Granisentrón	Retigabina	Amfotericina B	Quetiapina
Arsénico	Levofloxacino	Alfuzosina	Imipramina	Rilpivirina	Amisulpirida	Ranolazina
Avapritinib	Levomempromaz.	Apomorfina	Imatinib	Rispridona	Amitriptilina	Ritonavir
Azitrromicina	Levosulprida	Aripiprazol	Lantano	Rupatadina	Atazanavir	Sertralina
Bosutinib	Metadona	Asenapina	Lapatinib	Saquinavir	Bendroflumet.	Solifenacina
Carfilzomib	Midastaurina	Atomoxetina	Lenvatinib	Sertindol	Difenhidramina	Torasemida
Cilostazol	Moxifloxacino	Bambuterol	Leuproleina	Sildanafil	Doxepina	Trazodona
Ciprofloxacino	Nicardipino	Bendamustina	Litio	Sorafenib	Esomprazol	Voriconazol
Citalopram	Ondansetrón	Bortezomib	Lopinavir	Sunitinib	Fluoxetina	Ziprasidona
Claritromicina	Oxilaplatino	Buprenorfina	Maprotilina	Tacrolimus	Fluvoxamina	
Cloroquina	Pentamidina	Capecitabina	Mequitazina	Tadalafio	Furosemida	
Clorpromazina	Pimozida	Clomipramina	Mirabegron	Tamoxifeno	Galantamina	
Dasatinib	Procainamida	Clozapina	Mirtazapina	Telitromicina	Hidroclortizida	
Disoporamida	Propranolol	Crizotinib	Mizolastina	Tetrabenazina	Hidroxicina	
Domperidona	Quizartinib	Degarelix	Nilotinib	Tiaprada	Hidroxiclozoq.	
Donepezilo	Roxitromicina	Desloratadina	Norfloxacino	Tizanidina	Indapamida	
Dronedarona	Salbutamol	Dexmedetomid.	Nortriptilina	Tolterodina	Itraconazol	
Droperidol	Salmeterol	Ebastina	Ofloxacino	Transretinoico	Ivabradina	
Eritromicina	Servoflurano	Efavirenz	Oxitocina	Trimipramina	Ketoconazol	
Escitalopram	Sotalol	Erilubulina	Oxaliplatino	Trospio	Lansoprazol	
Fencainida	Sulridina	Espiramicina	Paliperidona	Vardenafil	Loperamida	
Fluconazol	Terbutalina	Famotidina	Palonosent.	Vemurafenib	Metronidazol	
Formoterol	Terlipresina	Fesoterodina	Panopanib	Venlafaxina	Mifepristona	
Gilertitnib	Vandetanib	Fingolimod	Pasideotida	Vernakalant	Olanzapina	
Haloperidol		Flufenazina	Perfenazina	Vinflumina	Omeprazol	
Indacaterol		Flupentixol	Prometazina		Paroxetina	

NIVEL DE EVIDENCIA: (D): Riesgo definido de TdP: La evidencia apoya que estos fármacos alargan el intervalo QT y tienen riesgo de causar TdP, cuando se utilizan en las indicaciones autorizadas. **(P):** Riesgo posible de TdP: La evidencia apoya que estos fármacos pueden causar prolongación del intervalo QT, pero no hay evidencias suficientes de que tengan riesgo de causar TdP, cuando se utilizan en las indicaciones autorizadas. **(C):** Riesgo condicional de TdP: La evidencia apoya que estos fármacos alargan el intervalo QT y aumentan el riesgo de TdP, pero sólo en determinadas circunstancias (dosis excesivas, interacciones con otros fármacos, etc.). **(*)**: Fármacos no incluidos en el listado AZCERT, incluidos en (10) y/o ficha técnica. **(**)**: Fármaco incluido en el listado AZCERT de fármacos con riesgo especial que se deben evitar en pacientes con Síndrome de QT largo congénito.

Chrome extension://efaidnbmnnnibpcajpcgclefindmkaj/https://cadime.es/images/documentos_archivos_web/BTA/2017/CADIME_BTA_32_02.pdf- (Actualizado marzo 2026)

Azoles. Prolongación de QT. Torsades de Pointes.

Panos G, Velissaris D, Karamouzou V, Matzaroglou C, Tylanakis M. Long QT Syndrome Leading to Multiple Cardiac Arrests After **Posaconazole** Administration in an Immune-Compromised Patient with Sepsis: An Unusual Case Report. *Am J Case Rep.* 2016 Apr 29;17:295-300.

Eiden C, Peyrière H, Tichit R, Cociglio M, Amedro P, Blayac JP, Margueritte G, Hillaire-Buys D. Inherited long QT syndrome revealed by antifungals drug-drug interaction. *J Clin Pharm Ther.* 2007 Jun;32(3):321-4.

Brown JD, Lim LL, Koning S. **Voriconazole** associated torsades de pointes in two adult patients with haematological malignancies. *Med Mycol Case Rep.* 2014 Mar 13;4:23-5

Elbey MA, Cil H, Onturk E, Islamoglu Y. QTc prolongation and torsade de pointes ventricular tachycardia in a small dose **voriconazole** therapy. *Eur Rev Med Pharmacol Sci.* 2012 Jan;16(1):100-2

Aypar E, Kendirli T, Tutar E, Çiftçi E, Ince E, Ileri T, Atalay S. **Voriconazole-induced** QT interval prolongation and torsades de pointes. *Pediatr Int.* 2011 Oct;53(5):761-763.

Reinhold JA, Sanoski CA, Russo AM, Cooper JM, Spinler SA. Torsades de pointes associated with methadone and **voriconazole**. *BMJ Case Rep.* 2009;2009. pii: bcr07.2009.2119.

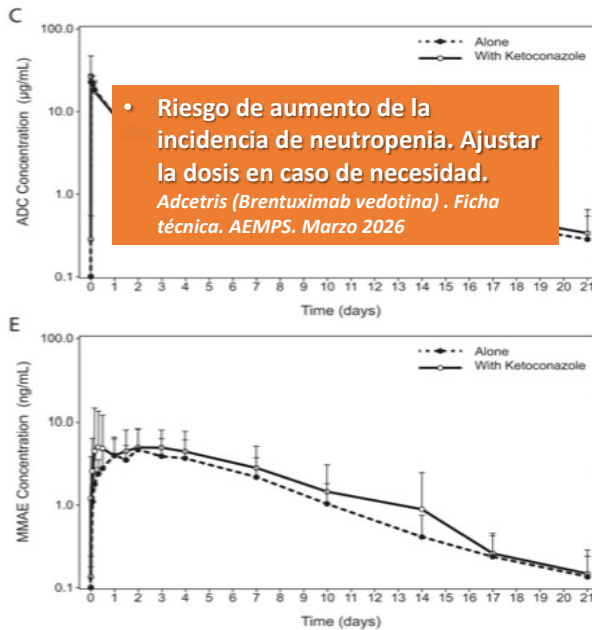
Barreto JN, Cullen MW, Mara KC, Grove ME, Sierzchulski AG, Dahl NJ, Tosh PK, Dierkhising RA, Patnaik MM, Ackerman MJ. QT prolongation in patients with acute leukemia or high-risk myelodysplastic syndrome prescribed antifungal prophylaxis during chemotherapy-induced neutropenia. *Leuk Lymphoma.* 2019 Dec;60(14):3512-3520.

Philips JA, Marty FM, Stone RM, Koplan BA, Katz JT, Baden LR. Torsades de pointes associated with **voriconazole** use. *Transpl Infect Dis.* 2007 Mar;9(1):33-6.

Alkan Y, Haefeli WE, Burhenne J, Stein J, Yaniv I, Shalit I. **Voriconazole-induced** QT interval prolongation and ventricular tachycardia: a non-concentration-dependent adverse effect. *Clin Infect Dis.* 2004 Sep 15;39(6):e49-52.

Eiden C, Peyrière H, Tichit R, Cociglio M, Amedro P, Blayac JP, Margueritte G, Hillaire-Buys D. Inherited long QT syndrome revealed by antifungals drug-drug interaction. *J Clin Pharm Ther.* 2007 Jun;32(3):321-4.

Brentuximab/Vedotina y azoles



Brentuximab vedotin is an antibody-drug conjugate (ADC) that selectively delivers monomethyl auristatin E (MMAE) into CD30-expressing cells. This study evaluated the CYP3A-mediated drug-drug interaction potential of brentuximab vedotin and the excretion of MMAE.

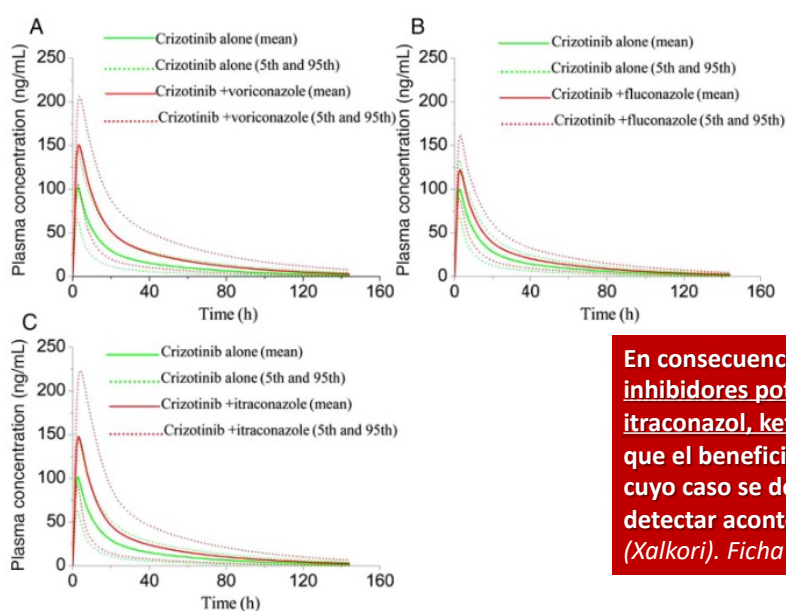
Two 21-day cycles of brentuximab vedotin (1.2 or 1.8 mg/kg intravenously) were administered to 56 patients with CD30-positive hematologic malignancies.

- The ADC Tmax and t1/2 were similar with and without concomitant ketoconazole.
- For MMAE, the AUC_{0-∞} GMR and the corresponding 90% CI were 1.34 and 0.98–1.84 and the Cmax GMR and corresponding 90% CI were 1.25 and 0.90–1.72. The MMAE Tmax and t1/2 were similar with and without concomitant ketoconazole.
- Using a model based-approach to account for the MMAE period effect, the adjusted GMR (90% CI) for MMAE AUC_{0-∞} was 1.73 (1.22, 2.46) with concomitant ketoconazole.

Han TH, Gopal AK, Ramchandren R, Goy A, Chen R, Matous JV, Cooper M, Grove LE, Alley SC, Lynch CM, O'Connor OA. CYP3A-mediated drug-drug interaction potential and excretion of brentuximab vedotin, an antibody-drug conjugate, in patients with CD30-positive hematologic malignancies. *J Clin Pharmacol*. 2013 Aug;53(8):866-77..

jra

Crizotinib y azoles



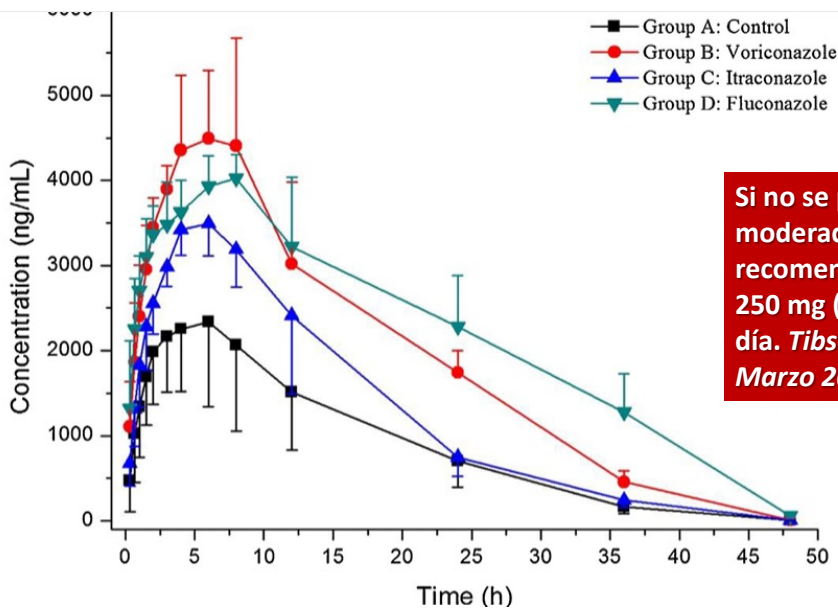
The geometric mean area under the plasma concentration–time curve (AUC) of crizotinib was increased by 84%, 58%, and 79% when coadministered with voriconazole, fluconazole, or itraconazole at multiple doses, respectively. (voriconazole>itraconazole>fluconazole).

En consecuencia, se debe evitar el uso concomitante de inhibidores potentes de CYP3A (incluidos, entre otros, itraconazol, ketoconazol, posaconazol y voriconazol), a menos que el beneficio potencial para el paciente supere el riesgo, en cuyo caso se debe vigilar estrechamente a los pacientes para detectar acontecimientos adversos de crizotinib. *Crizotinib (Xalkori). Ficha técnica. AEMPS. Febrero 2026.*

Chen L, Li L, Chen W. Use of Modeling and Simulation to Predict the Influence of Triazole Antifungal Agents on the Pharmacokinetics of Crizotinib. *Clin Pharmacol Drug Dev*. 2022 Jun;11(6):724-733. doi: 10.1002/cpdd.1049. Epub 2022 Jan 7. PMID: 34995400.

jra

Ivosidenib y azoles



Ivosidenib: Tibsovo (Ivosidenib). Ficha técnica . AEMPS. Marzo 2026

- Sustrato CYP3A4
- Induce CYP3A4
- Puede producir prolongación del espacio QT

Si no se puede evitar el uso de inhibidores moderados o potentes del CYP3A4, la dosis recomendada de ivosidenib se debe reducir a 250 mg (1 comprimido de 250 mg) una vez al día. Tibsovo (Ivosidenib). Ficha técnica . AEMPS. Marzo 2026.

Bolledula J, Ke A, Yang H, Prakash C. PBPK modeling to predict drug-drug interactions of ivosidenib as a perpetrator in cancer patients and qualification of the Simcyp platform for CYP3A4 induction. CPT Pharmacometrics Syst Pharmacol. 2021 Jun;10(6):577-588.

jra

Ivosidenib y azoles

Methods:

Patients treated with ivosidenib and concomitant triazole with at least one serum trough level were included. Subtherapeutic levels were defined as posaconazole <700 ng/mL and voriconazole <1.0 µg/mL. The incidences of breakthrough invasive fungal infections and QTc prolongation were identified at least 5 days after initiation of ivosidenib with concomitant triazole.

Results:

- Seventy-eight serum triazole levels from 31 patients receiving ivosidenib-containing therapy and concomitant triazole were evaluated. Of the 78 concomitant levels, 47 (60%) were subtherapeutic (posaconazole: n = 20 of 43 [47%]; voriconazole: n = 27 of 35 [77%]).
- Compared to levels drawn while patients were off ivosidenib, median triazole serum levels during concomitant ivosidenib were significantly reduced.
- There was no apparent increase in incidence of grade 3 QTc prolongation with concomitant azole antifungal and ivosidenib 500 mg daily.

Ivosidenib induce el CYP3A4 y podría, por lo tanto, disminuir la exposición sistémica a los sustratos del CYP3A4. Los pacientes deben ser monitorizados para detectar la pérdida de eficacia antifúngica si no se puede evitar el uso de itraconazol o ketoconazol . Tibsovo (Ivosidenib). Ficha técnica . AEMPS. Marzo 2026>

Dinh A, Savoy JM, Kontoyiannis DP, Takahashi K, Issa GC, Kantarjian HM, DiNardo CD, Rausch CR. Ivosidenib significantly reduces triazole levels in patients with acute myeloid leukemia and myelodysplastic syndrome. Cancer. 2026 Feb 10. doi: 10.1002/cncr.35251. Epub ahead of print. PMID: 38340331.

jra

Azoles/Inmunosupresores

This report summarizes phase 1 studies that evaluated pharmacokinetic interactions between the novel triazole antifungal agent isavuconazole and the immunosuppressants cyclosporine, mycophenolic acid, prednisolone, sirolimus, and tacrolimus in healthy adults.

Table 5. Interactions Between Triazole Antifungals and the Immunosuppressants Cyclosporine, Sirolimus, and Tacrolimus

CYP3A4 Substrate	Isavuconazole	Fluconazole	Itraconazole	Posaconazole	Voriconazole
Cyclosporine	↑ 1.3 ^a	↑ 2-3 ^{a,6}	↑ 2.7 ^{b,13}	↑ b,c,14	↑ 1.7 ^{a,7}
Sirolimus	↑ 1.8 ^a	↑ 3-4.7 ^{b,6}	NA	↑ 7.9 ^{a,14}	↑ 11 ^{a,7}
Tacrolimus	↑ 2.3 ^a	NA	↑ 5.6 ^{b,13}	↑ 3.6 ^{a,14}	↑ 3 ^{a,7}

NA, not applicable.

^aFold increases in area under the plasma concentration-time curve.

^bFold increases in trough concentration.

^cIncrease observed, but fold change not reported.

ajuste inicial
de la dosis?

↓ de la dosis
70-85%

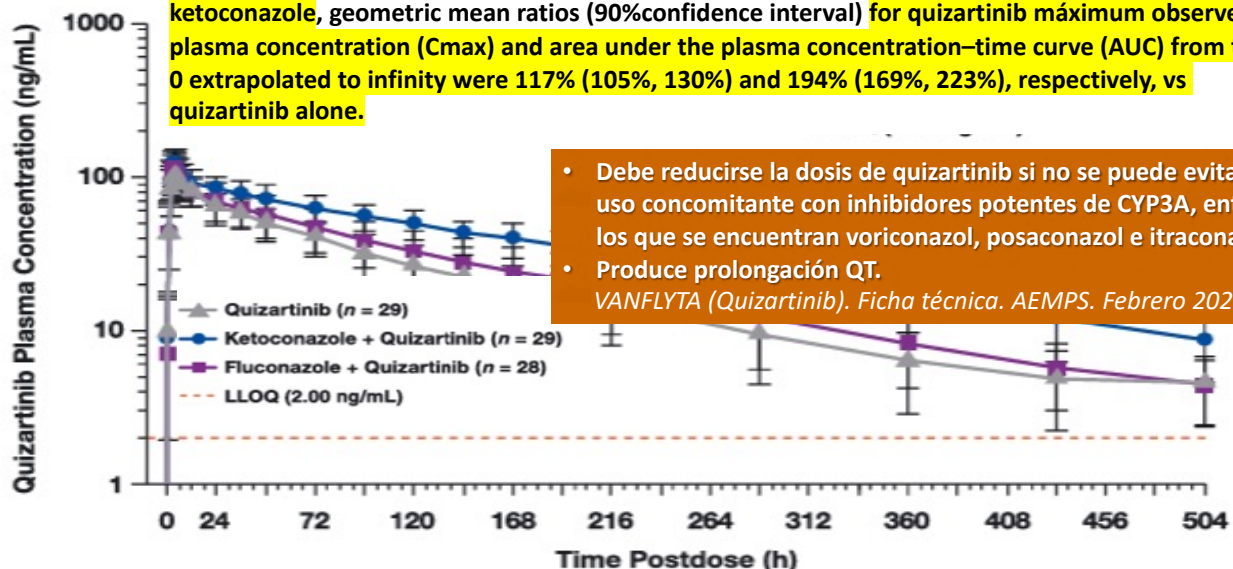
↓ de la dosis
80-90%

Groll AH, Desai A, Han D, Howieson C, Kato K, Akhtar S, et al. Pharmacokinetic Assessment of Drug-Drug Interactions of Isavuconazole With the Immunosuppressants Cyclosporine, Mycophenolic Acid, Prednisolone, Sirolimus, and Tacrolimus in Healthy Adults. *Clin Pharmacol Drug Dev*. 2017 Jan;6(1):76-85.

jra

Quizartinib y azoles

Ninety-three healthy subjects were randomised; 86 completed the study. When administered with ketoconazole, geometric mean ratios (90% confidence interval) for quizartinib maximum observed plasma concentration (C_{max}) and area under the plasma concentration-time curve (AUC) from time 0 extrapolated to infinity were 117% (105%, 130%) and 194% (169%, 223%), respectively, vs quizartinib alone.



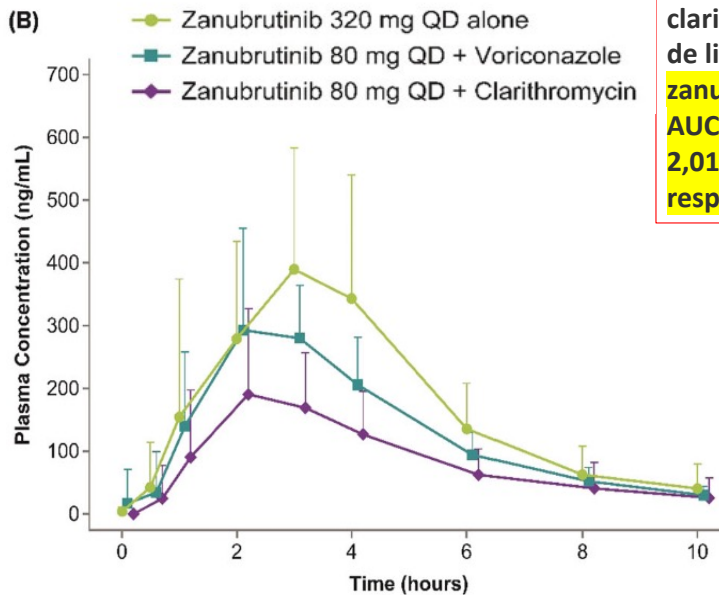
- Debe reducirse la dosis de quizartinib si no se puede evitar el uso concomitante con inhibidores potentes de CYP3A, entre los que se encuentran voriconazol, posaconazol e itraconazol.
- Produce prolongación QT.

VANFLYTA (Quizartinib). Ficha técnica. AEMPS. Febrero 2026

Li J, Kankam M, Trone D, Gammon G. Effects of CYP3A inhibitors on the pharmacokinetics of quizartinib, a potent and selective FLT3 inhibitor, and its active metabolite. *Br J Clin Pharmacol*. 2019 Sep;85(9):2108-2117.

jra

Zanubrutinib y azoles



La administración concomitante de dosis múltiples de los inhibidores potentes de CYP3A **voriconazol** y claritromicina en pacientes con neoplasias malignas de linfocitos B **aumentó las exposiciones a zanubrutinib en 3,30 veces y en 1,92 veces para el AUC_{0-24h} normalizada para la dosis y en 3,29 veces y 2,01 veces para la $C_{máx}$ normalizada para la dosis, respectivamente**

En caso de que se deba utilizar un inhibidor potente de CYP3A (p. ej., posaconazol, voriconazol, ketoconazol, itraconazol, claritromicina, indinavir, lopinavir, ritonavir, telaprevir), se debe reducir la dosis de zanubrutinib a 80 mg (una cápsula) durante el uso de inhibidor. Se debe vigilar al paciente con frecuencia para detectar toxicidad y seguir las directrices de modificación de la dosis. *Brukina (Zanubrutinib). Ficha técnica. AEMPS. Febrero 2026*

Tariq B, Ou YC, Stern JC, Mundra V, Wong Doo N, Walker P, Lewis KL, Lin C, Novotny W, Sahasranaman S, Opat S. A phase 1, open-label, randomized drug-drug interaction study of zanubrutinib with moderate or strong CYP3A inhibitors in patients with B-cell malignancies. *Leuk Lymphoma*. 2023 Feb;64(2):329-338. doi: 10.1080/10428194.2022.2150820. Epub 2022 Dec 8. PMID: 36480811.

jra

Ibrutinib. Interacciones

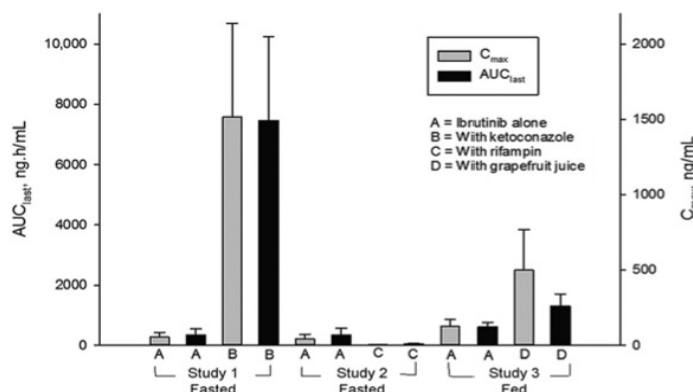


Figure 3. Mean (SD) AUC_{last} and C_{max} of ibrutinib following oral administration of ibrutinib alone and in combination with ketoconazole, rifampin, or grapefruit juice; data dose normalized to 560 mg.

Se deben evitar los inhibidores potentes del CYP3A4 ya que el uso concomitante de **IMBRUVICA** ya que puede aumentar la exposición de ibrutinib. En el caso de que se tenga que utilizar un inductor del CYP3A4, se debe vigilar estrechamente al paciente por si presentara signos de falta de eficacia (*Imbruvica. Ficha técnica. AEMPS. Abril 206*)

Se debe reducir la dosis de **IMBRUVICA** a 280 mg (dos cápsulas) durante el tiempo que se use el inhibidor. Se debe vigilar estrechamente al paciente por si presentara toxicidad y se deben seguir las normas de modificación de la dosis según sea necesario (*Imbruvica. Ficha técnica. AEMPS. Abril 2026*).

de Jong J, Skee D, Murphy J, Sukbuntherng J, Hellemans P, Smit J, de Vries R, Jiao JJ, Snoeys J, Mannaert E. Effect of CYP3A perpetrators on ibrutinib exposure in healthy participants. *Pharmacol Res Perspect*. 2015 Aug;3(4):e00156. doi: 10.1002/prp2.156. Epub 2015 Jun 24. PMID: 26171235; PMCID: PMC4492731.

jra



Modificaciones a las recomendaciones 2026 (1)

Busulfano

Se ha descrito reducción del aclaramiento de busulfano con aumento de las concentraciones por probable inhibición de la actividad de las FMO3 producida por voriconazol. Se recomienda precaución. El-Serafi I, Terelius Y, Abedi-Valuggerdi M, Naughton S, Saghaifan M, Moshfegh A, et al. Flavin-containing monooxygenase 3 (FMO3) role in busulphan metabolic pathway. *PLoS One*. 2017 Nov 9;12(11):e0187294. .

Citarabina Doxorubicina

Se ha descrito un paciente que presentó eritema palmoplantar en el que se sospechó la implicación de voriconazol y la posible alteración del metabolismo de citarabina y doxorubicina (Tavakoli-Ardakani). *ic pathway. PLoS One*. 2017 Nov 9;12(11):e0187294. doi: 10.1371/journal.pone.0187294. Erratum in: *PLoS One*. 2017 Dec 19;12 (12):e0190181. .

Dasatinib

En ratas, voriconazol y posaconazol aumentan el AUC dasatinib 4,12 veces, con el correspondiente riesgo de toxicidad. Luo X, Xue X, Li T, Zhang Y, Huang L, Cheng G. Differential Impacts of Azole Antifungal Drugs on the Pharmacokinetic Profiles of Dasatinib in Rats by LC-MS-MS. *Curr Drug Metab*. 2020;21(13):1022-1030.

Docetaxel

Se describe un aumento de las AUC, en ratas, al administrar docetaxel combinado con voriconazol.

Pei X, Li P, Jiang W, Sun Y, Lu L, Ding F, Wang G, Hao K. A robust LC-MS/MS method for the simultaneous determination of docetaxel and voriconazole in rat plasma and its application to pharmacokinetic studies. *Biomed Chromatogr*. 2018 Aug;32(8):e4246.

Ruxolitinib:

Inhibición del metabolismo de ruxolitinib por voriconazol con aumentos de C_{max} , $T_{1/2}$, AUC_{last} y AUC_{inf} de ruxolitinib del 50,4%, 81,3%, 110,1%, y 118,3%, respectivamente. Se recomienda reducir la dosis y monitorizar la respuesta clínica. Zhao Y, Chen P, Dou L, Li F, Li M, Xu L, et al. Co-Administration with Voriconazole Doubles the Exposure of Ruxolitinib in Patients with Hematological Malignancies. *Drug Des Devel Ther*. 2022 Mar 25;16:817-825.

jra

Modificaciones a las recomendaciones 2026 (2)

Venetoclax

- Se ha estimado que voriconazol aumenta la exposición de venetoclax entre 4,5 y 9,6 veces, dependiendo del polimorfismo CYP2C19. Se sugiere reducir la dosis de venetoclax a 100 mg. Dong J, Liu SB, Rasheduzzaman JM, Huang CR, Miao LY. Development of Physiology Based Pharmacokinetic Model to Predict the Drug Interactions of Voriconazole and Venetoclax. *Pharm Res*. 2022 Aug;39(8):1921-1933.
- Un paciente tratado con voriconazol que toleró el inicio de la dosis con venetoclax de 10 mg con un incremento paulatino hasta los 50 mg una vez al día, en el día 9. Krapfl A, McLeod C, Myers R, Venugopal P, Seddon A. Venetoclax ramp-up with concurrent voriconazole in a patient with chronic lymphocytic leukemia. *J Oncol Pharm Pract*. 2022 Dec;28(8):1898-1901.
- Se recomienda la MNP de venetoclax al administrar posaconazol. De Gregori S, Gelli E, Capone M, Gambini G, Roncoroni E, Rossi M, et al. Pharmacokinetics of Venetoclax Co-Administered with Posaconazole in Patients with Acute Myeloid Leukemia. *Pharmaceutics*. 2023 Jun 8;15(6):1680.
- Venetoclax es eliminado a través de la OATP1B-que es inhibida, por algunos azoles circunstancia que puede justificar la presencia de concentraciones elevadas del antineoplásico. Eisenmann ED, Garrison DA, Talebi Z, Jin Y, Silvaroli JA, Kim JG, Sparreboom A, Savona MR, Mims AS, Baker SD. Interaction of Antifungal Drugs with CYP3A- and OATP1B-Mediated Venetoclax Elimination. *Pharmaceutics*. 2022 Mar 23;14(4):694..
- Se recomienda la MNP las concentraciones de venetoclax (¿rango?). Tang Y, Li S, Rao P, Yu W, Jiang X, Liu J. Therapeutic Drug Monitoring: A New Hope for Individualised Treatment with Venetoclax. *Curr Drug Targets*. 2025;26(12):867-878. doi: 10.2174/0113894501376271250710221018. PMID: 40676794.

Vincristina

En 29 pacientes tratados con vincristina, que recibieron de forma asociada voriconazol con una reducción media de la dosis del 46,5%, se describió mayor incidencia de reducción del peristaltismo. Harnicar S, Adel N, Jurcic J. Modification of vincristine dosing during concomitant azole therapy in adult acute lymphoblastic leukemia patients. *J Oncol Pharm Pract*. 2009 Sep;15(3):175-82. doi: 10.1177/1078155208101959. Epub 2009 Mar 12. PMID: 19282418.

jra



Ajuste de dosis de venetoclax*. Inhibidores del CYP3A4 Venclyxto (Venetoclax). Ficha técnica. AEMPS. Noviembre 2023

Dosis convencional:

Dosis inicial:

LLC

Sem 1: 20 mg; Sem. 2: 50 mg; Sem. 3: 100 mg; Sem. 4: 200 mg. Sem.:5: 400 mg

LMA

Día 1: 100 mg; Día 2: 200 mg; Día 3: 400 mg.

Dosis mantenimiento:

400 mg/ día

Inhibidores potentes (posaconazol, itraconazol, voriconazol,):

Dosis inicial:

Contraindicado

Día 1: 10 mg; Día 2: 20 mg; Día 3: 50 mg; Día 4: 100 mg.

Dosis mantenimiento:

Reducir la dosis a 100 mg o menos del 75%

Inhibidores moderados (isavuconazol,):

Dosis inicial:

Reducir la dosis un 50%

Dosis mantenimiento:

*Comprimidos: 10, 50 y 100 mg.

jra

Interacciones

azoles/oncohematológicos

	Evitar	Precaución	S. R
Acalabrutinib	I, P, V (2)		Isa
Ascinimib		I, P, V (QT)	Isa
Avapritinib	I, P, V	Isa: Dosis (3)	
Belumosudil		I, P, V	Isa
Bortezomid		I, P, V	Isa
Bosutinib	I, P, V. QT	Isa. Dosis: reducir un 50%	
Brentuximab vedotina		I, P, V: neutropenia	Isa
Busulfano		I, P, V	Isa
Carfilzomib		(QT)	
Ciclofosfamida		I, P, V, Isa	
Crizotinib	I, P, V		Isa
Dasatinib	I, P, V	(QT)	Isa
Doxorubicina		I, P, V	Isa
Duvelisib	I, P, V. Dosis: 15 mg/día		Isa
Ibrutinib	I, P, V. Evitar o dosis: 140 mg/día	Isa. Dosis: 280 mg	Isa

	Evitar	Precaución	S. R
Idelalisib		I, P, V	Isa
Imatinib		I, P, V, QT	Isa
Inotuzumab ozogamicina		QT	Isa
Ivosidenib	I, P, V. Dosis: 250 mg/día	QT	Isa
Lenalidomida	I, P		Isa
Midostaurina		I, P, V, QT	Isa
Momelotinib		I, P, V	Isa
Nilotinib	I, P, V		Isa
Oxaliplatino		QT	Isa
Polatuzumab vedotina		I, P, V	Isa
Ponatinib		I, P, V. Dosis: 30 mg/día. QT	Isa
Prednisona	I, P, V		Isa
Quizartinib	I, P, V (4)	QT	Isa
Revumenib	I, P, V o 160 mg/2 vd		
Ruxolitinib	I, P, V. Dosis: reducir un 50%		Isa

	Evitar	Precaución	S. R
Sitotimus	I, P, V		Isa
Tacrolimus	I, P, V	QT	Isa
Tazemetostat	I, P, V Isa: Dosis: reducir un 50%		
Transretinoi.		QT	Isa
Treosulfano		I, P, V	Isa
T. de arsénio		I, P, V	Isa
Venetoclax	I, P, V. Evitar o ajustar la dosis (5)	Isa. Dosis: reducir un 50%	-
Vinca A.	I, P, V	Isa	
Zanabrutinib	I, P, V o Dosis: 80 mg/día	Isa. Dosis: 160 mg/día	

Precaución: Vigilar la eficacia y EA. QT: prolongación del QT. (2): I: itraconazol, P: posaconazol. V: voriconazol. Isa: isavuconazol.

(3): Reducir la dosis de 300 a 100 mg o de 200 mg a 50 mg. (4): Reducir la dosis desde 26,5/35,4 mg a 17,7 o desde 53 mg a 26,5 mg.

(5): *Inhibidor potente*: Inicio y fase de ajuste: LLC: evitar. LMA: día 1: 10 mg, día 2: 20 mg, día 3: 50 mg. día 4: 100 mg o menos. Dosis de mantenimiento: LLC y LMA: Dosis 100 mg/día o menos (un 75% como mínimo si ya se modificó por otros motivos). *Inhibidor moderado*: reducir la dosis 50%.

Fuentes: Fichas Técnicas. AEMPS. Abril 2026

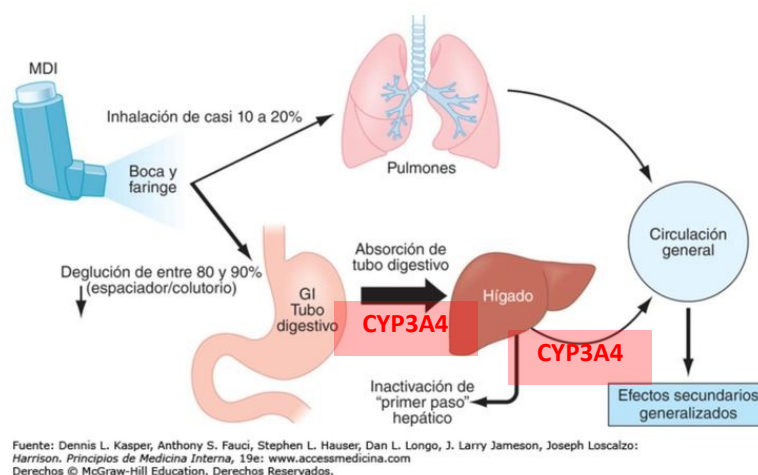
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Azoles y anticoagulantes orales

	Sustrato	<u>Voriconazol</u>	<u>Posaconazol</u>	<u>Isavuconazol</u>
Acenocumarol	CYP2C9	Precaución	Sin cambios	Sin cambios
Warfarina	CYP2C9	Precaución	Sin cambios	Sin cambios
Apixaban	CYP3A4 y GI-P	Evitar	Evitar	Sin cambios. P.
Rivaroxaban	CYP3A4 y GI-P	Evitar	Evitar	Sin cambios. P.
Edoxaban	GI-P	Sin cambios	Dosis: 30 mg/d	Sin cambios. P.
Dabigatran	GI-P	Sin cambios	Precaución	Sin cambios

AEMPS. Fichas técnicas. Abril 2023

jra



Farmacocinética de los corticosteroides inhalados. GI, tubo digestivo (gastrointestinal); MDI, inhalador con dosímetro (metered-dose inhaler).

Budesonida/Voriconazol

This prospective crossover study was conducted to evaluate what effect two commonly used antifungal agents, fluconazole, and voriconazole, would have on the trough (Cmin) and peak (Cmax) levels of budesonide in adult patients who had undergone allo-HSCT who subsequently developed clinical GI GVHD.

Fifteen subjects were enrolled and nine completed the study and were evaluable.

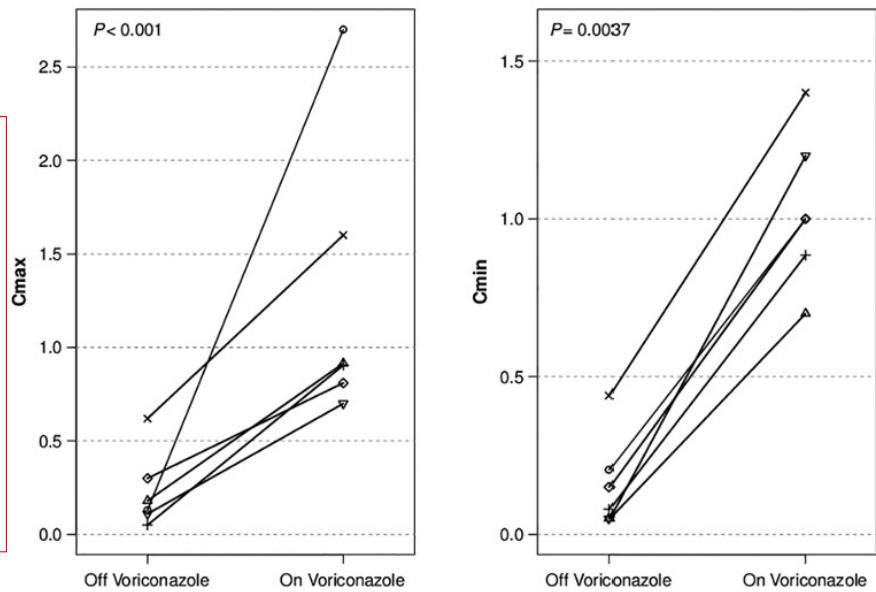


Figure 2. Plots of budesonide Cmax and Cmin values in the absence or presence of voriconazole (Cmax and Cmin values in mcg/dl)

Hughes TE, Stansfield L, Kumar P, Worthy T, Tian X, Childs RW. A prospective evaluation on the interaction of fluconazole and voriconazole on serum concentrations of budesonide in patients treated for gastrointestinal GVHD. Bone Marrow Transplant. 2020 Jun;55(6):1085-1092.

jra

Manejo de los antimicrobianos junto a los nuevos medicamentos en oncohematología

Antibacterianos

Evitar: rifampicina, macrólidos (3A4), fluoroquinolonas (3A4)

Antivíricos

Evitar: IP, ITINA, nirmaltrevir, remdesivir

Antifúngicos (3A4/QT)

Evitar/precauciones: Itraconazol, voriconazol, posaconazol

jra

Oncología. Nuevos medicamentos (Marzo 2026)

Afatinib (Sustato P-gp, BCRP)	Gefitinib (Sust. CYP3A4, 2D6)
Apitolisib	Itacitinib (Sust. CYP3A4)
Buparlisib (Sust. CYP3A4)	Lenvatinib (QT)
Cabozantinib (Sust. CYP3A4, QT)	Osimernib (QT)
Cediranib (R)	Pexidartinib (Sust. CYP3A4)
Copanlisib (Sust. CYP3A4)	Sonidegib (Sust. CYP3A4)
Dactolisib (QT)	Taselisib
Entospletinib	Vemurafenib (Ind. CYP3A4, inh 1A2)
Gedatolisib (QT)	Voxalisib
	Voxelotor (inh. CYP3A4)

¡Muchas gracias!

Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Taller. INFECCIONES EN LEUCEMIAS AGUDAS

Dr José Francisco Tomás Martínez

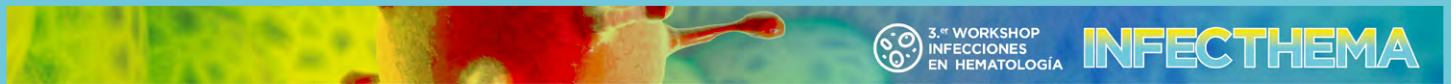
Hospital Sanitas Valdebebas / HU La Moraleja Madrid

OBJETIVOS

- Disponer de una perspectiva que ayude a comprender el manejo recogido en las principales guías
- Revisar y actualizar los puntos críticos en el manejo de estos pacientes
 - Tratamientos profilácticos (antibacterianos, antifúngicos, antivirales)
 - Interpretación pruebas microbiológicas
 - Duración del tratamiento antibiótico
 - El reto de los organismos multirresistentes
 - Los “nuevos neutropénicos” (pacientes ambulatorios Ven/AZA)
 - Recomendaciones manejo virus respiratorios (incluido Covid-19)
- Todo lo anterior debe consolidar nuestra práctica asistencial y mantener un espíritu crítico que ayude a seguir mejorando nuestros resultados clínicos

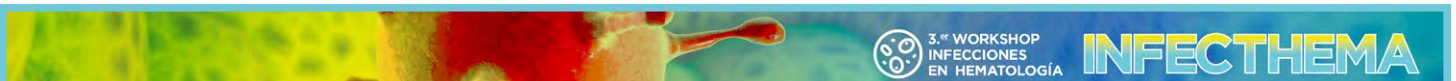
PERSPECTIVA HISTORICA

	Década 70	Década 80	Década 90	2000	2010	2020---
Agentes Infecciosos	P aeruginosa Gram neg	Cándidas Aumento G+	Prevalencia Gram+ Aspergilosis	Prevalencia Gram+ Fusarium Blastomyces Mucorales	Equilibrio G+/G-	Aumento G-
Fármacos	Ceftazidima Anfotericina B deox.	Ceftazidima Fluconazol Anfotericina B Vancomicina	Carbapenems Teicoplanina Anfo B lipos. Anidulafungina Voriconazol Ciprofloxacino Cefepime	Voriconazol Caspofungina Levofloxacino Linezolid	Posaconazol Micafungina	Isavuconazol Rezafungina
Dgto		Automatización hemocultivos	TAC Signo del Halo	Galactomanano Beta-d-Glucano	PCR	Microbioma Microbial cell-free DNA
Síndromes Clínicos	Fiebre neutropénica Ectima gangrenoso	Candidiasis hepatoesplénica Infecciones cateter	IFI			
“Issues”	Neutropenia por QT	Accesos venosos permanentes	Obras VHC		Multirresistencias	Ven/Aza COVID pandemia



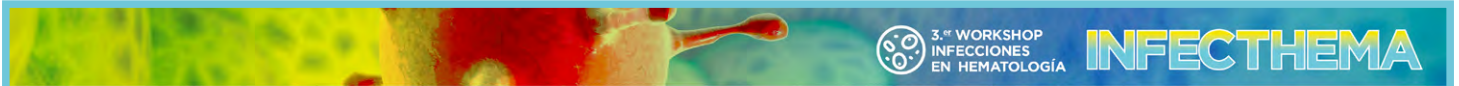
CASO CLÍNICO

- Varón de 77 años con AP de CI con 2 stent colocados 2021, HTA en tratamiento con enalapril, DM tipo II en tratamiento con metformina. Nuevo diagnóstico de LAM (NMP1+, IDH2+, FLT3ITD-, IDH1-, TP53-,), Cariotipo normal, ECOG 1, Hb: 9,7 g/L, L: $12.6 \times 10^9/L$ (82% blastos, Neutrófilos $0,6 \times 10^9/L$), Plaquetas: $18 \times 10^9/L$, CrCl: 62ml/min, ALT: 23, FA: 123, GGT: 32. Afebril. Ingresa para iniciar tratamiento y soporte hemoterápico.
- ¿Realiza/ría usted cultivos de colonización (nasal, heces etc)?
- ¿Indicaría profilaxis antibiótica? ¿Cuál?
- ¿Indicaría profilaxis antifúngica? ¿Cuál?
- ¿Indicaría profilaxis antivírica? ¿Cuál?



Screening Cultivos Colonización

- No hay ningún estudio robusto que confirme su utilidad de forma generalizada aunque pueden resultar de ayuda en situaciones concretas.
- Su realización no está incluida en ninguna guía
- ¿Cuál es su objetivo?
 - Averiguar si el paciente esta colonizado por organismos multirresistentes
- ¿En que circunstancias son más útiles?
 - Paciente que ha recibido tratamientos previos en las últimas semanas
 - Paciente que ha estado hospitalizado o cirugía previa en las últimas semanas y especialmente si estuvo en una UCI
 - Paciente que no responde o empeora tras tratamiento empírico



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ORIGINAL PAPER
Haematological Malignancy - Clinical

Prevention and management of febrile neutropenia in acute myeloid leukaemia and higher risk myelodysplastic syndrome: An international survey of current practice

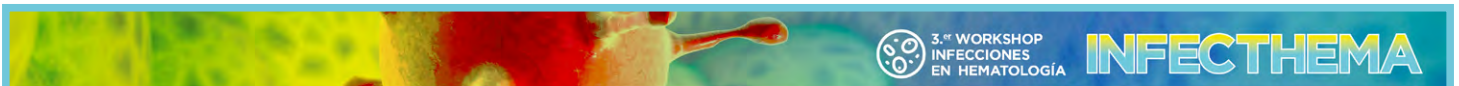
Aleec MacPhail^{1,2} | Justin Loke^{3,4} | Brett L. Houston^{5,6} | Claire Dendle^{1,2} |
Andrea S. Hendes^{7,8} | Robert Weinkens^{9,10,11} | Orla Morrissey^{12,13} |
Dionysios Neofytos¹⁴ | Niccolò Butti^{15,16} | Catriona Parker¹⁷ | Monica A. Slavin^{18,19,20,21} |
Charles Craddock^{22,23} | Simon J. Stanworth^{24,25,26} | Zoe McQuilten^{27,28} | on behalf of the
Australasian Leukaemia and Lymphoma Group Supportive Care Working Group and UK AML/
Supportive Care Working Parties

MACPHAIL ET AL.

BJHaem | 985

TABLE 2 Prophylaxis and empiric treatment of febrile neutropenia.

	ANZ (n=20)	Canada (n=14)	UK (n=30)	Europe (n=21)	Total (n=85)	p
Routine MDRO screening performed						
MRSA	7 (35%)	13 (93%)	18 (60%)	14 (67%)	52 (61%)	0.01
ESBL	8 (40%)	5 (36%)	8 (27%)	15 (71%)	36 (42%)	0.01
CRO	7 (35%)	3 (21%)	13 (43%)	11 (52%)	34 (40%)	0.42
VRE	9 (45%)	10 (71%)	8 (27%)	14 (67%)	41 (48%)	0.01
No MDRO screening	11 (55%)	1 (7%)	7 (23%)	5 (24%)	24 (28%)	0.02
Other/unknown MDRO screening ^b	2 (11%)	0 (0%)	7 (24%)	1 (5%)	10 (12%)	
If screening is performed, is the empiric antibiotic choice adjusted in the event of FN? (n = centres where any screening is performed)						
Yes	4 (44%)	6 (46%)	11 (61%)	14 (88%)	35 (63%)	0.08
Sometimes/it depends	1 (11%)	3 (23%)	5 (28%)	2 (13%)	11 (20%)	
No	3 (33%)	3 (23%)	2 (11%)	0 (0%)	8 (14%)	
Don't know	1 (11%)	1 (8%)	0 (0%)	0 (0%)	2 (4%)	
Regular information provided about local MDRO epidemiology in your institution	4 (20%)	3 (21%)	10 (33%)	9 (42%)	26 (31%)	0.59



Screening Cultivos Colonización

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Research note

Rectal colonization by multidrug-resistant Gram-negative bacteria and subsequent bacteraemia in haematological patients

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Patricia Mouzo-Gallo^{1,2}, Tullio Francesco Aiello^{1,2,3}, Ana Martínez-Urrea^{1,2},
Sabina Herrera¹, Ana Del Río¹, Christian Tejero-Lumbreras¹, Mariana Chumbita¹,
Carlos Jimenez-Vicente¹, Albert Cortés¹, Marta Bodro^{1,2}, Cristina Piatt¹, Elisa Rubio⁴,
Josep Mensa¹, Alex Soriano^{1,2}, Jose Antonio Martínez^{1,2}, Carolina García-Vidal^{1,2,3}

We collected **3024 rectal swabs** from 699 haematological patients with malignancies. Of these, 507 of 699 patients (72.5%) were not carriers of MDR-GNB (median 2 swabs per patient; interquartile range [IQR] 1–4), whereas **192 of 699 (27.5%) were carriers**, contributing 503 of 3024 (16.6%) positive swabs (median 5 swabs per patient; IQR 3–10; $p < 0.001$). Among colonized patients, the median number of prior negative swabs was 3 (IQR 1–6). Clinical data based on positive or negative rectal swab results are provided in Table 1.

The predominant microorganisms identified in swabs were ***Escherichia coli* (248/503, 49.3%)**, ***Klebsiella pneumoniae* complex (125/503, 24.9%)**, ***P. aeruginosa* (36/503, 7.2%)**, and ***Enterobacter cloacae* complex (30/503, 6.0%)**. Table S1 summarized MDR-GNB colonization results and resistance mechanisms. **CRE were identified in 59 of 503 (11.7%) swabs** from 28 of 192 (14.6%) colonized patients; from day 14 onwards, CRE represented 18.3% (44/241) of positive swabs.

Table 1
General characteristics of patients according to positive or negative rectal swab

Variable	Total (n = 699)	Positive rectal swabs (n = 192)	Negative rectal swabs (n = 507)	p
Sex (female)	307 (43.9)	69 (35.9)	238 (46.9)	0.011
Age (y), median (IQR)	59 (46–68)	56 (45–66)	60 (46–68)	0.052
Haematological malignancy				
Lymphoma	233 (33.3)	64 (33.3)	169 (33.3)	1.000
Acute leukaemia	206 (29.5)	73 (38.0)	133 (26.2)	0.003
Multiple myeloma	120 (17.2)	22 (11.5)	98 (19.3)	0.013
Chronic myeloid leukaemia	52 (7.4)	15 (7.8)	37 (7.3)	0.944
Myelodysplastic syndrome	35 (5.0)	14 (7.3)	21 (4.1)	0.131
HCT	248 (35.5)	82 (42.7)	166 (32.7)	0.018
Comorbidities				
Hypertension	197 (28.2)	57 (29.7)	140 (27.6)	0.653
Chronic heart disease	164 (23.5)	56 (29.2)	108 (21.3)	0.037
Previous solid tumour	136 (19.5)	31 (16.1)	105 (20.7)	0.210
Chronic pulmonary disease	112 (16.0)	28 (14.6)	84 (16.6)	0.601
Diabetes mellitus	85 (12.2)	26 (13.5)	59 (11.6)	0.577
Days of neutropenia during follow-up, median (IQR)	8 (0–19)	16 (3–30)	7 (0–15)	<0.001
Fluoroquinolone prophylaxis during follow-up	445 (63.7)	138 (71.9)	307 (60.6)	0.007
Mortality	142 (20.3)	50 (26.0)	92 (18.1)	0.027
Number of rectal swabs performed, median (IQR)	3 (1–5)	4 (3–10)	2 (1–4)	<0.001
Number of admissions during follow-up, median (IQR)	2 (1–4)	3 (2–5)	2 (1–3)	<0.001
Admission days during follow-up, median (IQR)	37 (21–68)	68 (38–101)	29 (17–49)	<0.001

HCT, haematopoietic stem cell transplantation; IQR, interquartile range.

Table 2
Performance of multidrug-resistant Gram-negative bacilli rectal colonization screening in predicting bloodstream infections by the same pathogen in haematology patients

Resistance phenotype / Colonizing organism	TP	FP	TN	FN	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR- (95% CI)
3CCyBBE	26	152	5	516	83.0% (67.4–92.9%)	77.2% (73.0–80.3%)	14.0% (10.2–20.5%)	99.0% (97.8–99.6%)	3.69	0.21
<i>Escherichia coli</i>	19	84	2	294	80.2% (71.1–87.3%)	87.8% (84.9–89.9%)	18.4% (12.1–27.0%)	99.7% (98.8–99.9%)	7.30	0.11
<i>Klebsiella pneumoniae</i> complex	5	31	0	663	100.0% (95.0–100.0%)	95.5% (93.7–96.8%)	13.9% (6.1–28.7%)	100.0% (99.4–100.0%)	22.39	0.00
<i>Enterobacter</i> (non- <i>cloacae</i>) complex	1	10	0	688	100.0% (93.0–100.0%)	98.8% (97.4–99.4%)	3.11% (1.2–6.1%)	99.9% (99.2–100.0%)	54.80	0.01
<i>Enterobacter cloacae</i> complex	1	16	1	681	60.0% (35.0–85.0%)	97.7% (96.3–98.8%)	5.9% (1.6–27.8%)	99.9% (99.2–100.0%)	21.78	0.01
CRE	7	21	1	670	87.5% (73.0–97.8%)	97.0% (95.4–98.0%)	25.0% (12.7–43.4%)	99.9% (99.2–100.0%)	28.80	0.13
<i>Escherichia coli</i>	1	2	0	696	100.0% (90.7–100.0%)	99.7% (99.0–99.9%)	33.3% (6.1–79.2%)	100.0% (99.5–100.0%)	349.00	0.00
<i>Klebsiella pneumoniae</i> complex	4	10	0	685	100.0% (91.0–100.0%)	98.8% (97.4–99.4%)	28.0% (11.7–54.6%)	100.0% (99.4–100.0%)	88.50	0.00
<i>Klebsiella</i> (non- <i>pneumoniae</i>) complex	0	5	0	694	NA	99.3% (98.3–99.7%)	0.0% (0.0–45.4%)	100.0% (99.4–100.0%)	NA	NA
<i>Enterobacter</i> (non- <i>cloacae</i>) complex	0	2	0	697	NA	99.7% (99.0–99.9%)	0.0% (0.0–45.0%)	100.0% (99.5–100.0%)	NA	NA
<i>Enterobacter cloacae</i> complex	2	2	0	695	100.0% (94.2–100.0%)	99.7% (99.0–99.9%)	50.0% (15.0–85.0%)	100.0% (99.5–100.0%)	348.50	0.00
<i>Ureaplasma</i> (non- <i>urealyticum</i>) complex	4	1	0	695	100.0% (94.2–100.0%)	99.8% (99.0–99.9%)	36.4% (12.2–64.6%)	99.9% (99.2–100.0%)	79.31	0.00
<i>Pseudomonas aeruginosa</i>	6	24	14	655	30.0% (14.5–51.9%)	96.5% (94.8–97.8%)	20.0% (9.5–37.3%)	97.9% (96.5–98.7%)	8.48	0.72

We assessed the diagnostic performance of MDR-GNB rectal colonization screening to predict concordant bloodstream infections (BSI). True positives (TP); colonized patients who developed concordant BSI; false positives (FP); colonized patients who did not develop concordant BSI. True negatives (TN); non-colonized patients who did not develop concordant BSI. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were expressed as percentages with 95% CIs. Positive and negative likelihood ratios (LR+ and LR-) were reported as absolute values with 95% CIs. NA indicates not applicable.

3CCyBBE, third-generation cephalosporin-resistant *Enterobacteriaceae*; CRE, carbapenem-resistant *Enterobacteriaceae*; DTR, difficult-to-treat resistance; MDR-GNB, multidrug-resistant Gram-negative bacilli.

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Research note

Rectal colonization by multidrug-resistant Gram-negative bacteria and subsequent bacteraemia in haematological patients

Antonin Gallardo-Pizarro ^{1,2,3}, Carlos Lopera ^{1,2,3}, Olivier Pymony ¹, Patricia Monzo-Gallo ^{1,2}, Tommaso Francesco Aiello ^{1,2}, Ana Martínez-Urrea ^{1,2}, Sabina Herrera ¹, Ana Del Río ¹, Christian Tejero-Lumbreras ¹, Mariana Chumbita ¹, Carlos Jiménez-Vicente ², Albert Cortés ¹, Marta Bodro ^{1,2}, Cristina Pitar ¹, Elisa Rubio ⁴, Josep Mensa ¹, Alex Soriano ^{1,2}, Jose Antonio Martínez ^{1,2}, Carolina García-Vidal ^{1,2,3}

Figure S1. Time from hospital admission to first positive swab.

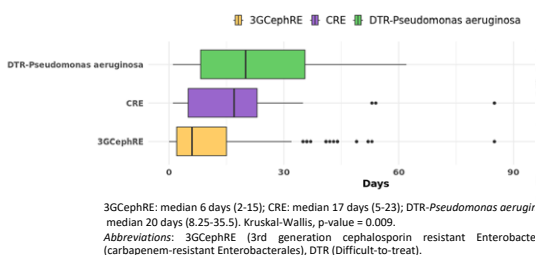
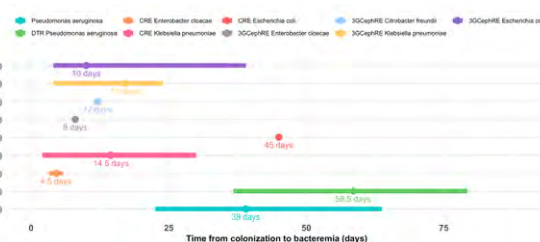


Figure S2. Time from colonization (detection of MDR-GNB in rectal swab) to onset of concordant bloodstream infection.



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Journal Pre-proof

Rectal colonization with multidrug-resistant organisms and subsequent bloodstream infections in hematological patients undergoing cellular therapies

Pineles Karakou, Charalampos Charalampidis, Ioannis Konstantinos, Konstantinos Glikas, Maria Stamouli, Ioanna Lazara, Christoforos Chatzidimitriou, Georgia Giallourou, Spiros Chondropoulos, Elissavet Mastroianni, Ioannis Grigoriadis, Penelope Christina Georgiou, Polyxeni Karakosta, Spyridon Katschis, Spyros Pournaras, Dimitra Kavatha, Penelope Tsirgolis, Sotirios Tsolotas, Konstantinos Thomas

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Reference: JTCT 55200

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Table 2. Microbiological results and prior antimicrobial use

Variable	N=182
Number of rectal samples, median (IQR)	4 (4-5)
≥2 rectal samples, n (%)	169 (93)
Days between admission and baseline rectal sample, median (IQR)	4 (3-6)
VRE colonization, last 6 months, n (%) ^a	19 (12)
CR-GNB colonization, last 6 months, n (%) ^a	10 (5.6)
Rectal colonization, baseline, n (%)	
- Negative for VRE/CR-GNB	172 (95)
- VRE	8 (4)
- CR-GNB	2 (1)
Vancomycin (≥4 weeks of cellular therapy)	86 (47.2)
Carbapenems (≥4 weeks of cellular therapy)	61 (33.5)
VRE colonization during follow-up, n (%) ^b	37 (23)
Time to VRE colonization (days), median (IQR)	14 (7-19)
CR-GNB colonization during follow-up, n (%) ^{b,c}	14 (8.4)
- KP-KPC	9
- KP-MBL	4
- <i>P. aeruginosa</i>	1
- <i>A. baumannii</i>	2
Time to CR-GNB colonization (days), median (IQR)	14 (7-21)
Patients with ≥1 episode of BSI, n (%)	79 (43.4)
Days from neutropenia onset to BSI, median (IQR)	6 (4-10)
Isolated microorganisms (1 st BSI event), n ^{††}	
- CoNS	88
- CS-GNB	40
- VRE	28
- Streptococci	8
- KP-KPC	4
- Staphylococcus aureus	3
- Other	5
Isolated microorganisms (2 nd BSI event), n ^{††}	
- CoNS	17
- CS-GNB	4
- VRE	7
- Enterococcus faecalis	2
- KP-KPC	1
- Candida spp	1
- Other	1

VRE: Vancomycin-resistant Enterococcus; CR-GNB: Carbapenem-resistant Gram-negative bacilli; KP-KPC: Klebsiella pneumoniae carbapenemase-producing Klebsiella pneumoniae; KP-MBL: Metallo-beta-lactamase-producing Klebsiella pneumoniae; BSI: bloodstream infection; CoNS: Coagulase-negative Staphylococci; CS-GNB: Carbapenem-resistant Gram-negative bacilli

^a ≥10 with existing data for prior VRE colonization and ≥4 with existing data for CR-GNB colonization

^b ≥10, VRE negative at baseline and ≥1 sample

^c ≥10, CR-GNB negative at baseline and ≥1 sample

^{††} ≥1 colonized with multiple CR-GNB microorganisms

^{†††} ≥2 with polymicrobial BSI

^{††††} ≥2 with polymicrobial BSI


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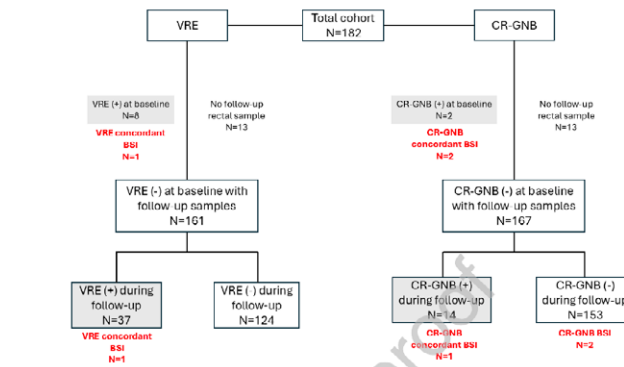
Journal Pre-proof

Rectal colonization with multidrug-resistant organisms and subsequent bloodstream infections in hematological patients undergoing cellular therapies

Pavlos Katsakos, Charalambos Charalampidis, Ioanna Konstantidou, Konstantinos Gkikas, Maria Stamouli, Ioanna Lazari, Chrysostomos Chatzidimitriou, Georgia Gellifonakou, Spiros Chondrosoulas, Elisavet Moutzouraki, Ioannis Grigoriadis, Panagiotis Christos Georgiou, Polymen Karakosta, Spyridon Katschis, Sigrun Papanicolaou, Dimitris Kavalas, Panagiotis Tsigalou, Salma Tassabehji, Konstantine Thomas

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VRE: Vancomycin-resistant *Enterococcus*, CR-GNB: Carbapenem-resistant Gram-negative bacilli

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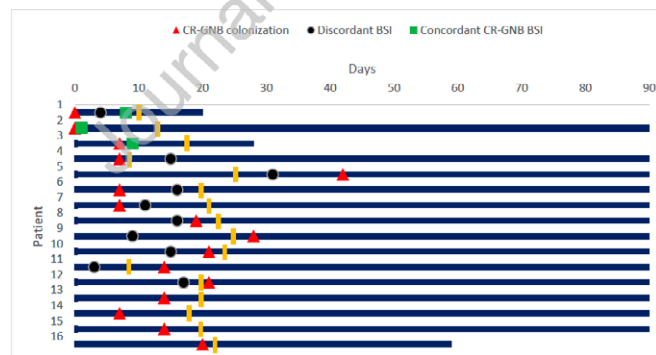
Pavlos Katsakos, Charalambos Charalampidis, Ioanna Konstantidou, Konstantinos Gkikas, Maria Stamouli, Ioanna Lazari, Chrysostomos Chatzidimitriou, Georgia Gellifonakou, Spiros Chondrosoulas, Elisavet Moutzouraki, Ioannis Grigoriadis, Panagiotis Christos Georgiou, Polymen Karakosta, Spyridon Katschis, Sigrun Papanicolaou, Dimitris Kavalas, Panagiotis Tsigalou, Salma Tassabehji, Konstantine Thomas

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Figure 4. Swimmer plot of CR-GNB colonized patients (n=16), showing timing of colonization and BSIs (concordant CR-GNB BSIs and discordant BSIs from other pathogens) up to 90 days after the initial rectal screening (Yellow vertical lines correspond to the time of recovery of neutrophils)








Screening Cultivos Colonización

Journal Pre-proof

Rectal colonization with multidrug-resistant organisms and subsequent bloodstream infections in hematological patients undergoing cellular therapies

Piretti Kazakou, Charalampou Charalampidou, Ioanna Konstantinou, Konstantinos Gkikas, Maria Stamouli, Ioanna Lazara, Chrysostomos Chatzidimitriou, George Gelleraopoulos, Spiros Chondrosoulas, Elisavet Mochizianou, Ioannis Grigoropoulos, Panagiotis Christos Georgiou, Polymni Karakosta, Spyridon Katschis, Spyros Papanicolaou, Dimitris Kavalas, Panagiotis Tzafaris, Salma Tassabehji, Konstantinos Triantafyllidis

PE: S2966-6367(2020)00234-4
DOI: <https://doi.org/10.1016/j.jct.2020.03.008>
Reference: JCT 5620

To appear in: Transplantation and Cellular Therapy

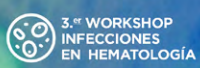
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Highlights

- In our cohort, 8.4% of carbapenem-resistant Gram-negative bacilli (CR-GNB) negative patients on baseline rectal screening, were colonized during follow-up, and 23% of vancomycin-resistant *Enterococcus* (VRE) negative patients were colonized, with prior colonization being associated with re-colonization.
- While 43% of patients experienced at least one BSI, only three concordant CR-GNB BSIs among 16 colonized patients (18.7%) and two concordant VRE BSIs among 45 colonized patients (4.4%) were observed.
- These concordance rates support antibiotics de-escalation in clinically stable patients empirically receiving carbapenems and vancomycin during febrile neutropenia.






CASO CLÍNICO

- Varón de 77 años con AP de CI con 2 stent colocados 2021, HTA en tratamiento con enalapril, DM tipo II en tratamiento con metformina. Nuevo diagnóstico de LAM (NMP1+, IDH2+, FLT3ITD-, IDH1-, TP53-,), Cariotipo normal, ECOG 1, Escala Hb: 9,7 g/L, L: 12.6 x 10⁹/L (82% blastos, Neutrófilos 0,6 x 10⁹/L), Plaquetas: 18 x 10⁹/L, CrCl: 62ml/min, ALT: 23, FA: 123, GGT: 32. Afebril. Ingresa para iniciar tratamiento y soporte hemoterápico.
- ¿Realiza/ría usted cultivos de colonización (nasal, heces etc)?
- ¿Indicaría profilaxis antibiótica? ¿Cuál?
- ¿Indicaría profilaxis antifúngica? ¿Cuál?
- ¿Indicaría profilaxis antivírica? ¿Cuál?

Profilaxis antibiótica

- Recomendaciones 2026 de las guías más relevantes

SI

- ECIL
- NCCN
- IDSA

NO

- ESMO
- Australian Guidelines

Profilaxis antibiótica

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DOI: 10.1111/bjh.16106

ORIGINAL PAPER
Haematological Malignancy - Clinical

Prevention and management of febrile neutropenia in acute myeloid leukaemia and higher risk myelodysplastic syndrome: An international survey of current practice

Aleecia MacPhail^{1,2} | Justin Loke^{3,4} | Brett L. Houston^{5,6} | Claire Dendle^{1,2} |
 Andrea S. Hendon^{1,8} | Robert Weinkove^{9,10,11} | Orla Morrissey^{1,12} |
 Dionysios Neofytos¹³ | Niccolò Buetti^{14,15} | Catriona Parker¹ | Monica A. Slavin^{16,17,18,19} |
 Charles Craddock^{20,21} | Simon J. Stanworth^{13,21,22} | Zoe McQuilten^{1,23} | on behalf of the
 Australasian Leukaemia and Lymphoma Group Supportive Care Working Group and UK AML/
 Supportive Care Working Parties

FIGURE 1 Routine prescription of antibiotic prophylaxis for febrile neutropenia in specific patient groups. ANZ, Australia and New Zealand; UK, United Kingdom.

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Profilaxis antibiótica

- Evidencia (Estudios randomizados)

The NEW ENGLAND JOURNAL of MEDICINE

DOI:10.1056/NEJM200507283531302

Levofloxacin to Prevent Bacterial Infection in Patients with Cancer and Neutropenia

Giuseppe Sazdovitch, M.D., Alessandra Muscarelli, M.D., Francesco Marzocchi, M.D., Pietro Martino, M.D., M. Bala Datta, M.D., Giovanni Martinelli, M.D., Rosanna Basso, M.D., Domenico D'Ercole, M.D., Maurizio Balli, M.D., A. Maria Nicosi, M.D., Daniela Ciliberto, M.D., Elena J. Zili, M.D., Simona Carli, M.D., Giorgio Speranza, M.D., Sergio Brindani, M.D., Francesco Tabbone, M.D., Giorgio Lombardi, M.D., Francesco Leone, M.D., Fabio Riva, M.D., and Roberto Di Fronzo, M.D.

For the Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) Infection Program*

A. All Patients

B. Patients with Acute Leukemia

Table 3. Mortality Rates in the Treated Population.

Variable	Levofloxacin (N=373)*	Placebo (N=363)	P Value
Death	10	18	0.15
Death due to infection	9	14	0.36
Microbiologically documented infection	4	7	0.25
Microbiologically documented infection with bacteremia	3	5	0.34
Single gram-positive isolate	2	2	
Single gram-negative isolate	0	2	
Polymicrobial (gram-positive and gram-negative) isolate	1	1	
Microbiologically documented infection without bacteremia	1	2	0.48
Single gram-positive isolate	0	1	
Single gram-negative isolate	1	1	
Clinically documented infection	2	4	0.33
Lung	1	2	
Other site	1	2	
Free of unexplained origin	3	3	0.64
Death from noninfectious causes	1	4	0.17

* Two patients were lost to follow-up.

3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

Profilaxis antibiótica

- Evidencia (Estudios randomizados)

ORIGINAL ARTICLE

Antibacterial Prophylaxis after Chemotherapy for Solid Tumors and Lymphomas

Michael Cutler, M.D., Neil Steven, Ph.D., Lucinda Billingham, Ph.D., Clare Gault, B.Sc., Mark Hastings, M.D., Peter Simmonds, M.D., Nicholas Storer, M.D., Daniel Fox, Ph.D., Mark Barnes, Ph.D., Indrajit Fernando, M.D., Robert Huddart, Ph.D., Simon Gillies, D.Phil., and Andrew Stanley, M.B. B.S., for the Simple Investigation in Neutropenic Individuals of the Frequency of Infection after Chemotherapy (SINIC) Antibiotic in a Number of Tumours (SIGNIFICANT) Trial Group*

Table 3. Incidence of Febrile Episodes, Probable Infections, and Hospitalization for Infection.*

Event	Levofloxacin (N=781)	Placebo (N=784)	Relative Risk (95% CI)	P Value†
Events occurring in first cycle				
Febrile episode				
Yes	27 (3.5)	62 (7.9)	0.44 (0.28–0.68)	<0.001
No	736	699		
Unknown	18	23		
Probable infection				
Yes	109 (14.0)	152 (19.4)	0.72 (0.57–0.90)	0.005
No	658	614		
Unknown	14	18		
Hospitalization for infection				
Yes	52 (6.7)	81 (10.3)	0.64 (0.46–0.90)	0.01
No	712	681		
Unknown	17	22		
Events occurring at least once in any cycle				
Febrile episode				
Yes for ≥1 cycles	84 (10.8)	119 (15.2)	0.71 (0.55–0.92)	0.01
No for all cycles	661	623		
Unknown for ≥1 cycles	36	42		
Probable infection				
Yes for ≥1 cycles	267 (34.2)	325 (41.5)	0.82 (0.73–0.94)	0.004
No for all cycles	489	432		
Unknown for ≥1 cycles	25	27		
Hospitalization for infection				
Yes for ≥1 cycles	173 (22.1)	269 (34.3)	0.73 (0.59–0.90)	0.004
No for all cycles	623	575		
Unknown for ≥1 cycles	35	40		
Severe infection and/or death from infection	8 (1.0)	16 (2.0)	0.50 (0.22–1.17)	0.15

Si evaluamos la prevención de fiebre neutropénica como endpoint primario deben tratarse 1000 pacientes con profilaxis para evitar a 44 un episodio de fiebre neutropénica

68

Profilaxis antibiótica

• Evidencia (Metaanálisis)



Antibiotic prophylaxis for bacterial infections in afebrile neutropenic patients following chemotherapy (Review)

Galer-Gvili A, Fraser A, Paul M, Vidal J, Lavielle TA, van de Bovenkamp MD, Rosner LDB, Leibovici L

13.579 pacientes
162 estudios

Summary of findings for the main comparison. Summary of findings: antibiotics versus placebo or no intervention

Antibiotics compared with placebo or no intervention for afebrile neutropenia

Patient or population: patients with afebrile neutropenia induced by chemotherapy

Settings: hospital or outpatient

Intervention: antibiotics

Comparison: placebo or no intervention

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Control	Antibiotic drug				
All cause mortality	88 per 1000	57 per 1000 (47 to 68)	RR 0.66 (0.55-0.79)	5,635 participants (46 trials)	0000 high	P = 20%. NNT to prevent one death from any cause is 34 (95% CI 28-56). The greatest effect was seen in the quinolone prophylaxis subgroup (10 trials; 3,796 participants; RR 0.54 (95% CI 0.40 to 0.74). Test for subgroup differences: P = 42%, P = 0.16. Quality was not downgraded despite a high risk of bias (allocation concealment was unclear in most of the trials) because when results of low risk allocation concealment were compared to unclear allocation concealment, they were similar.
Febrile patients and episodes	607 per 1000	406 per 1000 (449 to 526)	RR 0.60 (0.74-0.87)	6,658 participants (54 trials)	000 moderate	NNT to prevent one febrile patient or febrile episode was 7 (95% CI 5-10). Quality was downgraded because of heterogeneity and unit of analysis issues, not because of the high risk of bias (allocation concealment was unclear in most of the trials) as, when results between low risk allocation concealment were compared to unclear allocation concealment, the results were similar.
Bacteraemia	209 per 1000	195 per 1000 (88 to 325)	RR 0.50 (0.43-0.60)	6,390 participants (53 trials)	0000 high	This reduction occurred for all subgroups. NNT to prevent bacteraemia is 10 (95% CI 8-12).

Summary of findings 2. Summary of findings: quinolone prophylaxis compared with TMP-SMZ prophylaxis

Quinolones compared with TMP-SMZ for afebrile neutropenia

Patient or population: cancer patients with afebrile neutropenia following chemotherapy

Settings: hospital or outpatient

Intervention: quinolones

Comparison: TMP-SMZ

Outcomes	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)*	Comments
All cause mortality	RR 1.07 (0.66-1.72)	917 participants (10 trials)	000 moderate	Quality was downgraded due to imprecision.
Febrile patients and episodes	RR 0.92 (0.78-1.09)	931 participants (10 trials)	000 moderate	Quality was downgraded due to heterogeneity.
Bacteraemia	RR 0.89 (0.55-1.42)	931 participants (10 trials)	000 moderate	Quality was downgraded due to heterogeneity and imprecision.

In studies comparing antibiotic prophylaxis to placebo or no treatment in neutropenic patients, prophylaxis significantly reduced all-cause mortality and infection-related mortality. We estimated the NNT with antibiotic prophylaxis in order to prevent one death from all causes as 34 (95% CI 26 to 56). Prophylaxis significantly reduced febrile episodes.

Profilaxis antibiótica

• Evidencia (Metaanálisis)



8.123 pacientes
52 estudios

Effect of quinolone prophylaxis in afebrile neutropenic patients on microbial resistance: systematic review and meta-analysis

Anat Galer-Gvili □, Mical Paul, Abigail Fraser, Leonard Leibovici
Journal of Antimicrobial Chemotherapy, Volume 59, Issue 1, January 2007, Pages 5–22

Conclusions: Patients treated with quinolones have a non-significant increase in colonization by quinolone-resistant bacteria. There is no difference in the number of infections caused by pathogens resistant to quinolones. As quinolone prophylaxis reduces the risk of death in neutropenic patients, the risk associated with colonization and infections caused by quinolone-resistant organisms does not outweigh the gain. Future trials should focus on better documentation of infections caused by resistant organisms.

Profilaxis antibiótica

• Evidencia (Metaanálisis)

Meta-Analysis

• J Infect 2018 Jan;76(1):20-37.

doi: 10.1016/j.jinf.2017.10.009.Epub 2017 Oct 25.

Fluoroquinolone prophylaxis in haematological cancer patients with neutropenia: ECIL critical appraisal of previous guidelines

Malgorzata Mikulska¹, Diana Averbuch², Frederic Tisset³, Catherine Cordonnier⁴, Murat Akova⁵, Thierry Calandra⁶, Marcello Ceppi⁷, Paolo Bruzzi⁸, Claudio Viscoli⁹, European Conference on Infections in Leukemia (ECIL)

Abstract

Objectives: Fluoroquinolone (FQ) prophylaxis was recommended in 2005 by European Conference on Infections in Leukemia (ECIL) for patients with prolonged neutropenia. In consideration of a worldwide increase in antibiotic resistance, the issue of FQ prophylaxis during neutropenia was re-evaluated.

Methods: Literature review of randomised controlled trials (RCT) and observational studies published in years 2006-2014 was performed.

Their results were analysed in meta-analysis. Meta-regression model was applied to evaluate whether the rates of FQ resistance in community and hospital settings influenced the efficacy of FQ prophylaxis. The impact of FQ prophylaxis on colonisation and infection with resistant bacteria was reviewed.

Results: Two RCTs and 12 observational studies were identified. FQ prophylaxis did not have effect on mortality (pooled OR 1.01, 95%CI 0.73-1.41), but was associated with **lower rate of bloodstream infections (BSI)** (pooled OR 0.57, 95%CI 0.43-0.74) and **episodes of fever during neutropenia** (pooled OR 0.32, 95%CI 0.20-0.50). No effect of the background rate of FQ resistance on the efficacy of FQ prophylaxis was observed. In few studies, FQ prophylaxis resulted in an increased colonisation or infection with FQ- or multi-drug resistant strains.

Conclusions: **The possible benefits of FQ prophylaxis on BSI rate, but not on overall mortality, should be weighed against its impact in terms of toxicity and changes in local ecology in single centres**

Profilaxis antibiótica

• Levo Serie LAM Ven/Aza

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA

hivma

OXFORD

Levofloxacin to Prevent Bacterial Infection in Patients With Acute Myeloid Leukemia Treated by Venetoclax and Azacitidine: A Toulouse-Bordeaux DATAML Registry Study

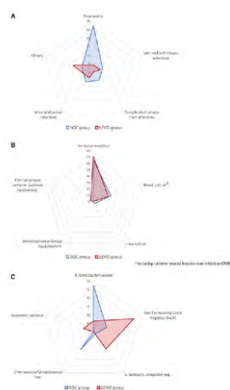
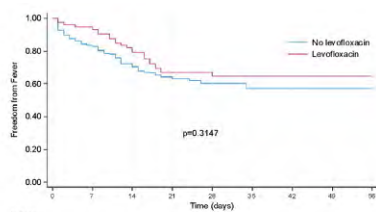
Xavier Breuer,^{1,2} Nicolas Benaïme,^{3,4} Emilie Barrot,^{5,6} Ramsey Lamy,⁷ Karim Delavigne,⁸ Nathan Mouton,⁹ Sébastien Tavitian,¹⁰ Fabrice Legrand,¹¹ Léonard Laperche,¹² Eric Delabranche,¹³ Audrey Bialek,¹⁴ Marie Cordier,¹⁵ Elise Lanté,¹⁶ Anne Bruneau,¹⁷ Jennifer Guinet,¹⁸ Pauline Fleck,¹⁹ Laëtitia Gherard,²⁰ Audrey Sarry,²¹ Anne-Charlotte de Grande,²² Clémentine Borgeron,²³ Christine Richier,²⁴ Arnaud Pigneau,²⁵ Sarah Berti,²⁶ and Pierre-Yves Dumas²⁷


Table 3. Incidence of Clinically Documented Infections, Fever of Unknown Origin in LEVO and SOC Groups, n (%)

	SOC Group n=186	LEVO Group n=72	P ^a Value
Fever of unknown origin	32 (17.2)	18 (25.0)	.155
Clinically documented	37 (19.9)	6 (8.3)	.028
Pneumonia	19 (10.2)	1 (1.4)	
Skin and soft-tissue infections	4 (2.1)	1 (1.4)	
Complicated urinary tract infection	4 (2.1)	0 (0.0)	
Intra-abdominal infections	5 (2.7)	1 (1.4)	
Others ^b	5 (2.7)	3 (4.2)	
Microbiologically documented	24 (12.9)	7 (9.7)	.481
Bloodstream infection ^b	20 (10.8)	6 (8.3)	
Urinary tract infection	3 (1.6)	0 (0.0)	
RAI, fluid	1 (0.5)	0 (0.0)	
Central venous catheter without bloodstream infection	0 (0.0)	1 (1.4)	
Overall documented infection	61 (32.8)	13 (18.1)	.019

Abbreviations: RAI, bronchoalveolar; LEVO, levofloxacin; SOC, standard of care.

^aCentral venous catheter infection, uncomplicated urinary tract infection.

^bIncluding central venous catheter-related bloodstream infections.


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

CASO CLÍNICO

- Varón de 77 años con AP de CI con 2 stent colocados 2021, HTA en tratamiento con enalapril, DM tipo II en tratamiento con metformina. Nuevo diagnóstico de LAM (NMP1+, IDH2+, FLT3ITD-, IDH1-, TP53-,), Cariotipo normal, ECOG 1, Hb: 9,7 g/L, L: $12.6 \times 10^9/L$ (82% blastos, Neutrófilos $0,6 \times 10^9/L$), Plaquetas: $18 \times 10^9/L$, CrCl: 62ml/min, ALT: 23, FA: 123, GGT: 32. Afebril. Ingresa para iniciar tratamiento y soporte hemoterápico.
- ¿Realiza/ría usted cultivos de colonización (nasal, heces etc)?
- ¿Indicaría profilaxis antibiótica? ¿Cuál?
- ¿Indicaría profilaxis antifúngica? ¿Cuál?
- ¿Indicaría profilaxis antivírica? ¿Cuál?


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

	Espectro	Comentarios
AZOLES		
Fluconazol	Activo frente a la mayoría de <i>Candida</i> spp. <i>Test in vitro de susceptibilidad recomendados</i>	<i>C. glabrata</i> resistente in vitro y <i>krusei</i> resistente No actividad frente a hongos (<i>Aspergillus</i> spp. <i>Mucorales</i>)
Itraconazol	Activo frente <i>Candida</i> , <i>Aspergillus</i> spp y otros hongos	Inotrópico negativo Variabilidad absorción (H2 bloqueantes reduce)
Voriconazol	Activo frente <i>Candida</i> , <i>Aspergillus</i> spp y otros hongos Standard of care para tratamiento primario de AI (A1)	Poca actividad frente a <i>Mucorales</i> Alt. Visuales, alucinaciones, PFH, interacciones
Posaconazol	Activo frente <i>Candida</i> , <i>Aspergillus</i> spp y otros hongos Efectivo en profilaxis LAM y SCT (GVHD) (A1)	Muy potente activador enzimático CYP3A4 (interacciones)
Isavuconazol	Activo frente a <i>Aspergillus</i> spp y <i>Mucorales</i>	Acorta QT / Menor actividad CYP3A4
FORMULACIONES ANFO		
Anfotericina deoxicolato	Mayor espectro antifúngico Excepto <i>A. terreus</i> , <i>Scedosporium</i> y <i>Lomentospora</i>	Muy nefrotóxico y reacciones infusionales
Anfotericina B complejo lipídico		Menor nefrotoxicidad y reacciones
Antotericina B liposómica		Posiblemente el de más fácil manejo y dosis altas
EQUINOCANDINAS		
Caspofungina	Tratamiento primario de candidemias (A1)	Pobre penetración en SNC, tracto urinario y ocular Excelente perfil de seguridad
Anidulafungina	Tratamiento primario de candidemias (A1)	idem
Micafungina	Tratamiento primario de candidemias (A1)	idem
Rezafungina	Pacientes con candidemia que no tiene otras opciones (A1)	idem


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Profilaxis antifúngica

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Posaconazole vs. Fluconazole or Itraconazole Prophylaxis in Patients with Neutropenia

Oliver A. Cornely, M.D., Johan Maertens, M.D., Drew J. Winston, M.D.,
John Perfect, M.D., Andrew J. Ullmann, M.D., Thomas J. Walsh, M.D.,
David Helligso, M.D., Jerry Holmbeck, M.D., Dirk Stockelberg, M.D.,
Yew-Teo Goh, M.D., Mario Pettini, M.D., Cathy Hurdale, M.D.,
Ramachandran Suresh, Ph.D., and David Angelo-Gonzalez, M.D.*

Table 2. Proven or Probable Invasive Fungal Infection during the Treatment Phase.*

Invasive Fungal Infection	Posaconazole (N=304)	Fluconazole or Itraconazole (N=298)	Fluconazole (N=249)	Itraconazole (N=58)	P Value	95% CI
Proven or probable†	7 (2)	25 (8)	19 (8)	6 (10)	<0.001	-9.7 to -2.5
Mold						
Invasive aspergillosis	2 (1)	20 (7)	15 (6)	5 (9)	<0.001	-9.1 to -3.1
<i>Aspergillus fumigatus</i>	0	2	1	1		
<i>A. flavus</i>	0	2	2	0		
<i>Aspergillus</i> species‡	2	16	12	4		
Rhizopus species	0	1	1	0		
<i>Scedosporium boydii</i>	0	1	1	0		
Mold, not otherwise specified	1	0	0	0		
Yeast						
Invasive candidiasis	3 (1)	2 (<1)	2 (<1)	0		
<i>Candida glabrata</i>	2	1	1	0		
<i>C. krusei</i>	0	1§	1§	0		
<i>C. parapsilosis</i>	0	1§	1§	0		
<i>C. tropicalis</i>	1	0	0	0		
Other						
<i>Pneumocystis jirovecii</i> ¶	1	1	0	1		

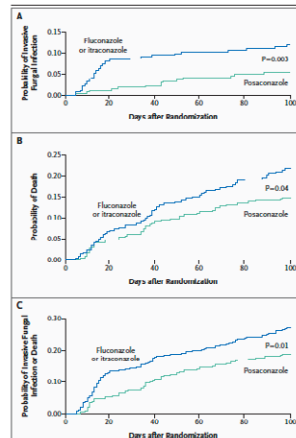


Figure 1. Kaplan-Meier Curves for Time to Invasive Fungal Infection (Panel A), Death from Any Cause (Panel B), and Invasive Fungal Infection or Death (Panel C) over the 100-Day Period after Randomization.

Table 3. Clinical Response and Reasons for Failure during the Treatment Phase.*

Clinical Response	Posaconazole (N=304)	Fluconazole or Itraconazole (N=298)	P Value	95% CI
Clinical success	155 (51)	160 (54)	0.908	-18.1 to -2.6
Clinical failure	109 (36)	138 (46)	<0.001	-9.7 to -2.5
Proven or probable invasive fungal infection	7 (2)	25 (8)	<0.001	-9.7 to -2.5
Use of systemic antifungal agent for adverse event (day 1 to 100 days after randomization)	68 (22)	101 (34)	0.002	-18.7 to -4.3
Adverse event possibly or probably related to study treatment, resulting in discontinuation	25 (8)	25 (8)	0.94	
Use of intravenous study drug for adverse event (day 1 to 100 days after randomization)	4 (1)	17 (6)	0.14	
Withdrawn for any reason and loss to follow-up	8 (3)	1 (0)	0.02	0.0 to 4.2

Profilaxis antifúngica

Posaconazole versus voriconazole for primary treatment of invasive aspergillosis: a phase 3, randomised, controlled, non-inferiority trial

Prof Johan A Maertens, MD^{a,b} · Prof Galia Rahav, MD^{c,d} · Prof Dong-Gun Lee, MD^e · Prof Alfredo Ponce-de-León, MD^f · Isabel Cristina Ramírez Sánchez, MD^g · Prof Nikolay Klimko, MD^h · et al.

LANCET 2021; 397: 499-509

The primary endpoint was cumulative all-cause mortality up until day 42 in the intention-to-treat (ITT) population (defined as randomly assigned participants who received ≥1 dose of study drug), with a 10% non-inferiority margin.

Between Oct 25, 2013, and Sept 10, 2019, of 653 individuals assessed for eligibility, 575 ITT participants were randomly assigned and received one or more doses of study drug (n=288 [50%] posaconazole, n=287 [50%] voriconazole). Mortality up until day 42 was 15% (44 of 288) in the posaconazole group and 21% (59 of 287) in the voriconazole group (treatment difference -5.3% [95% CI -11.6 to 1.0]; p<0.0001). Mortality up until day 42 in the full-analysis-set subpopulation (ITT participants with proven or probable invasive aspergillosis) supported this conclusion: 31 (19%) of 163 participants in the posaconazole group and 32 (19%) of 171 participants in the voriconazole group (treatment difference 0.3% [95% CI -8.2 to 8.8]). The most frequently reported treatment-related adverse events (incidence >3%) were increased aspartate aminotransferase (AST) or alanine aminotransferase (ALT), nausea, hypokalaemia, and vomiting in the posaconazole group and increased ALT, AST, or alkaline phosphatase, hallucination, increased γ-glutamyltransferase peptidase, nausea, and blurred vision in the voriconazole group. The overall incidence of treatment-related adverse event rates in the ITT population was 30% for posaconazole and 40% for voriconazole (treatment difference -10.2% [95% CI -17.9 to -2.4]).

Posaconazole was non-inferior to voriconazole for all-cause mortality up until day 42 in participants with invasive aspergillosis. Posaconazole was well tolerated, and participants had fewer treatment-related adverse events than in the voriconazole group. This study supports the use of posaconazole as a first-line treatment for the condition.






Profilaxis antifúngica

Metaanálisis

JAMA Network Open.

Original Investigation | Infectious Diseases

Comparison of Antifungal Prophylaxis Drugs in Patients With Hematological Disease or Undergoing Hematopoietic Stem Cell Transplantation: A Systematic Review and Network Meta-analysis

Jing Wang, MD, PhD; Min Zhou, MD, PhD; Jing Yan, MD, PhD; Hong-Ru Zhou, MD, PhD; Bing Chen, MD, PhD; Yuan Wan, PhD

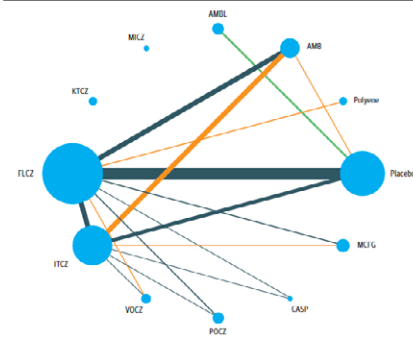
JAMA Network Open. 2020;3(01):e2017652. doi:10.1001/jamanetworkopen.2020.17652

14789 Pacientes

69 estudios randomizados

Comparación de 12 tratamientos

Figure 1. Schematic of the Network of Evidence Used in Network Meta-analysis for Invasive Fungal Infections

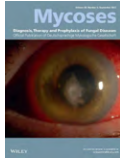


Conclusions

*This network meta-analysis assessed the performance of various antifungal prophylaxis treatment in patients with hematological disease or undergoing HSCT. Our findings suggest that, in terms of the prevention of IFIs and tolerance, voriconazole may be the best prophylactic option for patients undergoing HSCT, and **posaconazole may be the best prophylactic option for patients with AML or MDS.***

Profilaxis antifúngica

Metaanálisis



A systematic review and meta-analysis of efficacy and safety of isavuconazole for the treatment and prophylaxis of invasive fungal infections

[Hideo Kato](#), [Mao Hagihara](#), [Nobuhiro Asai](#), [Takumi Umemura](#), [Jun Hirai](#), [Nobuaki Mori](#), [Yuka Yamagishi](#), [Takuwa Iwamoto](#), [Hiroshige Mikamo](#)

Mycoses 2023;66:815-824

3037 Pacientes

10 estudios randomizados

Isavuconazole was **comparable with the control group in mortality and IFI rate** in the treatment and prophylaxis of IFIs, respectively (mortality, odds rate (OR) 1.11, 95% confidential interval (CI) 0.82–1.51; IFI rate, OR 1.02, 95% CI 0.49–2.12). **Isavuconazole significantly reduced the discontinuation rate in the treatment** (OR 1.96, 95% CI 1.26–3.07) and incidence of **hepatic function abnormalities** in the treatment and prophylaxis, compared with the control group (treatment, OR 2.31, 95% CI 1.41–3.78; prophylaxis, OR 3.63, 95% CI 1.31–10.05).

Conclusions

Our meta-analysis revealed that **isavuconazole was not inferior** to other antifungal agents for the treatment and prophylaxis of IFIs, with substantially **fewer drug-associated adverse events** and discontinuations. Our findings support the use of isavuconazole as the primary treatment and prophylaxis for IFIs.


3.º WORKSHOP
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INFECTHEMA

Profilaxis antifúngica

- Recomendaciones 2026 de las guías más relevantes


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INFECTHEMA

Profilaxis antifúngica

REVIEW ARTICLE OPEN
[Check for updates](#)

Primary antifungal prophylaxis in hematological malignancies.
Updated clinical practice guidelines by the European
Conference on Infections in Leukemia (ECIL)

Ulfö Pagano^{1,2,3}, Georg Maschmeyer⁴, Frederik Lamoth⁵, Ola Blennow^{6,7}, Alenor Xheard⁸, Mariela Spadea^{9,10},
Alessandro Buica¹¹, Catherine Cordonnier¹², Johan Maertens¹³ On behalf of ECIL*

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Table 2. Recommendations for antifungal prophylaxis in patients with AML receiving intensive remission induction/reinduction chemotherapy.

Intention	Intervention	SoR	QoE	ECIL 5-6
Prevent IFD in AML patients, excluding allogeneic HSCT	posaconazole, tablet 300 mg q24h p.o. (q12h on day 1)	A	1 ¹	A-I
	amphotericin B, liposomal, inhalation ^{1,3}	B	I	B-I
	10 mg twice weekly			
	fluconazole ⁴	B	I	B-I
	400 mg q24h p.o. or i.v.			
	voriconazole	B	IIu	B-II
	6 mg/kg/12h first day then 4 mg/kg q12h, i.v. or p.o.			
	isavuconazole ²	B	III	NR
	200 mg q8h p.o. first 2 days then 200 mg q24h			
	micafungin	B	II u,t	NR
	50 mg q24h i.v.			
	amphotericin B, liposomal, i.v. ²	C	II	C-II
	1-3 mg/kg q24h			
	caspofungin ²	B	III	NR

AML, acute myeloid leukemia; IFD, invasive fungal disease; HSCT, hematopoietic stem cell transplantation; NR, No recommendation.
1 = recommendation for AML under remission induction chemotherapy; 2 = no approval for prophylaxis of IFD; 3 = formulation not approved; 4 = Only recommended if the incidence of mold infections is low. Fluconazole may be part of an integrated care strategy together with a mold-directed diagnostic approach.

¹Should be combined with systemic fluconazole.

Amphotericin deoxycholate is not approved for prophylaxis and should not be considered due to drug-related toxicity.

Profilaxis antifúngica


3.º WORKSHOP
INFECCIONES
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INFECTHEMA

J Antimicrob Chemother 2019; 74: 1062–1068
doi:10.1093/jac/dky550 Advance Access publication 14 January 2019

Journal of
Antimicrobial
Chemotherapy

'Real-life' analysis of the role of antifungal prophylaxis in preventing invasive aspergillosis in AML patients undergoing consolidation therapy: Sorveglianza Epidemiologica Infezioni nelle Emopatie (SEIFEM) 2016 study

Maria Ilaria Del Principe^{1*}, Giulia Dragonetti², Luisa Verga³, Anna Candoni⁴, Francesco Marchesi⁵, Chiara Cattaneo⁶, Mario Delia⁷, Leonardo Potenza⁸, Francesca Farina⁹, Stelvio Ballanti¹⁰, Nunzia Decembrino¹¹, Carlo Castagnola¹², Gianpaolo Nadali¹³, Rosa Fanci¹⁴, Enrico Orsiola¹⁵, Barbara Veggia¹⁶, Massimo Offidani¹⁷, Lorella Melillo¹⁸, Sara Manetta¹⁹, Mario Tumbarello²⁰, Adriano Venditti²¹, Alessandro Busca²², Franco Aversa²³ and Livio Pagano²⁴ on behalf of the Sorveglianza Epidemiologica Infezioni nelle Emopatie (SEIFEM) Group†

N: 2588 pacientes
Restrospectivo
Real Life study
2011-2015
38 centros

Table 3. Distribution of patients in the different consolidation-course AP groups

IA	No AP	AP	Itraconazole	Posaconazole	Liposomal amphotericin B	Voriconazole
Yes	34 (2.9%)	22 (1.5%)	8 (1.03%)	8 (1.28%)	4 (12.9%)	2 (15.3%)
No	1103 (97.1%)	1429 (98%)	772 (98.97%)	619 (98.7%)	27 (87.1%)	11 (84.6%)
Total	1137 (44%)	1451 (56%)	780 (21%)	627 (15%)	31 (1%)	13 (1%)

Of 2588 patients, 56 (2.2%) developed IA [43 probable (1.7%) and 13 proven (0.5%)]. IA was diagnosed in 34 of 1137 (2.9%) patients receiving no AP and in 22 of 1451 (1.5%) who were given AP ($P=0.01$). Number-needed-to-treat calculation indicates that, on average, 71 patients should have received AP (instead of no AP) for one additional patient to not have IA. Initial antifungal therapy was 'pre-emptive' in 36 (64%) patients and 'targeted' in 20 (36%) patients. A good response to first-line therapy was observed in 26 (46%) patients, mainly those who received AP [16 of 22 (73%) versus 10 of 34 (29%); $P=0.001$]. The overall mortality rate and the mortality rate attributable to IA by day 120 were 16% and 9%, respectively. In multivariate analysis, age ≥ 60 years (OR 12.46, 95% CI 1.13–136.73; $P=0.03$) and high-dose cytarabine treatment (OR 10.56, 95% CI 1.95–116.74; $P=0.04$) independently affected outcome.

Conclusions: In our experience, AP appears to prevent IA from occurring during consolidation. However, although the incidence of IA was low, mortality was not negligible among older patients. Further prospective studies should be carried out particularly in elderly patients treated with high-dose cytarabine to confirm our data and to identify subsets of individuals who may require AP.

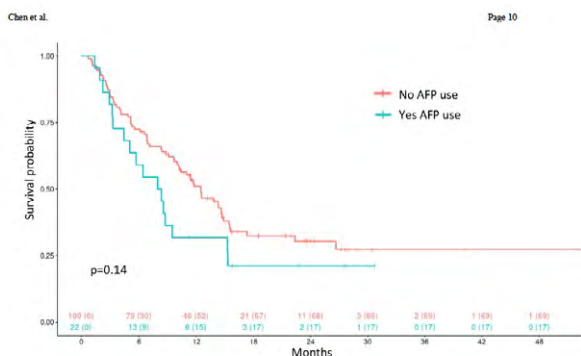
Profilaxis antifúngica


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Outcomes of antifungal prophylaxis for newly diagnosed AML patients treated with a hypomethylating agent and venetoclax

Evan C. Chen, MD¹, Yiwen Liu, MS², Courtney E. Harris, et al.

Department of Medical Oncology, Dana-Farber Cancer Institute
Leuk Lymphoma. 2022 August ; 63(8): 1934–1941


IFI outcomes.

	No AFP use N = 169	Yes AFP use N = 57	P value
All patients with IFI	15 (14%)	7 (9.1%)	0.74
Per infection[17]			>0.99
Possible	17	2	
Probable	1	0	
Proven	3	0	

Abbreviations: AFP = antifungal prophylaxis, IFI = invasive fungal infection


3.^{ra} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Profilaxis antifúngica

Am J Cancer Res 2024;14(12):5897-5908
www.ajcr.us/ /ISSN:2156-6976/ajcr0160111

Original Article

Safety and infection risk factors in elderly acute myeloid leukemia patients undergoing induction therapy with venetoclax combined with hypomethylating agents

Wenshan Zhu¹, Lijun Zhu², Xing Hu², Erling Chen², Lei Xue², Xingbing Wang², Xiaoyu Zhu², Changcheng Zheng², Juan Tong²

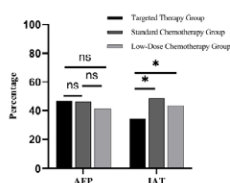


Figure 3. Comparison of patients undergoing pre-emptive antifungal prophylaxis and antifungal therapy for IFD among the three groups. ns, no statistical significance; *, P<0.05. Abbreviations: AFP, antifungal prophylaxis; IAT, initial antifungal therapy; IFD, invasive fungal disease.

Table 5. Univariate and multivariate analysis of risk factors for fungal infection during initial induction therapy in elderly AML patients

Variables	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Antifungal prophylaxis	0.625 (0.219-1.845)	0.404		
Nontargeted therapy	0.636 (0.130-2.970)	0.046	1.011 (0.194-5.262)	0.009
Neutropenic status	3.387 (0.428-26.777)	0.024		
Duration of neutropenia	1.068 (1.026-1.154)	0.005	1.072 (1.002-1.147)	0.043
Duration of fever	1.111 (1.008-1.225)	0.035	1.078 (0.983-1.203)	0.019

Abbreviations: UII, odds ratio; CI, confidence interval.

In this study, antifungal prophylaxis did not affect the incidence of IFD in elderly AML patients, and the overall incidence of diagnosed/clinically diagnosed IFD was low, regardless of antifungal prophylaxis use.


3.^{ra} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Profilaxis antifúngica

Is Antifungal Prophylaxis Needed for Acute Myeloid Leukaemia Patients Treated With Venetoclax-Based Regimens? A Systematic Review and Meta-Analysis

P. R. C. Passos, V. O. C. Filho, M. M. Noronha and C. M. O. Filho

Mycoses 2025 Vol. 68 Issue 7 Pages e70089

<https://www.ncbi.nlm.nih.gov/pubmed/40598802>

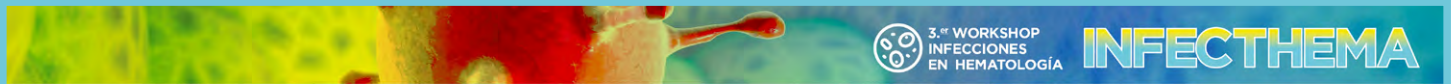
Seven retrospective studies involving 960 patients were included.

The pooled analysis yielded an odds ratio (OR) of 0.84 (95% credible interval: 0.39–1.59) for probable or confirmed IFIs with AFP use. The computed probability of OR < 1 for IFI infection was 74.8% for probable or confirmed IFIs and 71.8% for confirmed IFIs, indicating substantial uncertainty and no clear evidence of a real effect.

AFP did not significantly alter OS (hazard ratio = 0.82, 95% confidence interval: 0.58–1.16) or response rates.

Mould-active antifungals were underutilised in most studies, and the most used antifungals were fluconazole (35.2%) and posaconazole (34.8%).

Our analysis highlights the need for prospective studies and risk stratification to evaluate the role of mould-active agents in this population.

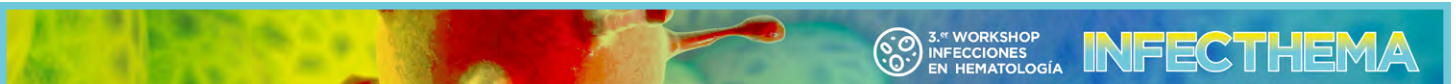


Profilaxis antifúngica

Aunque de los datos de la literatura se deduce que sólo un 3% de los pacientes con Aza/Ven desarrollan una IFI (probable/probada) parece razonable su uso

Idealmente empezarlo en el día 8 (una vez finalizada la azacitidina) con la dosis de carga y reduciendo la dosis de venetoclax a 50mg.

Otra opción es comenzarlo cinco días antes de iniciar Ven/Aza para asegurarnos que se alcanzan buenos niveles y comenzamos venetoclax desde el inicio a 50mg/24h



CASO CLÍNICO

- Varón de 77 años con AP de CI con 2 stent colocados 2021, HTA en tratamiento con enalapril, DM tipo II en tratamiento con metformina. Nuevo diagnóstico de LAM (NMP1+, IDH2+, FLT3ITD-, IDH1-, TP53-,), Cariotipo normal, ECOG 1, Hb: 9,7 g/L, L: $12.6 \times 10^9/L$ (82% blastos, Neutrófilos $0,6 \times 10^9/L$), Plaquetas: $18 \times 10^9/L$, CrCl: 62ml/min, ALT: 23, FA: 123, GGT: 32. Afebril. Ingresa para iniciar tratamiento y soporte hemoterápico.
- ¿Realiza/ría usted cultivos de colonización (nasal, heces etc)?
- ¿Indicaría profilaxis antibiótica? ¿Cuál?
- ¿Indicaría profilaxis antifúngica? ¿Cuál?
- ¿Indicaría profilaxis antivírica? ¿Cuál?

Profilaxis antivírica

Todas las guías recomiendan profilaxis para VHS con aciclovir en todos los pacientes seropositivos para evitar reactivación (hasta un 60-80% en estos pacientes) durante la fase de neutropenia.

1 December 1983
Acyclovir Prophylaxis Against Herpes Simplex Virus Infection in Patients with Leukemia: A Randomized, Double-Blind, Placebo-Controlled Study
Authors: [REIN SARAL, M.D.](#), [RICHARD F. AMBINDER, M.D.](#), [WILLIAM H. BURNS, M.D.](#), [CHRIS M. ANGELOPULOS, P.A.](#), [DIANE E. GRIFFIN, M.D., Ph.D.](#), [PHILIP J. BURKE, M.D.](#), and [PAUL S. LIETMAN, M.D., Ph.D.](#)
Publication: Annals of Internal Medicine
Volume 99, Number 6
<https://doi.org/10.7326/0003-4819-99-6-773>

Abstract
Twenty-nine adult patients with acute leukemia receiving timed sequential chemotherapy participated in a randomized, double-blind, placebo-controlled trial of acyclovir prophylaxis against reactivated herpes simplex virus infection. Patients with pretreatment antibody titers of 1:16 or greater received acyclovir or placebo starting 4 days after their initial chemotherapy. Treatment was given either for 32 days or until the patients were discharged from the hospital or until a culture-positive herpes simplex virus infection was found. Culture-positive herpes simplex virus infection developed in 11 of 15 patients who received placebo. No infection appeared in 14 patients who received acyclovir ($p < 0.00005$). No obvious acute drug toxicity was seen. Recurrent infection was seen in 6 of 14 patients after cessation of acyclovir when retreated with chemotherapy, suggesting no effect on viral latency in these 6 patients. Acyclovir provided highly effective prophylaxis against reactivated herpes simplex virus infections in adult patients with acute leukemia receiving timed sequential chemotherapy.

Profilaxis antivírica

Journal of Oral Pathology & Medicine

WILEY

ORIGINAL ARTICLE [OPEN ACCESS](#)

Characteristics of Acyclovir-Resistant Herpes Simplex Virus Infection in Hematological Patients

Reema Shehadeh¹ | Moe Bar Ilan² | Sara Dovrat³ | Ronit Yerushalmi^{4,5} | Michal Tepperberg Oikawa³ | Evangelia Piperi⁶ | Nikolaos G. Nikitakis⁷ | Noam Yarom^{1,2}

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Infrecuente
No hay estudios epidemiológicos comienza a ser un problema descrito sobre todo en pacientes hematológicos LAM / TPH


3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Profilaxis antivírica

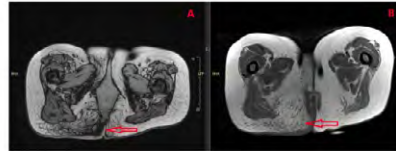
Open Access Case Report

Published via University of South Florida

Atypical Presentations of Acyclovir-Resistant Herpes Simplex Virus in Immunocompromised Patients: A Case Series

Keri Allen¹, Alan Wang², Matthew A. Hibdon³, Robert Castro⁴, John Greene⁵

1. Medicine, Morsani College of Medicine, University of South Florida, Tampa, USA 2. Osteopathic Medicine, Nova Southeastern University Dr. Kiran C. Patel College of Osteopathic Medicine, Clearwater, USA 3. Infectious Diseases, Moffitt Cancer Center, Tampa, USA


FIGURE 2: Axial pelvic MRI

(A) Axial T2-weighted MRI demonstrates a presacral/perineal fluid collection with peripheral rim hyperintensity (arrow), consistent with an abscess, extending into the right gluteal region. Associated surrounding fat stranding and soft tissue edema are also evident. (B) A more caudal axial slice shows further extension of the fluid collection into the perineal soft tissues (arrow), with asymmetric involvement of the right buttock, correlating with the site of the patient's ulcerated plaque.

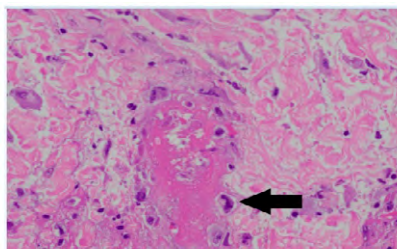
The following day (Day 1), wound cultures from the gluteal cleft grew *Staphylococcus epidermidis* and *Enterococcus faecalis*.

On Day 2, a dermatologic punch biopsy of the right buttock lesion was performed and demonstrated leukocytoclastic vasculitis with fibrin thrombi, early vascular necrosis, and viral cytopathic changes. Immunostaining confirmed HSV-1/2 infection, while stains for cytomegalovirus (CMV) and fungi (Periodic Acid-Schiff (PAS)/Grocott's Methenamine Silver (GMS)) were negative

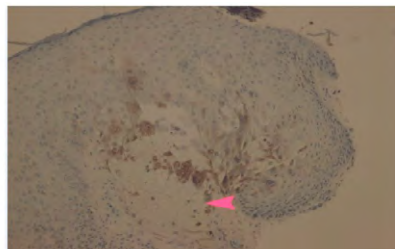

3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

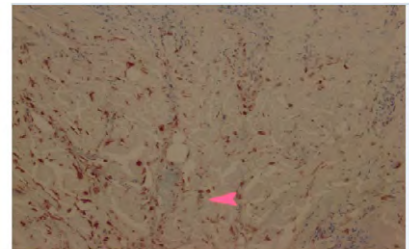
Profilaxis antivírica


FIGURE 3: Histopathology of right buttock biopsy

H&E staining shows a thrombosed vessel (arrow) with surrounding necrosis and viral cytopathic changes in endothelial cells, characterized by nuclear enlargement, chromatin margination, and multinucleation, consistent with HSV infection.


FIGURE 4: Immunohistochemical staining for HSV

Biopsy of the right buttock lesion demonstrates HSV antigen positivity in epidermal cells, highlighted by brown nuclear and cytoplasmic staining. The arrow indicates HSV-positive cells, confirming HSV infection.


FIGURE 5: Immunohistochemical staining for HSV in dermis

Immunohistochemistry demonstrates HSV antigen positivity in dermal cells, highlighted by brown nuclear and cytoplasmic staining. The arrow indicates HSV-positive cells, confirming viral involvement beyond the epidermis. This finding supports widespread cutaneous HSV infection with extension into deeper tissue layers.


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Profilaxis antivírica

Presentation	Clinical Description	Associations	Comments	Recommended initial Diagnostic Test	Typical Antiviral Response	Reference
Granulomas	Granulomatous inflammation, mimicking other chronic granulomatous diseases.	Rare; typically seen in immunocompromised patients.	Diagnosis may be delayed due to overlapping features with other granulomatous dermatoses.	Biopsy with histopathology + PCR	Often resistant; may require escalation to foscarnet	[6]
Vasculitis	Leukocytoclastic vasculitis with fibrin deposition and necrosis.	Reported in immunocompromised individuals.	May resemble autoimmune vasculitis; biopsy is key for diagnosis.	Punch biopsy with HSV PCR and immunostaining	Variable; resistance common; foscarnet often needed	[7]
Neuritizing Lesions	Cutaneous ulcerations with necrosis, mimicking pyoderma gangrenosum or erythema gangrenosum.	Can occur especially in immunocompromised patients.	Madiganosis can lead to inappropriate treatment and severe consequences.	Tissue biopsy + culture + PCR	Frequently acyclovir-resistant; foscarnet formerly required	[8]
Linear Erythema Lesions	Known as the "nailfold" sign; deep, linear fissures in skin folds in immunocompromised patients, mimicking the ulcers associated with metastatic Crohn's disease.	Classically seen in severely immunocompromised patients, can also involve patients with chronic diseases (chronic kidney disease, type 2 diabetes, morbid obesity) and acute systemic diseases.	Indicative of severe tissue compromise. Delayed diagnosis can lead to delayed treatment and potentially adverse outcomes.	Biopsy with HSV PCR; rule out Chikungunya	Mixed response; acyclovir may work, but resistance possible	[9]
Herpes Vegetans	Erythritic, verrucous, wart-like, proliferative lesions.	Common in HIV or severely immunocompromised patients.	It is crucial to differentiate herpes vegetans from other verrucous lesions (i.e., squamous cell carcinoma or HPV-related lesions) in the anogenital area.	Biopsy with immunostaining + HPV testing	Frequently acyclovir-resistant; foscarnet often required	[10]
Eczema Herpeticum	Sudden, painful, and widespread rash with vesicles, pustules, and erosions accompanied by fever.	Acute dermatitis is a major predisposing factor.	Dermatologic emergency; requires immediate systemic antiviral therapy.	Lesion swabs for HSV PCR + Tzanck smear	Usually responsive to acyclovir if treated promptly	[11]

TABLE 3: Summary of atypical presentations of HSV

HSV: Human Immunodeficiency virus; HPV: Human papillomavirus; HSV: Herpes simplex virus; PCR: polymerase chain reaction; BD: Infectious blood disease

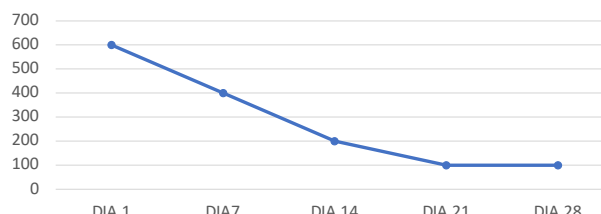

3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

CASO CLÍNICO

- El paciente inicia tratamiento con AZA/VEN, levofloxacin oral, posaconazol desde el día +8 y aciclovir. Se le coloca un acceso central no tunelizado. Se realiza determinación bisemanal de GM. El día +15 desde inicio del tratamiento tiene un pico febril de 38.7°C sin cambios hemodinámicos. No hay foco clínico, se toman hemocultivos, se realiza una Rx torax y se comienza tratamiento empírico antibiótico.
 - ¿Toma Hc de la vía y SP o solo de la vía de acceso?
 - ¿Realiza siempre una Rx de torax?
 - ¿Qué tratamiento antibiótico utilizar?

Neutrófilos



Hemocultivos

- La práctica habitual es la toma de dos muestras (via de acceso y periférica)
 - Diferencia en el tiempo para la positividad del cultivo apoya dgto de infección del acceso
 - Estudios de cultivo cuantitativos aumenta la sensibilidad y especificidad (95%)
 - Cultivo de distintas luces
 - Procesamiento correcto
 - El volumen es muy importante

JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 1997, p. 928-936
0095-1137/97/041001-0
Copyright © 1997, American Society for Microbiology

Diagnosis of Vascular Catheter-Related Bloodstream Infection: a Meta-Analysis

YARDENA SIEGMAN-IGRA,¹ ANNE M. ANGLIM,² DAVID E. SHAPIRO,¹ KARIM A. ADAL,² BARBARA A. STRAIN,² AND BARRY M. FARR^{3*}

Infectious Disease Unit, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel¹; Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts,² and University of Virginia Health Sciences Center, Charlottesville, Virginia³

Mahieu et al. Annals of Intensive Care (2020) 12:13
https://doi.org/10.1186/s13153-020-01107-y

RESEARCH **Open Access**

Impact of a strategy based on unique blood culture sampling on contamination rate and detection of bloodstream infections in critically ill patients

Rafael Mahieu^{1,2*}, Carole Lemarié³, Delphine Douillet^{1,5}, Alain Mercat⁶, Hélène Cornier¹, Matthieu Eveillard^{2,3}, Vincent Dubée^{1,2}, Jérémie Riou^{7,8} and Achille Koutchek⁴

CASO CLÍNICO

- El paciente inicia tratamiento con AZA/VEN , levofloxacin oral, posaconazol desde el día +8 y aciclovir. Se le coloca un acceso central no tunelizado. Se realiza determinación bisemanal de GM. El día +15 desde inicio del tratamiento tiene un pico febril de 38.7°C sin cambios hemodinámicos. No hay foco clínico, se toman hemocultivos, se realiza una Rx torax y se comienza tratamiento empírico antibiótico.
 - ¿Toma Hc de la vía y SP o solo de la vía de acceso?
 - ¿Realiza siempre una Rx de torax?
 - ¿Qué tratamiento antibiótico utilizar?

Neutrófilos

Día	Neutrófilos
DIA 1	~600
DIA 7	~400
DIA 14	~200
DIA 21	~100
DIA 28	~100


3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Estudio de imagen al inicio

- La práctica habitual incluye una Rx simple de torax (habitualmente un proyección AP portátil)

The Utility of Routine Chest Radiography in the Initial Evaluation of Adult Patients With Febrile Neutropenia Patients Undergoing HSCT

Deborah S. Yelin-Raley, PA-C¹; Binay Duggo-Jack, MD²; Heidi B. Niell, PA-C³; Robert J. Sciffler, MD⁴; Joseph H. Antin, MD⁵; Edwin P. Alyea III, MD⁶; and Brett E. Glotzbecker, MD⁷

J Natl Compr Canc Netw 2015;13:184–189

.1083 pacientes

.Estudio retrospectivo

-817 Primer fiebre neutropénica

-En 455 se tomo Rx simple

-En 76 síntomas respiratorios y en ellos en 24 (31.6%) datos en Rx

-En 379 no síntomas (en ninguno hallazgo en Rx) (p: 0,0001)

Conclusions: Indiscriminate routine CXR at the time of first neutropenic fever in asymptomatic adults with febrile neutropenia is unlikely to reveal an infectious process or change clinical practice


3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Estudio de imagen al inicio

- La práctica habitual incluye una Rx simple de torax (habitualmente un proyección AP portátil)

Research Article

Early Radiologic Diagnosis of Pulmonary Infection in Febrile Neutropenic Patients: A Comparison of Serial Chest Radiography and Single CT Chest

Wanaporn Burivong¹, Thanatorn Srirachoen, Apichart Thachang, Sunsree Soodchuen, Panitpong Maroongroge, and Vichit Leelasithorn

Chest low-dose computed tomography in neutropenic acute myeloid leukaemia patients

Demetris Patsios^{1,2,3}, Nimrod Maimon^{1,2}, TaeBong Chung⁴, Heidi Roberts⁴, Patricia Disperati⁵, Mark Minden⁶, Narinder Paul⁷

¹Department of Medical Imaging, University Health Network, Toronto General Hospital, 200 Elizabeth Street, Toronto, ON M5G 2C4, Canada
²Joint Division of Respiratory, Department of Medicine, University Health Network and Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada
³Department of Oncology, Princess Margaret Hospital, 610 University Avenue, Toronto, ON M5G 2M9, Canada

Received 20 February 2008; accepted 9 November 2009
Available online 16 December 2009

TABLE 2: Summary of consensus chest films and CT chest compared to the clinical diagnosis of early pulmonary infection.

	Clinical positive (n=48)	Clinical negative (n=59)	
Early pulmonary infection			
Chest film			
Radiological active (n=39)	24	15	PPV 61%
No radiological active (n=68)	24	44	NPV 64%
Early pulmonary infection			
Radiological active (n=19)	10	9	PPV 45.8%
No radiological active (n=2)	1	6	NPV 100%

PPV, positive predictive value; NPV, negative predictive value.

Table 2 Comparison of CXR with LDCT in the detection of radiological indicators of infection.

Modality	Consolidation N (%)	GGO N (%)	Nodules N (%)
CXR	18 (45)	11 (27.5)	8 (20)
LDCT	17 (42.5)	21 (52.5)	23 (57.5)
Significance	NS	p < 0.01	p < 0.01

GGO, ground-glass opacity; Nodules, focal opacity 3–30 mm in diameter.

Por su bajo costo y sencillez la realización de una Rx convencional puede mantenerse pero en los pacientes con sintomatología respiratoria optar por un TAC torácico

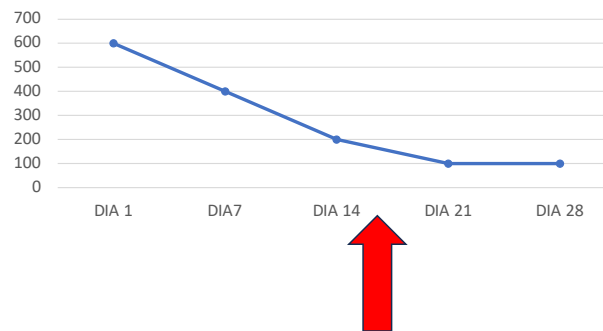

3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

CASO CLÍNICO

- El paciente inicia tratamiento con AZA/VEN, levofloxacin oral, posaconazol desde el día +8 y aciclovir. Se le coloca un acceso central no tunelizado. Se realiza determinación bisemanal de GM. El día +15 desde inicio del tratamiento tiene un pico febril de 38.7°C sin cambios hemodinámicos. No hay foco clínico, se toman hemocultivos, se realiza una Rx torax y se comienza tratamiento empírico antibiótico.
 - ¿Toma Hc de la vía y SP o solo de la vía de acceso?
 - ¿Realiza siempre una Rx de torax?
 - ¿Qué tratamiento antibiótico utilizar?

Neutrófilos


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Tratamiento antibiótico empírico

- OBJETIVO
 - Reducir mortalidad por sepsis y cobertura gramnegativos incluyendo *Pseudomonas spp*
 - Pacientes sin foco clínico
 - Piperacilina/Tazobactam (categoría 1)
 - Carbapenems: Imipenem/Cilastatina – Meropenem (categoría 1)
 - Cefalosporinas con espectro antipseudomonas (Cefepime-Categoría 1; Ceftazidima categoría 2B).
 - Pacientes con foco clínico:
 - Diarrea– Descartar infección por Clostridium difficile
 - Enterocolitis: añadir cobertura anaerobios y dgto diferencial con colitis por C difficile
 - Infección piel y partes blandas: valorar cobertura gram+ con daptomicina (no activa en pulmón)
 - Cobertura al inicio de Gram+
 - No se recomienda ya en ninguna guía
 - Valorar solo si:
 - Datos clínicos claros de infección sería del catéter
 - Cultivo + para grampositivo sin identificar en paciente inestable
 - Pacientes colonizados por MRSA o neumococos resistentes a penicilina/cefalosporina
 - Infecciones de tejidos blandos en centros con alta prevalencia de MRSA


3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Tratamiento antibiótico empírico

Meropenem Versus Ceftazidime in the Treatment of Cancer Patients With Febrile Neutropenia: A Randomized, Double-Blind Trial

Authors: [Ronald Feld](#), [Ben DePauw](#), [Steven Berman](#), [Armand Keating](#), and [Winston](#)

J Clin Oncol 18, 3690-3698(2000)

Volume 18, Number 21

The rate of **successful clinical response at the end of therapy was significantly higher for patients treated with meropenem** than for those on ceftazidime for all episodes (54% v 44%, respectively) and for episodes of fever of unknown origin (62% v 46%, respectively), but differences between groups were not statistically significant for clinically defined or microbiologically defined infections. Meropenem was significantly more effective than ceftazidime in severely neutropenic (≤ 100 cells/ μ L) patients (55% v 43%, respectively), bone marrow transplant patients (73% v 27%, respectively), and patients given antibiotic prophylaxis before study entry (71% v 52%, respectively). Common adverse effects of meropenem and ceftazidime therapy were rash, diarrhea, and nausea and vomiting.


3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Tratamiento antibiótico empírico

Treatment of Febrile Neutropenic Patients with Cancer Who Require Hospitalization

A Prospective Randomized Study Comparing Imipenem and Cefepime

CANCER September 1, 2003 / Volume 98 / Number 5

TABLE 2
Response to Therapy According to Type of Infection

Variable	Imipenem (n = 102)		Cefepime (n = 112)		P value
	No. of episodes	No. of responders (%)	No. of episodes	No. of responders (%)	
Intent-to-treat analysis	124	84 (68)	127	95 (75)	0.2
Total evaluable patients	102	72 (71)	112	84 (75)	0.5
Fever of unknown origin	33	25 (76)	43	36 (84)	0.4
Documented infections	69	47 (68)	69	49 (70)	0.9
Organisms identified	46	34 (74)	54	42 (78)	0.7
No organisms identified	23	13 (57)	15	6 (40)	0.3
Organisms identified*					
Monomicrobial gram-positive	25	17 (68)	37	29 (78)	0.4
Monomicrobial gram-negative	13	12 (92)	12	8 (67)	0.2
Polymicrobial	8	5 (63)	5	5 (100)	0.2
Discordant infections (with or without organism identified)					
Bacteremia	31	22 (71)	37	30 (81)	0.3
Pneumonia	16	7 (44)	18	8 (44)	1.0
Catheter related	15	12 (80)	9	6 (67)	0.6
Other	7	6 (86)	5	4 (80)	1.0

*The most common organisms identified for the imipenem (I) and cefepime (C) arms were gram-positive infections involving coagulase-negative staphylococci (I = 11 patients, C = 21 patients), *Staphylococcus aureus* (I = 3 patients, C = 5 patients), *Enterococcus* (I = 2 patients, C = 1 patient), *S. pneumoniae* (I = 1 patient), and *Moraxella* (I = 2 patients) and gram-negative infections involving *Pseudomonas aeruginosa* (I = 4 patients, C = 3 patients), *Klebsiella pneumoniae* (I = 2 patients, C = 1 patient), and *Acinetobacter* (I = 2 patients, C = 2 patients).

TABLE 5
Antibiotic-Related Adverse Events and Superinfections

Event	No. of patients		P value
	Imipenem	Cefepime	
Antibiotic-related adverse events			
Total (%)	17 (14)	13 (10)	NS
Diarrhea	3	7	—
Nausea/vomiting	4	2	—
Rash	6	2	—
Seizure	2	0	—
Others†	2	2	—
Superinfections			
Total superinfections (%)‡	14 (12)	12 (10)	NS
<i>Clostridium difficile</i>	8	3	—
<i>Candida</i>	2	3	—
VRE	2	1	—
<i>Stenotrophomonas maltophilia</i>	0	3	—
<i>Candida</i>	2	3	—
Others‡	6	4	—

NS, not significant; VRE, vancomycin-resistant enterococci.

†Some superinfections were polymicrobial, as a result the total number listed is smaller than the sum of the organism-specific superinfections.

‡Imipenem: *Aspergillus* (n = 2), *Pseudomonas* (n = 1), *Staphylococcus aureus* (n = 1), *Haemophilus* (n = 1), and *Pseudomonas* (n = 1). Cefepime: *Pseudomonas* (n = 1), VRE (n = 1), and *Pseudomonas* (n = 1).






Tratamiento antibiótico empírico

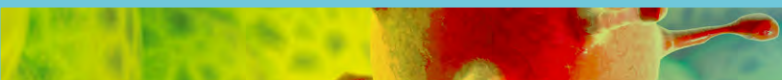


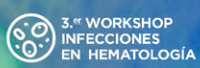
A Randomized, Open-Label, Multicenter Comparative Study of the Efficacy and Safety of Piperacillin-Tazobactam and Cefepime for the Empirical Treatment of Febrile Neutropenic Episodes in Patients with Hematologic Malignancies

E. J. Bow , C. Rotstein , G. A. Noskin ,
Clinical Infectious Diseases, Volume 43, Issue 4, 15 August 2006, Pages 447–459

Results. For 528 subjects (265 received piperacillin-tazobactam and 263 received cefepime), success rates were 57.7% and 48.3%, respectively ($P = .04$) at the 72-h time point, 39.6% and 31.6% ($P = .06$) at end of treatment, and 26.8% and 20.5% ($P = .11$) at the test-of-cure visit. The analyses demonstrated noninferiority for piperacillin-tazobactam at all time points ($P < .0001$). **Treatment with piperacillin-tazobactam was independently associated with treatment success in multivariate analysis** (odds ratio, 1.65; 95% confidence interval, 1.04–2.64; $P = .035$). Both regimens were well tolerated.

Conclusions. This study demonstrates **the noninferiority and safety of piperacillin-tazobactam monotherapy, compared with cefepime**, for the empirical treatment of high-risk febrile neutropenic patients with cancer.






Tratamiento antibiótico empírico

Efficacy and safety of cefepime: a systematic review and meta-analysis
[Lancet Infect Dis Volume 7, Issue 5 May 2007](#)
 Dafna Yahav, MD^a · Dr Mical Paul, MD^{a,b} [pil1p](#)
[el@zahav.net.il](#) · Abigail Fraser, MPH^{a,c}
 · Nadav Sarid, MD^{a,d} · Leonard Leibovici, MD^a



Meta-Analysis of a Possible Signal of Increased Mortality Associated with Cefepime Use

Peter W. Kim , Yu-te Wu , Charles Cooper ,
Clinical Infectious Diseases, Volume 51, Issue 4, 15 August 2010

Conclusions. In both trial-level and patient-level meta-analyses, we did not identify a statistically significant increase in mortality among cefepime-treated patients, compared with those treated with other antibacterials.

All-cause mortality—the primary outcome—was higher with cefepime than other β -lactams (risk ratio [RR] 1.26 [95% CI 1.08–1.49]).






Tratamiento antibiótico empírico

J Antimicrob Chemother 2011; **66**: 1207–1209
doi:10.1093/jac/dk138 Advance Access publication 6 April 2011

**Journal of
Antimicrobial
Chemotherapy**

Is cefepime safe for clinical use? A Bayesian viewpoint

Andre C. Kalil*

Infectious Diseases Division, University of Nebraska Medical Center, Omaha, NE 68198-5400, USA

A recent systematic review and meta-analysis by Yahav et al.2 published in 2007 concluded that cefepime was associated with a 26% (statistically significant) increase in the mortality of all included patients [risk ratio (RR) 1.26, 95% confidence interval (CI) 1.08–1.49]] and a 42% increase in the mortality of patients with neutropenic fever (RR 1.42, 95% CI 1.09–1.84), independently of the type of antibiotic used in comparator arms.

First, the FDA results show a potential mortality increase with cefepime by both trial-level and patient-level meta-analysis: risk difference (RD) 5.38 per 1000 (95% CI 21.53 to 12.28) and 4.83 per 1000 (95% CI 24.72 to 14.38), respectively (please note that FDA measured risk differences and Yahav et al. measured risk ratios). These results were not statistically significant, but the majority of the 95% CI clearly resided in the harm side

*So why continue administering cefepime?
Why use a drug that has a high probability of being associated with increased mortality (80%–99% for neutropenic fever and 87% for skin infections) and a clinically meaningful number needed to harm (NNH.54–109 for neutropenic fever and NNH.56 for skin infections), while there are several other available drugs (e.g. piperacillin, ticarcillin, ceftazidime, aztreonam, imipenem and meropenem), as well as a number of combinations of b-lactams with aminoglycosides or quinolones?*






Tratamiento antibiótico empírico

- El paciente inicia tratamiento empírico con Piperacilina/Tazobactam, la fiebre se resuelve a las 48h, no crecen microorganismos en los cultivos. El paciente sigue estable con necesidades hemoterápicas y el conteo de neutrófilos es de 100/mm³.
- Su actitud sería:
 - Suspendir tras 72h sin fiebre los antibióticos
 - Suspendir tras 72h sin fiebre los antibióticos y desescalar a Levo oral
 - Mantener antibióticos IV hasta recuperación de neutropenia (>1000)

Tratamiento antibiótico empírico

Durand et al. *Antimicrobial Resistance & Infection Control*
<https://doi.org/10.1186/s13756-023-01354-5>

(2024) 1:25

Antimicrobial Resistance & Infection Control

RESEARCH

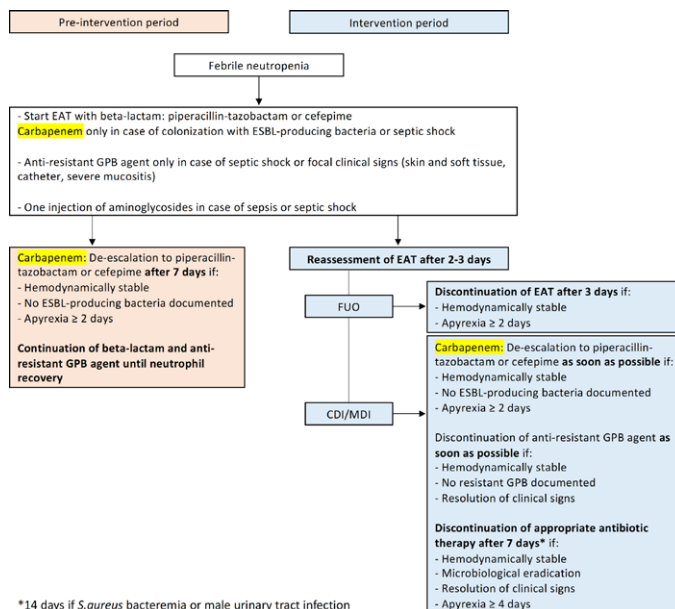
Open Access

Efficacy of an antimicrobial stewardship intervention for early adaptation of antibiotic therapy in high-risk neutropenic patients

Claire Durand^{1*}, Karine Hissu¹, Michael Loschi^{2,3}, Nicolas Bletu⁴, Audrey Emery⁵, Johan Courjon^{1,3}, Thomas Cluzeau^{2,3} and Michel Carles^{1,3}

No diferencia en mortalidad, ni duración ingreso, ni sobreinfección, ni resistencias

Menos uso y días de antibióticos



*14 days if *S. aureus* bacteremia or male urinary tract infection

Tratamiento antibiótico empírico

Early de-escalation of empiric antibiotic therapy in neutropenic fever: a single-center, retrospective study

Zachary Mostel MD¹ , Michelle Evans MD¹, Douglas Tremblay MD², Meenakshi Rana MD¹ , Samantha E. Jacobs MD¹, John Mascarenhas MD², Alla Kozmzer MD² , Daniel Park PharmD² and Risa Fuller MD¹

²Division of Infectious Disease, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, USA, ³Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, USA, and ⁴Department of Pharmacology, Icahn School of Medicine at Mount Sinai, New York, USA

Antimicrobial Stewardship & Healthcare Epidemiology (2025), **5**, e292, 1–3
doi:10.1017/ash.2025.10208

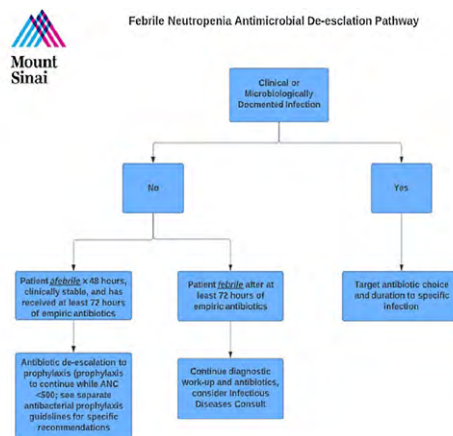
529 episodios

Todos con cefepime

Reducción significativa en los días de Abs

No diferencia en sobreinfección, mortalidad global y atribuida a infección

No diferencia en nuevos episodios de NF, descompensación clínica, ni días de hospitalización



Please note, the above does not exclusively apply to the first 72 hours of febrile neutropenia. Patients may be de-escalated at any point they meet criteria.

Use this pathway for the first neutropenic fever. If fever recurs after antimicrobial de-escalation, initiate new infectious work-up and resume antimicrobials as appropriate. Consider ID consult.

ES SEGURO

Caso Clínico

Antimicrobial Agents and Chemotherapy

Antimicrobial Chemotherapy | Full-Length Text

Efficacy and safety of early antibiotic de-escalation in febrile neutropenia for patients with hematologic malignancy: a systematic review and meta-analysis

Yu-Han Chen,¹ Andrea Yue-En Sun,¹ Karishma Narain,¹ Wei-Cheng Chang,¹ Chieh Yang,² Po-Huang Chen,³ Hong-Jie Zhou,⁴ Ming-Shen Dal,⁵ Natasha Rastogi,¹ Cho-Hao Lee¹

April 2025 Volume 69 Issue 4

Early de-escalation significantly reduced mortality risk (OR 0.20, 95% CI 0.06–0.69). Subgroup analyses showed mortality benefits in older patients (>55 years old, OR 0.42, 95% CI 0.18–0.98) and in higher-quality studies (OR 0.07, 95% CI 0.01–0.62). No significant differences were observed for infection-related ICU admissions, bacteremia, recurrent fever, or *Clostridium difficile* infection (CDI). In conclusion, early de-escalation of BSA in patients with hematologic malignancies and developing FN after treatment significantly reduces mortality risk without increasing major adverse events.

Tratamiento antibiótico empírico

Current antimicrobial practice in febrile neutropenia across Europe and Asia: the EBMT Infectious Disease Working Party survey

Antje Verhinden^{1,2,3}, Margareta Mikellius⁴, Nina Limousin-Kneale⁵, Lisa Auerbach⁶, Jan Nygren⁷, Jan van't Hof-Grootenboer⁸, on behalf of the Infectious Disease Working Party (IDWP) of the European Group for Blood and Marrow Transplantation (EBMT)

2018

194/567 centros EBMT (34%)

44.8% (North-West Europe)

42.8% (South-East Europe)

11.8% (Asia)

1992

A. Verhinden et al.

Table 2. Implementation of de-escalation/consolidation strategies.

Intervention	n (%)
Empirical de-escalation of combination therapy	71.50 (27.4%)
Combination therapy empirically in line with culture patients without history of resistant pathogens	2498 (93.3%)
Duration < 7 days	1398 (51.3%)
De-escalation of antibiotics in specific situations	
Positive blood culture with susceptible pathogen with uncomplicated presentation	1433.86 (56.8%)
Positive blood culture with susceptible pathogen with severe presentation, improved on empirical therapy	625.81 (24.4%)
Clinically documented infection with uncomplicated presentation, stable on empirical therapy	1133.83 (46.7%)
Clinically documented infection with severe presentation, improved and stable on empirical therapy	715.84 (28.6%)
Feasibility of unknown origin with uncomplicated presentation, stable on empirical therapy	1055.81 (41.3%)
Feasibility of unknown origin with severe presentation, improved and stable on empirical therapy	365.81 (14.3%)
Stop before successful recovery in specific situations	
Positive blood culture with susceptible pathogen with uncomplicated presentation	683.86 (26.6%)
Positive blood culture with susceptible pathogen with severe presentation, improved on empirical therapy	375.81 (14.8%)
Clinically documented infection with uncomplicated presentation, stable on empirical therapy	765.86 (29.9%)
Clinically documented infection with severe presentation, improved and stable on empirical therapy	365.81 (14.3%)
Feasibility of unknown origin with uncomplicated presentation, stable on empirical therapy	915.84 (35.7%)
Feasibility of unknown origin with severe presentation, improved and stable on empirical therapy	405.81 (15.8%)
Transfused red blood cells, sepsis with uncomplicated presentation, stable on empirical therapy	415.81 (16.4%)
Transfused red blood cells, sepsis with severe presentation, improved and stable on empirical therapy	335.81 (13.0%)
How long is antibiotic therapy generally continued	
Positive blood culture	
< 7 days	235.81 (9.3%)
7–10 days	515.81 (20.0%)
11–14 days	635.81 (24.6%)
15–20 days	1135.81 (44.8%)
Until end of neutropenia	555.81 (21.8%)
Clinically documented infection	
< 7 days	445.81 (17.5%)
7–10 days	575.81 (22.6%)
11–14 days	635.81 (24.6%)
15–20 days	745.81 (29.0%)
Until end of neutropenia	515.81 (20.0%)
Feasibility of unknown origin	
< 7 days	325.81 (12.6%)
7–10 days	405.81 (15.8%)
11–14 days	515.81 (20.0%)
15–20 days	555.81 (21.8%)
Until end of neutropenia	605.81 (23.8%)

This table summarizes all valid responses from centres on questions concerning implementation of de-escalation/consolidation strategies.

Tratamiento antibiótico empírico

Received: 18 December 2019 | Accepted: 20 January 2020
DOI: 10.1111/ajhp.70158

ORIGINAL PAPER

Haematological Malignancy – Clinical

Prevention and management of febrile neutropenia in acute myeloid leukaemia and higher risk myelodysplastic syndrome: An international survey of current practice

MACPITALL ET AL.

TABLE 3 Antibiotic de-escalation and cessation.

	ANZ (n=20)	Canada (n=14)	UK (n=30)	Europe (n=21)	Total (n=85)	P
In a patient with isolated, short-lived fever (<24–48h), with no positive microbiology results and no clear source of infection, who is otherwise well but remains neutropenic (ANC <1.0 × 10 ⁹ cells/L), how long are antibiotics continued after fever has resolved?						<0.001
≤72h	11 (55%)	2 (14%)	16 (53%)	10 (48%)	39 (46%)	
>72h	8 (40%)	3 (21%)	11 (37%)	7 (33%)	29 (34%)	
≤7 days	0 (0%)	1 (7%)	0 (0%)	2 (10%)	3 (4%)	
Until count recovery	0 (0%)	3 (21%)	0 (0%)	0 (0%)	3 (4%)	
Variable or unknown/missing	1 (5%)	3 (21%)	0 (0%)	1 (5%)	5 (6%)	
Missing	0 (0%)	2 (14%)	3 (10%)	1 (5%)	6 (7%)	
Scenario: a patient has febrile neutropenia (ANC <1.0 × 10 ⁹ cells/L) and is clinically stable. Vital signs are normal other than temperature. Blood cultures are positive for a clinically relevant bacterium other than mouth flora or skin flora and the organism is susceptible to a narrow-spectrum antibiotic (e.g. blood cultures are positive for <i>Enterobacteriaceae</i> sensitive to cefepime).						0.05
Change to narrower spectrum IV antibiotics (including if febrile and neutropenic)	3 (15%)	1 (7%)	14 (47%)	4 (20%)	24 (28%)	
Change to narrower spectrum IV antibiotics only once afebrile (including if neutropenic)	10 (50%)	9 (64%)	5 (17%)	4 (20%)	30 (35%)	
Change to oral antibiotics only once afebrile (including if neutropenic)	1 (5%)	0 (0%)	2 (7%)	1 (5%)	4 (5%)	
Continue broad-spectrum antibiotics until neutrophil count recovery	6 (30%)	3 (21%)	4 (13%)	5 (24%)	18 (21%)	
Other	0 (0%)	0 (0%)	3 (10%)	2 (10%)	5 (6%)	
Missing	0 (0%)	1 (7%)	2 (7%)	1 (5%)	4 (5%)	
Scenario: a patient has febrile neutropenia (ANC <1.0 × 10 ⁹ cells/L) and is clinically stable. Vital signs are normal other than temperature. Blood cultures are positive for an organism that represents mouth flora (e.g. <i>Streptococcus mitis</i>) or skin flora (e.g. <i>Staphylococcus epidermidis</i>) and no other organism.						0.42
Change to narrower spectrum IV antibiotics (including if febrile and neutropenic)	7 (35%)	3 (21%)	5 (17%)	2 (10%)	17 (20%)	
Change to narrower spectrum IV antibiotics only once afebrile (including if neutropenic)	4 (20%)	4 (29%)	10 (33%)	5 (24%)	27 (32%)	
Change to oral antibiotics only once afebrile (including if neutropenic)	2 (10%)	0 (0%)	5 (17%)	1 (5%)	8 (9%)	
Continue broad-spectrum antibiotics until neutrophil count recovery	9 (45%)	4 (29%)	5 (17%)	6 (29%)	27 (32%)	
Other	1 (5%)	0 (0%)	3 (10%)	3 (15%)	7 (8%)	
Missing	0 (0%)	1 (7%)	2 (7%)	1 (5%)	4 (5%)	
Scenario: a neutropenic patient has recently had a positive blood culture and has completed a course of antibiotics that would generally be considered sufficient for this infection (e.g. 10–14 days). The patient remains clinically well and afebrile. They have no other indication to continue treatment (including no persistent source of infection), but they remain neutropenic (ANC <1.0 × 10 ⁹ cells/L). What is your usual course of action in this scenario?						0.05
Cease antibiotics prior to neutrophil count recovery	14 (70%)	5 (36%)	11 (37%)	11 (52%)	41 (48%)	
Switch to oral antibiotics prior to neutrophil count recovery (if not usually on antibiotic prophylaxis)	3 (15%)	3 (21%)	1 (3%)	1 (5%)	8 (9%)	
Switch to prophylactic antibiotics prior to neutrophil count recovery (if usually on antibiotic prophylaxis)	1 (5%)	4 (29%)	14 (47%)	7 (33%)	26 (31%)	
Continue IV antibiotics until neutrophil count recovery	2 (10%)	1 (7%)	0 (0%)	1 (5%)	4 (5%)	
Other	0 (0%)	0 (0%)	2 (7%)	0 (0%)	2 (2%)	
Missing	0 (0%)	1 (7%)	2 (7%)	1 (5%)	4 (5%)	

Abbreviations: ANC, absolute neutrophil count; ANZ, Australia and New Zealand; UK, United Kingdom.

Tratamiento antibiótico empírico

Infection Control & Hospital Epidemiology 2016; 45, 1110–1175
doi:10.1017/ice.2016.101

Original Article

Antibiotic practice and stewardship in the management of neutropenic fever: a survey of US institutions

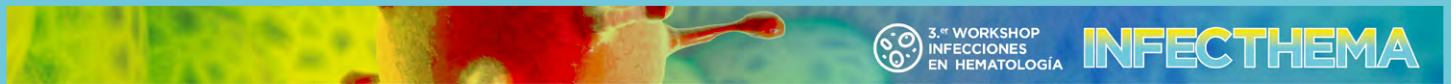
Xiao Wang MD¹, Swann V. Arya DO², Sonal Patel PharmD³, Stephen Saw PharmD⁴, Mary A. Decona MSN, RN, AOCNP, AGACNP-BC¹, Rebecca Hirsch MD¹, David A. Pegues MD⁵ and Matthew J. Ziegler MD, MSc⁶

¹Division of Hematology & Oncology, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA; ²Division of Hospital Medicine, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA; ³Department of Pharmacy, University of Pennsylvania, Philadelphia, PA, USA and ⁴Division of Infectious Diseases, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA

Table 1. Summary of selected survey studies regarding neutropenic fever management

Study	Location	Survey year(s)	Respondents	NI prophylaxis	NI-empiric treatment	Early de-escalation
Yoshida et al. 2004 ¹⁶	Japan	2001	175	50% for AML induction	72% cephalosporin alone 13% carbapenem alone 50% beta-lactam + aminoglycoside	Not assessed in survey
Ziglam et al. 2005 ¹⁷	UK	2005	161	72% for neutropenia	5% piperacillin-tazobactam alone 72% piperacillin-tazobactam + gentamicin	Not assessed in survey
Choi et al. 2008 ¹⁸	Korea	2005–2008	33	42.9% for chemotherapy, 90.9% for SCT	19% cephalosporin alone 50% cephalosporin + aminoglycoside	18.1% de-escalate before NR
Kojima et al. 2009 ¹⁹	Japan	2007	134	58% for AML induction	77% cephalosporin alone 11% carbapenem alone 20% cephalosporin + aminoglycoside	Not assessed in survey
Kimura et al. 2013 ²⁰	Japan	2013	141	64% for AML induction	84% cephalosporin alone 10% antipseudomonal penicillin alone 22% carbapenem alone 6% cephalosporin + aminoglycoside	Not assessed in survey
Verlinden et al. 2020 ²⁴	Europe/Asia	2017	194	52.1% (43.7% NW Europe, 71.6% SE Europe, 60.0% Asia)	47% piperacillin-tazobactam alone 70% cephalosporin or carbapenem alone 37% one of above + aminoglycoside	45.9% de-escalate before NR, with unknown source 36.6% (19.9% with complicated case) de-escalate before NR, with positive cultures + susceptibilities 40.9% (21.1% with complicated case) de-escalate before NR, with clinical infection
Kimura et al. 2019 ²¹	Japan	2019	163	62% for AML induction	79% cephalosporin alone 23% antipseudomonal penicillin alone 19% carbapenem alone 2% cephalosporin + aminoglycoside	22.6% switch to oral antibiotics before NR 18.6% stop antibiotics before NR
Barreto et al. 2022 ²²	US	2019	34	87% for high risk patients	50% cefepime alone 60% piperacillin-tazobactam alone 41% meropenem alone	30% with guidelines regarding empiric de-escalation before NR

Note. NI, neutropenic fever; AML, acute myeloid leukaemia; SCT, stem cell transplant; NR, neutrophil recovery. Multiple answers allowed for empiric treatment, so percentages may add up to

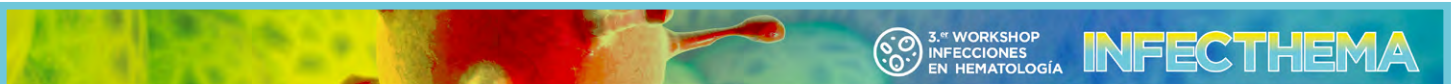


Tratamiento antibiótico empírico

Use of Procalcitonin as a Tool to Enhance Antimicrobial Stewardship

Paula A Politis , Thomas M File

Clinical Infectious Diseases, ciag166, <https://doi.org/10.1093/cid/ciag166>
15 April 2026



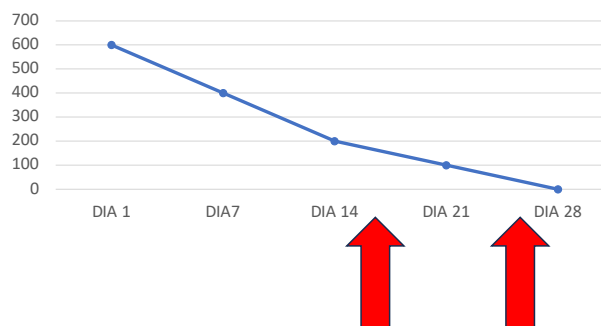
Caso Clínico

- El paciente suspendió Piperacilina/Tazobactam tras cinco días de tratamiento (día +20) y por persistencia de neutropenia (100mm³) y ree inició levofloxacin. Se practico una MO el día +21 que mostraba hipocelularidad en ausencia de blastos por lo que se suspendió venetoclax. El paciente continuo con posaconazol y desarrolló un nuevo pico febril (39.2°C) el día +27 con moderada hipotensión que remontó con sueroterapia sin necesidad de medidas adicionales y sin foco clínico. Los GM realizados hasta ese momento fueron negativos, una PCR y una procalcitonina obtenida ese día estaban elevadas. Se tomaron cultivos de vigilancia (rectal y fosas nasales).

Usted:

- Iniciaría de nuevo AB de amplio espectro
 - Piper/Tazo
 - Meropenem
 - Uno de los anteriores + cobertura gram +
- Realizaría una prueba de imagen
 - Rx Simple
 - TAC torácico

Neutrófilos



INFECTHEMA

Segundo episodio febril

En estos segundos episodios febriles en el contexto de una neutropenia mantenida:

- Infecciones por organismos resistentes
- Infecciones fúngicas

Neutrófilos

Día	Neutrófilos
DIA 1	~600
DIA 7	~400
DIA 14	~200
DIA 21	~100
DIA 28	~100

INFECTHEMA

Segundo episodio febril

Contents lists available at [ScienceDirect](http://ScienceDirect.com)

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Review

Epidemiology of resistant bacterial infections in patients with hematological malignancies or undergoing hematopoietic cell transplantation in Europe: A systematic review by the European Conference on Infections in Leukemia (ECIL)

Francesco Baccelli^{a,b,c}, Manuela Aguilar-Guisado^{c,d}, Carolina García Vidal^{d,e}, Malgorzata Mikulska^{f,g}, Yuri Vanbiervliet^h, Nicole Blijlevensⁱ, Patricia Muñoz^{j,k}, Dionysios Neofytos^h, Catherine Cordonnier^h, Thierry Calandra^{k,l}, Dina Averbuch^{m,n}, Murat Akova^{o,p,q}

Country	Resistance Patterns
Netherlands	FQ-R 76% (1) ESBL/3GCR 7% (1) CR 12% (1)
UK	FQ-R 32% (1)
Italy	FQ-R 75% (55-89) (4) ESBL/3GCR 33% (22-42) (5) CR 12% (1-58) (7) MDR 19.5% (6-33) (2) VRE 8% (2-16) (3) MRSA 32% (24-80) (2)
Spain	FQ-R 36.5% (29-44) (2) ESBL/3GCR 26% (6-30) (5) CR 25% (9-32) (3) MDR 20% (1-28) (5) VRE 3% (1) MRSA 28% (21-31) (3)
Russia	ESBL/3GCR 25% (1) CR 14% (1) MRSA 2% (1)
Greece	FQ-R 36% (1) ESBL/3GCR 34% (1) CR 30% (1) MDR 37% (1)
Türkiye	FQ-R 36% (35-37) (2) ESBL/3GCR 40% (37-43) (2) CR 9% (6-12) (2) MDR 13% (1) VRE 6% (1) MRSA 23% (1)
Israel	FQ-R 69% (1) ESBL/3GCR 27% (1) CR 19% (14-24) (2)

Fig. 2. Rate of bacterial resistance patterns across European countries. Number of studies in parentheses. FQ-R, fluoroquinolone-resistant; ESBL/3GCR, extended-spectrum beta-lactamase-producing/third-generation cephalosporin-resistant; CR, carbapenem-resistant; MDR, multidrug resistant; VRE, vancomycin-resistant enterococci; MRSA, methicillin-resistant *Staphylococcus aureus*.

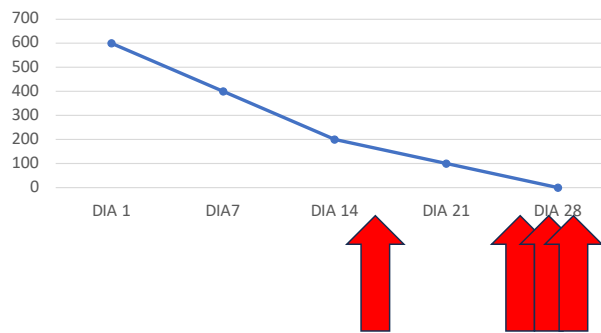

3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Segundo episodio febril

- El paciente se mantuvo estable pero permaneció febril durante los días consecutivos sin nuevos datos microbiológicos relevantes (cultivos de vigilancia, GM) ni foco clínico. El paciente seguía con posaconazol oral. Se repitió un CT que no observó imágenes patológicas.
- Usted:
 - Suspendería posaconazol e iniciaría un tratamiento antifúngico sistémico con:
 - Voriconazol IV
 - Anfotericina Liposomal
 - Micafungina
 - Si TAC normal y GM neg seguiría con posaconazol
 - Tratamiento empírico vs pre-emptive

Neutrófilos



Caso Clínico

Mycopathologia (2026) 191:29

https://doi.org/10.1007/s10255-025-01096-1

ORIGINAL ARTICLE

Clinical Characteristics and Outcomes of Invasive Aspergillosis in Patients with Hematological Malignancies and Transplantation and Cellular Therapies in the Contemporary Era

Christopher M. Lopez¹, Jose F. Suarez², Maria A. Mendez³, Anthony D. Anderson⁴, JR Eghosa⁵, Nicholas L. Lee⁶, Michael J. Murray⁷, Vicki S. Nadel⁸, Mohammed Raju⁹, Laurence J. Lebel¹⁰, Amer Hattaghi¹¹, Adnan Jassal¹², Mark Goodman¹³, Trent P. Wang¹⁴, Jay Spiegel¹⁵, Nae C. Hoffman¹⁶, David Prentice¹⁷, Thomas Green¹⁸, Krishna V. Komanduri¹⁹, Jose F. Camargo²⁰

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Mycopathologia (2026) 191:29

Page 5 of 15 29

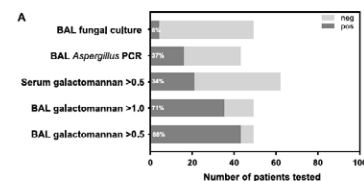


Fig. 1 Performance of diagnostic tests in the diagnosis of IA. A Bars represent various diagnostic tests in serum and bronchoalveolar lavage (BAL) specimens for diagnosis of IA. Percentage inserts correspond to the sensitivity for a given test (i.e., proportion of IA patients with a positive test). B Venn diagram for patients with BAL GM>1.0 (n=35), positive BAL Aspergillus PCR (n=16) and positive BAL fungal culture (n=4). Note how Aspergillus PCR in BAL facilitated diagnosis in patients with otherwise negative BAL testing, whereas culture added no diagnostic yield to BAL galactomannan>1.0 and BAL Aspergillus PCR (culture is still important for species identification and antifungal susceptibility testing)

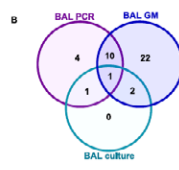


Table 2 Considerations for optimization of diagnostic evaluation and management of invasive aspergillosis in hematological patients

1. Consider early bronchoscopy to increase diagnostic yield^a
2. Consider early computed tomography of the chest in febrile patients with risk factors^b
3. Incorporate non-invasive molecular methods such as *Aspergillus* PCR or microbial cell-free DNA in blood^c
4. Close therapeutic drug monitoring in all patients receiving triazole antifungals during prophylaxis and treatment^d

^aNearly 90% of the patients had BAL GM>0.5 compared to only a third with positive serum GM. The yield of BAL is highest when bronchoscopy is performed early [66].

^bRadiologic halo sign, considered an early radiological finding in IA, was seen in less than 20% in this cohort suggesting delays in obtaining CT chest.

^cIn cases when tissue biopsy or bronchoscopy are not feasible or when results are unrevealing.

^dEspecially in those critically ill, overweight, rapid metabolizers or in cases of drug-drug interactions (e.g., co-administration of letermovir and voriconazole). If persistently subtherapeutic levels, bridging with echinocandin until therapeutic levels achieved can be considered.

Caso Clínico

2024 update of the AGIHO guideline on diagnosis and empirical treatment of fever of unknown origin (FUO) in adult neutropenic patients with solid tumours and hematological malignancies

Michael Senzberg,¹⁰⁰ Janik Stenke,¹⁰¹ Enisa Scholz,¹⁰² Tessa Hattenhausen,¹⁰³ Marcus Hentsch,¹⁰⁴ Bernd Hattenhausen,¹⁰⁵ Christian Hörmann,¹⁰⁶ Sylke C. Jellingshoff,¹⁰⁷ Gabiela Mergelhausen,¹⁰⁸ Christina Rieger,¹⁰⁹ Martin Schmalz-Huber/*Christine Spitzke*,¹¹⁰ Leonore Sties,¹¹¹ Ekkehard A. Conny,¹¹² Ludvig Harn,¹¹³ Gerd-Louis Harn,¹¹⁴ Bernd Grottel,¹¹⁵ Arvids Glazov,¹¹⁶ Udo Nöcker,¹¹⁷ Fritz,¹¹⁸ Malcol Knuths,¹¹⁹ Philipp Kneide,¹²⁰ Robert Koser,¹²¹ Jan-Nikolaus,¹²² Cornelia Lottmann,¹²³ Chafik Dadi,¹²⁴ Markus Scholz,¹²⁵ Florian Kuchler/*Sebastian Uhl*,¹²⁶ Florian Wiedner,¹²⁷ and Dore Bach.¹²⁸

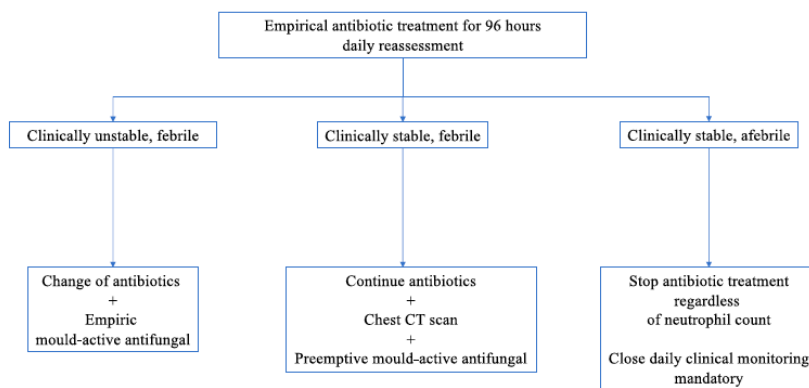


Fig. 4: Second-line antibiotic treatment in patients with FN. CT computed tomography.

www.thelancet.com Vol 51 April, 2025

Caso Clínico

Clinical Infectious Diseases
MAJOR ARTICLE

Infectious Diseases Society of America



OXFORD

Empiric vs Preemptive Antifungal Strategy in High-Risk Neutropenic Patients on Fluconazole Prophylaxis: A Randomized Trial of the European Organization for Research and Treatment of Cancer

Johan Maertens,¹ Tom Lodewyck,² J. Peter Donnelly,³ Sylvain Chantepie,⁴ Christine Robin,⁵ Nicole Blijlevens,⁶ Pascal Tardieu,⁷ Dominik Sellsatz,⁸ Frédéric Baron,⁹ Michael Aoun,¹⁰ Werner J. Heier,¹¹ Hartmut Bött,¹² Zdeněk Rálek,¹³ Bernard Vandecastee,¹⁴ Lubos Grunec,¹⁵ Valerie Collette,¹⁶ Cristina Castilla Llorca,¹⁷ Cornelia Schaefer-Prokop,¹⁸ Marianne Paesmans,¹⁹ Ljiljana Anđelić,²⁰ Iveta Anđelić,²¹ Lu Moert,²² Jin Xie Chang,²³ Deborah A. Hegler,²⁴ Jürgen Ledford,²⁵ Rosemary Barnes,²⁶ Oscar Marchetti,^{20,27} Paul Verwey,²⁸ Frederic Lamoth,²⁹ Pierre-Yves Bochet,³⁰ Michael Schwärzinger,³¹ and Catherine Couffignal,³² for the Infectious Diseases Group of the Action Leukemia Group of the European Organization for Research and Treatment of Cancer

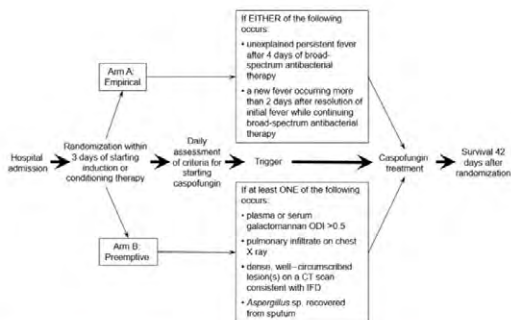


Figure 1. Study design. Abbreviations: CT, computed tomography; IFD, invasive fungal disease; ODI, optical density index.

Results. Of 556 patients recruited, 549 were eligible: 275 in arm A and 274 in arm B. Eighty percent of the patients had AML or MDS requiring high-dose chemotherapy, and 93% of them were in the first induction phase. At day 42, the OS was not inferior in arm B (96.7%; 95% confidence interval [CI], 93.8%–98.3%) when compared with arm A (93.1%; 95% CI, 89.3%–95.5%). The rates of IFDs at day 84 were not significantly different, 7.7% (95% CI, 4.5%–10.8%) in arm B vs 6.6% (95% CI, 3.6%–9.5%) in arm A. The rate of patients who received caspofungin was significantly lower in arm B (27%) than in arm A (63%; $P < .001$).

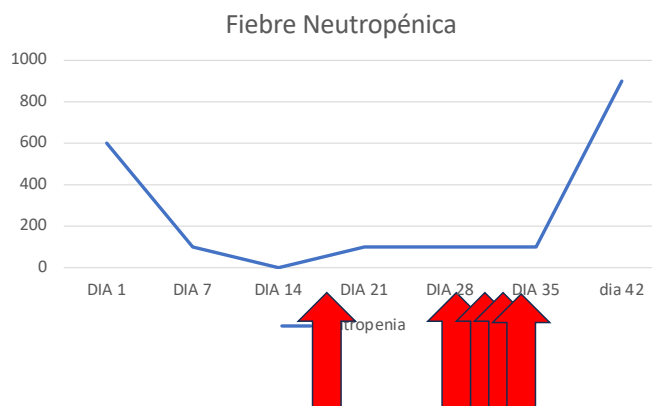
Conclusions. The preemptive antifungal strategy was safe for high-risk neutropenic patients given fluconazole as prophylaxis, halving the number of patients receiving antifungals without excess mortality or IFDs.


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Caso Clínico

- Al paciente se le seguía realizando GM bisemanal, se repitió un TAC torácico a la semana y la fiebre se resolvió tras 6 días anticipando la recuperación de los neutrófilos (día +38). Al paciente se le realizó de nuevo un AMO el día +43 que comprobó un RC morfológica y por citometría.
- El paciente fue dado de alta y el día +5º comenzó segundo curso de Aza/Ven reduciéndose el curso de venetoclax a 14 días.


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Taller Práctico:

Un marco de decisión para residentes: de la estratificación al manejo guiado (NCCN & ECIL)



1 | Anticipar

Estratificación de Riesgo



2 | Prevenir

Profilaxis



3 | Reaccionar

Algoritmo de Neutropenia Febril



4 | Adaptar

Infección Fúngica y COVID-19


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Reglas de Oro para Residentes


Regla 1: Profilaxis Anti-Fúngica es Ley en LMA

Posaconazol es el estándar de oro en inducción. No confíes en el fluconazol para prevención de mohos.


Regla 2: Vigila la Interacción CYP3A4

Azacitidina+Venetoclax exige profilaxis anti-fúngica, pero requiere reducir el Venetoclax en más del 50%.


Regla 3: Desescalada Precoz (72h)

No trates el número absoluto de neutrófilos. Si el paciente está clínicamente estable y afebril a las 72h, desescala a profilaxis.


Regla 4: Fiebre Día 4 = Piensa en Hongos


Fiebre refractaria a antibióticos de amplio espectro exige TC, Galactomanano y considerar terapia antifúngica anticipada (L-AmB/Isavuconazol).

Consideración Especial: COVID-19 en LMA


Shield (Prevención)

Cribado rutinario pre-quimioterapia.
Vacunación actualizada esencial (incluso con respuestas humores mitigadas).


Sword (Tratamiento Activo)

Integración rápida de Antivirales (Paxlovid/Remdesivir) o Anticuerpos Monoclonales (según directrices CDC/FDA vigentes).

Warning: La Trampa del Paxlovid (Nirmatrelvir/Ritonavir)

El **Ritonavir** es un inhibidor extremo del CYP3A4. **Interacción letal con Venetoclax, Inhibidores de FLT3 (Midostaurina) y Azoles.**

Regla: Preferir **Remdesivir IV** en pacientes bajo **terapia activa** con LMA para evitar toxicidad fatal por interacciones.

Leukemia www.nature.com/leu

REVIEW ARTICLE OPEN Check for updates

INFECTIOUS MEDICINE, VIROLOGY

Post-pandemic recommendations for the management of COVID-19 in patients with haematological malignancies or undergoing cellular therapy, from the European Conference on Infections in Leukaemia (ECIL-10)

Simone Cesaro ^{1,2}, Per Ljungman ^{2,3}, Malgorzata Mikulska ⁴, Hans H. Hirsch ⁵, David Navarro ^{6,7}, Catherine Cordonnier⁸, Varun Mehra ⁹, Jan Styczynski ¹⁰, Francesco Marchesi ¹¹, Jose Luis Pinana ¹², Gernot Beutel ¹³, Herman Einsele ¹⁴, Johan Maertens¹⁵, ECIL-10* and Rafael de la Camara ¹⁶

Leukemia (2025) 39:2061 – 2071

Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

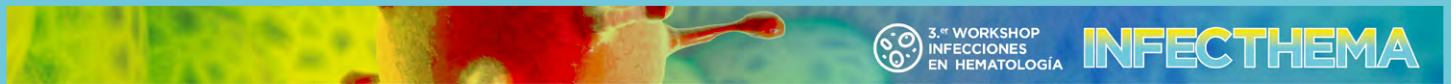
INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Taller. Caso clínico real en paciente con mieloma múltiple

Estrella Carrillo Cruz

Hospital Universitario Virgen del Rocío



51 años

Ingreso por síndrome constitucional y dolor generalizado progresivo e incapacitante en abril 2024.
Mieloma múltiple Bence Jones lambda, estadio IIIA de alto riesgo genético (t(4;14) y amplificación de 1q21) (>80% plasmocitos en MO). No inmunoparesia.

AP fumadora
Obesidad

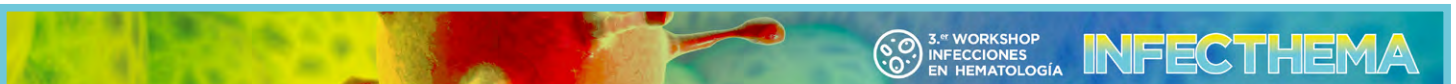
Inclusión en GemTectal con inicio de tratamiento el 14 de mayo siendo alta a domicilio el 18 de mayo

Inducción: bortezomib, lenalidomida, dexametasona y daratumumab x 4+ Teclistamab + daratumumab x 6 + mantenimiento teclistamab-daratumumab

25 de mayo: acude a urgencias por fiebre y tos: hemograma normal, PCR 138, rx tórax sin consolidaciones, se piden virus. Alta con amoxi-clavulánico.

26 mayo se le contacta por PCR SARS-Cov2 positiva

27 de mayo: vuelve por persistencia de fiebre, regular estado general, expectoración purulenta marrón, Sat O2 93%.



En urgencias

- Hemograma normal salvo linfopenia 270.
- PCR 202
- Rx tórax: patrón compatible con infección por SARS-Cov2
- Se toman hemocultivos
- Antigenurias legionella y neumococo → negativos



3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

- Disnea a mínimos esfuerzos, sat basal 93%, precisa oxigenoterapia y mantiene estabilidad hemodinámica, pero regular estado general.

¿y a continuación en planta?

- A) Mantendría tratamiento con amoxi-clavulánico y ver evolución. Si empeora solicitaría TAC.
- B) Cambiaría tratamiento a cefepima empírico y realizamos esfuerzo diagnóstico (HC, cultivo de esputo, TAC)
- C) Cambiaría tratamiento a piperacilina-tazobactam y realizamos esfuerzo diagnóstico (HC, cultivo de esputo, TAC)
- D) Suprimiría el tratamiento antibiótico puesto que ya tenemos documentación microbiológica.



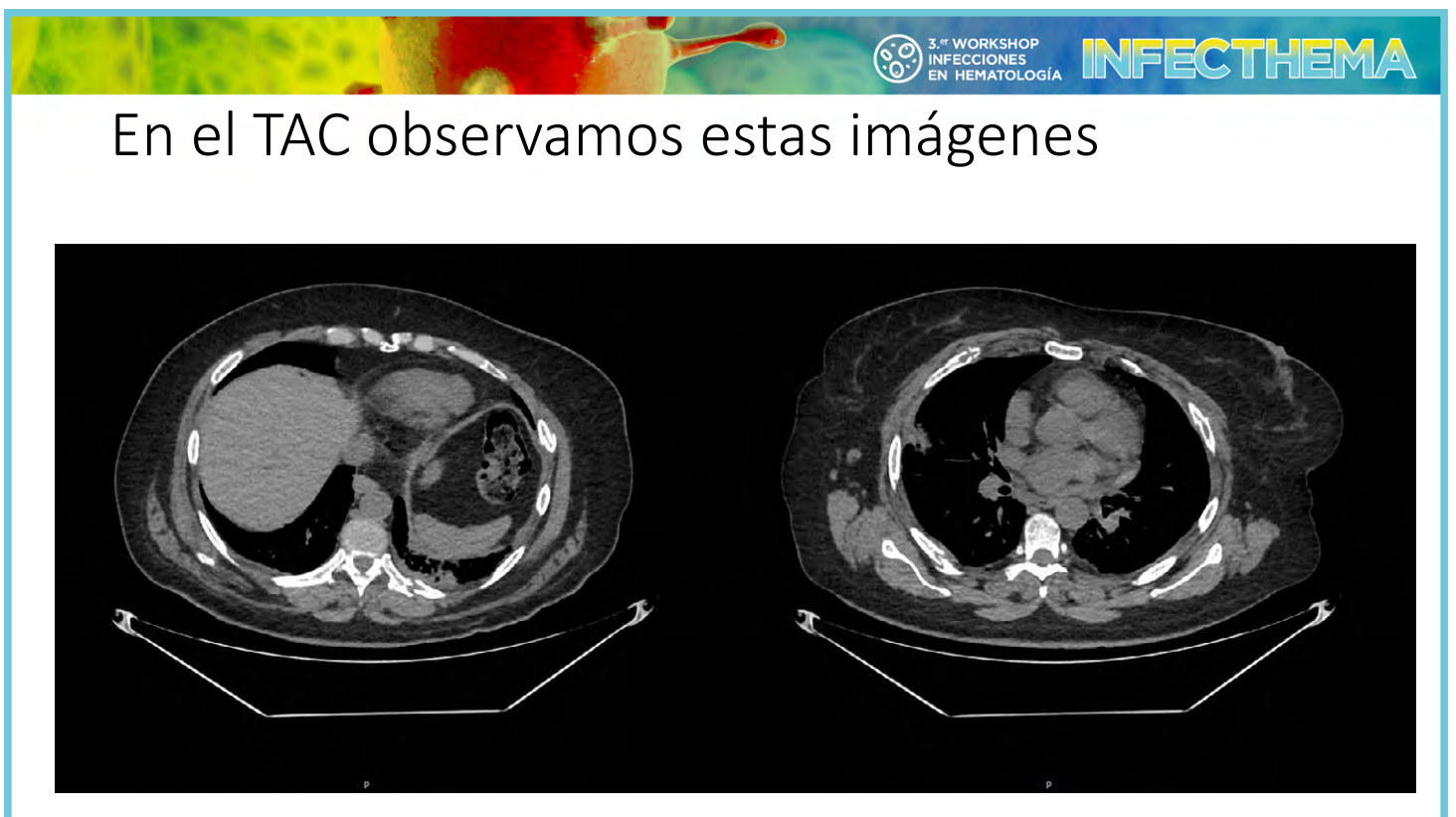
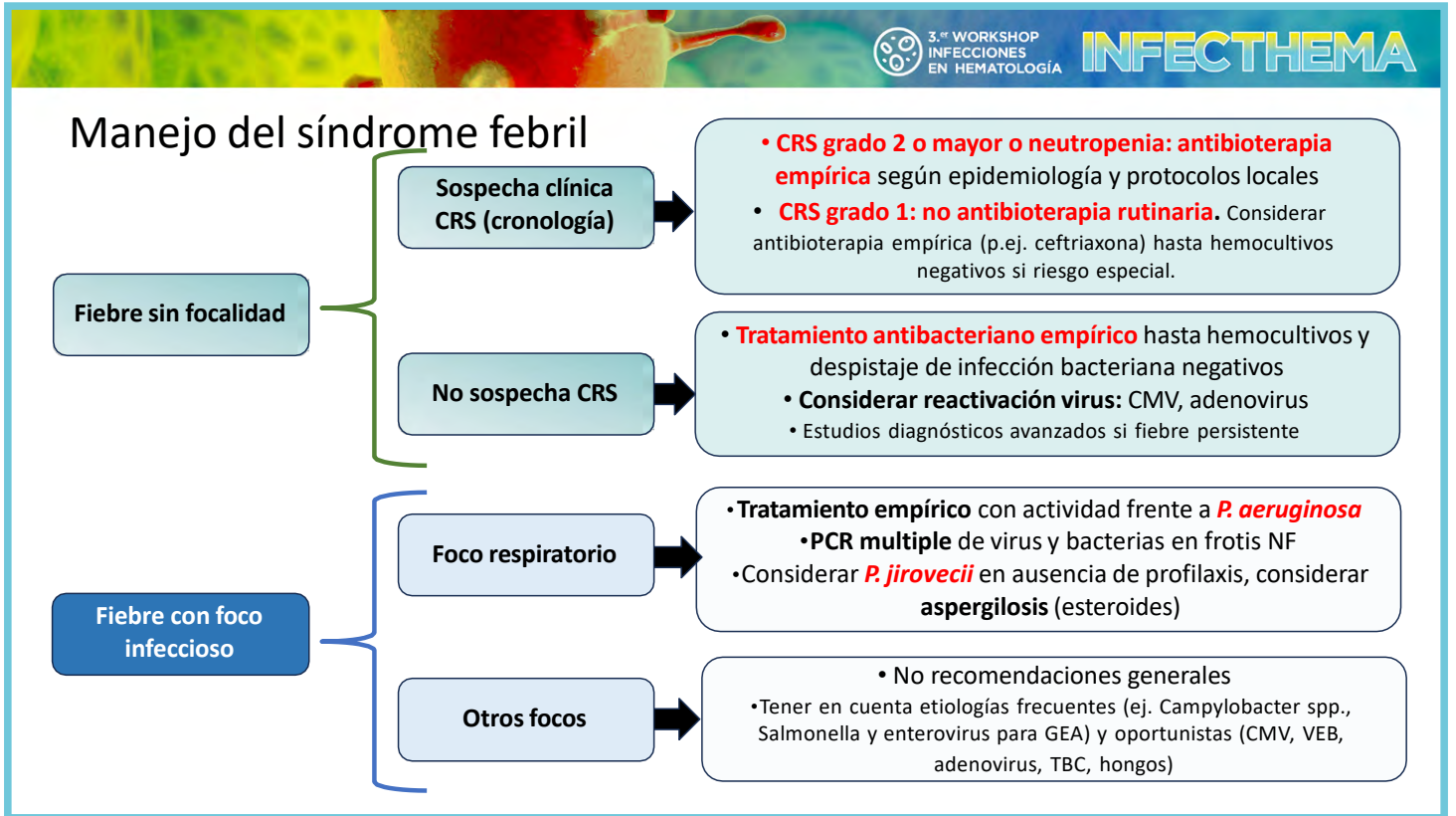
3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

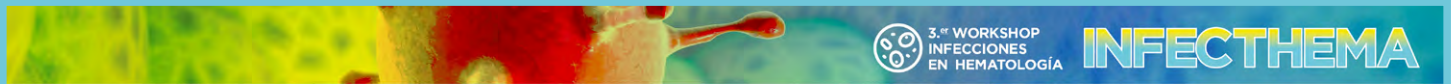
INFECTHEMA

- Disnea a mínimos esfuerzos, sat basal 93%, precisa oxigenoterapia y mantiene estabilidad hemodinámica, pero regular estado general.

¿y a continuación en planta?

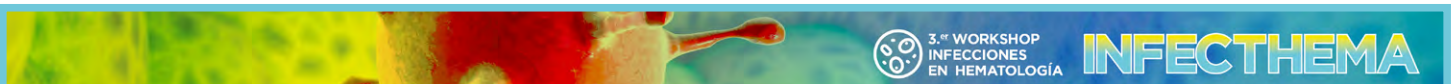
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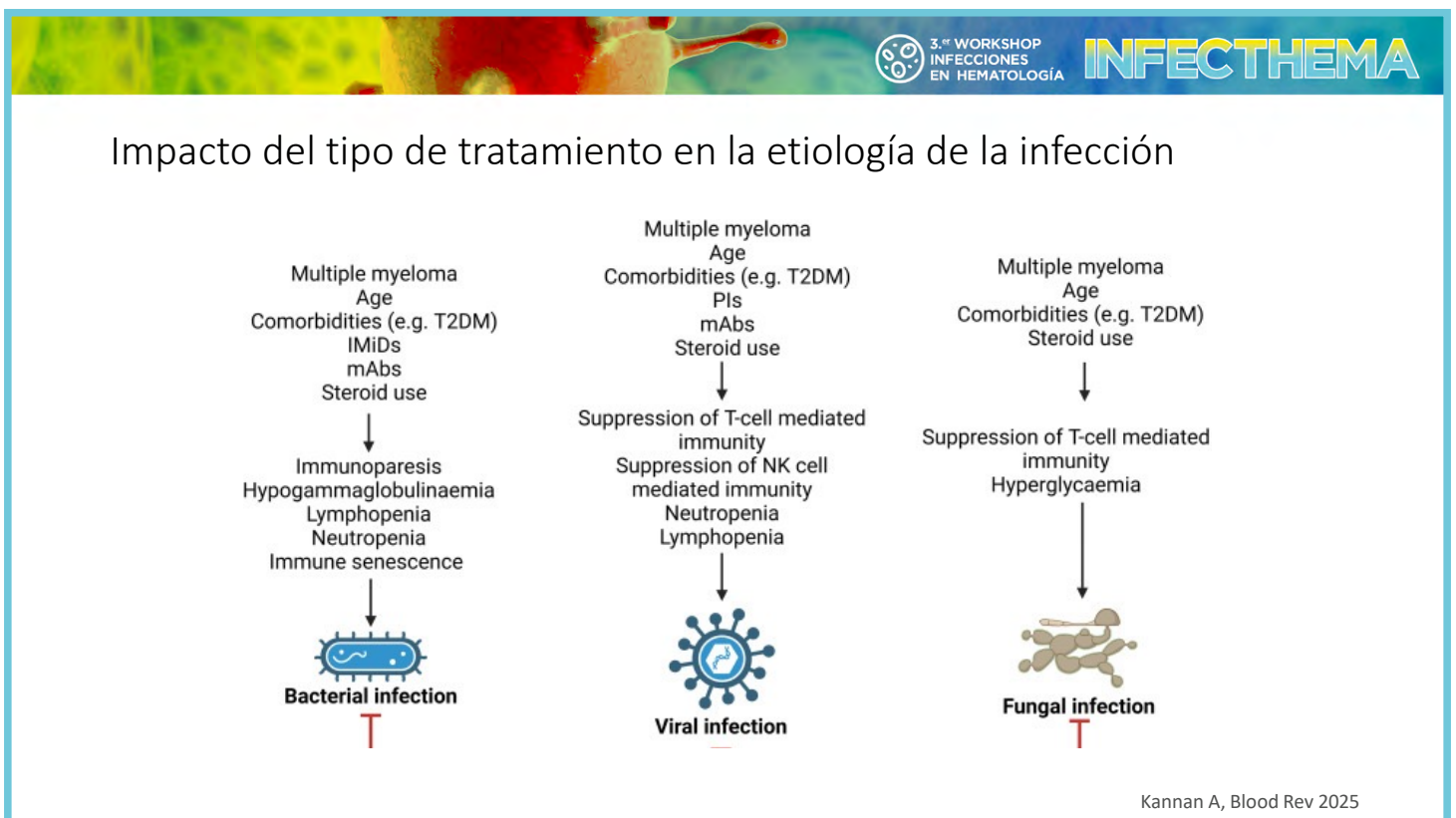
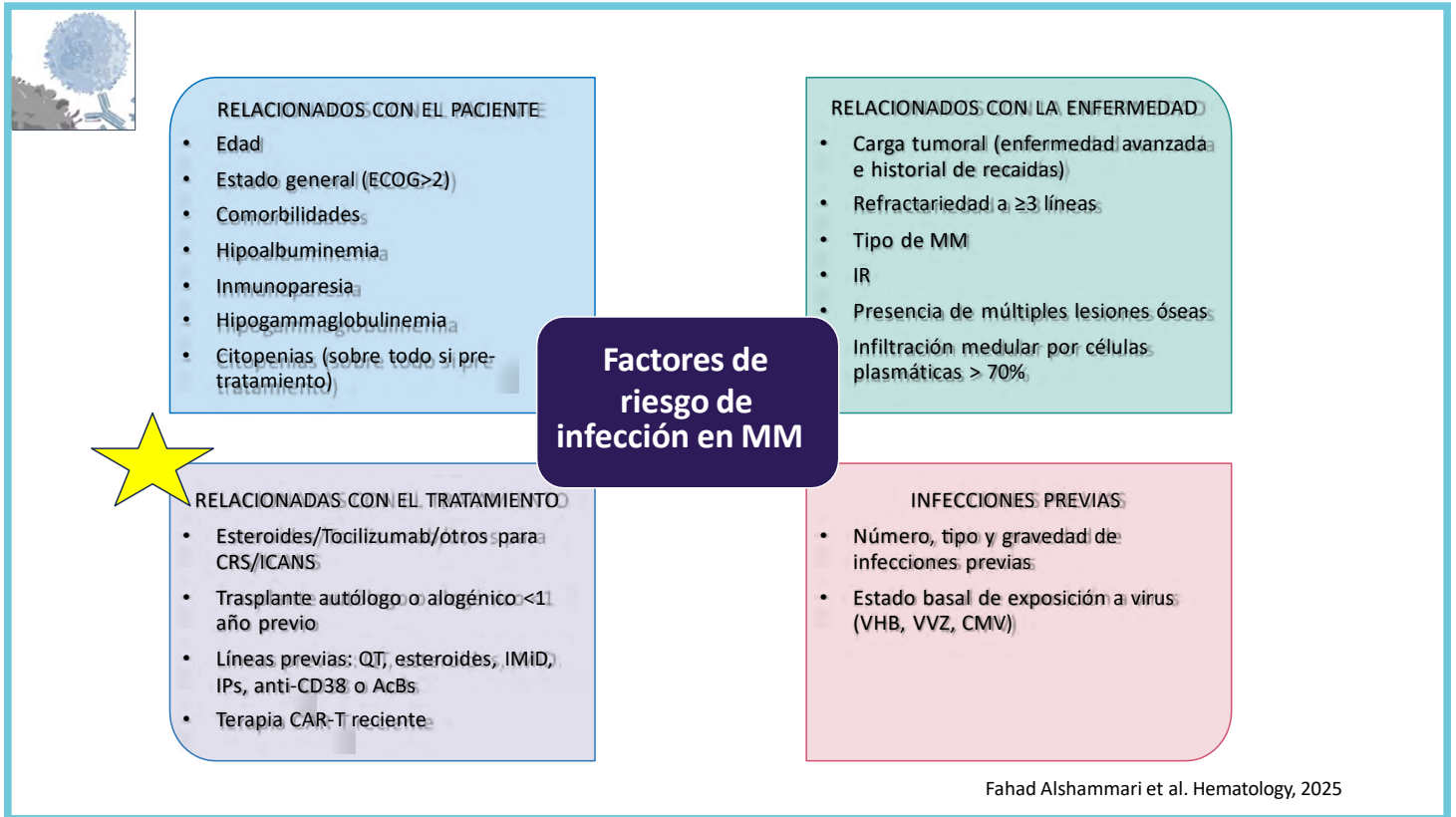
¿Qué harías a continuación?

- A) Parece que tiene una infección fúngica invasora por lo que iniciaría antifúngicos en espera de resultados de AGA y fibrobroncoscopia ASAP.
- B) No tengo claro que tenga factores de riesgo para IFI por lo que escalo en antibioterapia e inicio pipertazo
- C) No inicio tratamiento con antifúngicos dado que presenta estabilidad hemodinámica y voy a hacer pronto la FBC.
- D) No cambio tratamiento antimicrobiano y le pongo un poquito de corticoides que le va a venir muy bien para su inflamación ocasionada por su covid.



¿Qué harías a continuación?

- A) Parece que tiene una infección fúngica invasora por lo que iniciaría antifúngicos en espera de resultados de AGA y fibrobroncoscopia ASAP.**
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3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

¿Qué infecciones se asocian a los BsAbs?

SYSTEMATIC REVIEW

Infections following bispecific antibodies in myeloma: a systematic review and meta-analysis

Gemma Reynolds,^{1,2,*} Edward R. Scheffer Clift,^{3,*} Ghulam Rehman Mohyuddin,⁴ Rakesh Popat,⁵ Shonali Midha,⁶ Melissa Ng Liat Hing,⁷ Simon J. Harrison,^{7,8} Aaron S. Kesselheim,⁹ and Benjamin W. Teh,^{1,8}

- **1.666 pacientes** incluidos en 16 ensayos clínicos (Fase 1b a 3) +
- **141 pacientes** en 4 estudios observacionales.

Aspecto	Ensayos clínicos (n=1666)	Estudios observacionales (n=141)
Infecciones graves (≥G3)	24% (19–29%)	—
Mortalidad atribuible	3% (65 muertes/1604 pacientes)	2 muertes tardías documentadas
Distribución por tipo	Predominio de virales y bacterianas (sobre todo respiratorias)	49% virales , 45% bacterianas, 6% fúngicas
Etiología más común	Virus respiratorios (SARS-CoV-2, influenza, VRS), bacterianas por gramnegativos (<i>Pseudomonas spp.</i>, <i>Klebsiella spp.</i>, <i>E. coli spp.</i>)	Bacterias 64% BGN ; 8% reactivación CMV ; VRS, adenovirus , herpesvirus.
Infecciones fúngicas	<5% (casos aislados de aspergilosis y PJP)	6% (aspergilosis, candidiasis diseminada, PJP)

Fahad Alshammari et al. Hematology, 2025; Reynolds G. Blood Advances. 2023

3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

Evolución

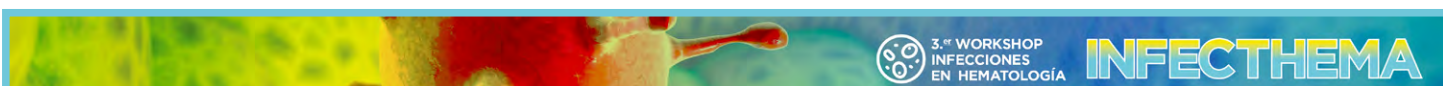
- Se confirmó Aspergillus en LBA
- AGA positivo
- Cultivo de esputo se aisló haemophilus influenzae.

- Se inició tratamiento con isavuconazol durante 9 días para posteriormente pasar a voriconazol y completar +14 días de tratamiento endovenoso.



Calendario vacunal en MM

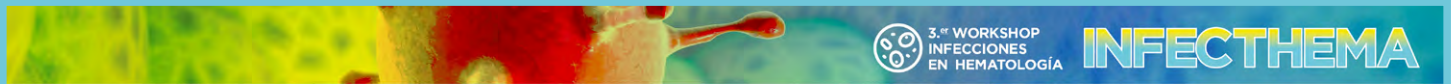
- Gripe (estacional)
- Neumococo (VNC20)
- Tétanos-difteria-tosferina (dTpa)
- COVID-19
- Hepatitis B, Hepatitis A
- Sarampión, Rubeola, Parotiditis,
- Varicela
- Virus herpes zóster
- Encapsulados: H. influenzae B (HiB) conjugada, meningococo ACWY, meningococo B.



Estrategia vacunal del paciente con mieloma múltiple

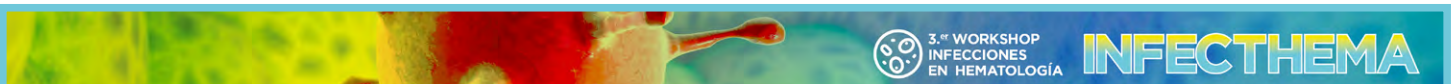
- Pocos estudios sobre indicación y respuesta a vacunas en los nuevos tratamientos del mieloma
 - Probable peor respuesta a la vacuna frente a SARS CoV-2 (daratumumab, BsAb) y encapsulados (BsAb)
 - Para CAR-T, calendarios extrapolados de HSCT
- Importante:
 - Vacunar lo antes posible, mejor al diagnóstico de la enfermedad e incluso en gammapatía monoclonal de significado incierto
 - Vacunar al menos 14 días antes de empezar tratamiento
 - En pacientes con alta carga tumoral vacunar cuando la enfermedad esté controlada
 - Revacunar si auto-TPH previo (>6-12 meses tras auto-TPH)
 - Evitar tratamiento concomitante con IgGIV
 - Profilaxis post-exposición en pacientes que contacten con enfermos de hepatitis A o varicela (mejor <96 horas) con IgGIV específica (aciclovir si no disponible y contacto con VVZ).





Evolución

- Un mes después del ingreso, el 25/06 reanuda tratamiento: había recuperado la linfopenia y la IgG 467.
 - 3 días más tarde comienza con diarreas, dolor abdominal, vómitos sin fiebre. PCR 3. Procalcitonina 0.13 ¿Qué harías?
- A) Dados los antecedentes iniciaría antibióticos, por supuesto interrumpir lenalidomida
 - B) Solicitaría coprocultivo
 - C) Solicitaría coprocultivo y toxina C. difficile, por supuesto interrumpir lenalidomida
 - D) Solicitaría coprocultivo y toxina C. difficile e iniciaría antibioterapia



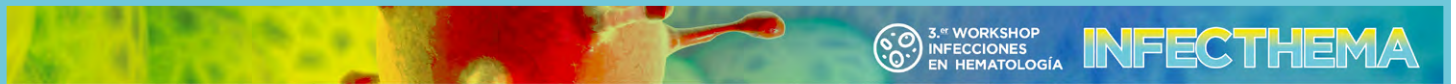
Evolución

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 - D) Solicitaría coprocultivo y toxina C. difficile e iniciaría antibioterapia

INMUNODIAGNÓSTICO INFECCIOSO	
<u>Clostridium difficile, toxina (heces)</u>	
Clostridium difficile, Ag GDH (heces)	Negativo
Clostridium difficile, toxina A (heces)	Negativo
Clostridium difficile, toxina B (heces)	Negativo
<i>Resultados validados por: Dr. A. Pulido</i>	
MICROBIOLOGÍA MOLECULAR	
<u>Bacterias, detección ADN (heces)</u>	
Bacterias, detección ADN (informe)	Ver informe completo en VIMOS
PCR de Salmonella	Se detecta ADN/ARN
PCR de Campylobacter	No se detecta ADN/ARN
PCR de Yersinia enterocolica	No se detecta ADN/ARN
PCR de Clostridium difficile (toxigénico)	No se detecta ADN/ARN
PCR de Shigella/enteroinvasiva E.coli (EIEC)	No se detecta ADN/ARN
PCR de Aeromonas	No se detecta ADN/ARN
PCR de Vibrio	No se detecta ADN/ARN
<u>Virus, detección ADN/ARN (heces)</u>	
PCR de Norovirus GI	No se detecta ADN/ARN
PCR de Norovirus GII	No se detecta ADN/ARN
PCR de Rotavirus	No se detecta ADN/ARN
PCR de Adenovirus F40/41	No se detecta ADN/ARN
PCR de Astrovirus	No se detecta ADN/ARN
PCR de Sapovirus	No se detecta ADN/ARN

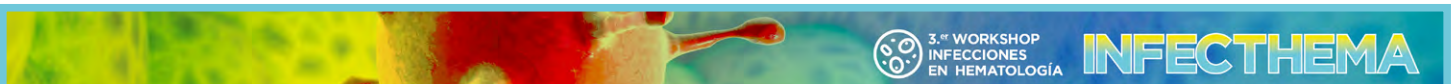
Evolución

- El episodio se resolvió de forma espontánea y cuando vimos el resultado ya estaba bien.
- C2, C3 y C4 sin incidencias
- Hipogammaglobulinemia progresiva desde julio 2024.

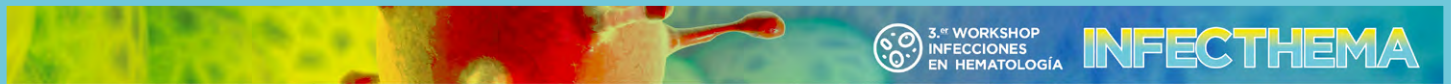


- Octubre 2024 inicia intensificación daratumumab+ teclistamab → caída de Ig a 200.
- Noviembre 2024 comienza con diarreas q se resuelven.
- Enero 2025 2 episodio de diarreas verdosas, con pérdida de 7 kg, dolor abdominal ocasional. Aporta orina con mucho sedimento. No síndrome miccional. inicia reposición de Ig.

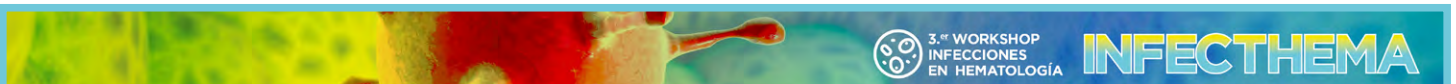
¿qué harías a continuación?



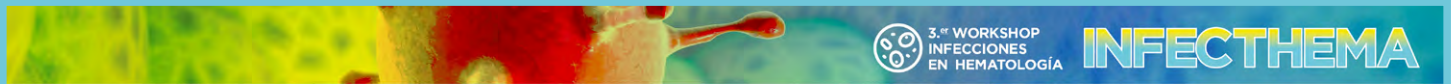
- A) Solicitar coprocultivo y continuar con tratamiento (daratumumab y teclistamab), si positivo ya trataré.
- B) Solicitar coprocultivo, interrumpir tratamiento, iniciar antibioterapia empírica.
- C) Solicitar coprocultivo y urocultivo puesto que la orina tiene sedimento.
- D) Solicitar coprocultivo, urocultivo puesto que la orina tiene sedimento e iniciar tratamiento antibiótico combinado.



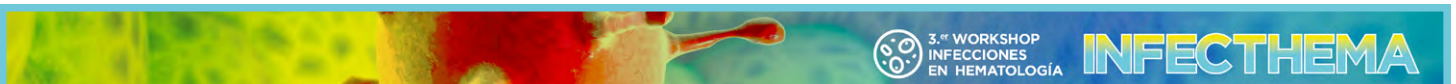
- A) Solicitar coprocultivo y continuar con tratamiento (daratumumab y teclistamab), si positivo ya trataré.
- **B) Solicitar coprocultivo, interrumpir tratamiento, iniciar antibioterapia empírica.**
- C) Solicitar coprocultivo y urocultivo puesto que la orina tiene sedimento.
- D) Solicitar coprocultivo, urocultivo puesto que la orina tiene sedimento e iniciar tratamiento antibiótico combinado.



- Se aísla campylobacter y tras realizar tratamiento la paciente queda asintomática.
- Continúa con tratamiento continuo con teclistamab + daratumumab.
- Inicia reposición de Ig bimensual.



- Noviembre 2025: la paciente lleva ya más de un año con teclistamab +daratumumab y comienza con diarreas que van aumentando progresivamente. No dolor abdominal.
- Abril 2026: Ha continuado todo este tiempo con diarreas y pérdida de peso progresiva ¡10 kilos!



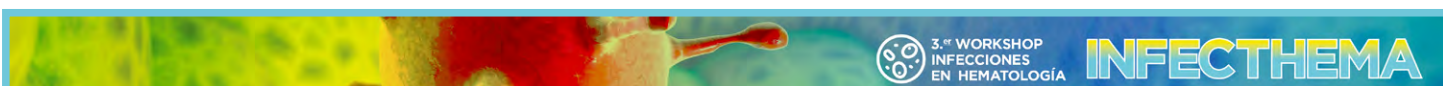
¿Qué harías?

- A) Suspendería tratamiento, solicitaría nuevo coprocultivo y toxina C. difficile y no iniciaría tratamiento empírico.
- B) Continuaría con el tratamiento y sin solicitar más pruebas iniciaría tratamiento empírico.
- C) Continuaría con el tratamiento ya que la causa más probable es el propio tratamiento del mieloma.
- D) Suspendería el tratamiento, revisaría niveles previos de IgG por si hay que cambiar esquema de reposición de Igiv, solicitaría nuevo coprocultivo y toxina C. difficile e iniciaría tratamiento empírico.



¿Qué harías?

- A) Suspendería tratamiento, solicitaría nuevo coprocultivo y toxina C. difficile y no iniciaría tratamiento empírico.
- B) Continuaría con el tratamiento y sin solicitar más pruebas iniciaría tratamiento empírico.
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Incidencia de infección en BsAbs en mielomas

SYSTEMATIC REVIEW

blood advances

Infections following bispecific antibodies in myeloma: a systematic review and meta-analysis

Gemma Reynolds,^{1,2,*} Edward R. Scheffer Clift,^{3,*} Ghulam Rehman Mohyuddin,⁴ Rakesh Popat,⁵ Shonali Midha,⁶ Melissa Ng Liet Hing,⁷ Simon J. Harrison,^{7,8} Aaron S. Kesselheim,⁹ and Benjamin W. Teh^{1,8}

- **1.666 pacientes** incluidos en 16 ensayos clínicos (Fase 1b a 3) +
- **141 pacientes** en 4 estudios observacionales.
- **Incidencia global** infecciones **56%** (24% de grado 3-4).
 - 90% de pacientes con **al menos una infección**
 - 41% con al menos una **infección grave** (grado 3-4)
- **Mayor tasa de infecciones graves con BCMA > no BCMA** (25% vs. 20%)
- **Tasa global de infección en combinaciones > monoterapia** (71% vs. 52%) pero no > infecciones graves.
- **Mortalidad atribuible del 3 %.**
- **Neutropenia grave 50-65%** (< con BsAb frente a GPRC5D), **hipogammaglobulinemia** (IgG <400 mg/dl): 60-70%.
- **Mayor riesgo de infección tardía (> día +100)** vs. CAR-T

Fahad Alshammari et al. Hematology, 2025; Reynolds G. Blood Advances. 2023

INFECTHEMA

¿Qué infecciones se asocian a los BsAbs?

SYSTEMATIC REVIEW

Infections following bispecific antibodies in myeloma: a systematic review and meta-analysis

Aspecto	Ensayos clínicos (n=1666)	Estudios observacionales (n=141)
Infecciones graves (≥G3)	24% (19–29%)	—
Mortalidad atribuible	3% (65 muertes/1604 pacientes)	2 muertes tardías documentadas
Distribución por tipo	Predominio de virales y bacterianas (sobre todo respiratorias)	49% virales , 45% bacterianas, 6% fúngicas
Etiología más común	Virus respiratorios (SARS-CoV-2, influenza, VRS), bacterianas por gramnegativos (<i>Pseudomonas spp.</i>, <i>Klebsiella spp.</i>, <i>E. coli spp.</i>)	Bacterias 64% BGN ; 8% reactivación CMV ; VRS, adenovirus , herpesvirus.
Infecciones fúngicas	<5% (casos aislados de aspergilosis y PJP)	6% (aspergilosis, candidiasis diseminada, PJP)

Fahad Alshammari et al. Hematology, 2025; Reynolds G. Blood Advances. 2023

INFECTHEMA

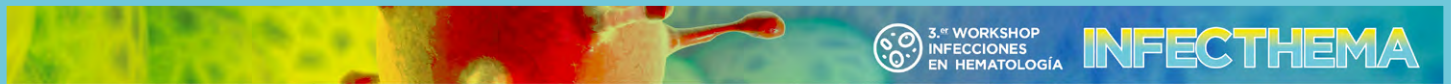
¿Qué infecciones se asocian a los BsAbs?

- Tasas elevadas de infección (**bacterianas y virales respiratorias**) pero
- Pensar también en **oportunistas**:
 - Salmonella spp.*
 - Reactivación de CMV.
 - Adenovirus diseminado.
 - Leucoencefalopatía multifocal progresiva.
 - VHS/VVZ
 - Otros...
- Infecciones oportunistas más típicas a priori de otros tratamientos intensivos e ID celular** (ej. Alo-TPH, alemtuzumab).

Notable opportunistic infections reported in patients with multiple myeloma treated with bispecific antibody therapy

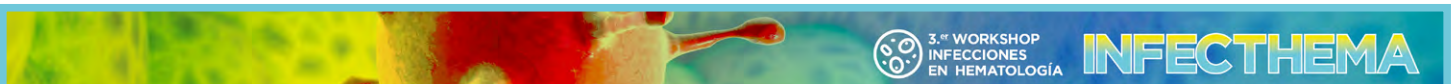
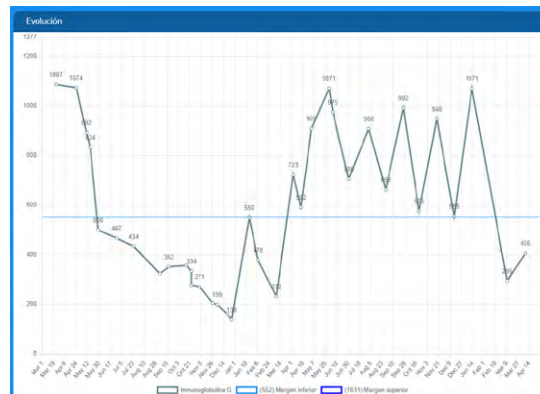
Bacterial infections
Salmonellosis
Viral infections
CMV viremia and end-organ disease
Adenovirus pneumonia and hepatitis
Disseminated zoster
JC virus infection causing progressive multifocal leukoencephalopathy
Parvovirus infection
Enterovirus infection
Fungal infections
Pneumocystis jirovecii pneumonia
Invasive aspergillosis
Candida esophagitis
Parasitic infections
Toxoplasmosis

Sarah P. Hammond. Blood advances.



Evolución

- La paciente actualmente está bajo tratamiento con azitromicina con mejoría de la clínica, tratamiento suspendido hasta que se resuelva la clínica
- Cambio a reposición de Ig mensual



Manejo de la hipogammaglobulinemia

- La hipogammaglobulinemia es más frecuente (53-75%), severa (41% IgG < 300 mg/dl) y prolongada tras CAR-T y biespecíficos frente BCMA que otras dianas.
- 75-87% de los pacientes tratados con BsAb tiene IgG < 400 mg/dl.

Monitorización del nivel de IgG basal, y después mensual hasta los 3-6 meses o más (CAR-T) o mientras dure el tratamiento (Biesp)

Considerar **tratamiento sustitutivo** si:

• IgG $\leq$ 400 mg/dl

Reposición mensual,
0,2-0,4 g/kg
Hasta IgG $\geq$ 400 mg/dl y
ausencia de infecciones
graves

- ≥ 2 **infecciones graves** por encapsulados con cualquier nivel de IgG
- Infección **grave, o que no responda** al tratamiento antimicrobiano

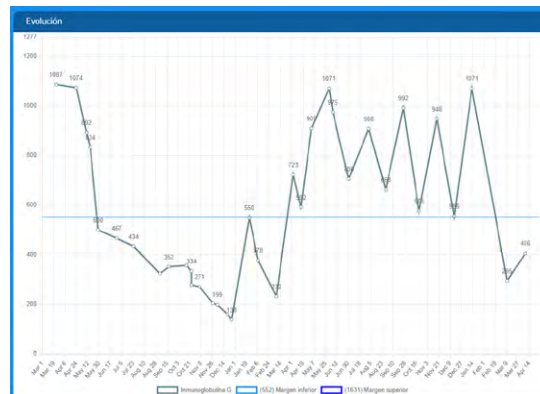


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Evolución

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Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

**TALLER PRÁCTICO.
DIAGNÓSTICO Y TRATAMIENTO DE PATOLOGÍA INFECCIOSA EN PACIENTE HEMATOLÓGICO**

IGNACIO MÁRQUEZ

SERVICIO DE ENFERMEDADES INFECCIOSAS
HOSPITAL REGIONAL UNIVERSITARIO DE MÁLAGA

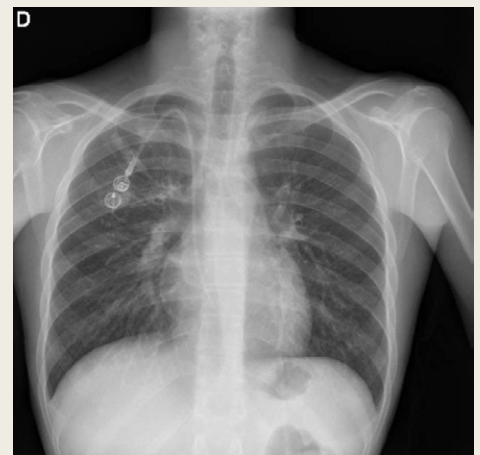
CASO CLÍNICO



- Varón de 18 años.
- Diagnosticado de LMA en Febrero de 2024, con buena respuesta a tto de inducción y consolidación con quimioterapia según esquema habitual.
- AloTPH haploidéntico en Julio de 2024 con complicaciones infecciosas entre las que destacan:
 - Neutropenia febril con bacteriemia relacionada con catéter por *Pseudomonas aeruginosa* multisensible.
 - Episodio recidivado de CI difícil tratado con Fidaxomicina en tapering.
- EICR cutáneo, intestinal y hepático severo que ha precisado tratamiento con esteroides, tacrólimus y fotoaféresis.
- Profilaxis actual con TMP/SMX L-X-V, Posaconazol 300 mg/24 horas.

CASO CLÍNICO

- Ingresa en el día + 200 por cuadro de fiebre de hasta 38.5°C con escalofríos sin tiritonas acompañado de dolor abdominal y deposiciones diarreicas sin productos patológicos.
- EF destacaba TA 88/56 mm Hg. Febril. Afectación con gran exantema descamativo cutáneo conocido (EICR cutáneo). HICKMANN de fotoaféresis canalizado sin signos de infección. PICC en miembro superior derecho. ACP sin hallazgos significativos. Abdomen blando y depresible, molestias a la palpación, no masa sin megalias.
- En complementarias destaca:
 - Hb 9, plaq 8.000, leucocitos 1.790, neutrófilos 1040, Glu 123, Cr 0.73, FG >90, lones sin alteraciones, AST 20, ALT 62, GGT 324, FA 124, Bt 2.59, BD 1.05 PCR 228, PCT 1.04



CASO CLÍNICO



- MICROBIOLOGÍA:
 - Coprocultivo: negativo. Toxina CI difficile negativo.
 - Hemocultivos ingreso: negativos.
 - GM en sangre negativo. BDG en sangre: 14.8
 - PCR CMV: 650 copias/mL.
- Se inició tratamiento con Ganciclovir a dosis de 5 mg/Kg /12 horas y se procedió a cambiar la profilaxis antifúngica a Anfotericina B liposomal 1 mg/Kg/24 horas dada la hepatotoxicidad.

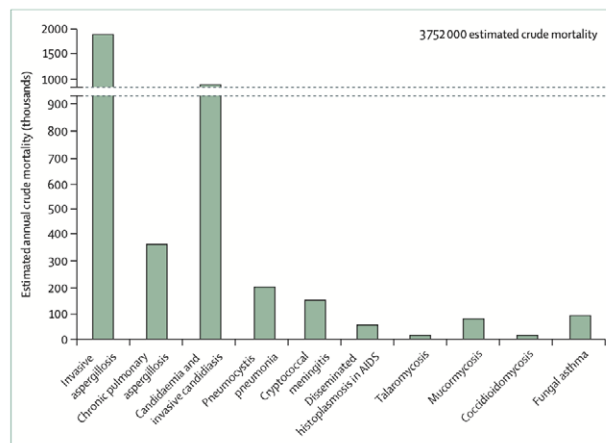
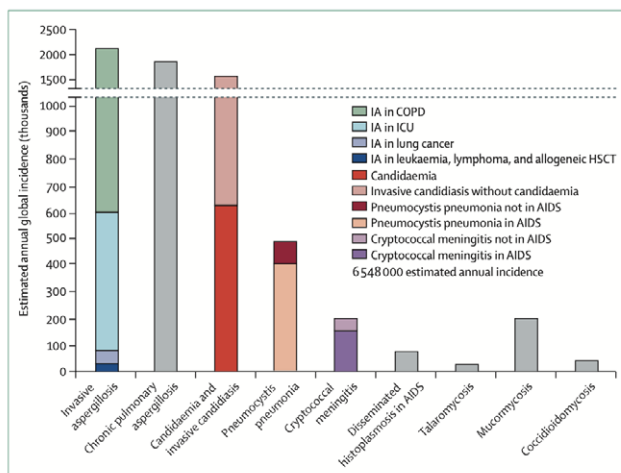
PREGUNTA I



Ante la situación clínica actual, usted

- a) Descartaría infección fúngica dado GM negativo.
- b) El valor de GM en suero no es valorable en este tipo de pacientes. Repetiría nueva extracción de BDG para descartar falso positivo.
- c) Mantendría posaconazol dada la hepatotoxicidad.
- d) Iniciaría anfotericina B liposomal a 3 mg/kg dado BDG positivo.

EL PROBLEMA DE LA INFECCIÓN FÚNGICA



Lancet Infect Dis 2024; 24: e428–38

	Mean annual incidence (thousands)	Treated mortality (%)	Untreated mortality* (%)	Ratio of treated to untreated cases*	Mean estimated deaths (thousands)	Percentage of deaths attributable to fungal infection (%)	Attributable deaths (thousands)
Invasive aspergillosis in COPD	1513 (753–2272)	43–72%	>95%	1:5	1325	~80%	1060
Invasive aspergillosis in ICU	519 (208–1038)	50% (46–82)	>95%	1:3	416	~50%	208
Invasive aspergillosis in leukaemia and lymphoma, and allogeneic HSCT	27	45% (30–57)	>95%	10:1	14	~80%	11
Invasive aspergillosis (lung cancer)	57*	51%	>95%	1:4	49*	~40%	19*
Chronic pulmonary aspergillosis	1837	8%	20%	1:12	340*	60% (0–85·7)	204*
Candida bloodstream infection	626	35% (8·7–77·3)	~90%	9:1	254	~65% (21–100)	165
Invasive candidiasis without positive blood culture	939	35% (27–60)	~90%	1:5	742*	~65% (21–100)	482*
Pneumocystis pneumonia in AIDS	400	15% (0–71)	>95%	4:1	140	90%	126
Pneumocystis pneumonia not in AIDS	105	40% (8–58)	100%	1:1	74	35% (30–90)	49*
Cryptococcal meningitis	194	60% (20–70)	100%	3:2	147	80% (63–68)	118
Disseminated histoplasmosis in AIDS	71 (47–95)*	30%	100%	1:10	66*	80%	53*
Talaromycosis	19	28%	>95%	3:1	9	90%	8
Mucormycosis	211	25%	100%	4:1	84	70%	59
Coccidioidomycosis (95% USA and Mexico)	30	..	..	10:1	2	90%	2
Fungal asthma	..	..	..	1:20†	92*	50%	46*
Totals	6548	NA	NA	NA	3752	NA	2548

Data are mean (range), unless stated otherwise. COPD=chronic obstructive pulmonary disease. ICU=intensive care unit. HSCT=haematopoietic stem cell transplant. NA=not applicable. *Low-confidence estimates requiring additional study. †Refers to antifungal treatment, not standard asthma therapy.

Table 2: Global incidence and mortality of invasive fungal diseases

Lancet Infect Dis 2024; 24: e428–38

PROFILAXIS ANTIFÚNGICA TPH

Table 5. Recommendations for allo-HSCT recipients: pre-engraftment.

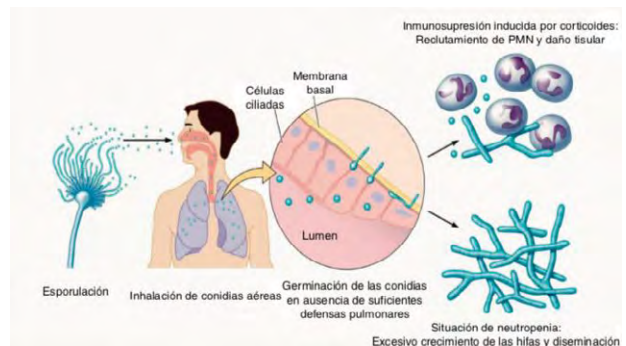
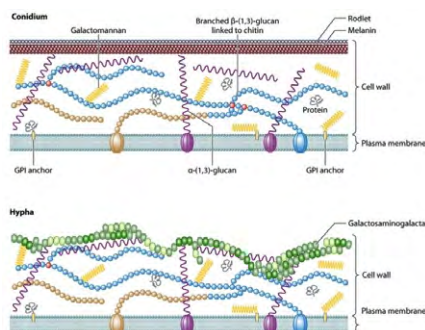
Antifungal agent	Pre-engraftment risk of mold infection		ECIL 5-6	
	low	high	low	High
Fluconazole 400 mg q24h	A-I ^a	D-III	A-I ^a	A-III against
Posaconazole tablet 300 mg q24h following a loading dose of 300 mg q12h on day 1 or oral solution 200 mg q8h	B-II	B-II	B-II	B-II
Itraconazole 2.5-7.5 mg/kg q24h i.v. or 200 mg q24h p.o.	B-I	B-I	B-I	B-I
Voriconazole 6 mg/kg q12h first day then 4 mg/kg q12h i.v. or p.o.	B-I	B-I	B-I	B-I
Micafungin 50 mg q24h	B-I	C-I	B-I	C-I
Caspofungin and anidulafungin	no data	no data	no data	no data
Liposomal amphotericin B	C-II	C-II	C-II	C-II
Aerosolized liposomal amphotericin B (10 mg twice weekly) in combination with systemic fluconazole 400 mg q24h	C-III	C-III	C-III	B-II
Isavuconazole 200 mg q24h following a loading dose of 200 mg q8h on days 1 and 2 ^b	B-II	B-II	no data	no data

Table 6. Recommendations for allo-HSCT recipients: post-engraftment.

Antifungal agent	Steroid treated acute GVHD	ECIL 5-6
Posaconazole tablet 300 mg q24h following a loading dose of 300 mg q12h on day 1, or oral solution 200 mg q8h	A-I ^{a, b}	A-I ^{a, b}
Itraconazole 2.5-7.5 mg/kg q24h i.v. or 200 mg q24h p.o.	B-I ^b	B-I ^b
Voriconazole 6 mg/kg q12h first day then 4 mg/kg q12h i.v. or p.o.	B-I ^b	B-I ^b
Micafungin 50 mg q24h	C-II	C-II
Caspofungin and anidulafungin	no data	no data
Liposomal amphotericin B	C-II	C-II
Aerosolized liposomal amphotericin B (10 mg twice weekly) in combination with systemic fluconazole 400 mg q24h	no data	no data
Fluconazole 400 mg q24h	D-III	D-III
Isavuconazole 200 mg q24h following a loading dose of 200 mg q8h on days 1 and 2 ^c	B-II	no data

Leukemia (2025) 39:1547 – 1557

Biomarcadores: GALACTOMANANO



- Polisacárido de la pared celular del *Aspergillus*
- Se libera durante el crecimiento fúngico
- Se detecta en el **suero y BAL**

Latgé J-P, Chamilo G. 2019. *Aspergillus fumigatus* and aspergillosis in 2019. Clin Microbiol Rev 33:e00140-18. <https://doi.org/10.1128/CMR.00140-18>.

García-Vidal C, Salavert Lletí M. Immunopatología de las micosis invasivas por hongos filamentosos [Immunopathogenesis of invasive mould infections]. Rev Iberoam Micol. 2014;31(4):219-228.

Biomarcadores: GALACTOMANANO

Falsos Positivos	Falsos Negativos
P. transfusionales	Profilaxis/TTª antifungico
Bifidobacterium	No neutropenicos
Ciclofosfamida,P, P/T A/C	Encapsulación

No neutropenia
Uso de antifúngicos



Angioinvasión

Latgé J-P, Chamilos G. 2019. *Aspergillus fumigatus* and aspergillosis in 2019. Clin Microbiol Rev 33:e00140-18. <https://doi.org/10.1128/CMR.00140-18>.

Biomarcadores: β -D-glucano

Marcador Panfúngico: Es un componente polisacárido de la pared celular de muchos hongos

No detecta *Cryptococcus sp* ni *zigomicetos* (mucorales)

Se libera durante la invasión fúngica

Sensibilidad baja y **alto VPN**

Aumenta la especificidad con **dos pruebas positivas**

Evitar la prueba en presencia de factores relacionados con falsos positivos

Cinética lenta

	Sensibilidad	Especificidad
1 prueba	60%	78%
2 pruebas	40%	93%



Falsos positivos	Falsos negativos
Curas con gasas o esponjas con glucano	Sueros hiperpigmentados (bilirrubina, tg)
Ttª albúmina, inmunoglobulinas, sulfamidas, f. coagulación	TTª azitromicina o pentamidina IV
Hemodiálisis con membranas de celulosa	
Bacteriemias	
Ttª con AC/PT	
Mucositis por radioterapia y/o quimioterapia	
•Contaminación por material no libres de glucano	

Mikulska, A. Beta-D-Glucan in Patients with Haematological Malignancies. J. Fungi 2021, 7, 1046.

DIAGNÓSTICO DE INFECCIÓN FÚNGICA EN HEMATOLÓGICOS

2. – What microbiological methods can be used to diagnose invasive aspergillosis (IA)? Are all diagnostic methods useful in all populations?

Searched Keywords: Diagnosis; Aspergillosis; Aspergillus diagnostic tests; Galactomannan; Glucan; BDG; Aspergillus LFD; Aspergillus PCR.

Executive summary

1. Diagnosis of IA in patients with suspected infection is mainly based on culture (AI), galactomannan antigen quantification (GM) (AII) and techniques based on the amplification of fungal DNA by the polymerase chain reaction (PCR) (AII).
2. Sensitivity of cultures is usually low but provides information on epidemiology and antifungal susceptibility (AII).
3. GM serum quantification is recommended in neutropenic and hematological patients who are not in prophylaxis (AII).
4. The PCR-based techniques have been extensively used and might improve diagnosis in hematological and ICU patients (AII) albeit an effort in standardization and harmonization of the techniques is still needed.

Searched Keywords: Invasive Aspergillosis; Oncologic patients; Haematologic patients; Neutropenia; Diagnostic.

Executive summary

1. – In neutropenic patients with suspicion of IPA the recommended approach is: (a) chest computed tomography (CT) scan (AII), (b) serum and/or BAL GM detection (AII), and (c) bronchoscopy (AII). Bronchoscopy allows for performing fungal culture, GM and PCR determinations that increase the probability of ruling in IPA diagnosis and ruling out other infections (AI).
2. – Histopathologic examination of tissues and fluid specimens are recommended whenever possible (AI), particularly to rule out other infections or diseases in patients with pulmonary nodules and negative biomarkers results (BII).

García-Vidal C, Alastruay-Izquierdo A, Aguilar-Guisado M, et al. Executive summary of clinical practice guideline for the management of invasive diseases caused by Aspergillus: 2018 Update by the GEMICOMED-SEIMC/REIP. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2019;37(8):535-541.

CASO CLÍNICO



- Tras el inicio del tratamiento con Ganciclovir, el paciente presenta mejoría clínica persistiendo mínimas deposiciones diarreicas en contexto de EICR ya conocido.
- Se repitió BDG en suero, resultado negativo.
- En el día + 236, presenta de nuevo pico febril de hasta 39°C asociando tos con expectoración mucopurulenta y leve dolor costal izquierdo de características pleuríticas, procediéndose al inicio de antibioterapia con meropenem 1 gr/8 horas + vancomicina 1 gr/12 horas + anfotericina B 3 mg/kg cada 24 horas.

PREGUNTA II



Ante la situación clínica actual, usted

- a) Mantendría tratamiento con anfotericina B 3 mg/kg /24 horas.
- b) Solicitaría TAC tórax y, según hallazgos, BAL.
- c) Valoraría anidulafungina a dosis plenas para cambiar de grupo farmacológico.
- d) La probabilidad de una fungemia de brecha en este paciente es baja.

CASO CLÍNICO





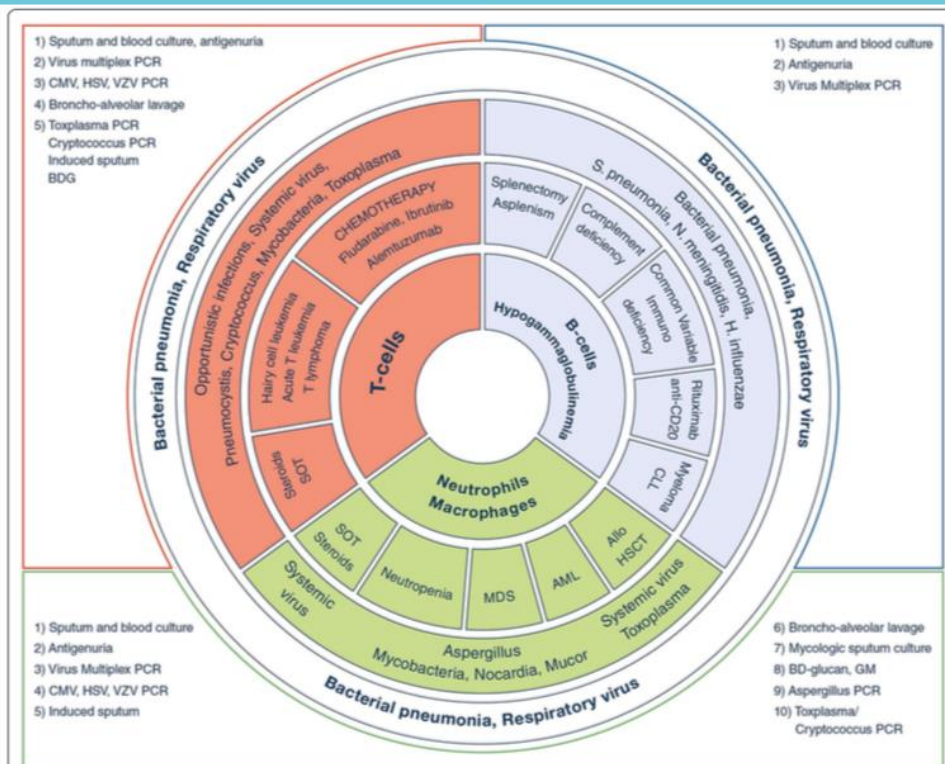
PREGUNTA III

Ante la situación clínica actual, usted

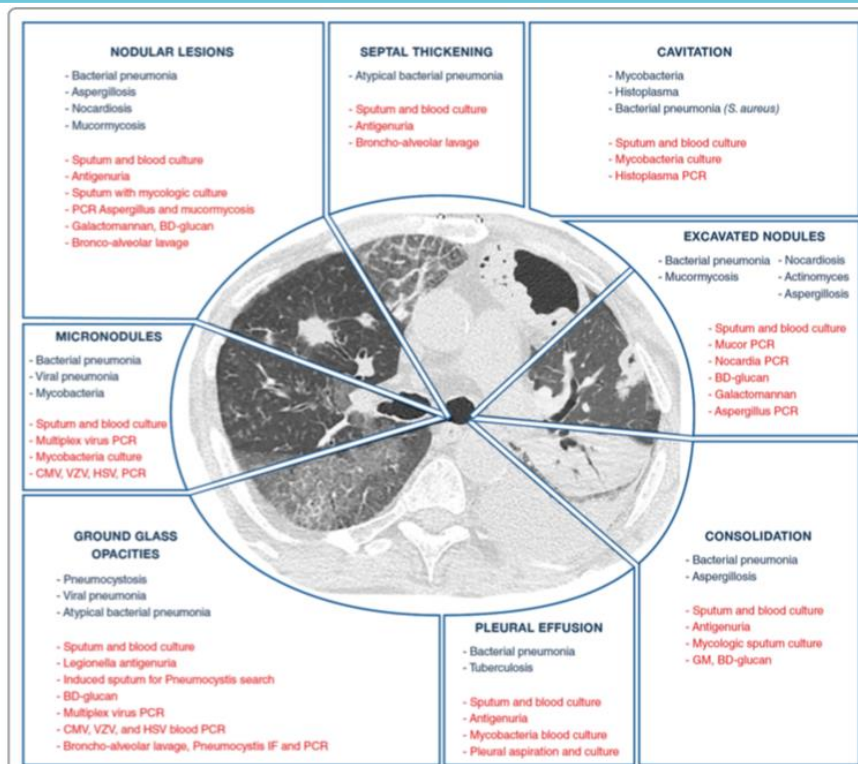
- a) Podría tratarse de una Aspergilosis Pulmonar Invasiva.
- b) Podría tratarse de una Mucormicosis pulmonar.
- c) Podría tratarse de Nocardiosis pulmonar.
- d) Podría tratarse de una infección por bacterias atípicas.

Legionella: neoplasias, corticosteroides, terapias biológicas

Rhodococcus: enfermedad hematológica



Intensive Care Med (2020) 46:298–314



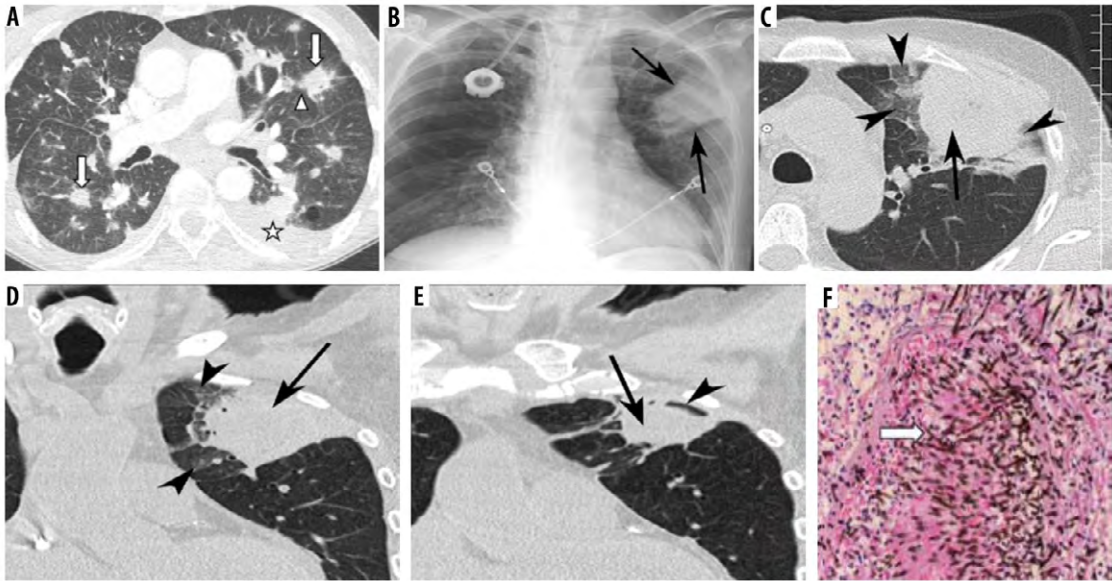
Intensive Care Med (2020) 46:298–314

Table 1

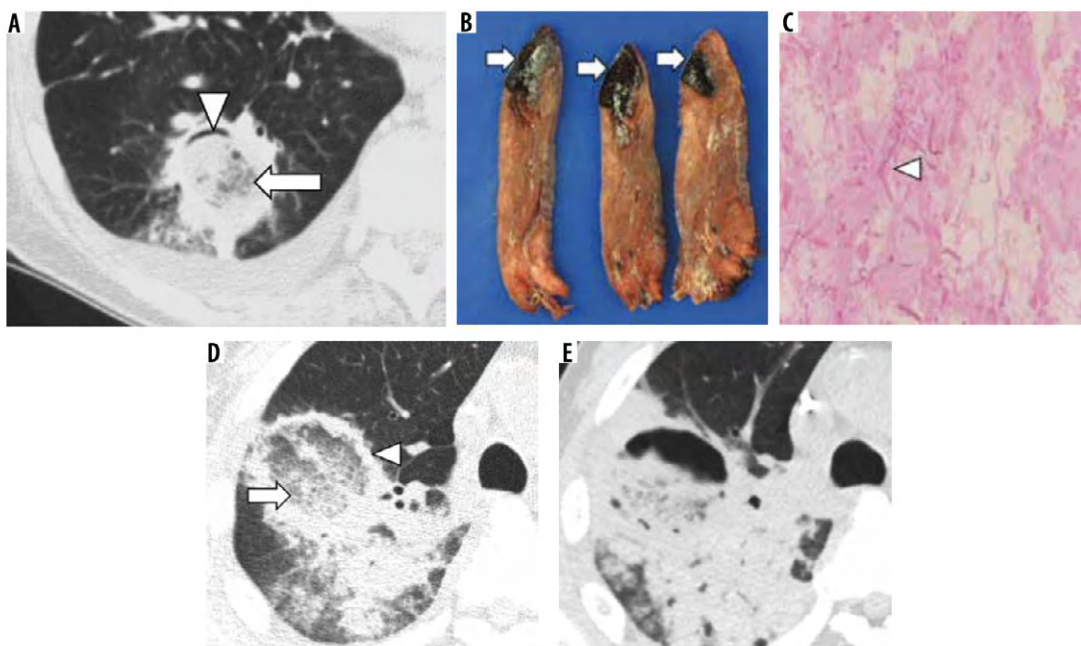
Imaging findings in IFD

Image findings	Type of IFD	Type of underlying conditions	Differential diagnosis
Nodules without halo sign	IPA (most frequent) Other IMD, endemic mycoses, cryptococcosis (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions	Bacterial abscess Nocardiosis Other bacterial infection (actinomycosis, legionellosis, Q fever) Tuberculosis/other mycobacterial infections Septic emboli Bronchogenic carcinoma Post-transplant lymphoproliferative disorder
Nodules with halo sign	IPA (most frequent) Other IMD, endemic mycoses, cryptococcosis (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions	Viral pneumonia (CMV, herpes) Mycobacterial infections Granulomatous polyangiitis Haemorrhagic metastasis
Reverse halo sign	IM (most frequent) IPA, other IMD, endemic mycoses, Pneumocystis pneumonia (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions	Tuberculosis Bacterial Pneumonia OP Pulmonary infarct Sarcoidosis, granulomatous polyangiitis Lymphomatoid granulomatosis Post-radiotherapy, post-radiofrequency
Hypodense sign	IPA (most frequent) Other IMD, endemic mycoses (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions	Any necrotic process (infectious or non-infectious)
Air crescent sign	IPA (most frequent) Other IMD, endemic mycoses (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions ^a ICU	Bacterial abscess Septic emboli Pulmonary infarct Cavitated metastasis Post-infectious scar
Cavity	IPA (most frequent) Other IMD, endemic mycoses (rare)	Haematologic cancer (most frequent) Other immunosuppressive conditions ^a ICU	Mycetoma Bacterial abscess, necrotizing pneumonia (tuberculosis/other mycobacterial infections tumoural, trauma) Non-infectious cavitating process (Vasculitis, tumoural, trauma)
Alveolar consolidation	IPA (most frequent) IM, other IMD (rare)	Haematologic cancer Other immunosuppressive conditions ^a ICU	Bacterial, viral infections OP, AOP, alveolar damage Aspiration pneumonia, post-obstructive atelectasis Pulmonary haemorrhage Adenocarcinoma, lymphoma Drug-induced/radiation pneumonitis Viral, atypical bacterial pneumonia (e.g. Mycoplasma, ...) Pulmonary oedema Alveolar haemorrhage Diffuse alveolar damage (e.g. ARDS) Drug-induced/radiation pneumonitis Interstitial pneumonitis Acute interstitial pneumonia, alveolar proteinosis
Ground-glass attenuation	Pneumocystis pneumonia (most frequent) IPA, IM, other IMD (rare)	Haematologic cancer Other immunosuppressive conditions ^a ICU	Viral pneumonia OP Lymphoma, adenocarcinoma Drug-induced/radiation pneumonitis Granulomatous or inflammatory bronchiolitis
Peribronchovascular density	IPA (most frequent) Other IMD (rare)	Other immunosuppressive conditions ^a (most frequent) Haematologic cancer ICU	Other infectious or inflammatory bronchiolitis
Bronchovascular wall thickening and tree-in-bud nodules	IPA (most frequent) Other IMD (rare)	Other immunosuppressive conditions ^a (most frequent) Haematologic cancer ICU	
Pleural effusion	IM, IPA (most frequent) Other IMD (rare)	Haematologic cancer Other immunosuppressive conditions ^a ICU	Bacterial empyema or parapneumonic effusion Non-infectious pleural effusion

Clinical Microbiology and Infection 30 (2024) 296e305



Pol J Radiol 2021; 86: e335-e343



Pol J Radiol 2021; 86: e335-e343

MUCORMICOSIS EN HEMATOLÓGICOS

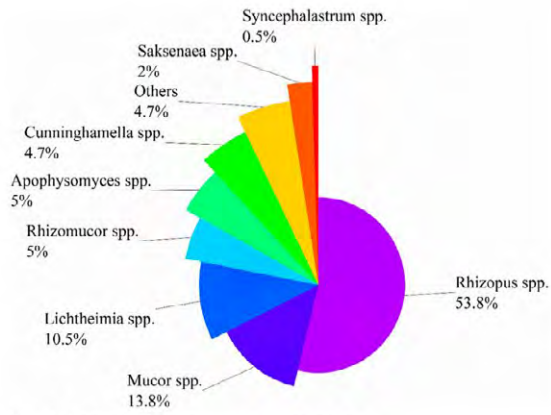
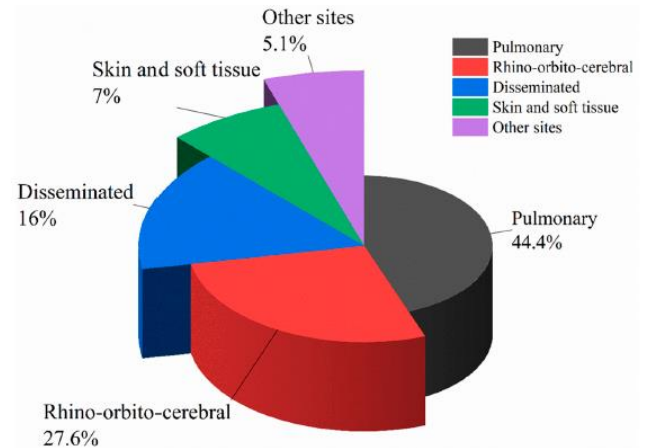
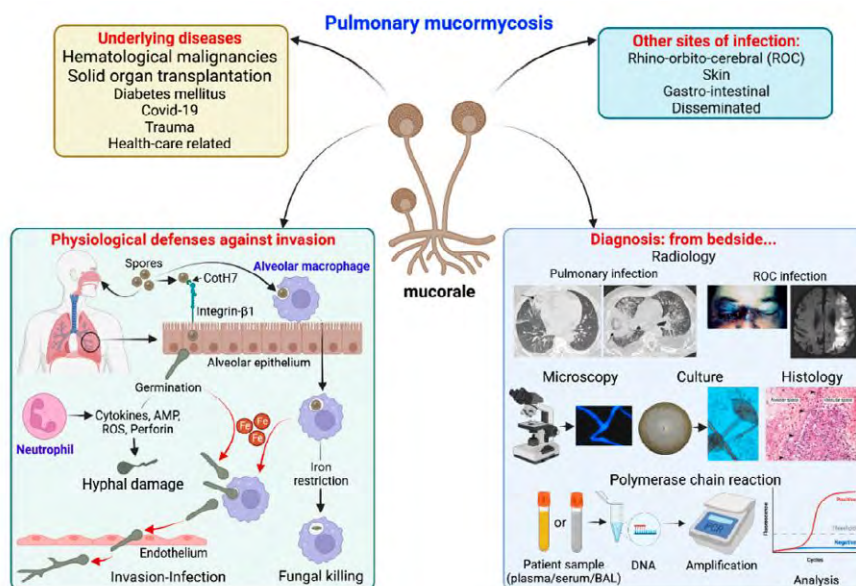


Figure 1. Distribution of Mucorales organisms causing infection.

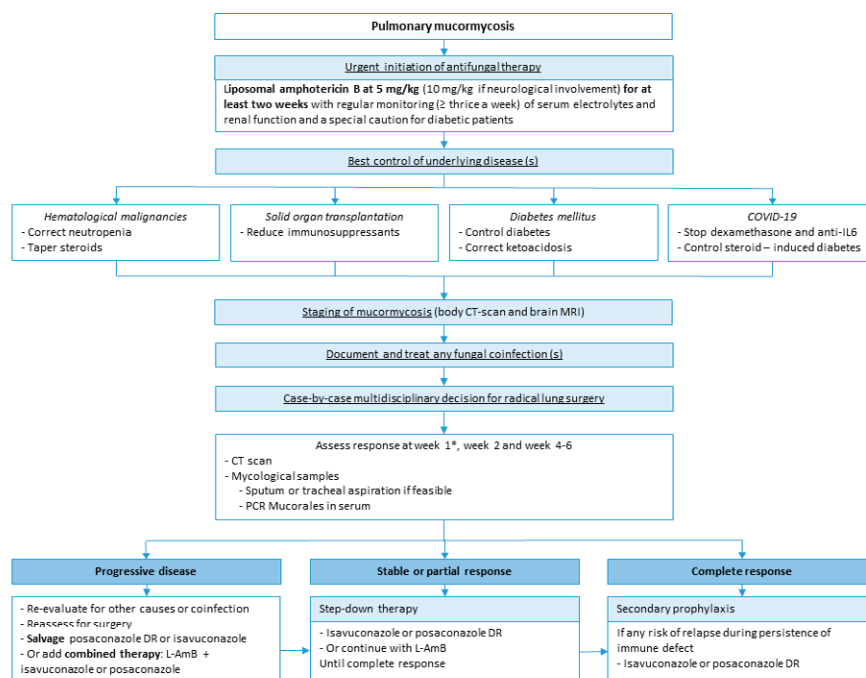


J. Fungi 2023, 9, 592.

MUCORMICOSIS EN HEMATOLÓGICOS



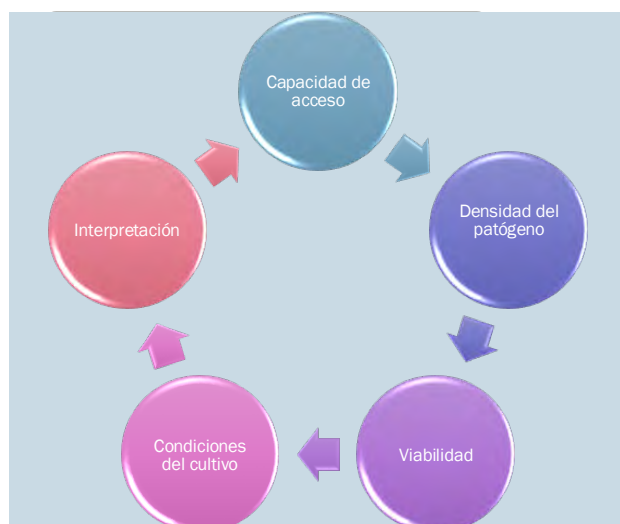
J. Fungi 2023, 9, 307



J. Fungi 2023, 9, 307

Diagnóstico microbiológico: Tinción y cultivo

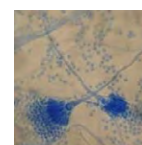
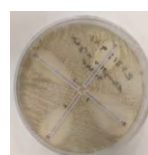
BAL



Cultivo:

- Diagnóstico etiológico
- Estudio de sensibilidad

S	<70%
VPP	<70%



Diagnóstico microbiológico: Biomarcadores

BAL

Galactomanano:

- > sensible BAL que en suero.
- Se ve afectada por la calidad de la muestra.
- En paciente no neutropénico > Sensibilidad en LBA vs sérico.
- En pac. con profilaxis antifúngica para mohos tiene una S: 52%

ELISA/CLIA

- Suero/BAL
- **Alta** sensibilidad y especificidad
- Sirve para **monitorizar** la infección
- Indicador de **enfermedad activa**

Lateral flow assay (LFA, ImmyTM)

- Detecta GM (ME-A5 mAB)
- Evaluado en poblaciones mixtas inmunocomprometidas y no neutropénicos
- **Sensibilidad similar a GM** (PlateliaTM assay, Paris, France)

Lateral flow device(LFD, OhmTM)

- detecta una glicoproteína extracelular de Aspergillus sp (JF5 glicoproteína extracelular)

Diagnóstico microbiológico

PCR

- Alta sensibilidad para Aspergillus
- Alto VPN en pacientes inmunosuprimidos sin profilaxis antifúngica
- Marcador precoz
- La profilaxis afecta menos a la sensibilidad en el BAL

La combinación de múltiples pruebas diagnósticas basados en estudio micológico, PCR y biomarcadores pueden ayudar al diagnóstico de las IFI

Desafío diagnóstico:

- Presentación clínica atípica
- Disminución de la sensibilidad de las pruebas
- Combinación de biomarcadores
- Métodos invasivos en pacientes frágiles.



Table 1. Comparative overview of different diagnostic methods used to detect various fungal infections, including *Aspergillus*, *Candida*, *Cryptococcus*, and *Mucorales*. The table outlines the advantages and disadvantages of each method, such as microscopy, culture, antigen biomarkers, and PCR, highlighting their effectiveness and limitations for each type of fungal pathogen.

Method	<i>Aspergillus</i>		<i>Candida</i>		<i>Cryptococcus</i>		<i>Mucorales</i>	
	Advantages (+)	Disadvantages (-)	Advantages (+)	Disadvantages (-)	Advantages (+)	Disadvantages (-)	Advantages (+)	Disadvantages (-)
Microscopy	* Rapid diagnosis * Increased sensitivity with fluorescent stains	* Limited sensitivity (max. 50%) * Lack of specificity * Sufficient expertise of the examinee required	* Gold standard for detection and identification of fungal pathogens * Rapid results, simple and cost-effective * Simple procedure	* Limited sensitivity (50%-70%) * Limited specificity	* Provides rapid results	* Requires skilled personnel	* Rapid presumptive diagnosis possible	* Genus or species identification not possible * Artificial septa can cause misinterpretation * Differentiation from other filamentous fungi can be difficult
Culture	* High specificity * Identification of the exact fungal strain * Long-term storage of samples	* Time-consuming * Material requirements * Overgrowth by other species	* High sensitivity * Species identification * Quantitative information	* False negative results possible * Large volumes needed (Issue in neonates and children) * Time-consuming	* High sensitivity and specificity * Allows for standardized antifungal resistance testing	* Time-consuming process	* Species identification possible * Antifungal susceptibility testing possible * Positive culture from sterile site confirms diagnosis	* Up to 50% false-negative results * Tissue homogenization can damage fungi * Some strains require specific media * Species identification requires expertise
Antigen Biomarkers	GM-Testing * High specificity * Foundation for most treatment initiation decisions BDG-Testing * Faster test than PCR * Can indicate fungal infections	GM-Testing * false-negative results BDG-Testing * False-positives with contaminated infusions, especially in hematological patients * Not specific for <i>Aspergillus</i>	GM-Testing * Not applicable BDG-Testing * High sensitivity * Strongly recommended for diagnosis of candidemia	BDG-Testing * False positive results (patients with hemodialysis, liver cirrhosis or after abdominal surgery) * Lower sensitivity for non-albicans species	Cryptococcal antigen (CrAg) * Easily accessible * Delivers quick results	CrAg * Negative serum test does not exclude CNS disease	GM-Testing * May help rule out mucormycosis in high-risk patients BDG-Testing * Limited use; some <i>Rhizopus</i> spp. might be detected	GM-Testing * False positives, mixed infections possible BDG-Testing * Most <i>Mucorales</i> have low BDG, below detection limits
PCR	* Can directly detect <i>Aspergillus</i> * Can be combined with other biomarkers for increased accuracy	* More expensive test than GM * Requires specialized equipment and expertise * Can sometimes give false-positive results	* Requires specialized equipment and trained staff	* High sensitivity and specificity * Results within 90 min – 3 hours	* High sensitivity in HIV patients (90%)	* Lower performance in immunocompetent individuals * Not suitable for resource-limited settings * Lacks resistance testing capabilities (currently)	* Detects <i>Mucorales</i> DNA in tissues * Enables earlier diagnosis than traditional methods * Non-invasively detects in blood and other fluids * Promising for identifying specific <i>Mucorales</i> species	* Lack of standardization across different PCR techniques and targets * Most in-house techniques lack external validation * Limited availability and clinical validation of commercial assays * Performance typically better with fresh tissues than formalin-fixed tissues



Target	Assay Reference	Assay Type	Specimen	Manufacture
Antibodies	<i>Aspergillus fumigatus</i> IgA ELISA Kit	ELISA	Serum	QED Bioscience Inc.
	<i>Aspergillus</i> IgG Antibody Detection K-Set	Lateral flow assay	Serum	Era Biology
	<i>Aspergillus</i> IgM Antibody Detection K-Set	Lateral flow assay	Serum	Era Biology
	<i>Aspergillus fumigatus</i> IgG ELISA	ELISA	Serum	Demeditec
Target	Assay Reference	Assay Type	Specimen	Manufacture
Antibodies	<i>Aspergillus fumigatus</i> IgG ELISA Kit	ELISA	Serum	Aviva Systems Biology
	<i>Aspergillus fumigatus</i> IgG ELISA Kit	ELISA	Serum	QED Bioscience Inc.
	<i>Aspergillus fumigatus</i> IgE ELISA	ELISA	Serum	Demeditec
	<i>Aspergillus fumigatus</i> IgM ELISA Kit	ELISA	Serum	Aviva Systems Biology
	<i>Aspergillus fumigatus</i> IgM ELISA Kit	ELISA	Serum	QED Bioscience Inc.
	Dynamiker <i>Aspergillus fumigatus</i> IgG	ELISA	Serum	Dynamiker
	QuicIgG <i>Aspergillus</i> IgG Ab Lateral Flow Assay	Lateral flow assay	Serum	Dynamiker

J. Fungi 2026, 12, 259

Galactomannan	<i>Aspergillus</i> Galactomannan Ag VIRCLIA	Sandwich chemiluminescent immunoassay	Serum and BAL	Vircell S.L.			
	<i>Aspergillus</i> Galactomannan Detection K-Set	Lateral flow assay	Serum and BAL	Era Biology			
	Dynamiker <i>Aspergillus</i> Galactomannan Assay	ELISA	Serum and BAL	Dynamiker			
	FungiXpert® <i>Aspergillus</i> Galactomannan	ELISA	Serum and BAL	Era Biology			
	<i>Aspergillus</i> Galactomannan (CLIA)	Chem immu	AsperGenius	Real-time PCR (species ID and azole resistance)	BAL	PathoNostics	
	Platelia <i>Aspergillus</i> Ag	ELISA	GeneProof <i>Aspergillus</i> PCR Kit	Real-time PCR (ITS2/28S rDNA)	Whole blood, plasma, serum, BAL, sputum, CSF	GeneProof	
	Sōna <i>Aspergillus</i> GM Lateral Flow Assay	Later	Goldstream® <i>Aspergillus</i> Molecular Test (China and Europe)	Real-time PCR	Whole blood and BAL	Era Biology	
Mannoprotein	QuickGM <i>Aspergillus</i> Galactomannan Ag	Later					
	<i>Aspergillus</i> Antigen ELISA	ELISA					
1,3-β-D-glucan	Beta-Glucan Test	Enzy	DNA detection	MycAssay <i>Aspergillus</i>	Real-time PCR	Lower respiratory tract samples and serum	Myconostica UK
	Dynamiker Fungus (1-3)-β-D-Glucan	ELISA		MycogenIE® <i>Aspergillus fumigatus</i> and resistant TR34/L98H	Real-time PCR	Serum, biopsy, lower respiratory tract samples	Ademtech
	Goldstream® Fungus (1-3)-β-D-glucan Test (available in China and Europe)	Enzy		MycogenIE <i>Aspergillus</i> species—Mucorales species	Real-time PCR	Serum, biopsy, lower respiratory tract samples	Ademtech
	Fungitell Assay	Enzy (singl		VIASURE <i>Aspergillus</i> differentiation Real Time PCR Detection Kit	Real-time PCR (<i>A. fumigatus</i> , <i>A. flavus</i> , <i>A. terreus</i>)	BAL, bronchial aspirate, sputum	Certest
	Fungitell STAT Assay	Enzy					

J. Fungi 2026, 12, 259

Diagnosis of Aspergillosis Using Biomarkers

Multiple biomarkers can be used to diagnose **aspergillosis**. Each has different strengths and weaknesses depending on the host population and clinical setting and how to.

Serum β -D-Glucan	Serum and BAL Galactomannan	Antibody Detection
 Detects (1-3)-β-D-glucan, a component of many fungal cell walls. Useful in various patient populations, but not specific to aspergillosis. Strengths: Broad fungal detection, good for screening. Priority: Useful as screening marker, not definitive for aspergillosis.	 Detects galactomannan, a component of the <i>Aspergillus</i> cell wall. Highly sensitive and specific in hematologic patients, but may be reliable in other populations. Strengths: Well-studied, specific in hematologic patients. Priority: First-line markers in hematologic patients.	 Detects antibodies (IgG, IgM) against <i>Aspergillus</i> species. Useful to screen for chronic and allergic manifestations of aspergillosis. Strengths: Useful to screen for chronic and allergic manifestations of aspergillosis.

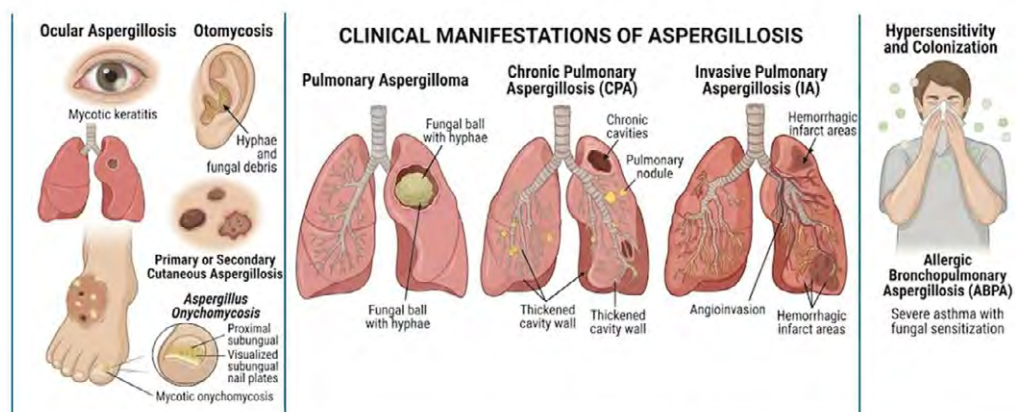
Aspergillus PCR

-  Detects *Aspergillus* DNA in blood or respiratory specimens.
- ☒ Highly specific, direct detection of *Aspergillus* DNA.

Assess the clinical context and patient population to choose the most appropriate biomarker, balancing sensitivity, specificity, and invasiveness to ensure accurate diagnosis.



J. Fungi **2026**, *12*, 259



Clinical presentation	Superficial aspergillosis	<i>Aspergillus</i> colonization (Aspergilloma)	Chronic pulmonary aspergillosis	Acute invasive pulmonary aspergillosis and disseminated disease	Allergic (ABPA / AFRS)
Host immunity	Immunocompetent	Immunocompetent	Immunocompetent or mildly immunocompromised	Severely immunocompromised	Atopic / Hyperimmune
Primary biomarker	No diagnostic value	IgG (Anti- <i>Aspergillus</i> Antibodies)	IgG (Anti- <i>Aspergillus</i> Antibodies)	GM/LB, PCR in serum	Total IgE, Specific IgE
Complementary biomarker	No diagnostic value	PCR/GM in sputum (non-serum)	GM in serum (monitoring)	BDG (for IFIs in general)	Specific IgG, Eosinophilia

J. Fungi **2026**, *12*, 259

TRATAMIENTO ASPERGILOSIS

TREATMENT

1. – What is the treatment for IA in hematological patients?

a) Which drug has been associated with better outcomes?

Searched Keywords: Aspergillosis; Aspergillus; Treatment; Therapy; Guidelines

Executive summary

1. Voriconazole and Isavuconazole should be considered drugs of choice for primary treatment of IA in hematological patients (AI).
2. Liposomal amphotericin B is an alternative for primary or salvage treatment for patients who are intolerant, had hepatitis or are refractory to voriconazole or isavuconazole. Also for patients with suspected or confirmed triazole resistance, or when triazole use is not desirable due to drug interactions (AII).
3. Echinocandins and posaconazole are not recommended as primary treatment of IA in oncohematological patients (AII), but they are an alternative as salvage therapy when other azoles and liposomal amphotericin B cannot be used (BII).

b) When should we use combination therapy and what are the best regimens?

Executive summary

1. Antifungal combination therapy should not be generally recommended for primary treatment of IA, but it could be considered in selected hematological patients with documented IA (BI).
2. Regarding class of antifungal compounds to be combined, combinations including triazole and echinocandin are the most commonly recommended and specifically voriconazole with anidulafungin would be the best regimen (BI).
3. For salvage treatment of refractory IA, the addition to another agent to initial therapy is in general not recommended, although combination therapy may be considered in individual patients (CIII).

García-Vidal C, Alastruéy-Izquierdo A, Aguilar-Guisado M, et al. Executive summary of clinical practice guideline for the management of invasive diseases caused by Aspergillus: 2018 Update by the GEMICOMED-SEIMC/REIP. *Enferm Infect Microbiol Clin (Engl Ed)*. 2019;37(8):535-541.

CASO CLÍNICO



LAVADO BRONCOALVEOLAR

Técnica	Pato.	Resultado	Unidades
Estudio: INMUNODIAGNÓSTICO INFECCIOSO			
Ag galactomanano Aspergillus (CLIA)		Positivo	
Índice		2,305 (Positivo >0,20)	
Estudio: MUESTRAS RESPIRATORIAS			
Tinción de Gram		Abundantes leucocitos	
Cultivo standard		Microbiota desplazada.	
		Crecimiento escaso de Aspergillus spp y Coryneb.	





PREGUNTA IV

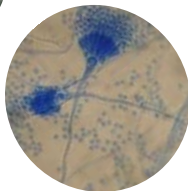
Ante las pruebas anteriormente aportadas, usted decide

- a) Iniciar biterapia con anfotericina B 3 mg/kg + anidulafungina.
- b) Mantener monoterapia con anfotericina B 3 mg/kg hasta sensibilidad de cultivo.
- c) Modificar tratamiento a Isavuconazol.
- d) La opción más lógica sería biterapia con anfotericina B 3 mg/kg + isavuconazol.

Aspergillus terreus

Section Terrei

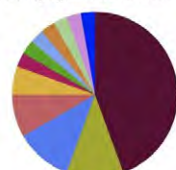
A. alabamensis
A. allahabadii
A. ambiguus
A. aureoterreus
A. bicephalus
A. carneus
A. citrinoterreus
A. floccosus
A. hildiae
A. hortae
A. iranica
A. microcysticus
A. neoaficanus
A. neoindicus
A. niveus
A. pseudoterreus
A. terreus



- *A.fumigatus* es la causa mas frecuente de AI, seguido de *A.flavus*, *A.niger* y *A.terreus*.
- *A.terreus* 3-12%:
 - Tasa < de respuesta al TT
 - > mortalidad
 - >diseminación
 - >frecuencia en fungemia de brecha
 - >frecuencia tras administración de antifúngicos

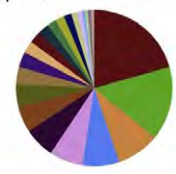
- 21 países
- 370 casos de *A. terreus* (5,25) → 25,1% AI
- Especies crípticas 14,9%: *A. citrinoterreus* 65,5%
- *A. terreus sensu stricto* (n 315), *A. citrinoterreus* (n 36), *A.alabamensis* (n 6), *As. hortai* (n 10)

(a) *Aspergillus citrinoterreus*



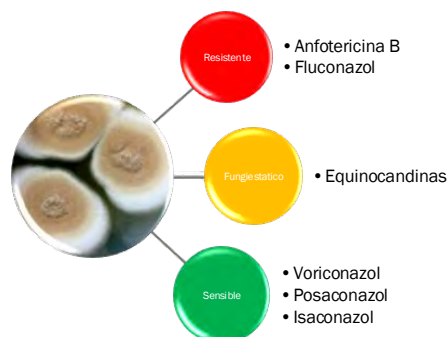
Total=36

(b) *Aspergillus terreus sensu stricto*

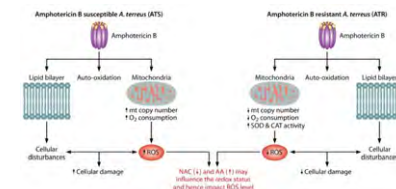


Total=315

Aspergillus terreus



Resistencia intrínseca anfotericina B



Aspergillus species	Amphotericin B MICs, mg/L								
	0.125	0.25	0.5	1	2	4	8	16	32
<i>A. terreus sensu stricto</i>	3	7	10	14	36	81	86	55	23
<i>A. citrinoterreus</i>					3	13	8	7	5
<i>A. hortai</i>					1	2	5	2	
<i>A. alabamensis</i>					2	3	1		
<i>A. floccosus</i>						1			
<i>A. neoafrikanus</i>									1
Potential new species							1		

B. Risslegger et al. A prospective international Aspergillus terreus survey: an EFISG, ISHAM and ECOMM joint study. Cornella lass et al. Aspergillus terreus species complex. Clinical microbiology review. octubre 2021, volumen 34 issue 4 e00311-20

Received: 21 June 2019 | Revised: 26 June 2019 | Accepted: 27 June 2019
DOI: 10.1111/myc.13296

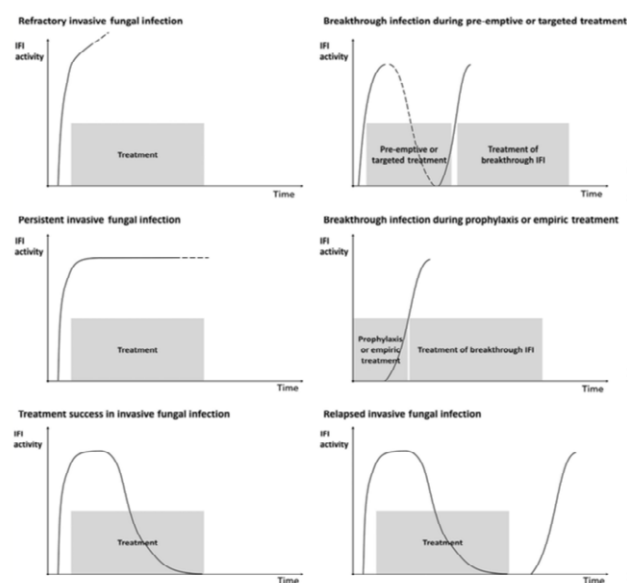
REVIEW ARTICLE

WILEY

Defining breakthrough invasive fungal infection—Position paper of the mycoses study group education and research consortium and the European Confederation of Medical Mycology

TABLE 1 Summary of definitions for invasive fungal infection

Term	Definition
Persistent IFI	IFI unchanged from baseline, may precede treatment success
Refractory IFI	IFI with worsening or new attributable clinical signs or symptoms or radiological findings attributable to IFI while on treatment
Relapsed IFI	IFI occurring after antifungal treatment discontinuation. IFI is caused by the same pathogen at the same site with or without dissemination
Breakthrough IFI	IFI occurring during exposure to an antifungal drug. Including fungi outside the spectrum of activity of an antifungal (treatment emergent IFI is a synonym). The time point of breakthrough IFI is the first attributable clinical sign or symptom, mycological findings or radiological feature. The period of breakthrough IFI depends on the pharmacokinetic properties of the antifungal evaluated



Cornely OA, Hoenigl M, Lass-Flörl C, et al. Defining breakthrough invasive fungal infection—Position paper of the mycoses study group education and research consortium and the European Confederation of Medical Mycology. *Mycoses*. 2019;62(9):716–729.

FACTORES DE RIESGO IFI DE BRECHA

Risk factor	Mechanism increasing risk of IFI
Acute leukaemia ^{18,22,34,81,101,102}	Increased proliferation of leukaemic cells leads to decreased production of normal neutrophils ¹⁸
Neutropenia ^{19,20,22,34,36,92,101,102}	Decreased production of normal neutrophils ¹⁸
Immunosuppression including glucocorticoids ^{20,22,89,102}	Impaired innate and/or adaptive immune response ¹⁰⁵ ; Glucocorticoid-associated dysregulation of immunity ¹⁰⁶
Mucositis ^{35,36,81,102} fungal translocation ^{109,110,146}	Impaired mucosal barrier with translocation of pathogens, primarily <i>Candida</i> , to the blood ^{107,109,110,146}
Central venous catheters ^{34,81,102}	Port of entry and nidus of infection for fungal pathogens, primarily <i>Candida</i> ¹²²
Broad-spectrum antibiotic use ^{20,22,35,81,101}	Alters gut flora and increases colonisation from <i>Candida</i> spp., increasing risk for IC; selective pressures and increase in <i>Candida</i> spp. resistance; alterations in host immune response to <i>Candida</i> spp. ¹²³
Genetic factors ^{27-29,126,127}	Impaired adaptive and/or innate immune function ^{27-29,126,127}

TABLE 1 Mechanism of risk increase of major predisposing host factors for breakthrough invasive fungal infections

Mycoses. 2020;63:1021–1032.

IFI DE BRECHA

4. – What antifungal drugs should be used in case of breakthrough aspergillosis (BrA)?

Searched terms: Breakthrough aspergillosis, Breakthrough fungemia, Posaconazole, Micafungin, Caspofungin, Amphotericin B.

Executive summary

1. In patients with BrA is recommended initiating empirical treatment with an alternative class of antifungal with *Aspergillus* activity until the diagnosis is established and a response to treatment can be documented (**BIII**).

García-Vidal C, Alastruey-Izquierdo A, Aguilar-Guisado M, et al. Executive summary of clinical practice guideline for the management of invasive diseases caused by *Aspergillus*: 2018 Update by the GEMICOMED-SEIMC/REIPI. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2019;37(8):535-541.

Question 12: What is breakthrough IA and how should it be managed?

Recommendations

- Verification of adherence to antifungal therapy together with TDM should be performed in suspected breakthrough IA (Strong recommendation, Level III evidence).
- If breakthrough IA occurs on triazole prophylaxis or therapy, a switch to liposomal amphotericin B is strongly recommended (Strong recommendation, Level III evidence).
- If breakthrough IA occurs on liposomal amphotericin B therapy, a switch to voriconazole or isavuconazole is strongly recommended (Strong recommendation, Level III evidence).
- Where possible, definitive treatment targeted towards the specific fungal pathogen and with an agent confirmed to be effective on antifungal susceptibility is strongly suggested (Strong recommendation, Level III evidence).

Douglas AP, Smibert OC, Bajel A, et al. Consensus guidelines for the diagnosis and management of invasive aspergillosis, 2021. *Intern Med J*. 2021;51 Suppl 7:143-176.

IFI DE BRECHA

Table 3
BtIFI diagnosis, site of infection, and microbiological results.

	ALL EPISODES N = 121 (%)
IFI classification	
Proven	41 (33.9)
Probable	53 (43.8)
Possible	27 (22.3)
Diagnosed IFI classified as Proven or Probable^a	94 (77.7)
Invasive aspergillosis ^b	55 (45.5)
Candidemia ^c	23 (19)
Mucormycosis ^d	7 (5.8)
Other mould infections ^e	6 (5)
Other fungemias ^f	5 (4.1)
IFI site	
Pulmonary	71 (58.7)
Disseminated	43 (35.5)
Sinonasal infection	6 (5)
CNS infection	1 (0.8)
Source of fungemia (n = 30)	
Unknown source	13 (43.3)
Catheter-related	11 (36.7)
Abdominal source	5 (16.7)
Urinary source	1 (3.3)
Microbiological results	
Positive galactomannan antigen in plasma	32 (26.4)
Mean (SD) galactomannan value in plasma ^g	3.14 (2.40)
Positive galactomannan antigen in bronchoalveolar lavage	33 (27.3)
Mean (SD) galactomannan value in bronchoalveolar lavage ^h	4.09 (2.95)
Positive culture or PCR	65 (53.7)
Positive pan-fungal PCR	5 (4.1)
Antifungal susceptibility to a prior antifungal in isolated species (n = 48)	
Susceptible	8 (16.7)
Resistant/Non-susceptible	40 (83.3)

13 hospitales
36 meses
> 7 días de tto antifúngico

Table 4
Antifungal therapy and outcomes of invasive fungal infection episodes.

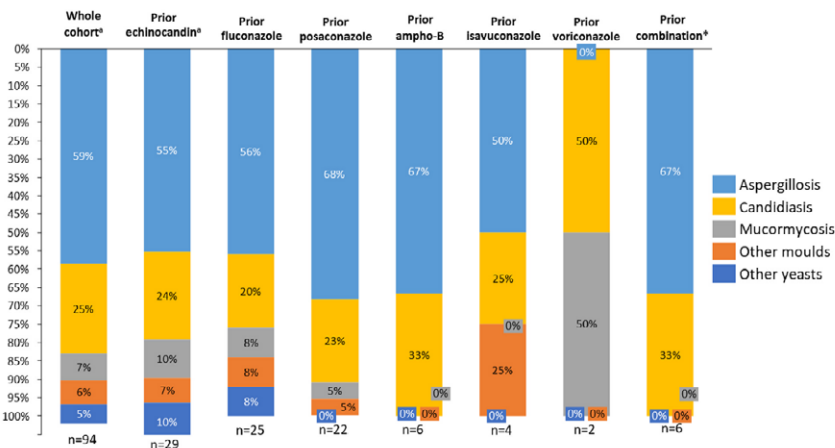
	ALL EPISODES ^a (N = 121 (%))
Antifungal change after BtIFI suspicion/ diagnosis	110 (90.9)
Change of antifungal class after BtIFI suspicion/diagnosis	97 (80.2)
Empirical antifungal therapy	
Liposomal amphotericin-B	59 (48.8)
Voriconazole	36 (29.8)
Echinocandins	32 (26.4)
Posaconazole	9 (7.4)
Isavuconazole	7 (5.8)
Fluconazole	1 (0.8)
Empirical antifungal combination	23 (19)
Definitive antifungal therapy^b	
Voriconazole-containing regimen ^c	52 (43)
Liposomal amphotericin-B-containing regimen ^d	44 (36.4)
Echinocandin-containing regimen ^e	37 (30.6)
Isavuconazole-containing regimen ^f	22 (18.2)
Posaconazole-containing regimen ^g	15 (12.4)
Fluconazole-containing regimen ^h	5 (4)
Amphotericin-B lipid complex	1 (0.8)
Definitive antifungal combination	34 (28.1)
Management/evolution of patients with fungemia (n = 30)	
Persistent fungemia at 48 h	8 (26.7)
Ophthalmoscopic evaluation	14 (46.7)
Secondary septic metastases	4 (13.3)
Catheter removal	28 (93.3)
Other source control procedures	3 (10)
Echocardiography performance	11 (36.7)
Overall outcomes	
Inappropriate empirical antifungal therapy	15 (12.4)
ICU requirement	33 (27.3)
Invasive mechanical ventilation requirement	24 (19.8)
Clinical IFI response at 100 daysⁱ	
Complete response	48 (39.7)
Partial response	23 (19)
Stable infection	13 (10.7)
Fungal infection progression	37 (30.6)
100-day mortality	57 (47.1)
IFI was the cause of the death	36 (28.1)
IFI had an essential role in the death	39 (32.3)
IFI had a secondary role in the death	12 (10)
Death was unrelated to the IFI	10 (7.5)

Puerta-Alcalde P, Monzó-Gallo P, Aguilar-Guisado M, et al. Breakthrough invasive fungal infection among patients with haematologic malignancies: A national, prospective, and multicentre study. J Infect. 2023;87(1):46-53.

IFI DE BRECHA

P. Puerta-Alcalde, P. Monzó-Gallo, M. Aguilar-Guisado et al.

Journal of Infection 87 (2023) 46–53



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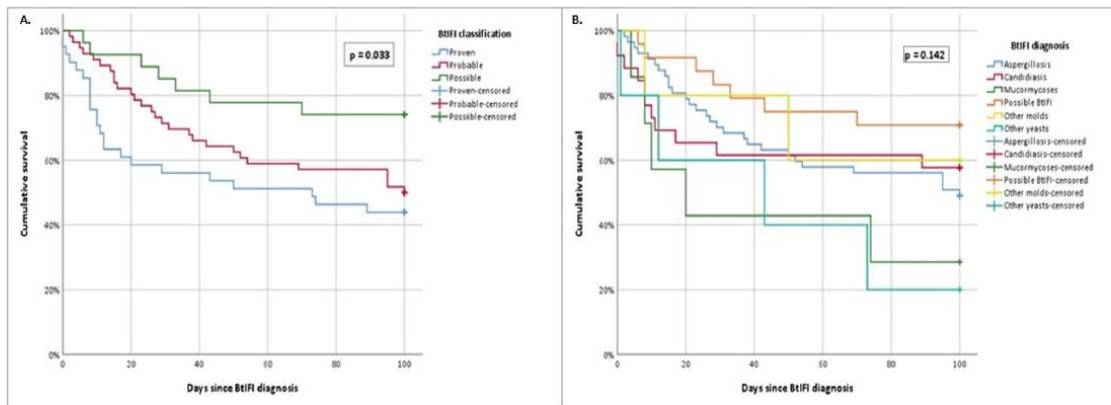
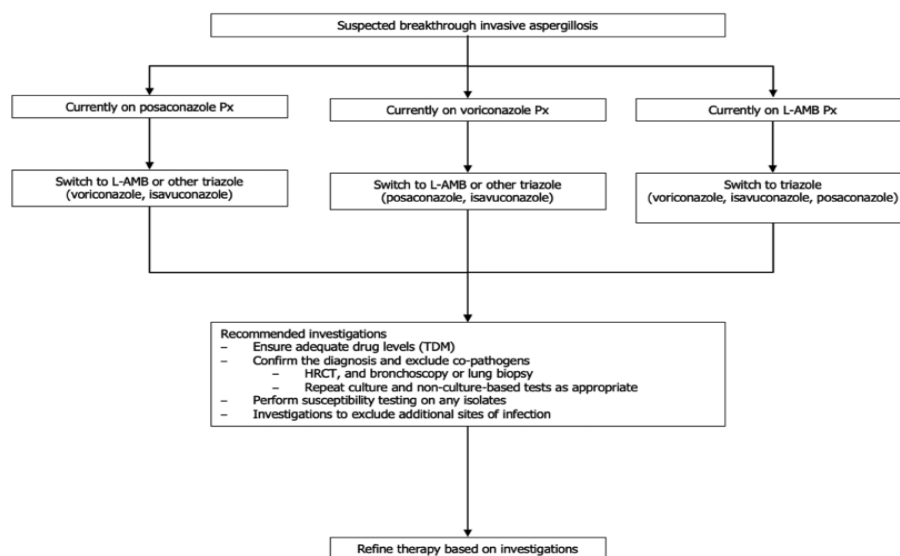


Fig. 2. Kaplan-Meier survival curves at 180 days based on breakthrough fungal infection classification (A) and diagnosis (B).

Puerta-Alcalde P, Monzó-Gallo P, Aguilar-Guisado M, et al. Breakthrough invasive fungal infection among patients with haematologic malignancies: A national, prospective, and multicentre study. J Infect. 2023;87(1):46-53.

Douglas et al.

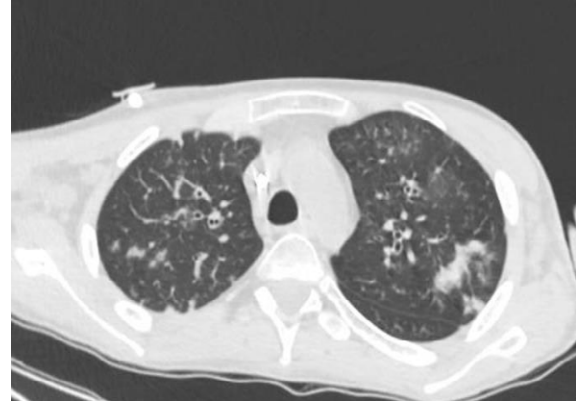
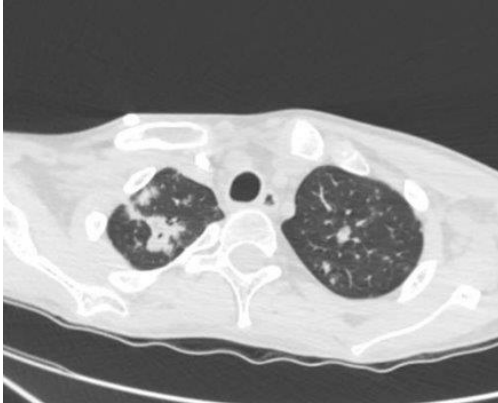


Douglas AP, Smibert OC, Bajel A, et al. Consensus guidelines for the diagnosis and management of invasive aspergillosis, 2021. Intern Med J. 2021;51 Suppl 7:143-176.

CASO CLÍNICO



- Se inició Isavuconazol 200 mg/8 horas las primeras 48 horas y posteriormente 200 mg/24 horas con buena tolerancia clínica y sin repercusión en el perfil hepático.
- En TAC de evaluación a las 3 semanas, se objetivan incremento de las lesiones nodulares pulmonares respecto al TAC diagnóstico.



PREGUNTA V



Ante el TAC de control, usted

- Iniciar biterapia con anfotericina B 3 mg/kg + anidulafungina.
- Mantener monoterapia con Isavuconazol ya que se trata de un posible efecto paradójico.
- Añadiría triple terapia con Anfotericina B 3 mg/kg + anidulafungina + Isavuconazol.
- La opción más lógica sería biterapia con anfotericina B 3 mg/kg + isavuconazol.

Received: 5 August 2018 | Revised: 3 October 2018 | Accepted: 7 October 2018
DOI: 10.1111/myc.12860

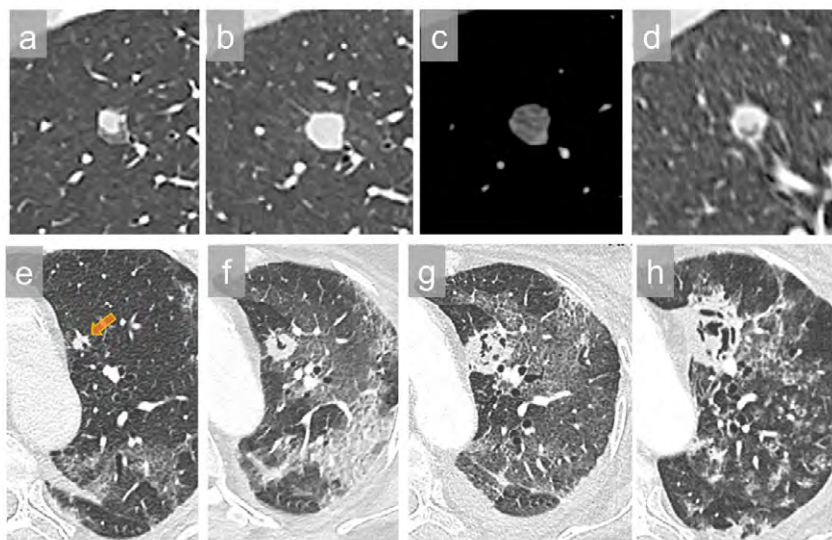
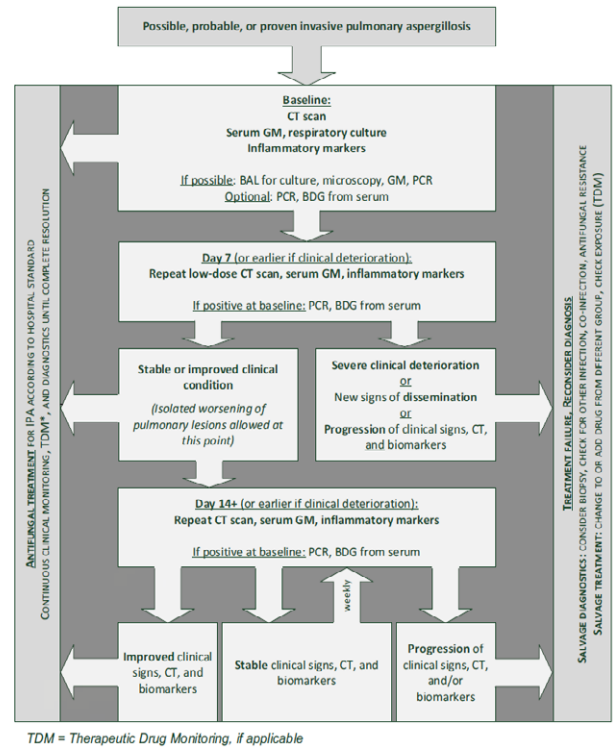
REVIEW ARTICLE

WILEY **mycoses**

Diagnostic work up to assess early response indicators in invasive pulmonary aspergillosis in adult patients with haematologic malignancies

Even under appropriate treatment, size and number of pulmonary lesions observed in a CT scan tend to increase before reaching a plateau, while actual radiologic remission may take weeks or months. Treatment-emergent cavities are suggestive of treatment response and associated with favourable survival outcomes,¹⁷ but they may prolong the time until complete radiological remission and may sometimes become a source of relapses.

Heinz WJ, Vehreschild JJ, Buchheidt D. Diagnostic work up to assess early response indicators in invasive pulmonary aspergillosis in adult patients with haematologic malignancies. *Mycoses*. 2019;62(6):486-493



CASO CLÍNICO



- Tras 6 semanas de tratamiento antifúngico, el paciente presenta un discreto ascenso de enzimas hepáticas a favor de colestasis.
- Tras comprobar interacciones con antifúngicos, se mantuvo tratamiento con isavuconazol y seguimiento estrecho de enzimas hepáticas con resolución progresiva.
- La situación clínica del paciente es de estabilidad, sin presentar clínica respiratoria ni otros datos de infección.
- Se solicitó TAC de control a las 8 semanas y, según hallazgos, se dirigió la duración del tratamiento.

MONITORIZACIÓN Y DURACIÓN DE TTO

c) Should we monitor treatment response? How?
Searched terms: Aspergillosis, *Aspergillus*, Response
Executive summary

1. Response assessment of antifungal therapy should be based on a composite of clinical, radiological and mycological criteria in an appropriate period evaluation (AI).
2. A follow-up chest CT scan is recommended to assess the radiological response of invasive aspergillosis to treatment after a minimum of 2 weeks of treatment (CIII).
3. Monitoring of serum galactomannan titers can be used in patients with hematological malignancies and hematopoietic stem cell transplantation recipients to assess therapeutic responses earlier and predict outcomes (AII).

13. – When should we stop treatment for invasive aspergillosis?
Searched terms: Aspergillosis, *Aspergillus*, Neutropenia, Solid organ transplant immunosuppression, Treatment, Therapy

Executive summary

1. Treatment for IA should be continued for a minimum of 6–12 weeks. The duration of the antifungal therapy should be individualized, depending on the degree and duration of neutropenia and other immunosuppressive conditions, the site of the disease, and evidence of disease improvement (BIII).

García-Vidal C, Alastruey-Izquierdo A, Aguilar-Guisado M, et al. Executive summary of clinical practice guideline for the management of invasive diseases caused by *Aspergillus*: 2018 Update by the GEMICOMED-SEIMC/REIPI. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2019;37(8):535-541.

PREGUNTA VI



Ante esta situación, usted decide

- a) Indicaría finalización de tratamiento a las 12 semanas.
- b) Realizaría TAC de control y según hallazgos, indicaría finalización de tratamiento.
- c) Realizaría PET/TAC de control y según hallazgos, indicaría finalización de tratamiento.
- d) La evolución favorable del paciente permite finalizar el tratamiento.

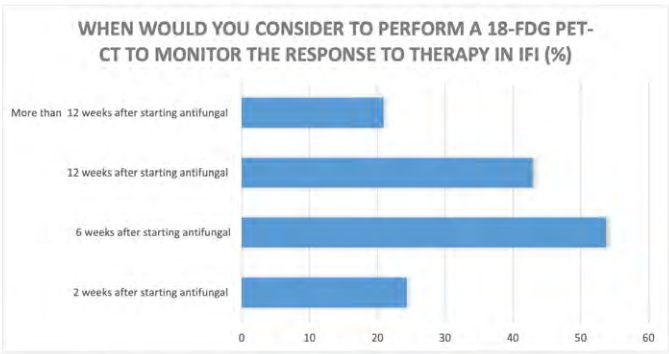
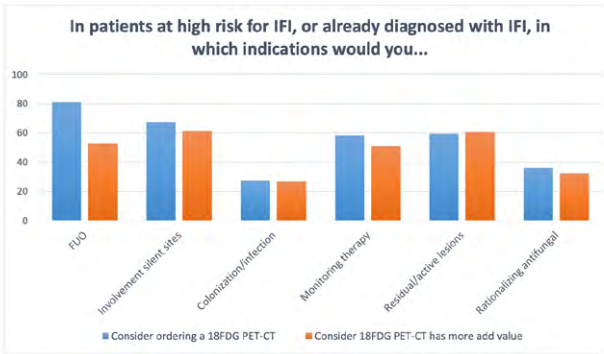
CASO CLÍNICO



El paciente completó un total de 14 semanas con Isavuconazol con recuperación completa clínica y radiológica.

EL ROL DEL PET/TAC

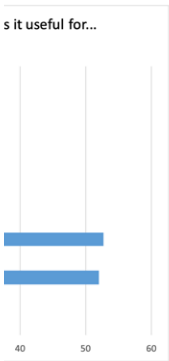
180 encuestados.
60,5% Enfermedades Infecciosas de España e Italia



Mycopathologia (2024) 189:84

Table 2 Areas of uncertainty regarding usefulness of 18F-FDG PET-CT for IFI management to be addressed by future research

Area	Evidence gap/research question	Required investigations
Diagnosis	Value of 18F-FDG PET-CT for the differential diagnosis between colonization and infection in patients with positive cultures from non-sterile sites	Prospective study that analyzes the results of performing 18F-FDG PET-CT to assess active lesions in patients with fungal isolates and whether it determines modification of management
	Value of 18F-FDG PET-CT for the differential diagnosis between bacterial and fungal infection	Multicenter registry that compares the type of uptake of the different etiologies
	Value of 18F-FDG PET-CT for the differential diagnosis between fungal species infection	Multicenter registry that compares the type of uptake of the different fungal species
	Value of 18F-FDG PET-CT for the differential diagnosis between cancer and fungal infection	Multicenter registry that compares the type of uptake of the different etiologies
Staging	Added value of 18F-FDG PET-CT performed at diagnosis to rule out or confirm dissemination	Head to head comparison with conventional techniques
Follow-up	Normal duration of glucose uptake in 18F-FDG PET-CT in the case of a good outcome, and to what extent is it influenced by immunological status	Serial 18F-FDG PET-CT at different time points in patients with different types of underlying immunocompromise and correlation with outcome
	Optimal timing of follow-up 18F-FDG PET-CT	Protocolized 18F-FDG PET-CT at different time points of IFI follow-up
	Optimal glucose uptake threshold to stop antifungals	Correlation of 18F-FDG PET-CT SUV values with clinical parameters and fungal biomarkers
Prognosis	18F-FDG PET-CT parameters such as TLG (total lesion glycolysis) and MV (metabolic volume) showed the ability to predict whether a patient will achieve a complete metabolic response	Prospective study that analyzes patient's outcome through these parameters
Efficiency	Disagreement about the indication of 18F-FDG PET-CT for IFI as compared to conventional imaging	Cost-effectiveness studies
	Lack of reimbursement of 18F-FDG PET-CT in this indication	



Mycopathologia (2024) 189:84

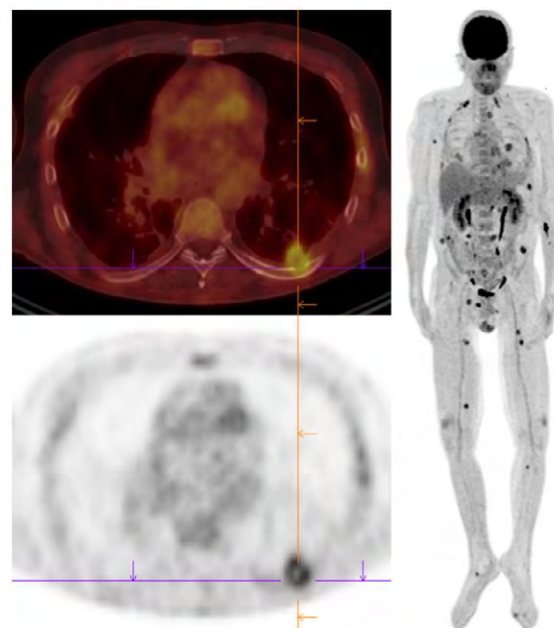
Table 1. ^{18}F -FDG PET/CT results obtained in the whole population and in patients with *Candida* spp. or *Aspergillus* spp. infection

	Nb. of patients	Nb. of PET/CT	PET/CT indication	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All aetiologies	51	83	Overall	93	81	95	72	90
	29	29	Primary staging	93	—	100	—	93
	22	54	Follow-up	92	81	92	81	89
<i>Aspergillus</i> spp.	23	39	Overall	97	63	91	83	90
	11	11	Primary staging	100	—	100	—	100
	28	28	Follow-up	95	63	86	83	86
<i>Candida</i> spp.	17	30	Overall	83	100	100	60	87
	13	13	Primary staging	85	—	100	—	85
	17	17	Follow-up	82	100	100	75	88

PPV, positive predictive value; NPV, negative predictive value.

Table 2. ^{18}F -FDG PET/CT results according to per-organ analysis and comparison with conventional imaging (CT/MR)

Pathogen (Nb. of patients)	Nb. of patients (%)	Nb. of PET/CT (%)	SUV _{max} mean $\pm$ SD (range) §	PET/CT vs. CI (per patient analysis)	Added value of ^{18}F -FDG PET/CT (per patient analysis)
Lung <i>Aspergillus</i> (27)	37 (73%)	44 (50%)	5.2 $\pm$ 3.6 (0.7–18.9)	PET/CT = CI: 14 PET/CT > CI: 5 PET/CT < CI: 1	Influence in diagnostic work-up ^a : 7 Treatment intensification ^b : 1 Treatment reduction ^c : 9
Liver <i>Candida</i> (7)	9 (18%)	13 (16%)	8.7 $\pm$ 4.6 (2.9–15.9)	PET/CT = CI: 5 PET/CT > CI: 4 PET/CT < CI: 0	Influence in diagnostic work-up ^a : 8 Treatment intensification ^b : 3 Treatment reduction ^c : 4
Spleen <i>Candida</i> (11)	12 (23%)	14 (17%)	5.8 $\pm$ 2.6 (2.8–10)	PET/CT = CI: 1 PET/CT > CI: 6 PET/CT < CI: 0	Influence in diagnostic work-up ^a : 3 Treatment intensification ^b : 0 Treatment reduction ^c : 4
Bone <i>Candida</i> (5)	6 (12%)	8 (10%)	6.3 $\pm$ 2.6 (3.5–10.8)	PET/CT = CI: 2 PET/CT > CI: 4 PET/CT < CI: 1	Influence in diagnostic work-up ^a : 5 Treatment intensification ^b : 3 Treatment reduction ^c : 3



QJM: An International Journal of Medicine, 2018, Vol. 111, No. 9

Clinical Microbiology and Infection xxx (xxxx) xxx

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Narrative review

How to safely discontinue antifungal treatment in invasive pulmonary aspergillosis?—clinical considerations in haematology

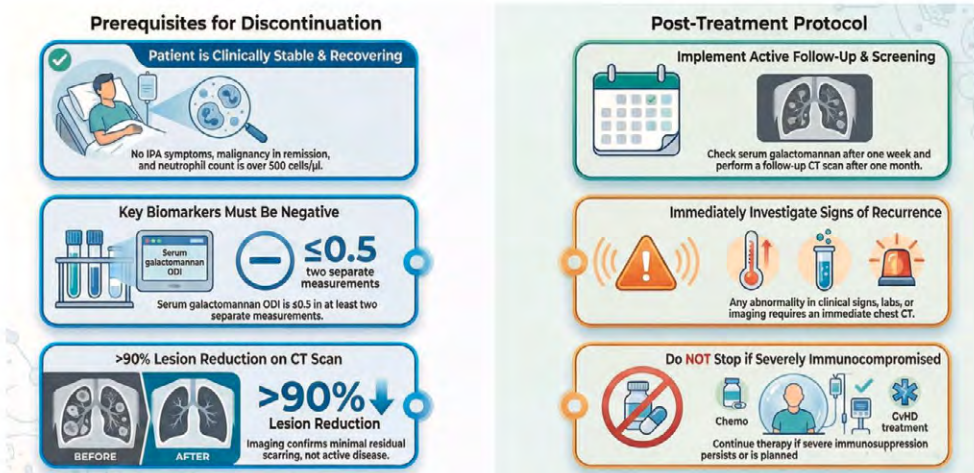


Fig. 1. Criteria to discontinue antifungal treatment and follow-up in patients with haematological malignancies

CONCLUSIONES

- Importancia de seleccionar bien la profilaxis adecuada según el paciente de riesgo.
- Diagnóstico de fungemia de brecha. Microbiología. Imprescindible la sospecha clínica. Hallazgos Radiológicos inespecíficos.
- Manejo terapéutico de la fungemia de brecha. ¡Especies y sensibilidades!
- Posible efecto paradójico en TAC de control: NO ENTRAR EN PÁNICO.
- Siempre comprobar interacciones de antifúngicos.
- En caso de duda, consulte con su infectólogo de confianza.

Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

ESCENARIO CLÍNICO DESAFIANTE: FIEBRE Y NEUTROPENIA

Bianca Rafaela Mendoza Zambrano

Complejo Asistencial Universitario de Segovia



3.º WORKSHOP
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INFECTHEMA

DESCRIPCIÓN DEL CASO CLÍNICO



Edad 35

Sexo Mujer

Diagnóstico LMA con mutación NPM1 — según la clasificación OMS 2022, con pronóstico favorable.

Situación Actual

Remisión completa tras inducción según esquema 3+7.

Motivo de Ingreso

1º consolidación según el mismo esquema.

Antecedentes Relevantes

- **Ingreso anterior:** Fiebre y enterocolitis neutropénica durante inducción → tratada con cefepime, meropenem y teicoplanina (*sin documentación microbiológica*) → resolución completa.
- **Previo a este ingreso:** Episodio de flebitis en MSD tratado con ácido fusídico y amoxicilina/clavulánico → resolución completa.



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INFECTHEMA

DESCRIPCIÓN DEL CASO CLÍNICO



Día +15 de consolidación



Neutropenia grado 4



Fiebre 39°C y escalofríos



Sin foco infeccioso evidente

✓ Amplia toma de cultivos + ATB empírica con **Cefepime 2g/8h** → Persistencia de fiebre → **Nuevos hallazgos de mucositis oral grado 1 + diarrea** (sin productos patológicos)

Aumento de parámetros inflamatorios

✓ **Cambio a Meropenem** por mala evolución y cobertura de posible foco abdominal → Persiste fiebre con escalofríos...



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INFECTHEMA

ESTUDIO DIAGNÓSTICO



ANALÍTICA SANGUÍNEA:

- **Hemograma:** Leucocitos $0,13 \times 10^3/\mu\text{L}$; **neutrófilos $0,02 \times 10^3/\mu\text{L}$** ; Hb 8,6 g/dL; Plaquetas $10 \times 10^3/\mu\text{L}$.
- **Bioquímica:** AST 24/UL; ALT 77/UL; GGT 57 U/L; FA 154 U/L; Bilirrubina total 1.9 mg/dL con 58% directa. **PCR 145 mg/L (N: <5 mg/L)**; procalcitonina 4.6 ng/mL (N:<0.5 ng/mL).



TC ABDOMINO-PÉLVICO:

- Realce de la mucosa de ciego y colon ascendente proximal compatible con enterocolitis de ciego-colon derecho.



Imágenes obtenidas del servicio de Radiología del HGSE

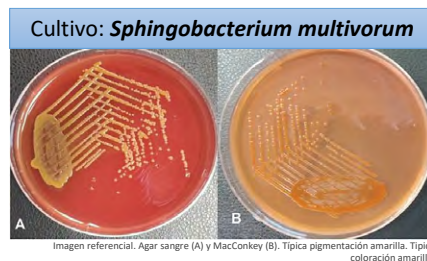


MICROBIOLOGÍA INICIAL:

- Urocultivo: negativo
- Hemocultivos: **positivos**



Tinción de gram: Bacilos gramnegativos



Cultivo: *Sphingobacterium multivorum*

Imagen referencial. Agar sangre (A) y MacConkey (B). Típica pigmentación amarilla. Típica coloración amarilla.

ESTUDIO DIAGNÓSTICO



ANALÍTICA SANGUÍNEA:

- **Hemograma:** Leucocitos $0,13 \times 10^3/\mu\text{L}$; **neutrófilos $0,02 \times 10^3/\mu\text{L}$** ; Hb 8,6 g/dL; Plaquetas $10 \times 10^3/\mu\text{L}$.
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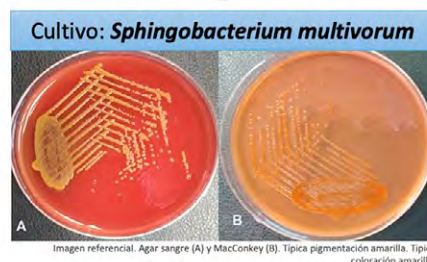
- Urocultivo: negativo
- Hemocultivos: **positivos**



Tinción de gram: Bacilos gramnegativos

Antibiograma inicial (*Sphingobacterium multivorum*):

- ✓ **Sensible a Trimetoprim/Sulfametoxazol**
- ✓ Resistente a Ceftazidima, Piperacilina/Tazobactam, Meropenem y Levofloxacina-lo que explicaba el fracaso terapéutico.



Cultivo: *Sphingobacterium multivorum*

Imagen referencial. Agar sangre (A) y MacConkey (B). Típica pigmentación amarilla. Típica coloración amarilla.



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INFECTHEMA

IDENTIFICACIÓN DEL AGENTE CAUSAL

La muestra fue enviada al laboratorio de referencia para la tipificación avanzada mediante:

MALDI-TOF MS

Espectrometría de masas por desorción/ionización láser asistida por matriz-tiempo de vuelo. Técnica **de referencia** para identificación de microorganismos difíciles de detectar con métodos convencionales.

RESULTADO FINAL

El agente causal fue reclasificado, diagnóstico final:
Bacteriemia por *Chryseobacterium indologenes* — bacilo gramnegativo no fermentador.

Perfil de resistencia de *C. Indologenes*



Resistencia intrínseca amplia:

- Múltiples β -lactámicos
- Carbapenémicos (incluido Meropenem)
- Cefalosporinas (Ceftazidima)
- Piperacilina/Tazobactam
- Fluoroquinolonas (Levofloxacina)



Sensible:

- Trimetoprim/Sulfametoxazol

El diagnóstico puede ser complejo mediante métodos convencionales, contribuyendo a su infradiagnóstico.

- ✓ Hemocultivos diferenciales positivos para el mismo microorganismo → confirma **bacteriemia relacionada con catéter PICC.**
- ✓ Frotis rectal: aislamiento de *Serratia marcescens* productora de KPC → medidas de aislamiento de contacto.



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INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

CONTEXTO CLÍNICO Y EPIDEMIOLÓGICO

Factores de Riesgo en esta Paciente



Neutropenia profunda y prolongada

Neutropenia grave → supresión medular 2º a quimioterapia intensiva.



Catéter venoso central (PICC)

Dispositivo intravascular → puerta de entrada y reservorio para microorganismos ambientales *C. indologenes*.



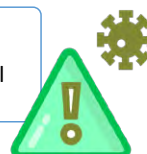
Exposición previa a antibióticos de amplio espectro

Tratamiento previo con carbapenémicos → favorece la selección de patógenos con resistencias intrínsecas, eliminando la flora competidora protectora.



Mucositis y enterocolitis neutropénica

Alteración de la barrera mucosa → facilita la translocación bacteriana de patógenos ambientales hacia el torrente sanguíneo.





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EN HEMATOLOGÍA

INFECTHEMA

DIAGNÓSTICO DIFERENCIAL Y ENFOQUE CLÍNICO

Una estrategia efectiva para abordar la neutropenia febril requiere distinguir entre los patógenos más comunes y aquellos con perfiles de resistencia complejos.

1

PATÓGENOS HABITUALES

Responden a antibioterapia estándar

- *Pseudomonas aeruginosa*
- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Staphylococcus aureus* / SCN

2

NO FERMENTADORES RAROS

Resistencias intrínsecas, requieren identificación temprana

- ***Chryseobacterium indologenes* ✓**
- *Stenotrophomonas maltophilia*
- *Acinetobacter* spp.
- *Burkholderia cepacia*

3

HONGOS (SI PERSISTE >72-96H)

Considerar si no hay respuesta a antibióticos

- *Candida* spp.
- *Aspergillus* spp.
- Mucormicosis

Clave Clínica

La falta de respuesta a la antibioterapia empírica estándar debe alertar sobre patógenos con resistencias intrínsecas o inusuales. La identificación microbiológica temprana y el antibiograma son determinantes para optimizar el tratamiento.



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INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

TRATAMIENTO Y EVOLUCIÓN

Antibioterapia empírica

Cefepime → Meropenem por fallo inicial.

Control del foco

Retirada de PICC → hemocultivos diferenciales positivos.

Antibiograma disponible

Sensible a TMP/SMX → cambio dirigido

Resolución clínica

Afebril a las 24h → 14 días TMP/SMX, alta.

Pilares del Tratamiento

- 1 Antibioterapia dirigida**
TMP/SMX como 1ª línea, dada sensibilidad de *C. indologenes*.
- 2 Retirada precoz del PICC**
En bacteriemias asociadas a dispositivos intravasculares, es tan importante como el tratamiento antibiótico dirigido.
- 3 Medidas de aislamiento**
Aislamiento de contacto por colonización rectal con *Serratia marcescens* productora de KPC. Vigilancia epidemiológica activa.



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EN HEMATOLOGÍA

INFECTHEMA

DISCUSIÓN

La bacteriemia en pacientes con LMA sometidos a quimioterapia intensiva constituye una complicación grave, especialmente en el contexto de neutropenia profunda y prolongada, con **morbimortalidad del 20–40%**.

C. indologenes

Infección nosocomial

Las infecciones por *C. indologenes* son principalmente nosocomiales, asociadas a **dispositivos intravasculares, ventiladores y soluciones de agua** dentro de hospitales.

Patógeno oportunista

Afecta a pacientes con enfermedad subyacente grave, exposición prolongada a antibióticos, hospitalización prolongada, inmunodeprimidos, etc.

Resistencia intrínseca

Bacilo gramnegativo no fermentador con **amplio perfil de resistencia intrínseca** (múltiples β -lactámicos incluidos carbapenémicos), mediada por **metalo- β -lactamasas** y otros mecanismos.

Reto diagnóstico

El diagnóstico puede ser complejo con métodos convencionales. **MALDI-TOF MS y métodos moleculares** son clave para su identificación y contribuyen a reducir su infradiagnóstico.



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EN HEMATOLOGÍA

INFECTHEMA

CONCLUSIONES Y MENSAJES PARA LLEVAR

Los **patógenos emergentes** como *Chryseobacterium indologenes*, aunque infrecuentes, representan un reto real en pacientes de alto riesgo. La **identificación temprana, el ajuste antibiótico dirigido y el control del foco** son los determinantes clave para mejorar la supervivencia en neutropenia febril con mala respuesta empírica.

Alto índice de sospecha clínica



Ante la **falta de respuesta a la antibioterapia empírica estándar**. El cambio precoz a tratamiento dirigido es determinante para mejorar el pronóstico.

Abordaje multidisciplinar



La complejidad microbiológica exige coordinación entre **Hematología, Microbiología e Infectología**, junto con medidas de vigilancia epidemiológica y control de infección nosocomial.

Técnicas microbiológicas avanzadas



La implementación de **MALDI-TOF MS** y métodos moleculares facilita la identificación de patógenos emergentes como *C. indologenes*. El acceso a laboratorios de referencia es esencial.

Prevención



Control ambiental, correcta higiene de manos y precauciones de barrera, vigilancia microbiológica activa, profilaxis antimicrobiana, uso racional de antibióticos, etc.



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INFECTHEMA

REFERENCIAS BIBLIOGRÁFICAS

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- Chang J, Kim S, Kwak YG, Um TH, Cho CR, Song JE. Clinical and Microbiological Characteristics of Chryseobacterium indologenes Bacteremia: A 20-Year Experience in a Single University Hospital. Infection and Chemotherapy. 2023;55.
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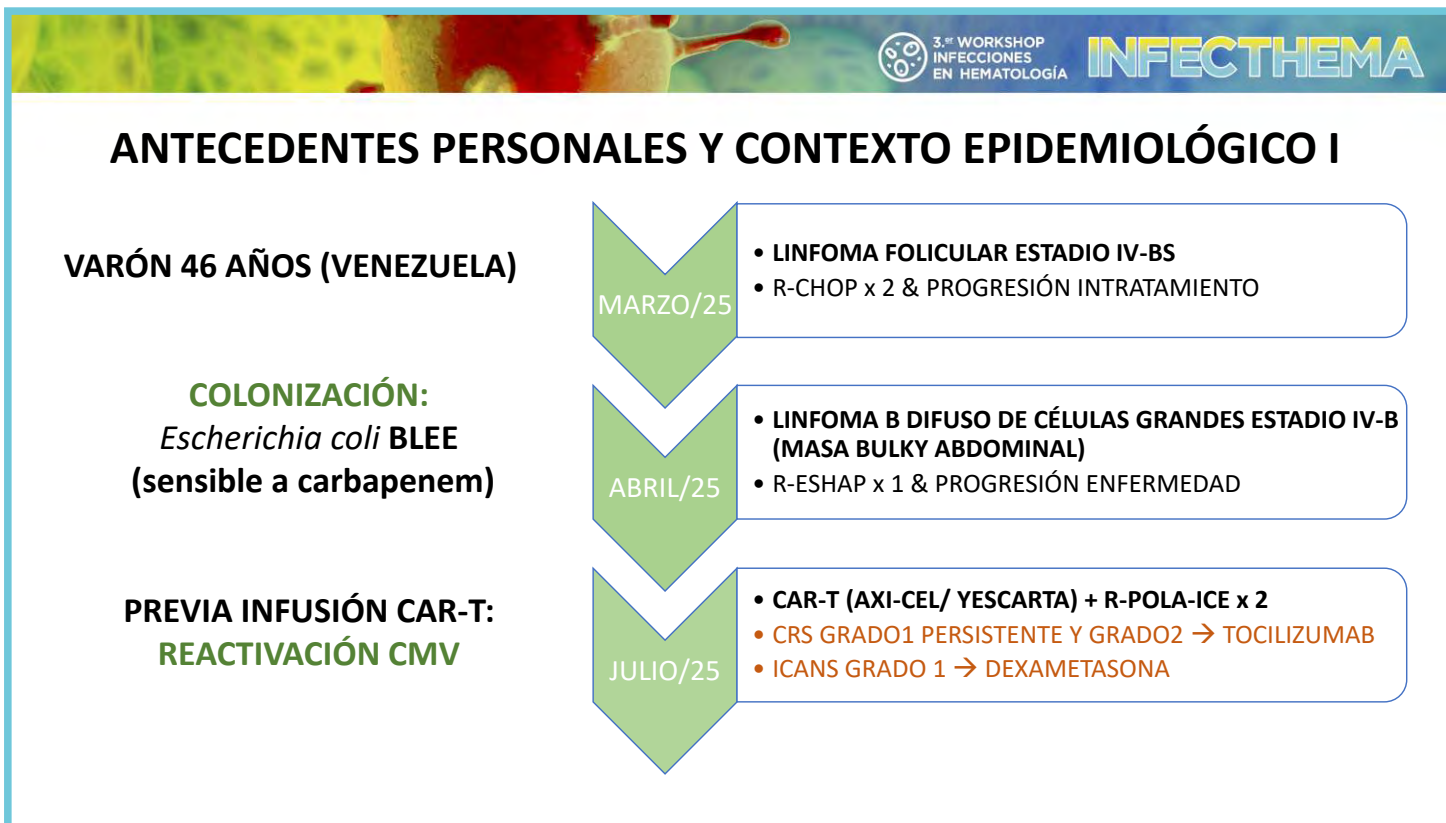
INFECTHEMA

Valencia, 16 y 17 de abril de 2026

FIEBRE EN EL PRIMER MES POST-INFUSIÓN DE CART-T

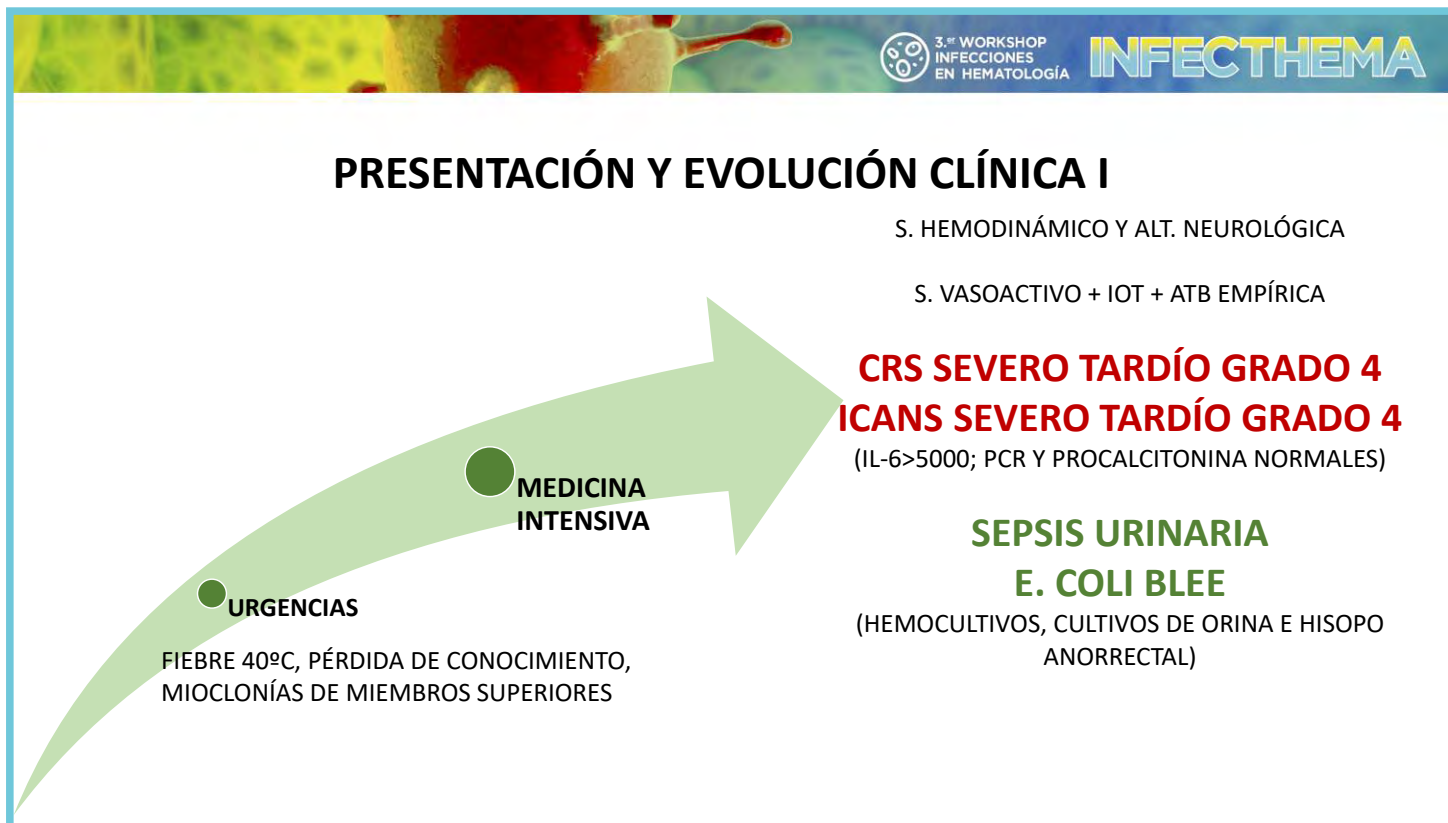
Soler Pérez, Miguel

Hospital Universitario Reina Sofía de Córdoba

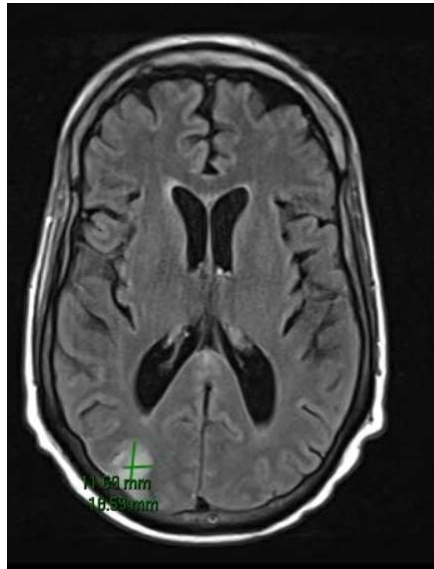
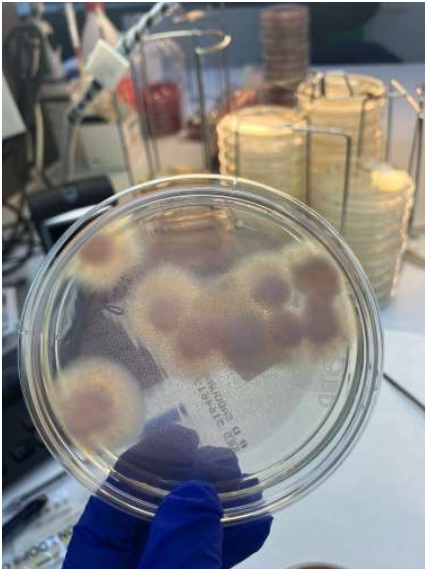


ANTECEDENTES PERSONALES Y CONTEXTO EPIDEMIOLÓGICO II

DÍA POST-INFUSIÓN	CÉLULAS CAR-T	VALOR DE IL-6
DÍA 0	-	45.09
DÍA +7	25/microlitro CD3+:12% [3/μL] Células CAR-T.	24814.64
DÍA +14	26/ microlitro CD3+ (11% CAR-T; 3/microlitro).	240
DÍA +21	Se detecta un 19% de células CAR-T+, estudio de subpoblaciones no evaluable teniendo en cuenta bajo numero de eventos.	258.88
DÍA +28	No es posible realización de inmunofenotipo debido al bajo recuento celular.	2786.69



PRESENTACIÓN Y EVOLUCIÓN CLÍNICA III



AISLAMIENTOS MICROBIOLÓGICOS:

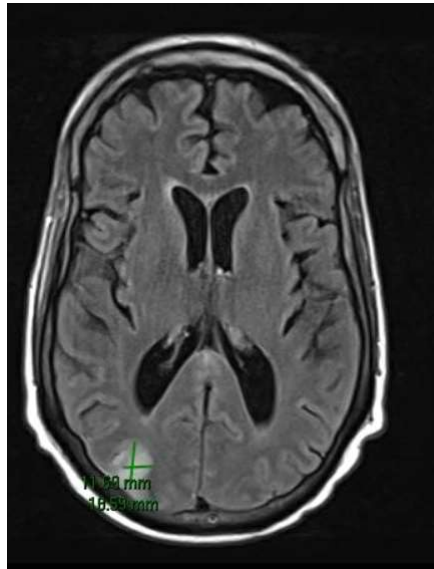
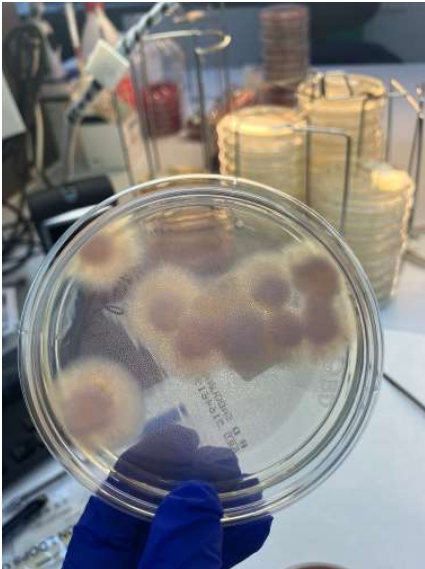
- 1.-*FUSARIUM PROLIFERATUM*
(ESPUTO Y PIEL)
- 2.-*ESCHERICHIA COLI* BLEE
(HEMOCULTIVOS)
- 3.-*ENTEROCOCCUS FAECIUM*
(HEMOCULTIVOS Y UROCULTIVOS)

FIEBRE PERSISTENTE
EMBOLOS SÉPTICOS
BILATERALES

CONCLUSIONES



PRESENTACIÓN Y EVOLUCIÓN CLÍNICA III



AISLAMIENTOS MICROBIOLÓGICOS:

- 1.-*FUSARIUM PROLIFERATUM*
(ESPUTO Y PIEL)
- 2.-*ESCHERICHIA COLI* BLEE
(HEMOCULTIVOS)
- 3.-*ENTEROCOCCUS FAECIUM*
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FIEBRE PERSISTENTE
EMBOLOS SÉPTICOS
BILATERALES

CONCLUSIONES





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EN HEMATOLOGÍA



INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Infiltrados pulmonares extensos y rápido deterioro respiratorio en un paciente con LMA

Uxía Taboada Rodríguez

Complejo Hospitalario Universitario A Coruña



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INFECTHEMA

Presentación del caso clínico

VARÓN DE 35 AÑOS

ALERGIAS

Sin alergias medicamentosas conocidas

FRCV

Sin factores de riesgo cardiovascular

ANTECEDENTES PERSONALES

No antecedentes médico-quirúrgicos relevantes

SITUACIÓN FUNCIONAL

IABVD
Funciones cognitivas superiores conservadas.
Trabaja de electricista.



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INFECTHEMA

MOTIVO DE CONSULTA

Ingres a el 6 de julio por síndrome constitucional de varias semanas de evolución, astenia intensa, pérdida de peso no cuantificada, sudoración profusa y febrícula.

EXPLORACIÓN FÍSICA

Eupneico.
Adenopatías laterocervicales e inguinales subcentimétricas y leve esplenomegalia.

CONSTANTES

Tª 38.4°
TA: 100/67
FC: 120 lpm
SatO2 basal 96%



HEMATOLOGÍA-Hematimetría

Leucocitos	147.8	x 10 ⁹ /L	[4.0 - 11.5]*
Hemoglobina	6.5	g/dL	[13.0 - 18.0]*
Plaquetas	22.0	x 10 ⁹ /L	[130.0 - 450.0]*
LUC/LYC	82.7	%	[0.0 - 5.0]*
Linfocitos	7.06	x 10 ⁹ /L	[1.0 - 4.0]*
Monocitos	5.31	x 10 ⁹ /L	[0.2 - 1.0]*
Neutrófilos	10.97	x 10 ⁹ /L	[2.5 - 7.5]*
Eosinófilos	0.19	x 10 ⁹ /L	[0.0 - 0.4]
Basófilos	2.02	x 10 ⁹ /L	[0.0 - 0.2]*
VSG 1ª hora	26.0	mm	[1.0 - 20.0]*

HEMATOLOGÍA-Coagulación (A.C.)

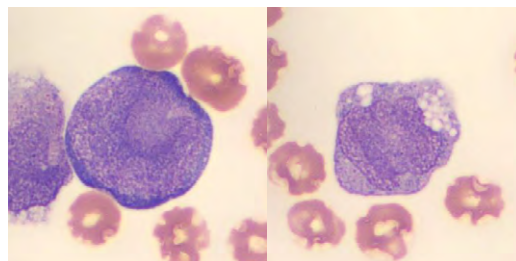
T.P. (cociente)	1.63	[0.85 - 1.2]*
TTPA (cociente)	1.15	[0.85 - 1.3]
I.N.R.	1.61	[-]
	2 - 3: Rango bajo	
	2.5 - 3.5: Rango alto	
	<1.7 o >5: Ver tabl	
Fibrinógeno	168.0	mg/dL [170.0 - 470.0]*

BIOQUÍMICA-Sero / Plasma

Glucosa	93.0	mg/dL	[70.0 - 110.0]
Urea	49.0	mg/dL	[10.0 - 50.0]
Creatinina	1.68	mg/dL	[0.72 - 1.18]*
Acido Úrico	<0.5	mg/dL [Valor Ref.: 3.4-7.0]	
Sodio	138.0	mEq/L	[135.0 - 145.0]
Potasio	3.1	mEq/L	[3.5 - 5.0]*
Cloro	101.0	mEq/L	[98.0 - 108.0]
Proteínas totales	7.1	g/dL	[6.0 - 8.0]
Albumina (verde de bromocresol)	2.8	g/dL	[3.5 - 5.0]*
Bilirrubina Total	0.98	mg/dL	[0.1 - 1.3]
Fosfatasa Alcalina	144.0	U/L	[46.0 - 116.0]*
LDH	1068.0	U/L	[120.0 - 246.0]*
GOT (AST)	173.0	U/L	[5.0 - 40.0]*
GPT (ALT)	249.0	U/L	[5.0 - 45.0]*
GGT	141.0	U/L	[8.0 - 61.0]*
Amilasa	49.0	U/L	[30.0 - 118.0]

Se observa un 23% de promonocitos y monoblastos (alguna célula se ha observado con invaginación nuclear tipo "cup cell") y un 70% de monocitos. No se observan bastones de Auer ni astillas.

Frotis de sangre periférica sugiere leucemia aguda mieloide con diferenciación monoblástica/monocítica



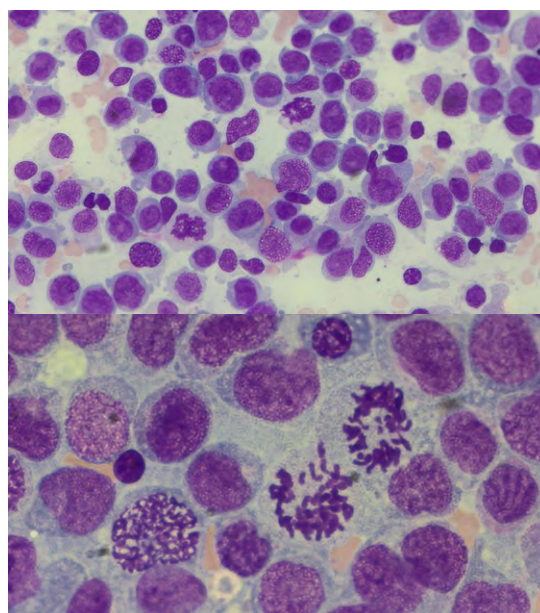
INGRESO EN HEMATOLOGÍA

TRATAMIENTO INICIAL

- 1) Profilaxis síndrome lisis tumoral
- 2) Citorreducción con hidroxiurea
- 3) Soporte transfusional

REALIZACIÓN DE ESTUDIO

- 1) Aspirado de MO
- 2) Citometría de flujo
- 3) Genética
- 4) Muestras para Pethema

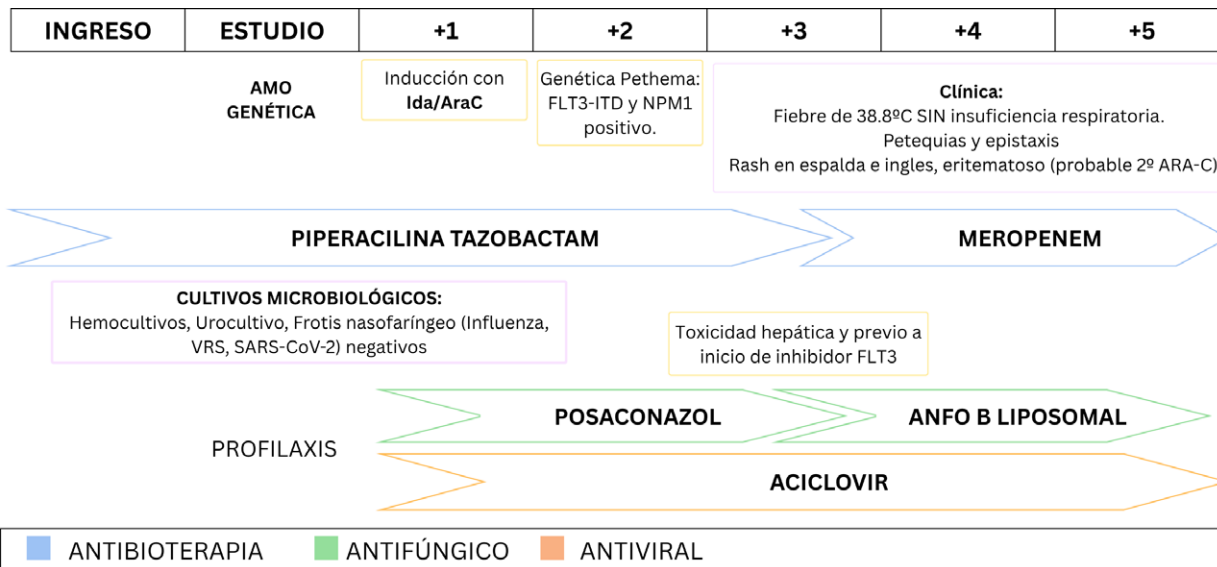




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EN HEMATOLOGÍA

INFECTHEMA

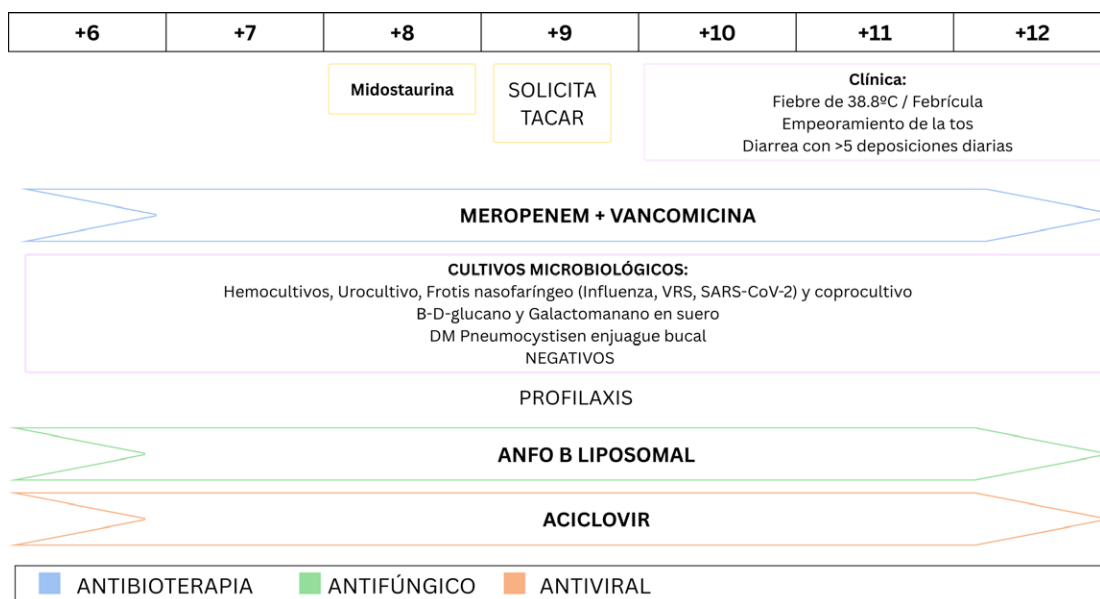
1 SEMANA DE INGRESO



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INFECTHEMA

2 SEMANA DE INGRESO

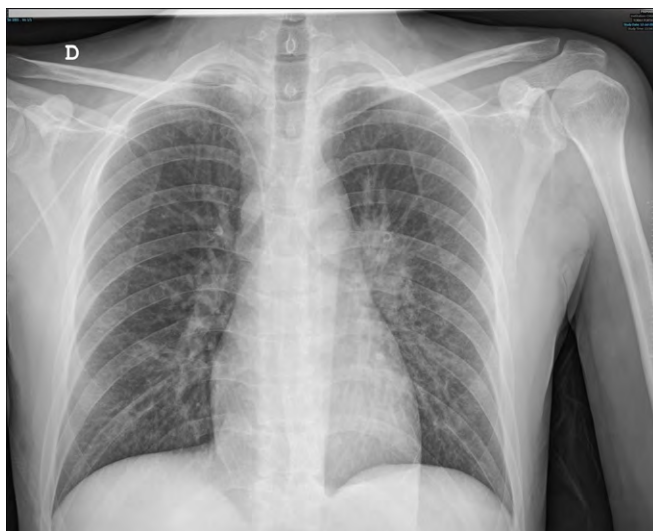




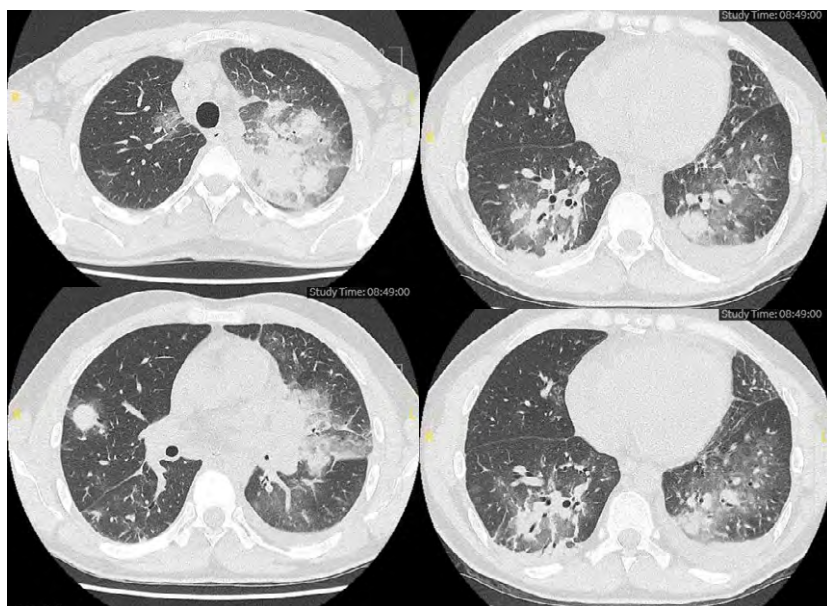
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INFECTHEMA

¿Fiebre infecciosa vs. Tumoral vs. Farmacológica?



TACAR



Consolidación parenquimatosa con **broncograma aéreo** que ocupa prácticamente todo el lóbulo superior izquierdo.

En el resto de los lóbulos se observan **lesiones parcheadas redondeadas con halo en vidrio deslustrado** y tendencia a la coalescencia.

Los hallazgos son compatibles con **proceso inflamatorio/infeccioso**, dada la patología de base del paciente no podemos descartar sangrado asociado.



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INFECTHEMA

FBC



Broncoscopia diagnóstica:

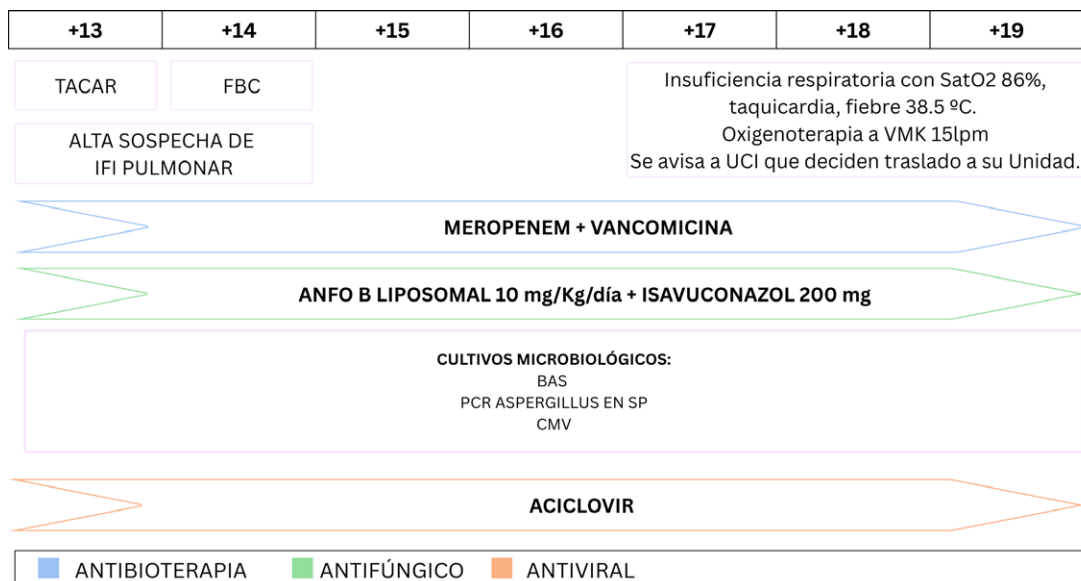
Disminución del calibre en el bronquio principal izquierdo y edema, con lesiones mamelonadas en mucosa, e imposibilidad para acceder a los diferentes bronquios segmentarios, no siendo posible realizar un lavado broncoalveolar y obteniéndose solamente muestra de broncoaspirado.



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INFECTHEMA

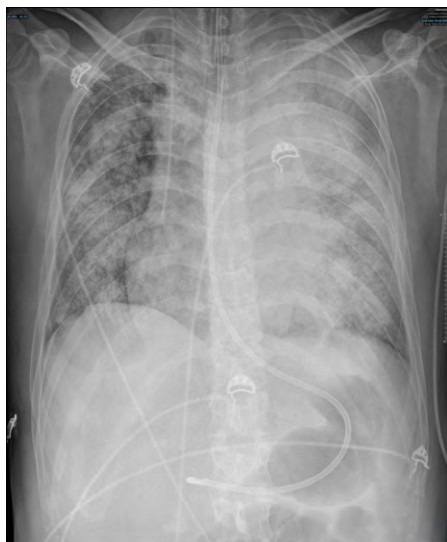
3 SEMANA DE INGRESO





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INFECTHEMA



MICROBIOLOGÍA:

- Examen en fresco calcoflúor
 - Se observan hifas tabicadas
- Cultivo de Hongos:
 - Positivo
- Solicitud de estudio molecular en centro externo:
 - Instituto de Salud Carlos III



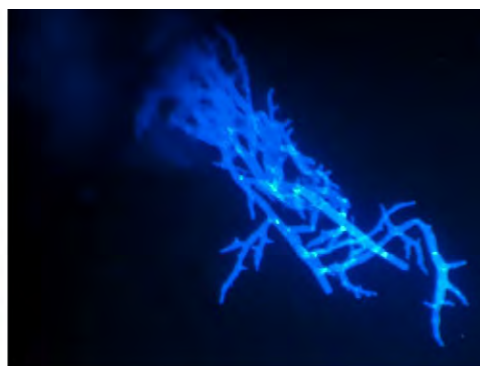
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INFECTHEMA

MICROBIOLOGÍA



MICROSCOPIO ÓPTICO



CALCOFLÚOR

ANTIFÚNGICO

CMI

Anfotericina B	12
Itraconazol	4
Voriconazol	> 32
Posaconazol	2
Isavuconazol	8
Candinas	> 32

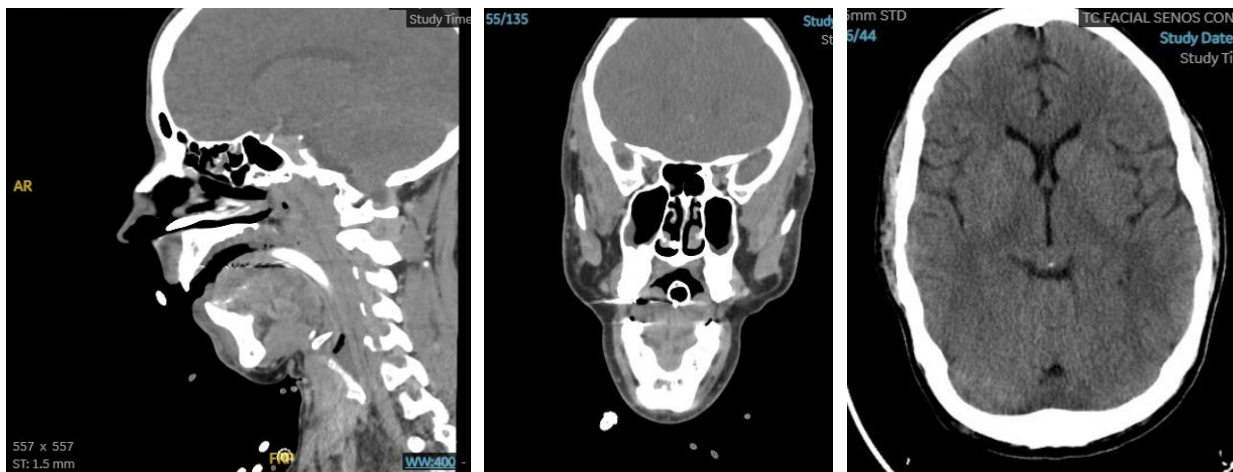
Cunninghamella bertholletiae



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INFECTHEMA

Completamos el estudio



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INFECTHEMA

00	00	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
----	----	---	---	---	---	---	---	---	---	---	----	----	----	----	----	----	----	----	----	----	----	----

Clínica del paciente:

Fiebre persistente + tos + aislada hemoptisis secundaria a trombocitopenia severa

Ingreso en UCI por insuficiencia respiratoria

PIPERACILINA
TAZOBACTAM

MEROPENEM

MEROPENEM + VANCOMICINA

POSACONAZOL
Profilaxis

ANFOTERICINA B LIPOSOMAL
Profilaxis

ANFO B LIPO + ISAVUCONAZOL

Aciclovir en Profilaxis

Inducción con Ida/AraC

TACAR
extensa consolidación en
lóbulo superior izquierdo,
múltiples lesiones
parcadas bilaterales
con halo en vidrio
deslustrado.

Fibrobroncoscopia
en la UCI

Cultivo de hongos BAS:
Se aísla *Cunninghamella bertholletiae*

El paciente presenta situación de:

1. Shock con necesidad de aminas vasoactivas.
2. Pancytopenia con soporte diario.
3. Fracaso renal oligúrico con soporte con hemodiafiltración venovenosa continua.
4. Fibrilación auricular que no responde a cardioversión eléctrica ni farmacológica.
5. Insuficiencia respiratoria

En shock profundo y distrés respiratorio severo que condiciona el fallecimiento en UCI.

ANTIBIOTERAPIA

ANTIFÚNGICO

ANTIVIRAL





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INFECTHEMA

EPIDEMIOLOGÍA DE LA MUCORMICOSIS

MUCORMICOSIS

Infección oportunista causada por hongos filamentosos del orden Mucorales

VÍAS DE INFECCIÓN

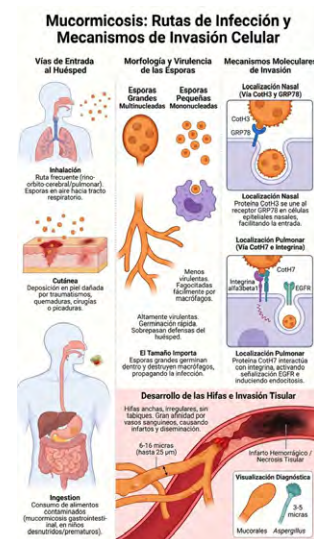
Inhalación de esporas de Mucorales a través de las vías respiratorias
Ingestión de alimentos contaminados
Invasión a través de heridas cutáneas

INCIDENCIA EN EUROPA

<0.04 - 0.12 por 100.000 habitantes/año

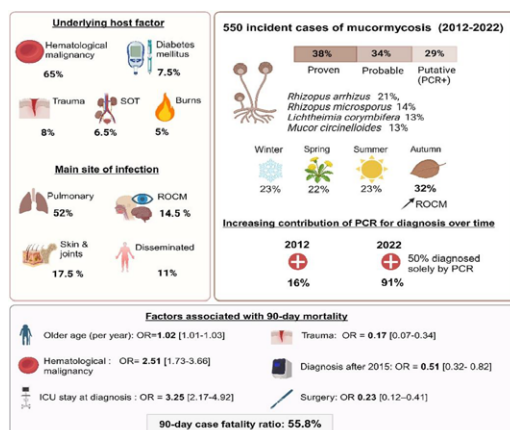
- Mayor incidencia en países como España, Francia, Bélgica y Suiza

Mei Liang, Jian Xu, Yanan Luo & Junyan Qu (2024) Epidemiology, pathogenesis, clinical characteristics, and treatment of mucormycosis: a review, *Annals of Medicine*, 56:1, 2396570, DOI: 10.1080/07853890.2024.2396570



Epidemiology and prognostic factors of mucormycosis in France (2012–2022): a cross-sectional study nested in a prospective surveillance programme

Laura Gouzien,^{a,b} Didier Che,^c Sophie Cassaing,^{d,e} Olivier Lortholary,^{a,c,f} Valérie Letscher-Bru,^{f,g,h} Olivier Paccoud,^c Thomas Obadia,^{a,m} Florent Morio,^h Maxime Moniot,ⁱ Estelle Cateau,^j Marie Elisabeth Bougnoux,^{k,l} Taleb Chouaki,^m Lilia Hasseine,ⁿ Guillaume Desoubreux,^{o,p} Cecile Gautier,^q Caroline Mahinc-Martin,^q Antoine Huguenin,^{r,s} Julie Bonhomme,^t Karine Sitbon,^u Julien Durand,^c Alexandre Alania,^{a,u,v,w} Laurence Millon,^{x,y,z} Dea García-Hermoso,^{a,z} and Fanny Lanterrier,^{a,b,e,z} the French Mycoses Study Group



MORTALIDAD

Pacientes hematológicos a 90 días es del 64%

PERFIL DEL PACIENTE

- LAM 62,5%
- Neutropenia reciente 72,6%
- Alo-TPH 31,5%

The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports

W. Jeong¹, C. Keighley^{2,3}, R. Wolfe⁴, W.L. Lee¹, M.A. Slavin^{5,6}, D.C.M. Kong^{1,7,8}, S.C.-A. Chen^{2,3,*}

CUNNINGHAMELLA SPP

Más frecuentes en pacientes con:

- Enfermedad pulmonar (57 % frente a 20 %; $p < 0,001$)
- Enfermedad diseminada (33 % frente a 13 %; $p < 0,002$)

MORTALIDAD

Fue significativamente mayor que la causada por otros Mucorales (71 % frente a 44 %; $p < 0,001$)

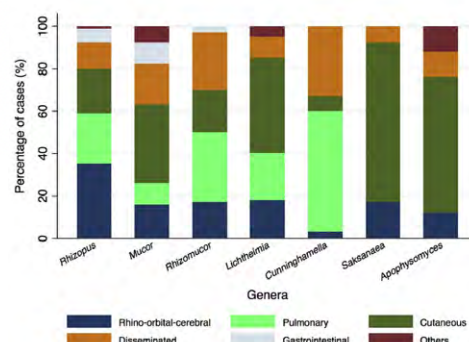
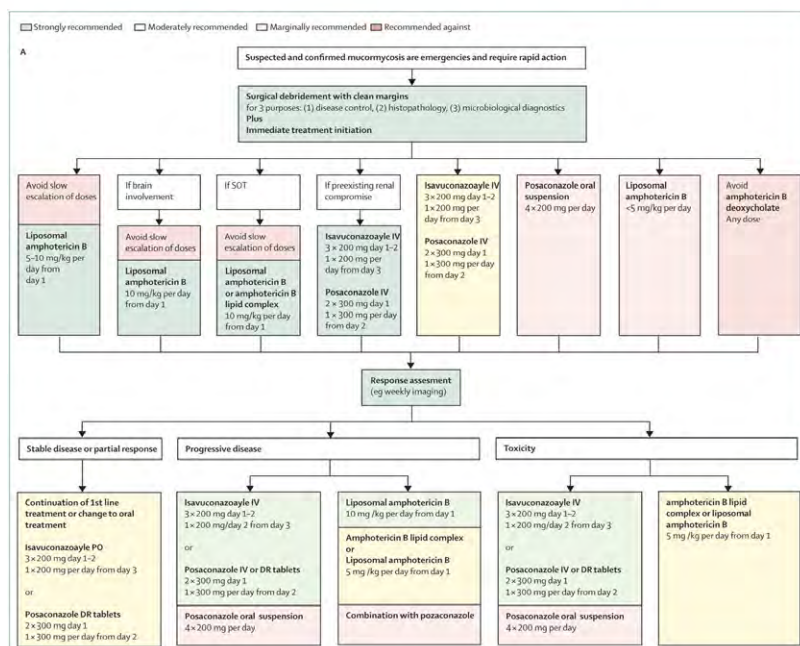


Fig. 2. Genera of causative Mucorales organism according to disease manifestations.

MUCOR	N = 821	MORTALIDAD
<i>Rhizopus</i>	213	(101) 47%
<i>Mucor</i>	63	(26) 41%
<i>Lichtheimia</i>	60	(21) 35%
<i>Cunninghamella</i>	30	(23) 77%
<i>Apophysomyces</i>	34	(15) 44%
<i>Rhizomucor</i>	28	(11) 39%
<i>Saksenaea complex</i>	7	(5) 71%

Published in final edited form as:
Lancet Infect Dis. 2019 December ; 19(12): e405–e421. doi:10.1016/S1473-3099(19)30312-3.

Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium



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EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

**Retinitis en paciente con mieloma múltiple en
tratamiento con anticuerpo biespecífico antiBCMA**

Diana Casares Aguiar

Hospital General Universitario Gregorio Marañón, Madrid



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INFECTHEMA

Presentación del caso



Varón de 43 años,
Mieloma Múltiple IgG-kappa (2022).

1L VRd (RP) + TASPE MEL 200 (VGPR).

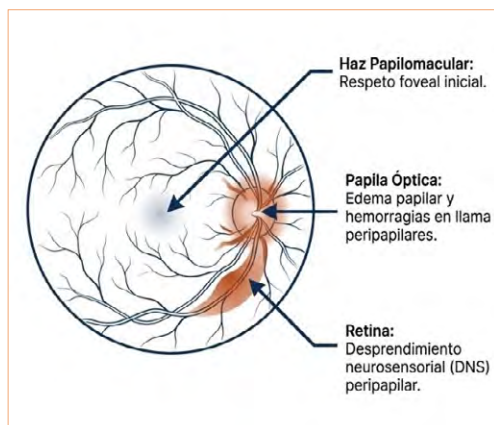
- TVP yugular asociada a catéter
- TEP segmentario de bajo riesgo

Mantenimiento: **antiBCMA (EC) → RC EMR-**

- Reactivaciones de CMV: tratamiento anticipado
- Hipogammaglobulinemia severa: inmunoglobulinas periódicas.

No otras enfermedades crónicas.
No antecedentes epidemiológicos de interés.
Profilaxis con Aciclovir y SMX-TMP.
Vacunas: SARS-CoV2, Influenza.

Motivo de consulta:
Escotoma campo temporal superior OI.



Exploración neurológica normal. ICE 10/10.



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INFECTHEMA

Estudios iniciales

Pruebas complementarias:

- **TC craneal** sin alteraciones.
- **RMN craneal/órbitas** sin alteraciones.
- **Punción lumbar:** Presión de partura elevada (26cmH2O). BQ normal. CMF-. **→Microbiología**
- **Anticuerpos onconeuronales** negativos.
- **Potenciales evocados visuales** anodinos.
- **PCR virus JC.**

LCR:

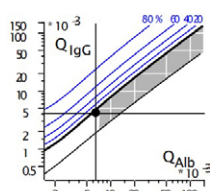
PCR VHS-1
PCR HSV2
PCR VVZ
PCR CMV
PCR VEB
PCR VHH-6
PCR VHH-7
PCR Adenovirus
PCR Parechovirus
PCR Parotiditis
PCR Parvovirus B19
PCR Enterovirus
PCR T. whipplei
PCR toxoplasma
Cultivo bacteriológico
Cultivo de hongos
Cultivo de micobacterias

Serología neuroborreliosis

Borrelia IgM (CLIA) - LCR
Borrelia IgG (CLIA) - LCR

Serología neurosífilis

Screening Treponémico (CLIA) - LCR
VDRL (LÁTEX) - LCR



Proteínas normales en el LCR



Neuritis óptica isquémica anterior



Neurotoxicidad por antiBCMA



Hipertensión intracraneal



Infiltración MM



Etiología infecciosa



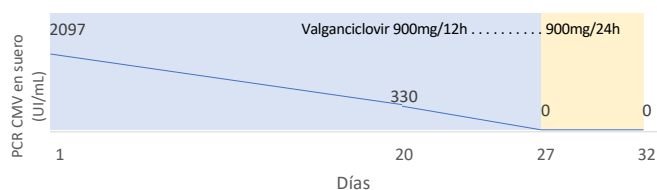
AAS 100mg



Prednisona 1mg/kg/día



STOP antiBCMA





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INFECTHEMA



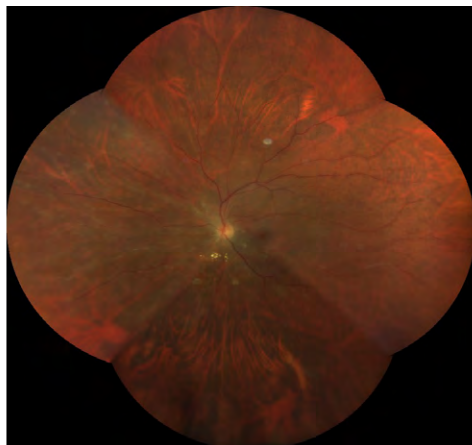
RETINITIS POR CITOMEGALOVIRUS

Reevaluación por Retina:

Evidencia de nuevos focos de retinitis en haz papilomacular y vasculitis nasal.
Tyndall positivo. Hipertensión ocular (28mmHg).



Viremia CMV 3838 UI/mL



VALGANCICLOVIR oral a dosis terapéuticas.

Negativización rápida de
la carga viral en sangre

Cese de la actividad inflamatoria.
Inicio de cicatrización retineana.

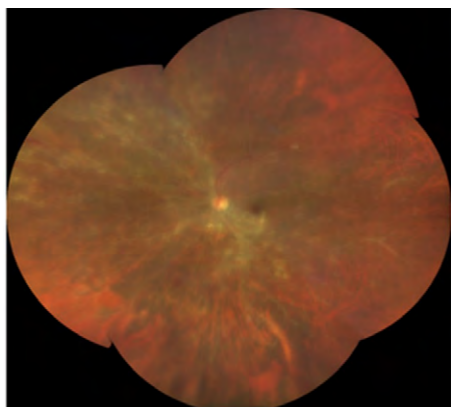
Suspensión a las 12 semanas de tratamiento ininterrumpido

Secuela inicial: Atrofia residual del haz papilomacular confirmada por OCT.



3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA



A las 3 semanas de suspender el valganciclovir, **empeoramiento súbito:**
vitritis severa, vasculitis florida y extensión a la arcada temporal inferior.

Sospecha de recidiva

¿IRIS/reconstitución inmune?

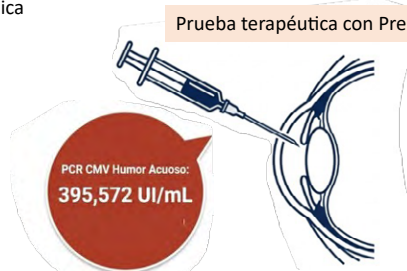
Vacuna VVZ , infusión de inmunoglobulinas

Reinicio de VALGANCICLOVIR... pero:

- Exploración oftalmológica atípica
- Carga viral reciente negativa

Viremia 786 UI/mL

Prueba terapéutica con Prednisona 30mg/día

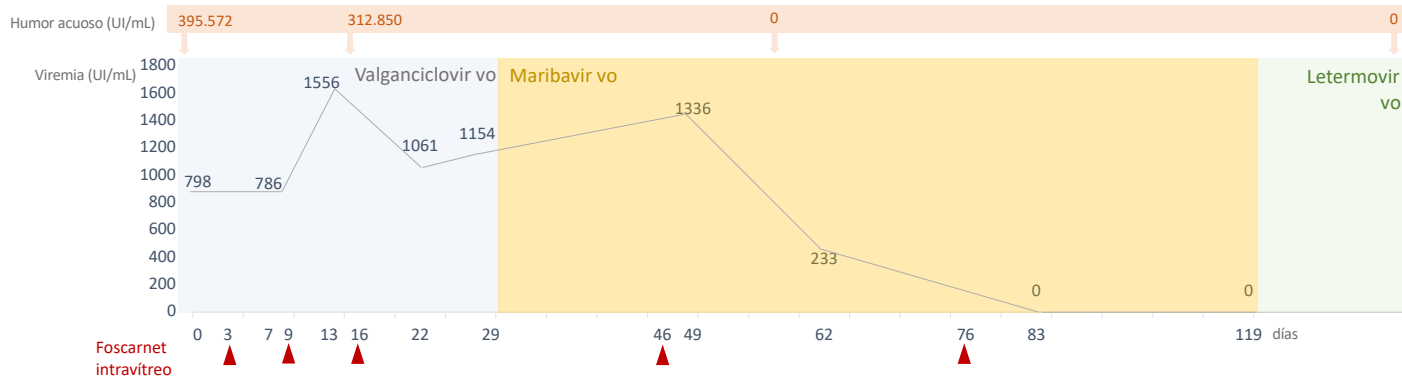




3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Manejo de la refractariedad



Respuesta virológica:
Carga viral indetectable en suero y humor acuoso tras maribavir 400mg/12h 3 meses y foscarnet intravítreo 5 dosis.

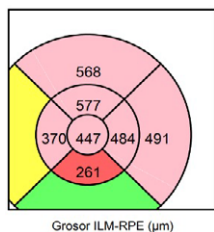
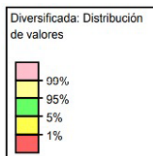


3.º WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

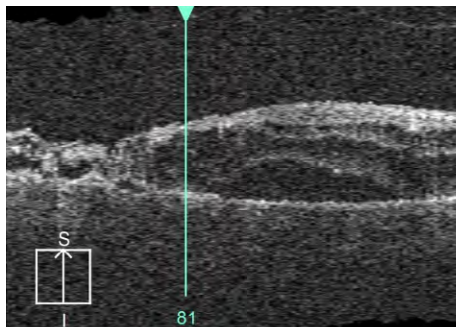
INFECTHEMA

Manejo de las secuelas

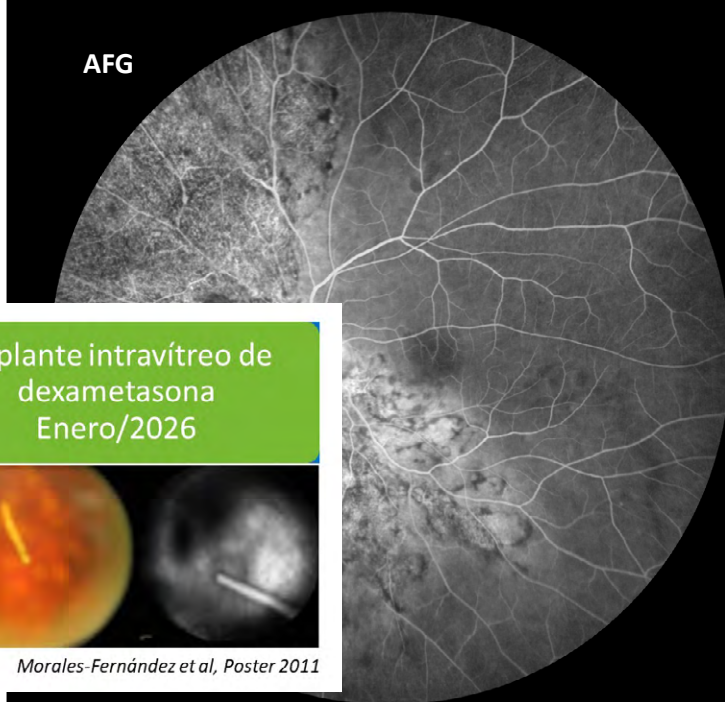
OCT



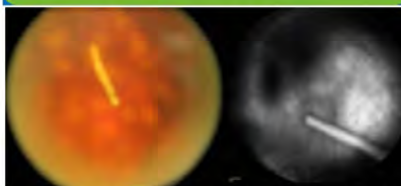
Grosor ILM-RPE (µm)



AFG



Implante intravítreo de dexametasona
Enero/2026



Morales-Fernández et al, Poster 2011

En la actualidad

Hematología

- MM: respuesta completa estricta
- Suspensión definitiva de antiBCMA
- Hipogammaglobulinemia recuperada

Infectología

- Desde enero/2026 CMV indetectable en suero y en humor acuoso
- Seguimiento de PCR CMV en suero al menos mensual
- Letermovir como profilaxis secundaria (uso compasivo)

Oftalmología

- Seguimiento estrecho
- Manejo de secuelas
- Vitritis de etiología incierta

Reflexiones finales

- Importancia de mantener un alta sospecha clínica frente a infecciones oportunistas en la época de las nuevas terapias celulares.
- Importancia del manejo interdisciplinar (Hematología, Neurología, Infecciosas/Microbiología, Oftalmología).
- Combinación de terapias locales con fármacos sistémicos para el tratamiento de la enfermedad por CMV ocular.
- ¿Debería estandarizarse la monitorización de carga viral de CMV en suero en pacientes asintomáticos en tratamiento con anticuerpos biespecíficos?
- ¿Habría que indicar profilaxis secundaria, en pacientes de alto riesgo de enfermedad por CMV que hayan presentado reactivaciones previas?

Organizado por:



3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

**TRATAMIENTO ANTIFUNGICO ANTICIPADO (PRE-EMPTIVE) EN PACIENTES DE
ALTO RIESGO:
una estrategia guiada por diagnóstico**

ISABEL IZQUIERDO GARCIA

HOSPITAL MIGUEL SERVET, ZARAGOZA



INTRODUCCIÓN

-  **Problema clínico**
 - Alta mortalidad
 - Diagnóstico **difícil y tardío**
 - Síntomas **poco específicos**
-  **Dilema**
 - Retrasar tratamiento → peor pronóstico
 - Tratar a todos → sobretratamiento
-  **Estrategia clásica**
 - Tratamiento **empírico** basado en fiebre



UN POCO DE HISTORIA

Años 80–90 → Estrategia empírica



Fiebre persistente



Sin biomarcadores



Diagnóstico muy limitado

Años 2000 → Nace el enfoque preemptive



Galactomanano



PCR Aspergillus



TC de alta resolución



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INFECTHEMA

GALACTOMANANO

- 362 episodios AI probable (Enero 1997-Febrero 2000)

- LMA/AloTpH/LLA/SMD/LMC
- Neutropenia >10 días
- Profilaxis: Itraconazol o Anfo B
- Tratamiento: Anfo B
 - Fiebre persistente
 - Infiltrados pulmonares de novo
 - TC sugestivo infección fúngica
 - Aislamiento de moho
 - Alteraciones neurológicas

- IFI: ~23 casos
- Sensibilidad: ~90%
- Especificidad: ~85–90%
- VPP: ~60–70%
- VPN: ~95–98%

Johan Maertens J, et al. Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients. *J Infect Dis.* 2001
Kieren A Marr KA, Balajee SA, McLaughlin L, et al. Detection of galactomannan antigenemia by enzyme immunoassay for diagnosis of invasive aspergillosis. *Clin Infect Dis.* 2004;



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EN HEMATOLOGÍA

INFECTHEMA

PCR ASPERGILLUS

- 2000 → Hebart → PCR seriada
- 2010 → EAPCRI → estandarización
- 2015 + → metaanálisis + guías
 - ~25–30 estudios incluidos
 - >2000 pacientes
 - Sensibilidad ~80–90%
 - Especificidad ~75–85%
 - VPN Muy alto



WORKING GROUP
EUROPEAN ASPERGILLUS PCR INITIATIVE
EAPCRI



Comparative Study > Clin Infect Dis. 2015 Oct 15;61(8):1293–303. doi: 10.1093/cid/civ507.
Epub 2015 Jun 25.

Aspergillus Polymerase Chain Reaction: Systematic Review of Evidence for Clinical Use in Comparison With Antigen Testing

P Lewis White ¹, John R Wingard ², Stéphane Bretagne ³, Jürgen Löffler ⁴,
Thomas F Patterson ⁵, Monica A Slavin ⁶, Rosemary A Barnes ⁷, Peter G Pappas ⁸,
J Peter Donnelly ⁹

- Incorporación a guías: (ECIL-6 / ECIL-8)

- 2020 → EORTC/MSGERC: Incluyen PCR como criterio microbiológico

Johan Maertens J, et al. Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients. *J Infect Dis.* 2001
Kieren A Marr KA, Balajee SA, McLaughlin L, et al. Detection of galactomannan antigenemia by enzyme immunoassay for diagnosis of invasive aspergillosis. *Clin Infect Dis.* 2004;

	Galactomanano	PCR Aspergillus	β-D-glucano
Especificidad	Aspergillus	Aspergillus	Panfúngico
Detección precoz	✓✓	✓✓✓	✓✓
Screening seriado	✓✓✓	✓✓✓	✓✓
VPN	✓✓✓	✓✓✓	✓✓
Limitaciones	Profilaxis	Estandarización	Baja especificidad





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INFECTHEMA

EMPÍRICO VS PREEMPTIVE

Estrategia empírica:

Inicio de antifúngicos por:

- Fiebre persistente
- Sin evidencia microbiológica
- Basada en **riesgo clínico**

Estrategia preemptive

Inicio de antifúngicos por:

- Biomarcadores (galactomanano, PCR)
- Imagen (TC precoz)
- Basada en **evidencia de infección**

EVIDENCIA CIENTÍFICA

- **Objetivo:**
 - Tratamiento antifúngico **empírico** vs Estrategia **preemptive**
 - Pacientes: Hematológicos con Neutropenia febril de alto riesgo
- **EC aleatorizado, multicéntrico**
 - n ≈ 293 pacientes
 - Empírico → antifúngico por fiebre persistente
 - Preemptive → basado en:
 - TC torácico
 - Galactomanano
 - Hallazgos clínicos
- **RESULTADOS**
 - Uso de antifúngicos: Empírico: ~63% vs Preemptive: ~39%
 - IFI probada/probable: Ligeramente mayor en preemptive
 - Mortalidad global: Sin diferencias significativas

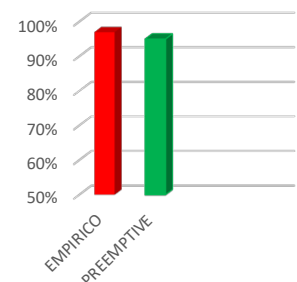
JOURNAL ARTICLE

Empirical versus Preemptive Antifungal Therapy for High-Risk, Febrile, Neutropenic Patients: A Randomized, Controlled Trial

Catherine Cordonnier, Cécile Pautas, Sébastien Maury, Anne Vekhoff, Hassan Farhat, Felipe Suarez, Nathalie Dhedin, Françoise Isnard, Lionel Ades, Frédérique Kuhnowski ...
[Show more](#)

Clinical Infectious Diseases, Volume 48, Issue 8, 15 April 2009, Pages 1042–1051,
<https://doi.org/10.1086/597395>

SUPERVIVENCIA A 14 DIAS



Cordonnier C, et al. Empirical versus preemptive antifungal therapy for high-risk, febrile, neutropenic patients: a randomized, controlled trial. Clin Infect Dis. 2009



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INFECCIONES
EN HEMATOLOGÍA

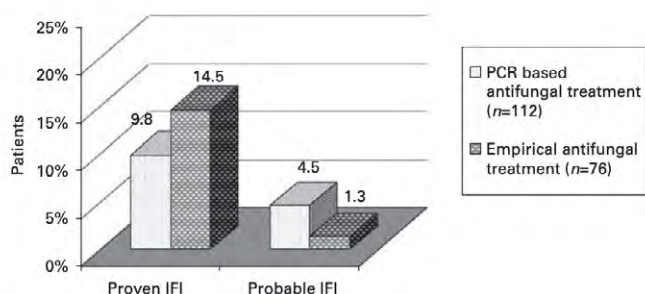
INFECTHEMA

EVIDENCIA CIENTÍFICA

Randomized Controlled Trial > Bone Marrow Transplant. 2009 Apr;43(7):553-61.
doi: 10.1038/bmt.2008.355. Epub 2008 Dec 15.

A prospective randomized controlled trial comparing PCR-based and empirical treatment with liposomal amphotericin B in patients after allo-SCT

H Hebert¹*, L Klingspor, T Klingebiel, J Loeffler, J Tollemer, P Ljungman, H Wandt,
K Schaefer-Eckart, H J Dornbusch, C Meisner, C Engel, N Stenger, T Mayer, O Ringden, H Einsele



- **Diseño**
- Pacientes hematológicos de alto riesgo
- Monitorización con **PCR Aspergillus seriada**

- **Resultados en grupo pre-emptive**
- ↓ uso de antifúngicos
- = mortalidad
- ↑ diagnóstico precoz

Hebert H, et al. A prospective randomized controlled trial comparing PCR-based and empirical treatment with liposomal amphotericin B in patients after allo-SCT. Bone Marrow Transplant. 2009



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EVIDENCIA CIENTÍFICA

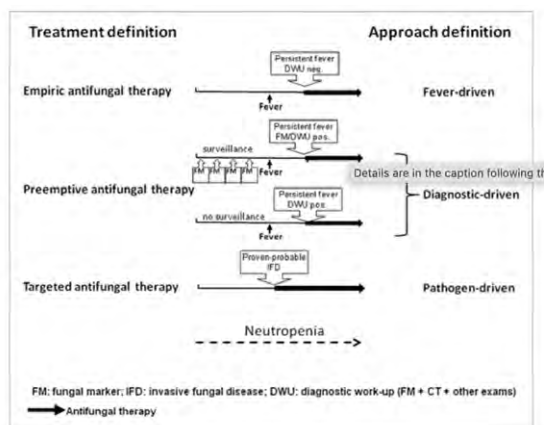
- Documento de consenso

Hematological Oncology
Haematol Oncol 2010; 31: 117-126
Published online 5 October 2012 in Wiley Online Library
(wileyonlinelibrary.com) DOI: 10.1002/hon.2031

Review

A hematology consensus agreement on antifungal strategies for neutropenic patients with hematological malignancies and stem cell transplant recipients

Corrado Girmenia¹*, Franco Aversa², Alessandro Busca³, Anna Candoni⁴, Simone Cesaro⁵, Mario Luppi⁶,
Livio Pagano⁷, Giuseppe Rossi⁸, Adriano Venditti⁹ and Anna Maria Nisanti¹⁰



EAT: inicio de tratamiento antifúngico en paciente con fiebre neutropénica sin respuesta a antibioterapia sistémica. 3-7 días

PAT: inicio de tto antifúngico en paciente neutropénico (con/sin fiebre) con hallazgos clínicos o microbiológicos que sugieren IFI Pero sin criterios de IFI probada/probable

TAT: IFI PROBADA/PROBABLE, tto dirigido

Corrado Girmenia C, Aversa F, Busca A, et al. A hematology consensus agreement on antifungal strategies for neutropenic patients with hematological malignancies and stem cell transplant recipients. *Haematologica*. 2010;






EVIDENCIA CIENTÍFICA

- **DDAT (DIAGNOSTIC DRIVEN ANTIFUNGAL THERAPY)**
 - Hallazgos Clínicos
 - Fiebre neutropénica persistente
 - Hallazgos microbiológicos
 - Galactomanano/Beta D glucano/PCR
 - Hallazgos radiológicos
 - Infiltrados pulmonares de novo

• Biomarcador positivo → TC confirma/localiza

• Biomarcador negativo → TC ayuda a descartar

Corrado Girmenia C, Aversa F, Busca A, et al. A hematology consensus agreement on antifungal strategies for neutropenic patients with hematological malignancies and stem cell transplant recipients. *Haematologica*. 2010;

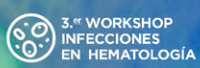
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Corrado Girmenia^{1*}, Franco Aversa², Alessandro Busca³, Anna Candoni⁴, Simone Cesaro⁵, Mario Luppi⁶, Livio Pagano⁷, Giuseppe Rossi⁸, Adriano Venditti⁹ and Anna Maria Nicosi¹⁰






EVIDENCIA CIENTÍFICA

Biomarcadores evaluados:

- **Galactomanano**
 - ✓ Uso en **screening seriado**
 - ✓ Detección precoz
 - ✓ Alta utilidad en neutropenia
- **β-D-glucano**
 - ✓ Marcador **panfúngico**
 - ✓ Útil como apoyo diagnóstico
- **PCR**
 - ✓ Prometedora
 - ⚠ Requiere estandarización

Estrategia recomendada:

Uso combinado de biomarcadores + imagen

Oscar Marchetti O, Lamoth F, Mikulska M, et al. ECIL recommendations for the use of biological markers for the diagnosis of invasive fungal diseases in leukemic patients and hematopoietic SCT recipients. *Lancet Infect Dis*. 2012;

EUROPEAN
CONFERENCE on
INFECTIONS in
LEUKAEMIA



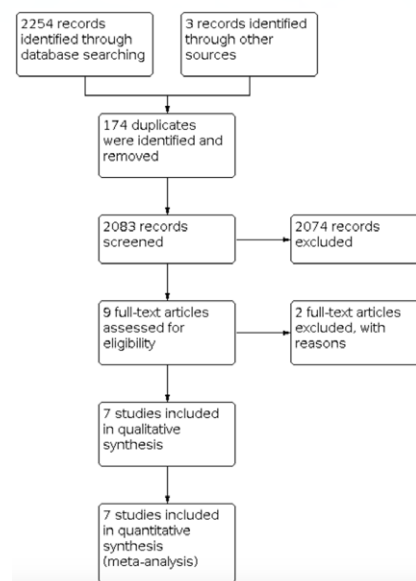
EVIDENCIA CIENTÍFICA

• RESULTADOS

- ⚠ Mortalidad
 - Sin diferencias significativas
- 🦠 IFI
 - Tendencia a más IFI en preemptive
- 💊 Uso de antifúngicos
 - Significativamente menor en preemptive

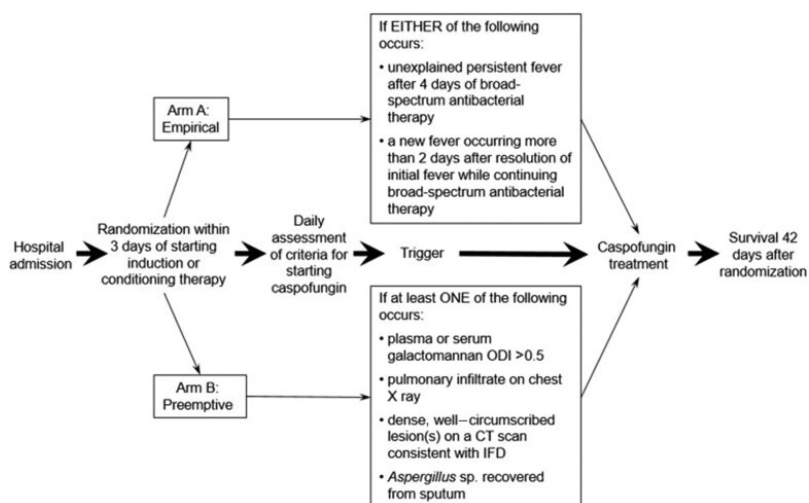
• Limitaciones del metaanálisis

- Heterogeneidad de estrategias
- Variabilidad diagnóstica
- Bajo número de eventos
- EC no ciegos
- Práctica no actual
- Evidencia baja–moderada



Uneno Y, Imura H, Makuuchi Y, Tochitani K, Watanabe N. Pre-emptive antifungal therapy versus empirical antifungal therapy for febrile neutropenia in people with cancer. Cochrane Database Syst Rev. 2022

EVIDENCIA CIENTÍFICA



Supervivencia global

- ✓ No diferencias significativas

Uso de antifúngicos

- ✓ Significativamente menor en preemptive

IFI

- ✓ Ligero aumento de IFI en preemptive

Maertens J, et al; Infectious Diseases Group and the Acute Leukemia Group of the European Organization for Research and Treatment of Cancer. Empiric vs Preemptive Antifungal Strategy in High-Risk Neutropenic Patients on Fluconazole Prophylaxis: A Randomized Trial of the European Organization for Research and Treatment of Cancer. Clin Infect Dis. 2023

Profilaxis antifúngica: cambia el juego

La profilaxis antifúngica

- Reduce incidencia de IFI
- Mortalidad

Pero también...

- ! Presentación clínica más atípica
- ! ↓ sensibilidad de biomarcadores (GM, PCR)
- ! Infecciones “breakthrough”

El manejo actual combina profilaxis y diagnóstico precoz = PRE EMPTIVE

Review

Antifungal prophylaxis and pre-emptive therapy: When and how?

Rosanne Sprute^{a b c}, Julia A. Nacov^{a b c}, Dionysios Neofytos^d, Matteo Oliverio^a, Juergen Prattes^{a b c e}, Ilana Reinhold^f, Oliver A. Cornely^{a b c g}, Jannik Stemler^{a b c}

GUÍAS Y CONSENSOS

- **European Conference on Infections in Leukemia**
 - Reconoce estrategia **preemptive**
 - Recomendada en centros con diagnóstico disponible
 - Enfoque: **diagnostic-driven**
- **Infectious Diseases Society of America**
 - Acepta ambas estrategias
 - Preemptive válido con monitorización estrecha
 - Destaca:
 - Galactomanano
 - Imagen precoz
- **Girmeria et al. consensus**
 - Estrategia **individualizada**
 - Preemptive = alternativa real
 - Énfasis en diagnóstico

Haematologica. 2016 Dec 20;102(3):433–444. doi: 10.3324/haematol.2016.152900

ECIL-6 guidelines for the treatment of invasive candidiasis, aspergillosis and mucormycosis in leukemia and hematopoietic stem cell transplant patients

Frederic Tisserand^{1*}, Samir Agrawal², Livia Pavano³, Georgios Petrakos⁴, Andreas H. Groll⁵, Anna Skiada⁶, Cornelia Lass-Floet⁷, Thierry Calandra⁸, Claudio Viscoli⁹, Basoul Herbrecht⁹

ECIL	Año	Aportación clave
ECIL-3	~2012	Introduce biomarcadores (GM, β-D-glucano, PCR) → base del enfoque diagnostic-driven
ECIL-6	~2016	Consolida uso de GM seriado + TC precoz → integración en práctica clínica
ECIL-8	~2019–2020	Refuerza estrategias individualizadas y uso combinado de herramientas diagnósticas



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INFECTHEMA

GUÍAS Y CONSENSOS

- **European Conference on Infections in Leukemia**
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 - Preemptive = alternativa real
 - Énfasis en diagnóstico

• Clin Infect Dis. 2016 Jun 29;63(4):e1–e60. doi: [10.1093/cid/ciw326](https://doi.org/10.1093/cid/ciw326) [↗](#)

Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America

[Thomas F Patterson](#)^{1,4,5}, [George R Thompson III](#)², [David W Denning](#)³, [Jay A Fishman](#)⁴, [Susan Hadley](#)⁵, [Raoul Herbrecht](#)⁶, [Dimitrios P Kontoyiannis](#)⁷, [Kieren A Marr](#)⁸, [Vicki A Morrison](#)⁹, [M Hong Nguyen](#)¹⁰, [Brahm H Segal](#)¹¹, [William J Steinbach](#)¹², [David A Stevens](#)¹³, [Thomas J Walsh](#)¹⁴, [John R Wingard](#)¹⁵, [Jo-Anne H Young](#)¹⁶, [John E Bennett](#)^{17,8}

PREEMPTIVE: A FAVOR



1. **Menos toxicidad**
 - Menos exposición a antifúngicos
2. **Coste-efectividad**
 - Menos tratamiento
 - Menos efectos adversos
3. **Medicina de precisión**
 - Tratamiento dirigido, no “a ciegas”
4. **Stewardship antifúngico**
 - Reduce presión selectiva
5. **No inferior en mortalidad**



PREEMPTIVE: EN CONTRA

1. Retraso en el tratamiento

- Monitorización seriada → detección precoz

2. No todos los centros pueden hacerlo

- En centros terciarios es el estándar emergente

3. Los biomarcadores no son perfectos



CONCLUSIONES

- Las IFI siguen siendo un problema crítico, con una alta mortalidad y un diagnóstico difícil
- La estrategia empírica sigue siendo el estándar en la mayoría de centros
- La estrategia pre-emptive es válida y segura, no empeora supervivencia
- Misma eficacia, mayor eficiencia
- El verdadero cambio no es terapéutico, es diagnóstico



Organizado por:



FUNDACIÓN
PETHEMA
Programa Español de
Trasplantes en Hematología

3.^{er} WORKSHOP
INFECCIONES
EN HEMATOLOGÍA

INFECTHEMA

Valencia, 16 y 17 de abril de 2026

Abordaje integral del paciente con neoplasias hematológicas en las unidades de cuidados intensivos (UCI)

Pedro Castro Rebollo
Hospital Clínic Barcelona

Programa académico
**Enfermo crítico
y emergencias**



Clínic
Barcelona



UNIVERSITAT DE
BARCELONA



DISCLOSURES

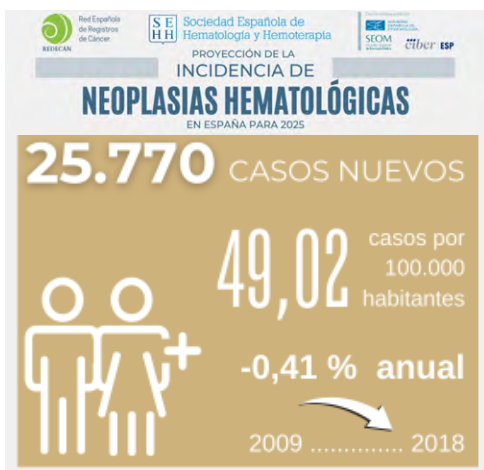
- Honoraria for scientific collaboration (Pfizer, MSD, Gilead, Alexion, Abbvie, Mundipharma)
- Advisory Board (Alexion, Janssen, Gilead, Sanofi)
- **Hematologist Husband!**

AGENDA

- Landscape of critically ill patients with HM
- Prognosis factors of critically ill patients with HM
- Sepsis and septic shock outcomes in the critically ill patient with HM
- Strategies to improve prognosis in the critically ill patient with HM
- Take home messages

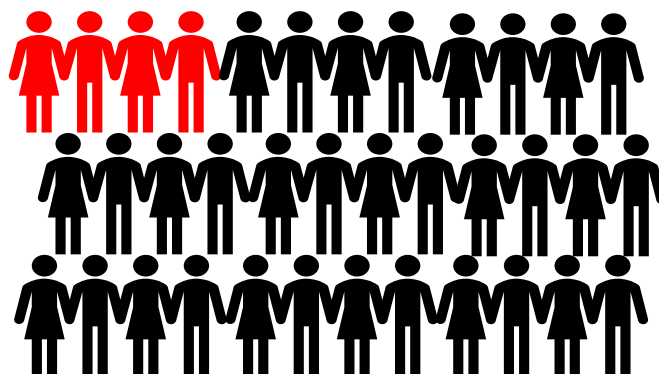
THE CRITICALLY ILL PATIENT WITH HEMATOLOGICAL MALIGNANCY: CURRENT LANDSCAPE

HEMATOLOGICAL MALIGNANCIES IN SPAIN



Las cifras del cáncer sanguíneo en España; 2025. REDECAN y SEHH

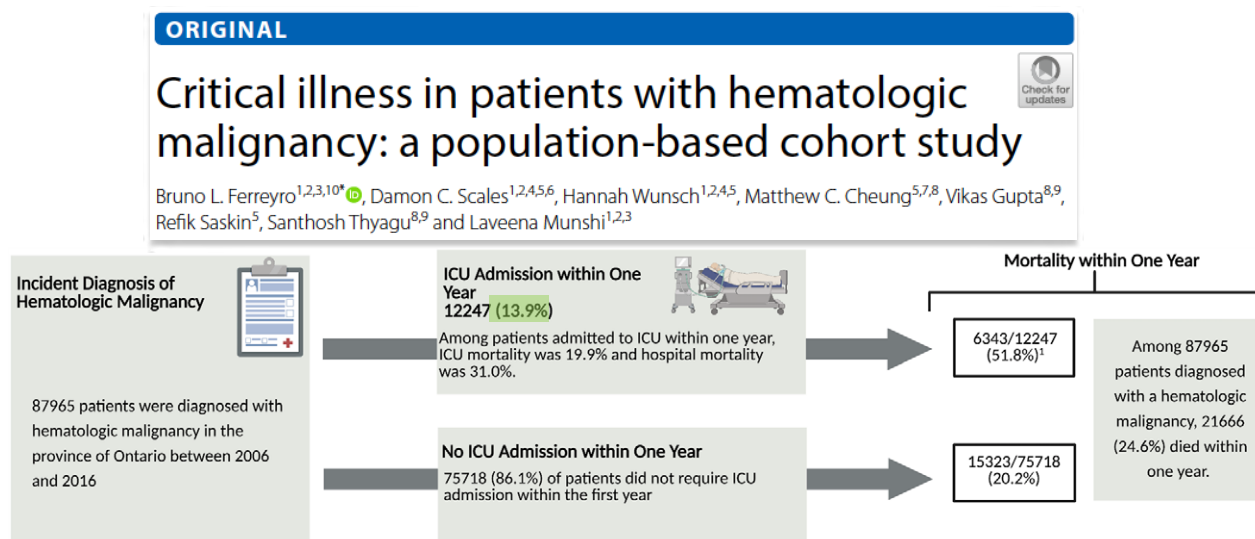
INCREASING PREVALENCE OF CRITICALLY ILL ONCOHEMATOLOGICAL PATIENTS. ICU ADMISSION



↑ Probability of ICU admission

P.Castro

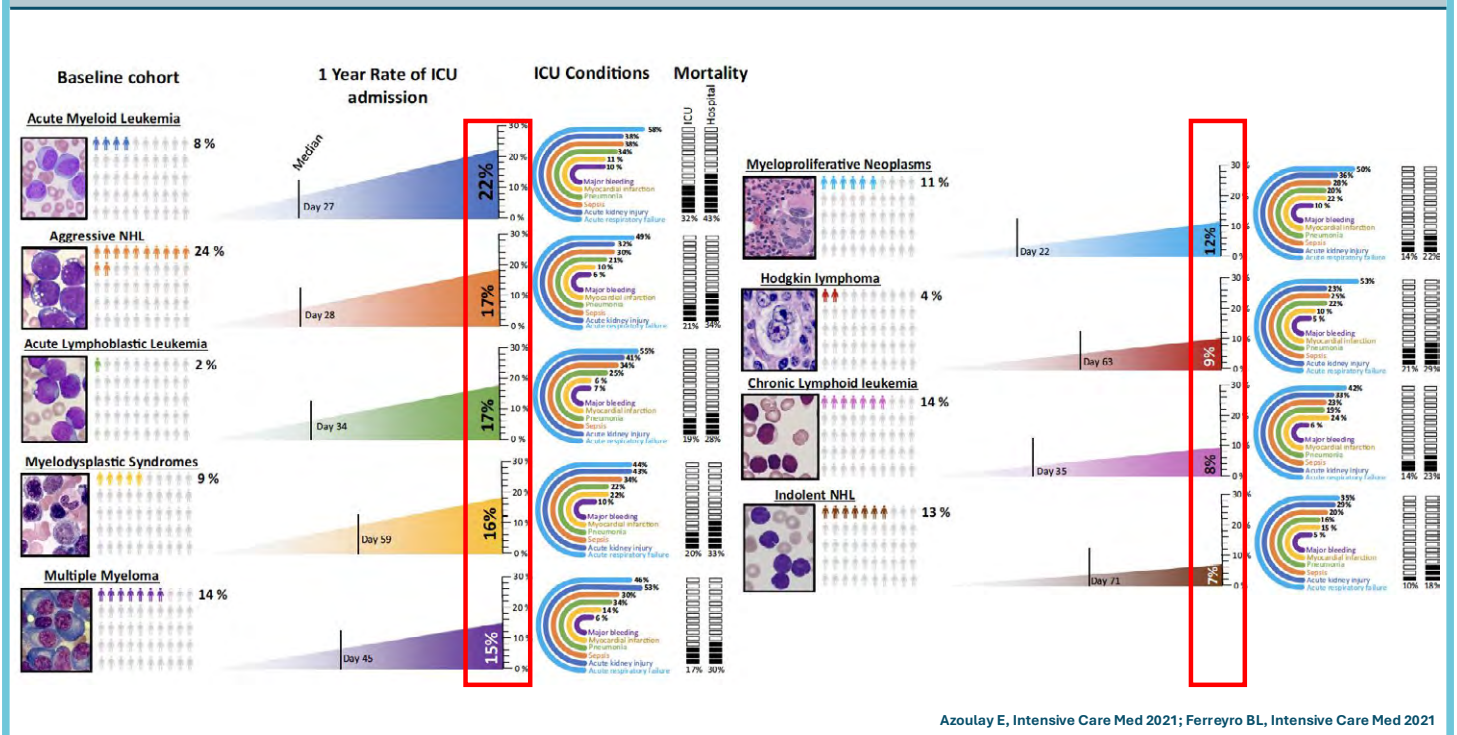
HM AND ICU: CURRENT LANDSCAPE. ICU ADMISSION



Ferreyro BL, Intensive Care Med 2021



HM AND ICU: CURRENT LANDSCAPE. ICU ADMISSION



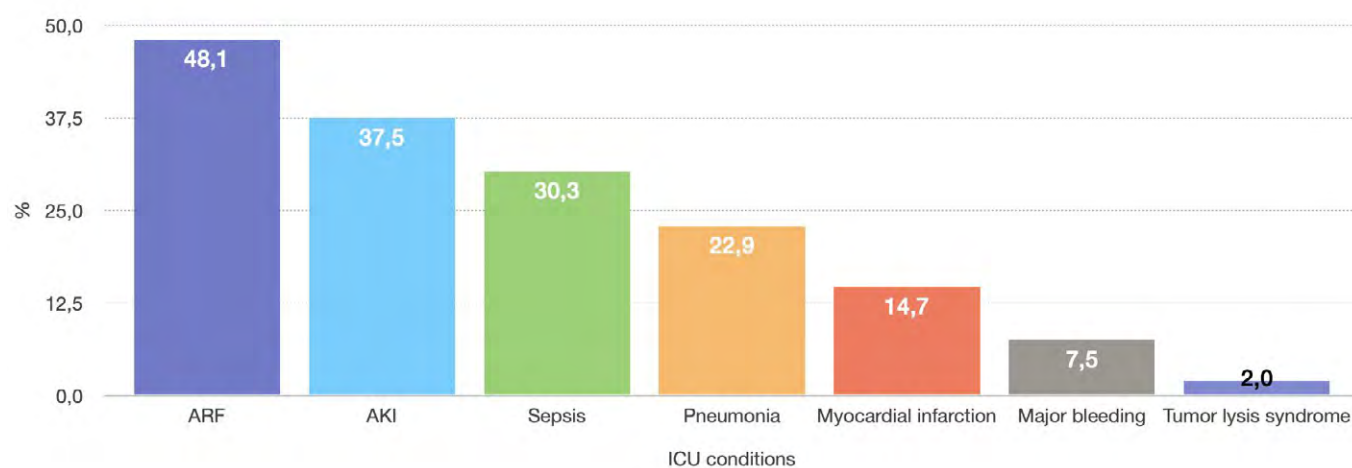
RATE OF ICU ADMISSION AMONG PATIENTS WITH HM

7-22%

of patients with HM will present life-threatening complications requiring ICU admission in the first year after diagnosis

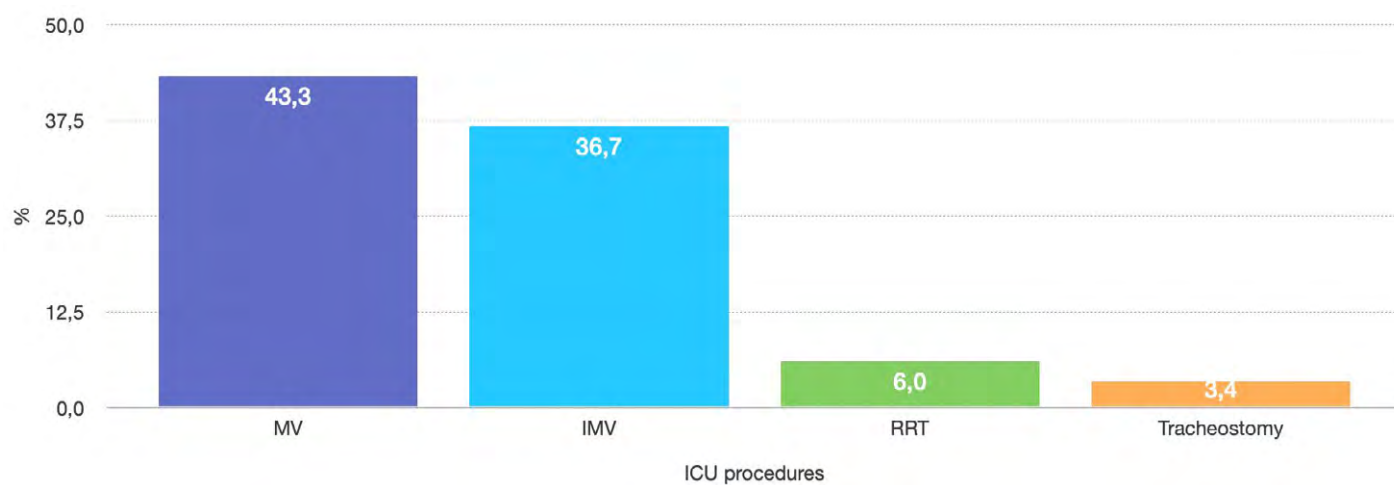


HM AND ICU: CURRENT LANDSCAPE. CAUSES OF ADMISSION



Ferreyro BL, Intensive Care Med 2021

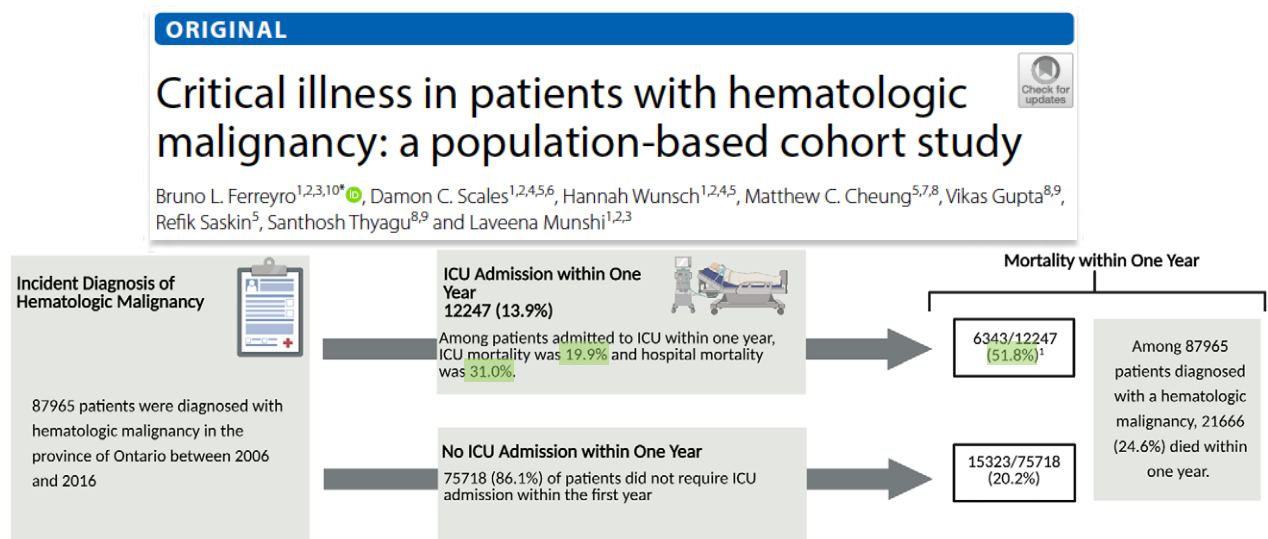
HM AND ICU: CURRENT LANDSCAPE. ICU PROCEDURES



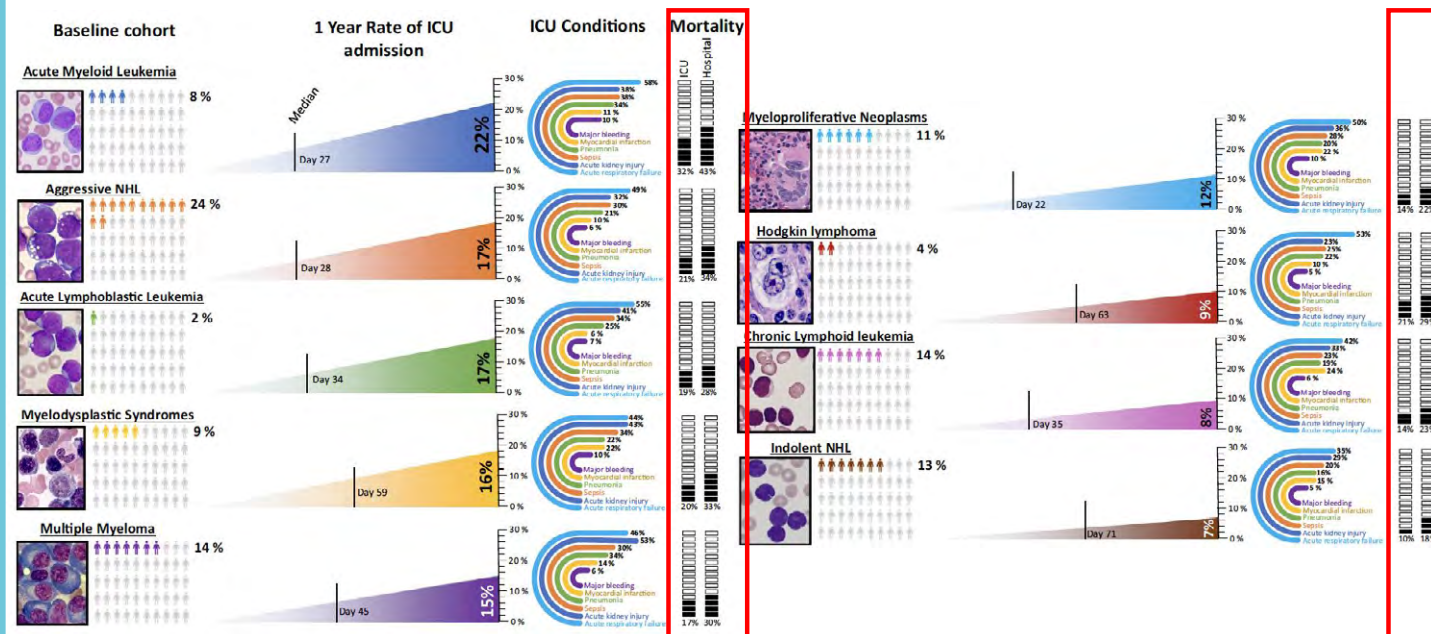
Ferreyro BL, Intensive Care Med 2021

THE CRITICALLY ILL PATIENT WITH HEMATOLOGICAL MALIGNANCY: PROGNOSIS

HM AND ICU: MORTALITY



HM AND ICU: MORTALITY



Azoulay E, Intensive Care Med 2021; Ferreyro BL, Intensive Care Med 2021

HM AND ICU: MORTALITY

Disease	1-y rate ICU admission	ICU mortality	Hospital mortality
AML	22%	32%	43%
Aggressive NHL	17%	21%	34%
ALL	17%	19%	28%
MDS	16%	20%	33%
MM	15%	17%	30%
Myeloproliferative neoplasm	12%	14%	22%
Hodgkin lymphoma	9%	21%	29%
CLL	8%	14%	23%
Indolent NHL	7%	10%	18%

Azoulay E, Intensive Care Med 2021; Ferreyro BL, Intensive Care Med 2021



CANCER PATIENTS IN THE ICU HAVE IMPROVED THEIR PROGNOSIS

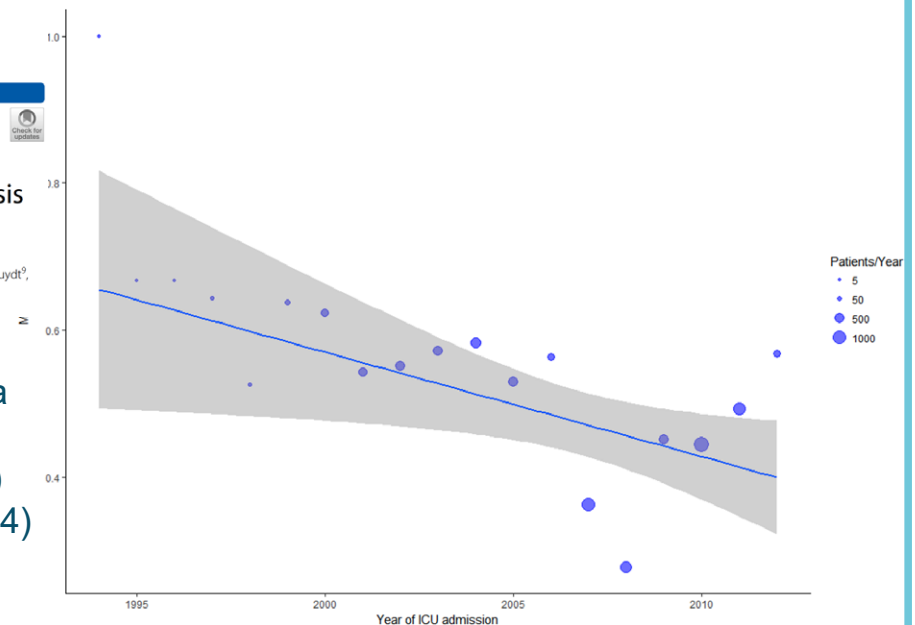
Intensive Care Med (2019) 45:977–987
<https://doi.org/10.1007/s00134-019-05653-7>

SYSTEMATIC REVIEW

Changes in critically ill cancer patients' short-term outcome over the last decades: results of systematic review with meta-analysis on individual data

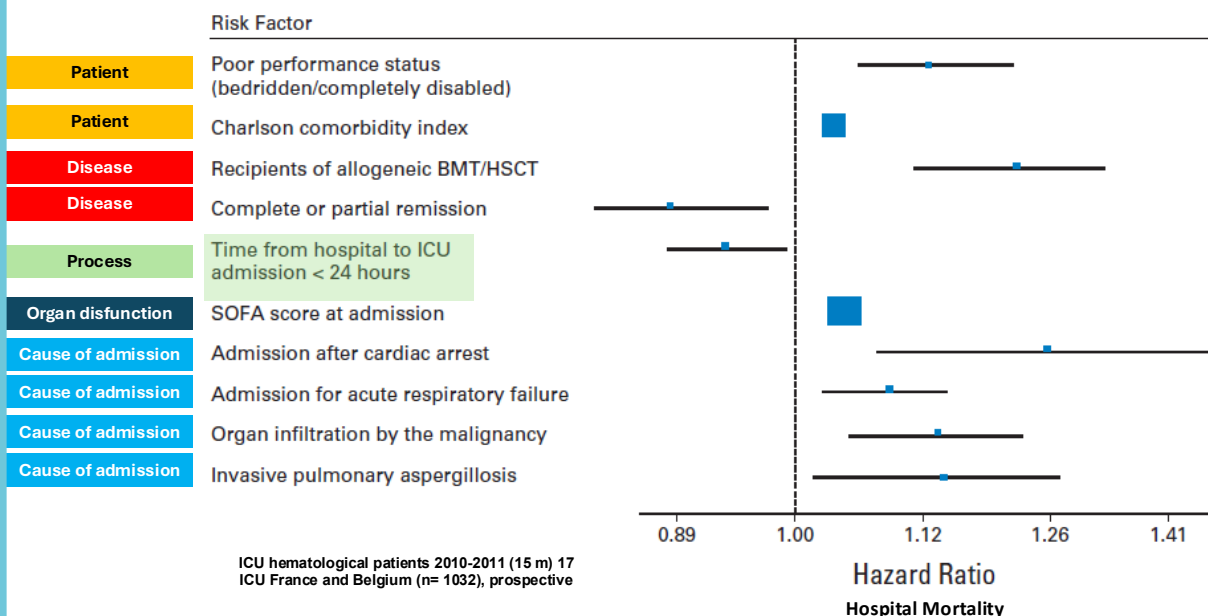
Michaël Darmon^{1,2,3*}, Aurélie Bourmaud^{4,5}, Quentin Georges⁶, Marcio Soares⁷, Kyeongman Jeon⁸, Sandra Oeyen⁹, Chin Kook Rhee¹⁰, Pascale Gruber¹¹, Marlies Ostermann¹², Quentin A. Hill¹³, Pieter Depuydt⁹, Christelle Ferra¹⁴, Anne-Claire Toffart¹⁵, Peter Schellongowski¹⁶, Alice Müller¹⁷, Virginie Lemiale¹, Djamel Mokart¹⁸ and Elie Azoulay^{1,2,3}

Meta-analysis of individual data from published studies (2005–2015) including cancer (mixed) patients admitted to ICU (n=7,354)



Darmon M, Intensive Care Med 2019

MORTALITY RISK FACTORS OF CRITICALLY ILL PATIENTS WITH HM



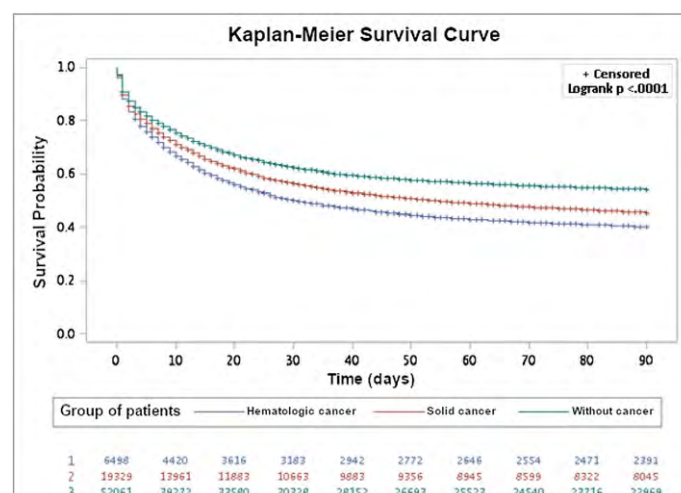
Prospective multicenter (17 ICU France and Belgium) observational study of ICU HM patients (2010–2011) (n=1032)

Azoulay E, J Clin Oncol 2013

SEPSIS OUTCOMES IN THE CRITICALLY ILL PATIENT WITH HEMATOLOGICAL MALIGNANCY

SEPSIS IN CRITICALLY ILL HEMATOLOGICAL PATIENTS. INCREASED MORTALITY...

Mortality of cancer patients with septic shock: A nation-based cohort analysis of 77,888 patients



Retrospective populational study (France) of patients hospitalized with SS (2017-2018)(n= 77,888 patients, 6,498 with HM and 19,329 with ST)

Bianchi A, Anaesth Crit Care Pain Med 2025

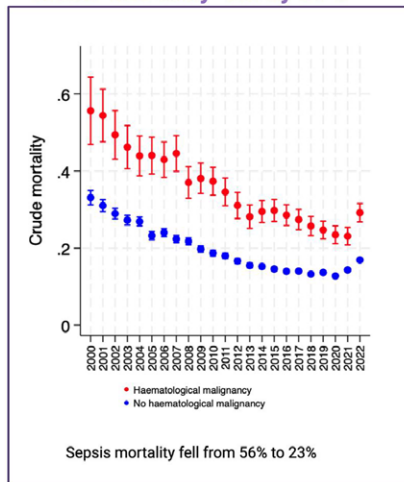


SEPSIS IN CRITICALLY ILL HEMATOLOGICAL PATIENTS. MORTALITY RISK FACTORS

Sepsis mortality among patients with haematological malignancy admitted to Intensive Care 2000 to 2022: a binational cohort study

A retrospective cohort study of 17,313 patients with sepsis and haematological malignancy using binational intensive care registry data from Australia and New Zealand

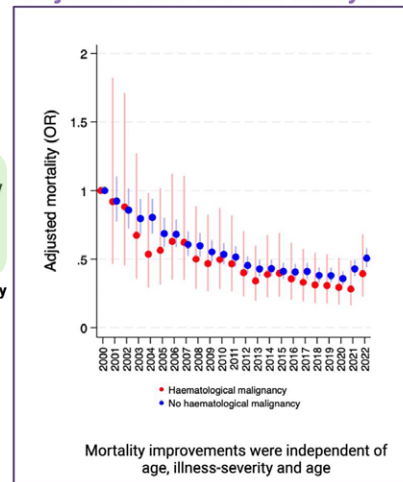
Crude mortality fell by 50%



Risk factors for mortality
Age
SOFA-score
Chronic comorbidities
Mechanical ventilation

Not predictive of mortality
Neutropenia

Adjusted odds of death fell by 50%



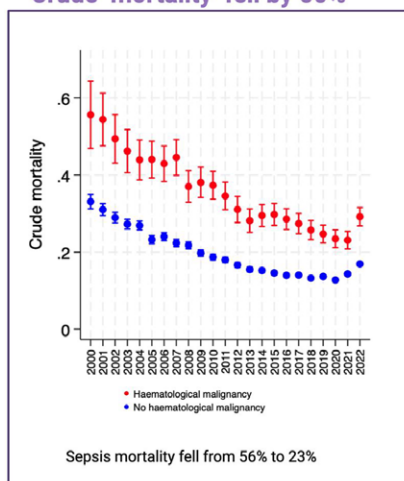
MacPhail A, Crit Care 2024

SEPSIS IN CRITICALLY ILL HEMATOLOGICAL PATIENTS. MORTALITY RISK FACTORS

Sepsis mortality among patients with haematological malignancy admitted to Intensive Care 2000 to 2022: a binational cohort study

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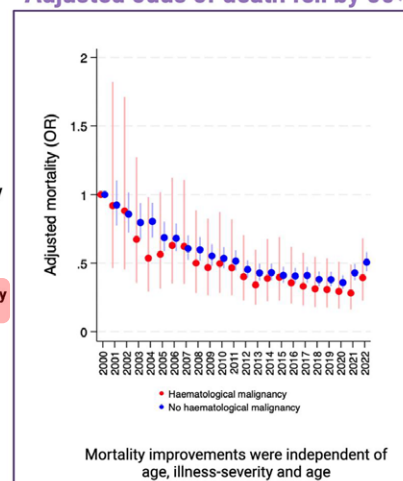
Crude mortality fell by 50%



Risk factors for mortality
Age
SOFA-score
Chronic comorbidities
Mechanical ventilation

Not predictive of mortality
Neutropenia

Adjusted odds of death fell by 50%



MacPhail A, Crit Care 2024

LONG TERM OUTCOMES OF ICU SURVIVORS WITH HM

LONG TERM OUTCOMES ICU SURVIVORS WITH HM

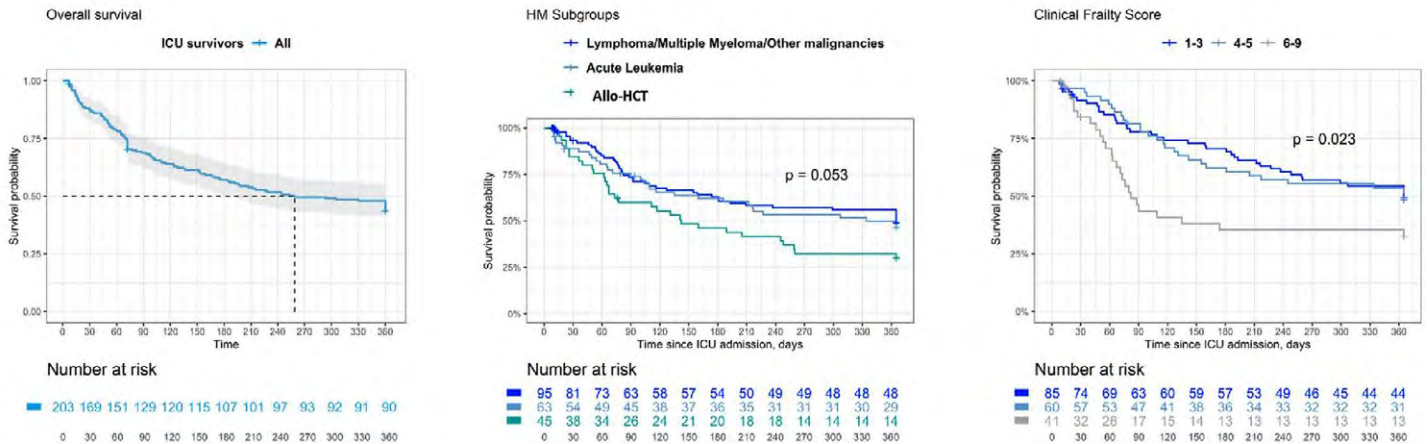
Long-term survival and functional outcomes of critically ill patients with hematologic malignancies: a Canadian multicenter prospective study



Prospective multicenter (7 ICU Canada) observational study of ICU HM (2018-2020) (n=414) (12 months)

LONG TERM OUTCOMES ICU SURVIVORS WITH HM

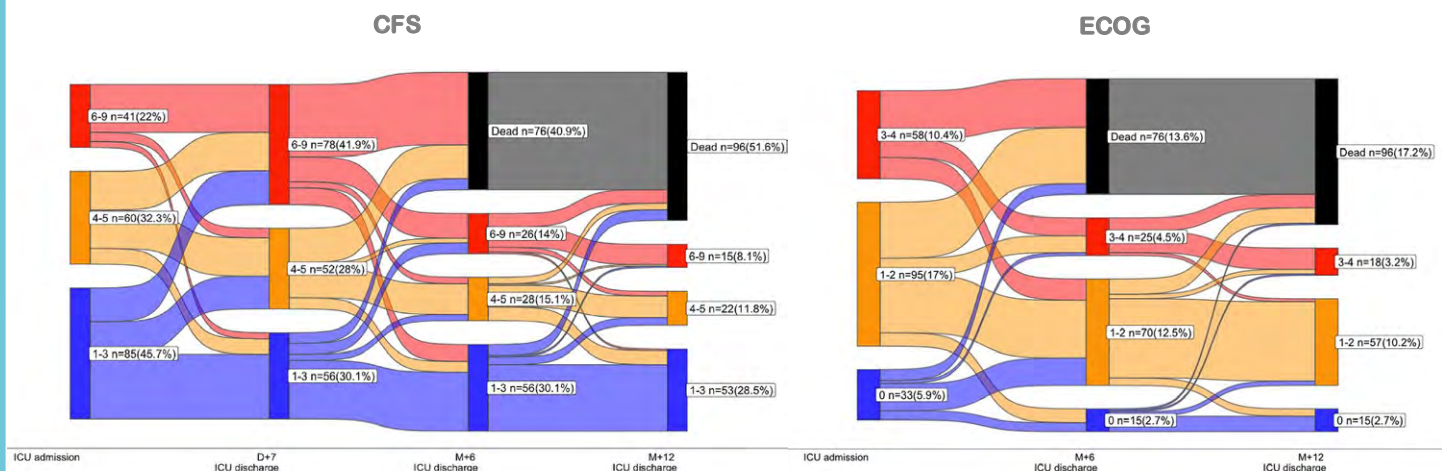
ICU survivors



Prospective multicenter (7 ICU Canada) observational study of ICU HM (2018-2020)
(n=414) (12 months)

Munshi L, Intensive Care Med 2024

LONG TERM OUTCOMES ICU SURVIVORS WITH HM



Prospective multicenter (7 ICU Canada) observational study of ICU HM (2018-2020)
(n=414) (12 months)

Munshi L, Intensive Care Med 2024

IMPACT OF ICU ADMISSION IN PROGNOSIS OF HM PATIENTS

Bredin et al. *Annals of Intensive Care* (2024) 14:143
<https://doi.org/10.1186/s13613-024-01372-5>

Annals of Intensive Care

RESEARCH **Open Access**

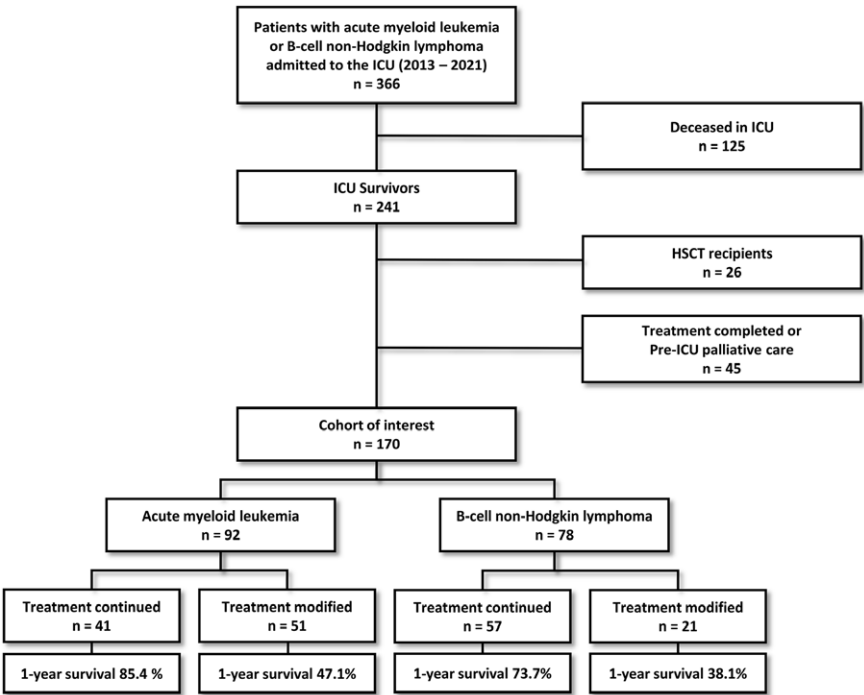


Impact of critical illness on continuation of anticancer treatment and prognosis of patients with aggressive hematological malignancies

Retrospective single-centre observational study including adult patients with AML and B-NHL survivors of ICU admission (2013-2021, France) (n=170 (92 + 78) out of 366)

Bredin S, Ann Intensive Care 2024

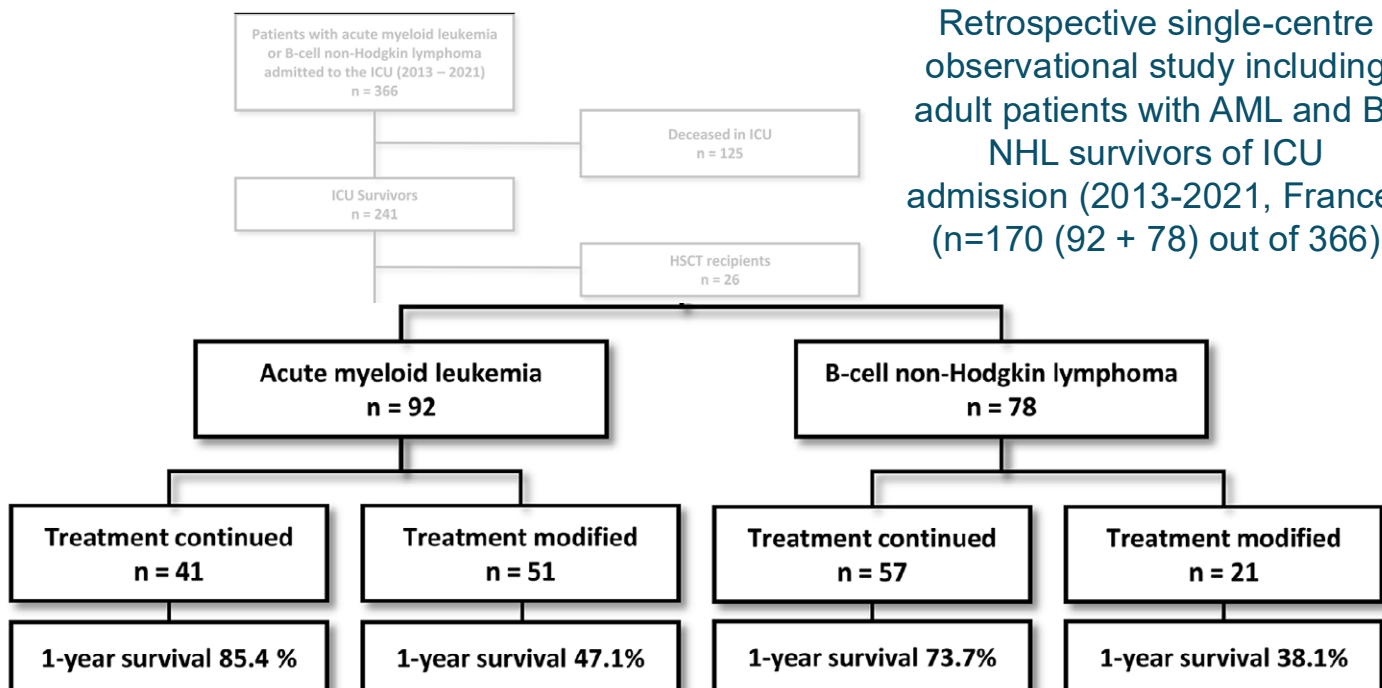
IMPACT OF ICU ADMISSION IN PROGNOSIS OF HM PATIENTS



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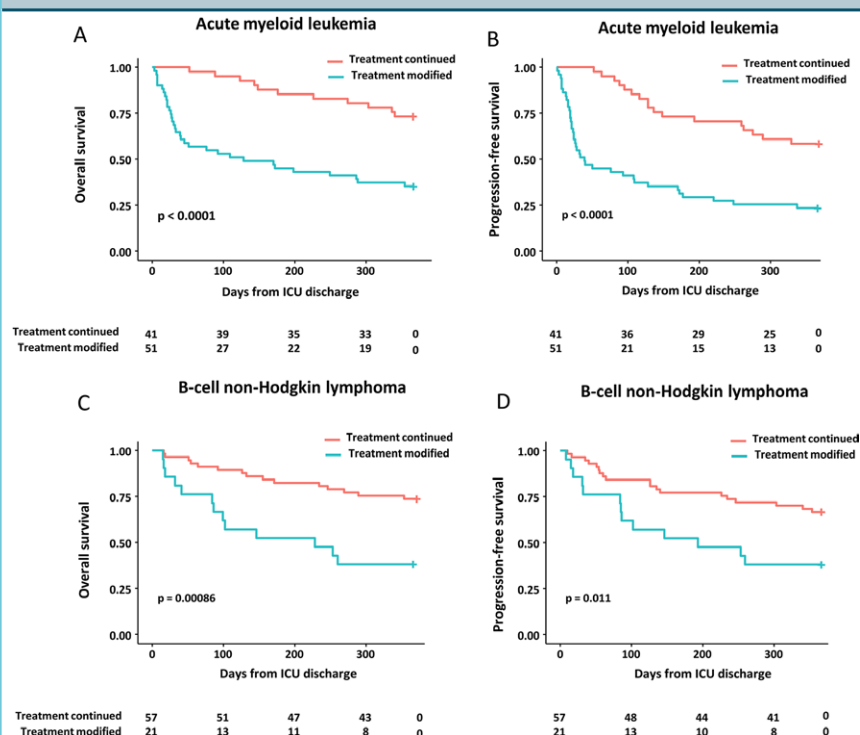
Bredin S, Ann Intensive Care 2024

IMPACT OF ICU ADMISSION IN PROGNOSIS OF HM PATIENTS



Bredin S, Ann Intensive Care 2024

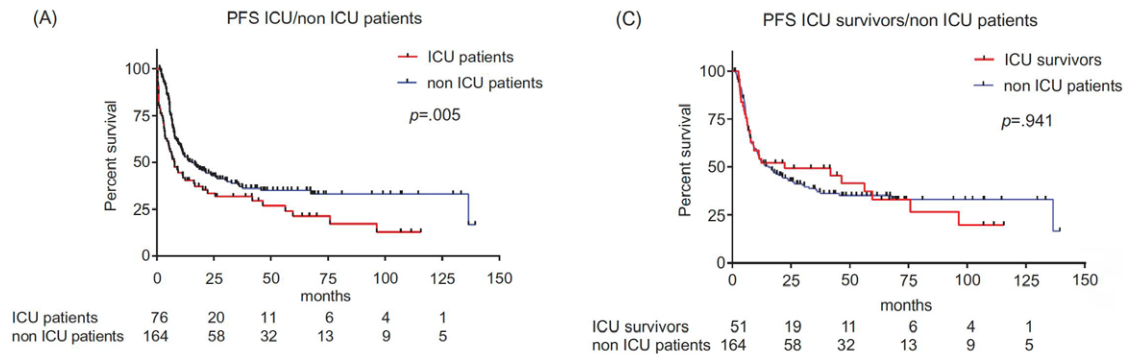
IMPACT OF ICU ADMISSION IN PROGNOSIS OF HM PATIENTS



Retrospective single-centre observational study including adult patients with AML and B-NHL survivors of ICU admission (2013-2021, France) (n=170 (92 + 78) out of 366)

Bredin S, Ann Intensive Care 2024

IMPACT OF ICU ADMISSION IN PROGNOSIS OF HM PATIENTS

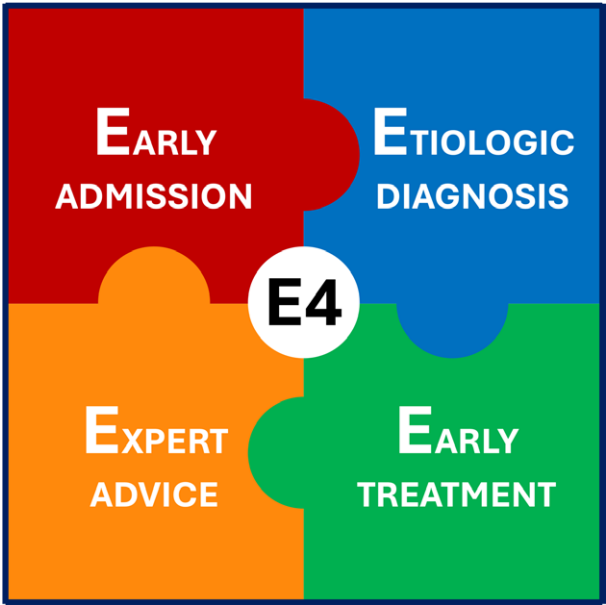


Retrospective unicenter (Switzerland) observational study of AML patients receiving intensive chemotherapy (n=240) (2006-2016)

Fassbind P, Leuk Lymphoma 2019

STRATEGIES TO IMPROVE PROGNOSIS IN THE CRITICALLY ILL HEMATOLOGICAL PATIENT

MANAGEMENT OF THE CRITICALLY ILL HEMATOLOGICAL PATIENT



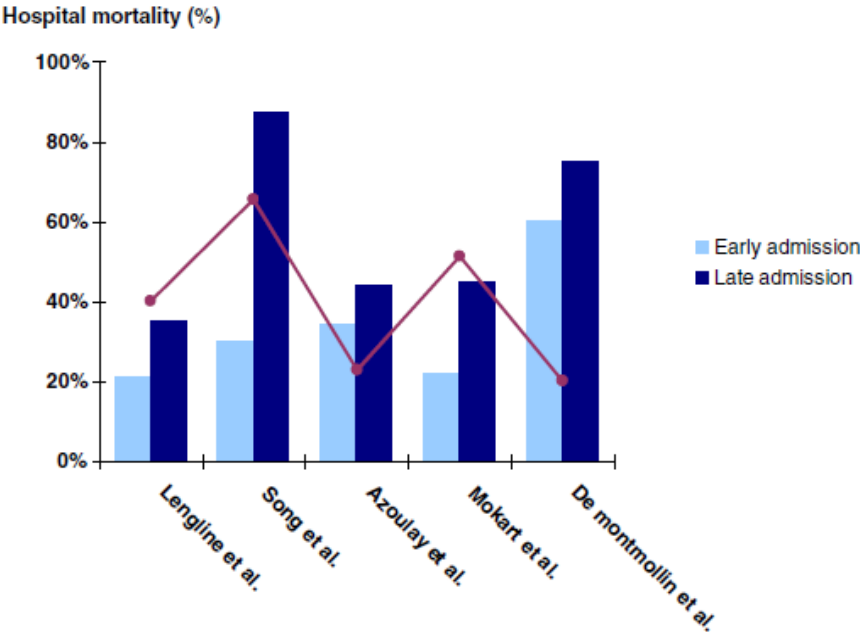
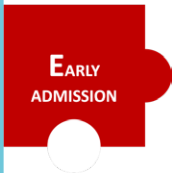
Castro P, Intensive Care Med 2026

IMPORTANCE OF EARLY ADMISSION IN CRITICALLY ILL CANCER PATIENTS



Castro P, Intensive Care Med 2026

IMPORTANCE OF EARLY ADMISSION IN CRITICALLY ILL PATIENTS WITH HM

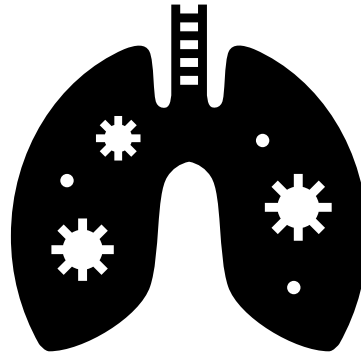


Azoulay E, Blood Rev 2015

IMPORTANCE OF ETIOLOGIC DIAGNOSIS IN CRITICALLY ILL CANCER PATIENTS



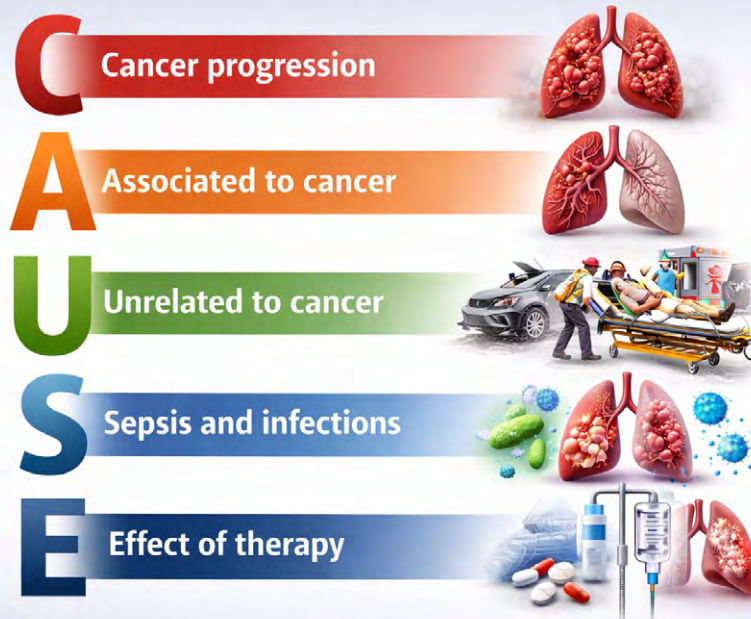
HIGH DIAGNOSTIC COMPLEXITY



Critically ill cancer patient
with ARF

P.Castro

ETIOLOGIC DIAGNOSIS IN CRITICALLY ILL CANCER PATIENTS



ETIOLOGIC
DIAGNOSIS

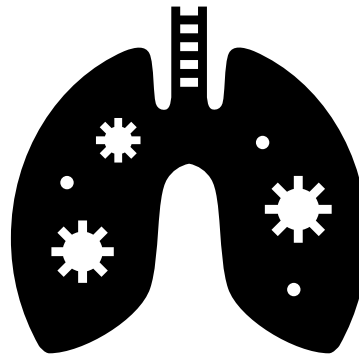
P.Castro AI-generated image (ChatGPT, OpenAI) adapted from Castro P, Intensive Care Med 2026.

HIGH DIAGNOSTIC COMPLEXITY

Infections

- Bacterial
- Viral
- Fungal

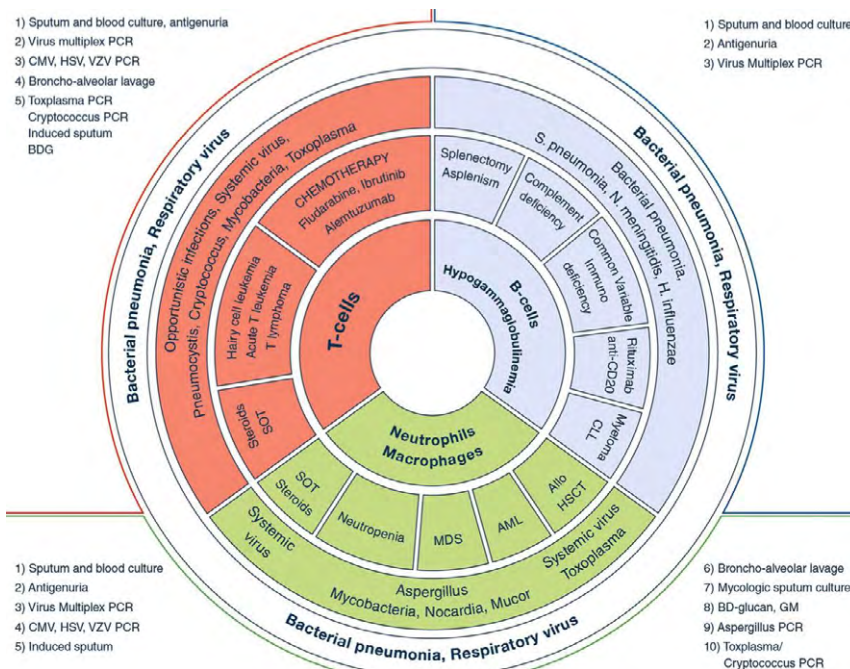
60%



Critically ill cancer patient
with ARF

P.Castro

HIGH DIAGNOSTIC COMPLEXITY



Azoulay E, Intensive Care Med 2020

HIGH DIAGNOSTIC COMPLEXITY

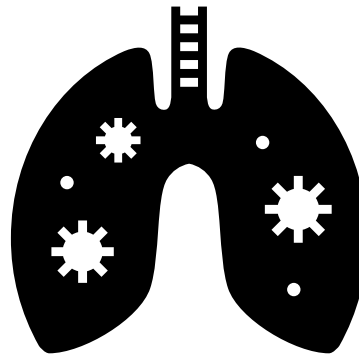
Infections

- Bacterial
- Viral
- Fungal

60%

Disease related

- Infiltration
- Leukostasis
- Compression/obstruction



Critically ill cancer patient
with ARF

Treatment toxicity

- Chemotherapy
- Radiotherapy
- Immunotherapy

Others

- GVHD
- Inflammatory
- Heart failure
- Non-cancer related ARDS

P.Castro

DD OF SEPSIS IN HM PATIENTS: SEPSIS MIMICKERS

Unrelated to Cancer

Common ICU
Entities
(Pancreatitis, AMI, PE)

Uncommon ICU
Conditions
(Adrenal Crisis,
Thyroid Storm, Refeeding)

Related to Cancer

HLH

CRS /
Immunotherapy

TMA

Tumor Lysis
Syndrome

Leukostasis

Cancer
Progression

Differentiation
Syndrome

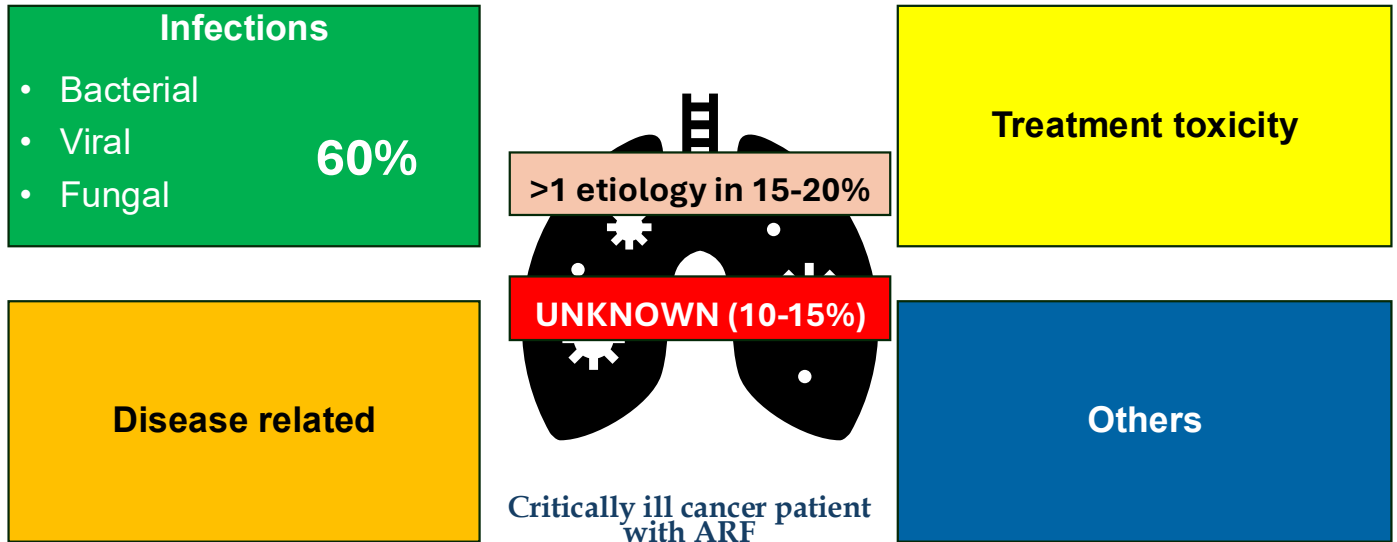
Ruxolitinib
Withdrawal

Sepsis

ETIOLOGIC
DIAGNOSIS

P.Castro AI-generated image (ChatGPT, OpenAI)

HIGH DIAGNOSTIC COMPLEXITY



P.Castro

ARF AND ETIOLOGY IN CANCER PATIENTS

Contejean et al. *Ann. Intensive Care* (2016) 6:102
DOI 10.1186/s13613-016-0202-0

Annals of Intensive Care

RESEARCH

Open Access



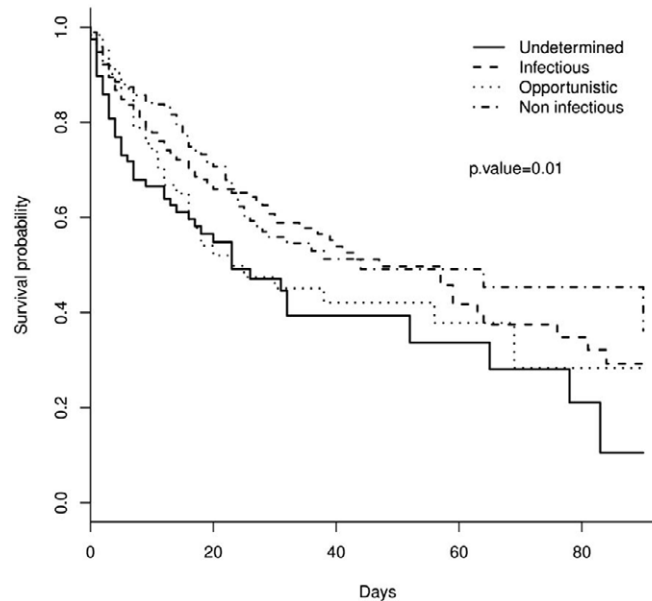
Increased mortality in hematological malignancy patients with acute respiratory failure from undetermined etiology: a *Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologie* (Grrr-OH) study

Post hoc analysis prospective multicenter cohort, with HM patients admitted to ICU due to ARF (n=604) (2010-2011)

Contejean A, *Ann Intensive Care* 2016



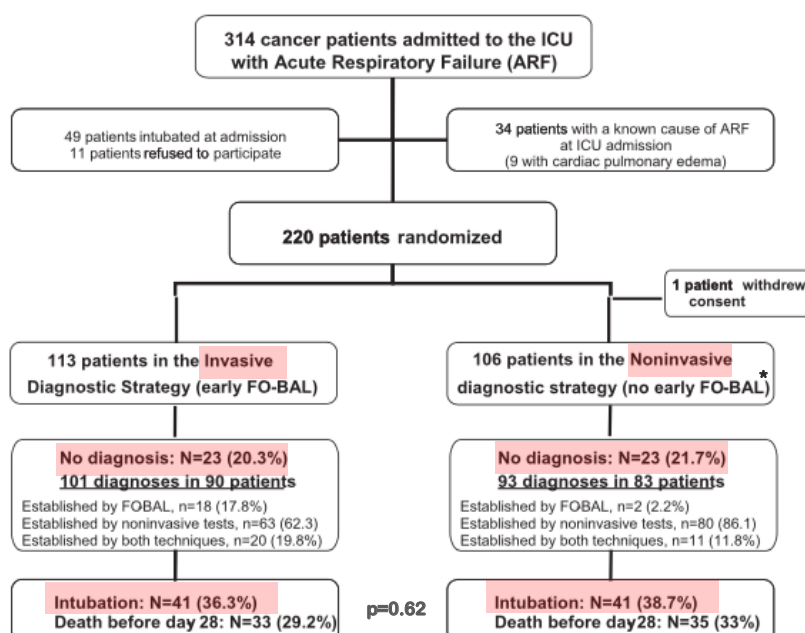
ARF AND ETIOLOGY IN CANCER PATIENTS



Post hoc analysis prospective multicenter cohort, with HM patients admitted to ICU due to ARF (n=604) (2010-2011)

Contejean A, Ann Intensive Care 2016

ROLE OF BAL IN ARF ETIOLOGIC DIAGNOSIS IN CRITICALLY ILL CANCER PATIENTS

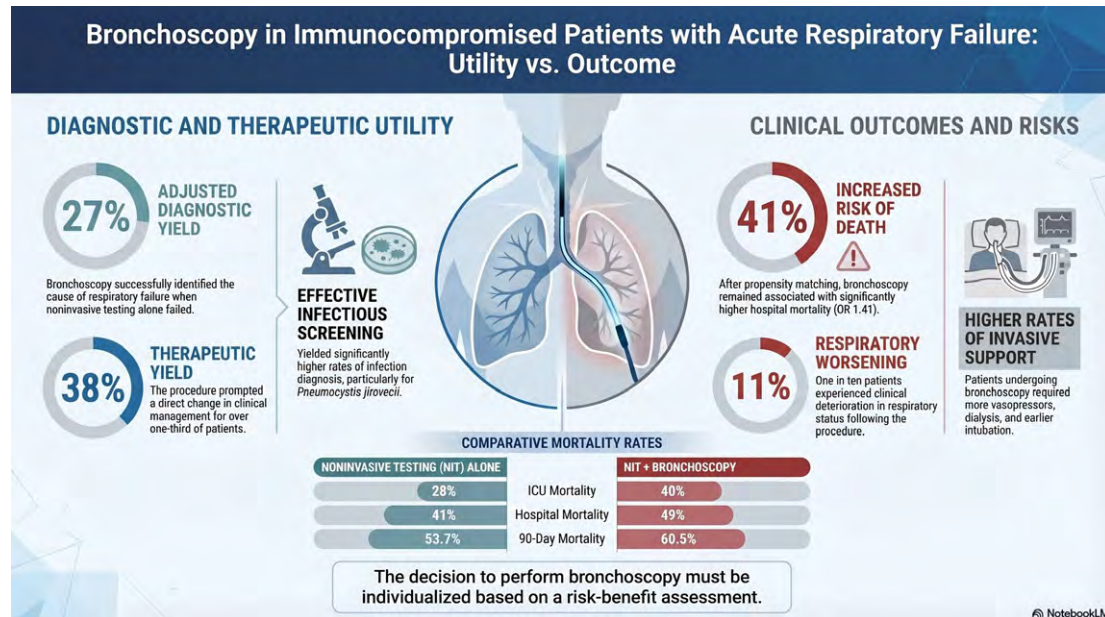


Multicenter (16 French ICU) RCT: patients with cancer + ARF of unknown cause without ventilatory support and admitted to ICU, comparing early FO-BAL + non-invasive tests (n=113) vs non-invasive tests only (n=106) (2005-2007)

* 38 (36%) patients underwent FO-BAL either at intubation or after Day 3, which provided a diagnosis not found by noninvasive tests in 2 patients.

Azoulay E, Am J Respir Crit Care Med 2010

ROLE OF BAL IN ARF ETIOLOGIC DIAGNOSIS IN CRITICALLY ILL CANCER PATIENTS



Pre-planned secondary analysis of Efrain study (prospective multicenter study of immunosuppressed patients admitted to ICU due to ARF) (n= 1611) (2015-2016)

Bauer P, Eur Respir J 2019

IMPORTANCE OF EARLY AND EFFECTIVE TREATMENT IN CRITICALLY ILL CANCER PATIENTS



Castro P, Intensive Care Med 2026



IMPORTANCE OF MULTIDISCIPLINARY MANAGEMENT IN CRITICALLY ILL CANCER PATIENTS

JOURNAL OF CLINICAL ONCOLOGY

Effects of Organizational Characteristics on Outcomes and Resource Use in Patients With Cancer Admitted to Intensive Care Units

Retrospective study of critically ill cancer patients (n=9,946, 8,956 ST and 990 HM) in 70 ICUs (51 general hospitals and 19 in cancer centers) in Brazil in 2013.

EXPERT
ADVICE

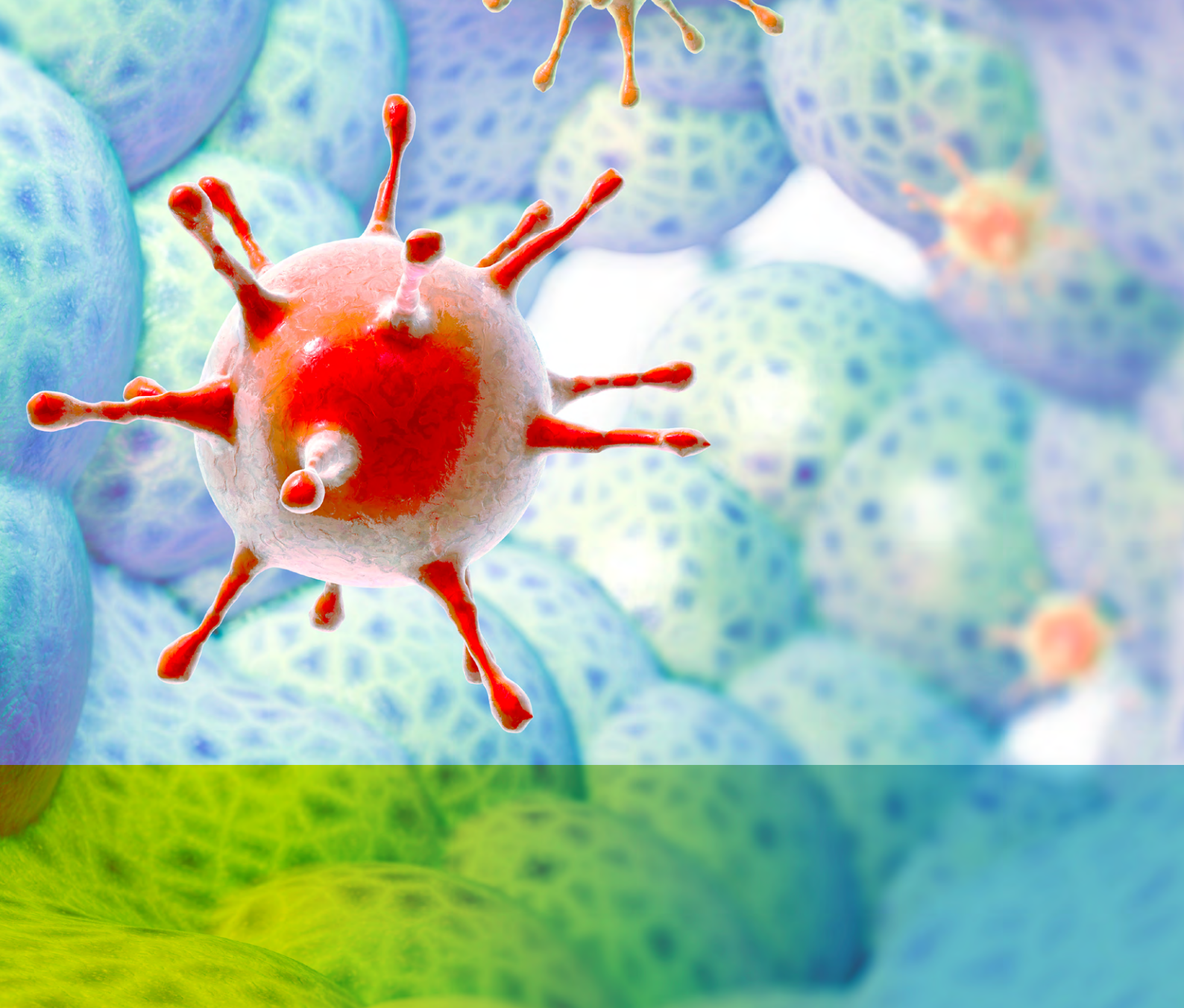
Table 4. Multilevel Multivariable Analysis of Characteristics Associated With Hospital Mortality

Variable	OR (95% CI)	P
Center level		
Type of hospital		
General	1.000	
Referral cancer center	1.210 (0.893 to 1.638)	.217
Training programs in critical care in ICU		
No	1.000	
Yes	1.376 (1.048 to 1.808)	.021
Presence of clinical pharmacist in ICU		
No	1.000	
Yes	0.666 (0.492 to 0.900)	.008
Daily meetings between oncologists and intensivists for care planning in all patients		
No	1.000	
Yes	0.688 (0.520 to 0.910)	.009
Implemented clinical protocols†	0.923 (0.865 to 0.984)	.015

Soares M, J Clin Oncol 2016

TAKE HOME MESSAGES

- Prevalence and survival of critically ill patients with HM is increasing
- Infection and sepsis are the most important cause of ICU admission
- Prognosis factors include aspects related to the patient, the baseline disease and the cause and severity of ICU admission
- Early admission, Etiologic diagnosis, Early and Effective treatment and Expert advice are strategies that reduce mortality in this population



ENTIDADES COLABORADORAS

