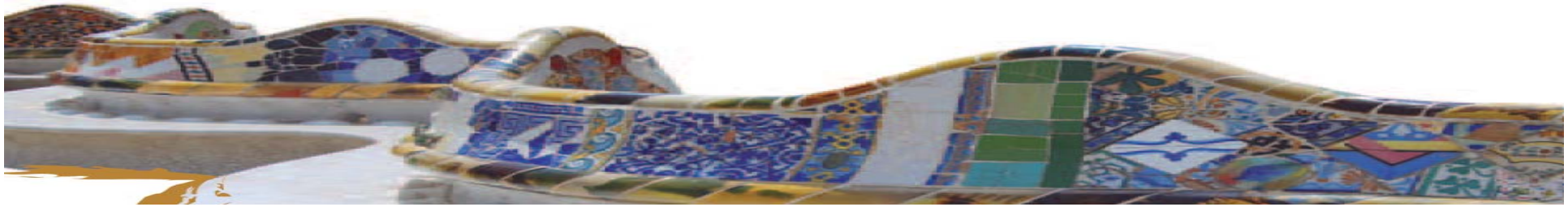
12.30-13.00
SIMPOSI SATÈL·LIT ▸ PFIZER
AVANTATGES D'ANIDULAFUNGINA EN EL TRACTAMENT DE LES INFECCIONS FÚNGIQUES EN EL PACIENT CRÍTIC
Ponent ▾ Javier González de Molina.
Hospital Universitari Mútua de Terrassa

34 REUNIÓ SOCIETAT CATALANA **Medicina Intensiva i Crítica**

Nous reptes, noves solucions

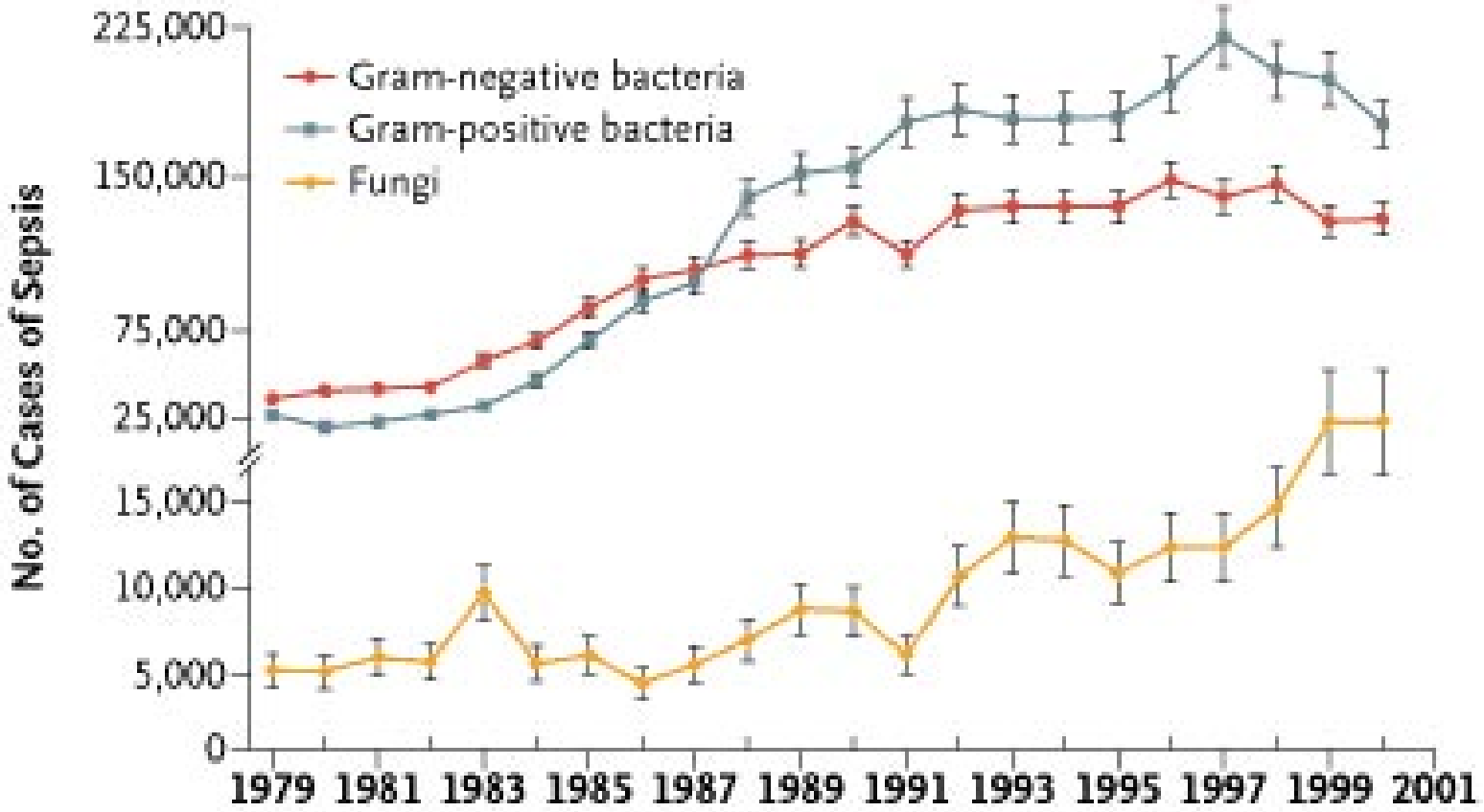
Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Dr. Francisco Javier González de Molina Ortiz
Servei de Medicina Intensiva.
Hospital Universitari Mutua Terrassa



Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Epidemiología:



Epidemiología:

Escenario clínico: UCI *versus* salas de hospitalización

Patógeno	UCI	Salas	RR* (IC 95%)
Estafilococos coagulasa (-)	59	41	1.34 (1.28-1.42)
Staphylococcus aureus	44	56	0.74 (0.68-0.81)
Enterococos	53	47	1.07 (0.97-1.18)
Candida spp	57	43	1.25 (1.10-1.41)
Escherichia coli	33	67	0.47 (0.40-0.54)
Enterobacter	62	38	1.56 (1.32-1.85)
Serratia	60	40	1.41 (1.04-1.90)
Pseudomonas spp	54	46	1.11 (0.94-1.31)

Edmond MB et al. Clin Infect Dis 1999; 29: 239

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Epidemiología:

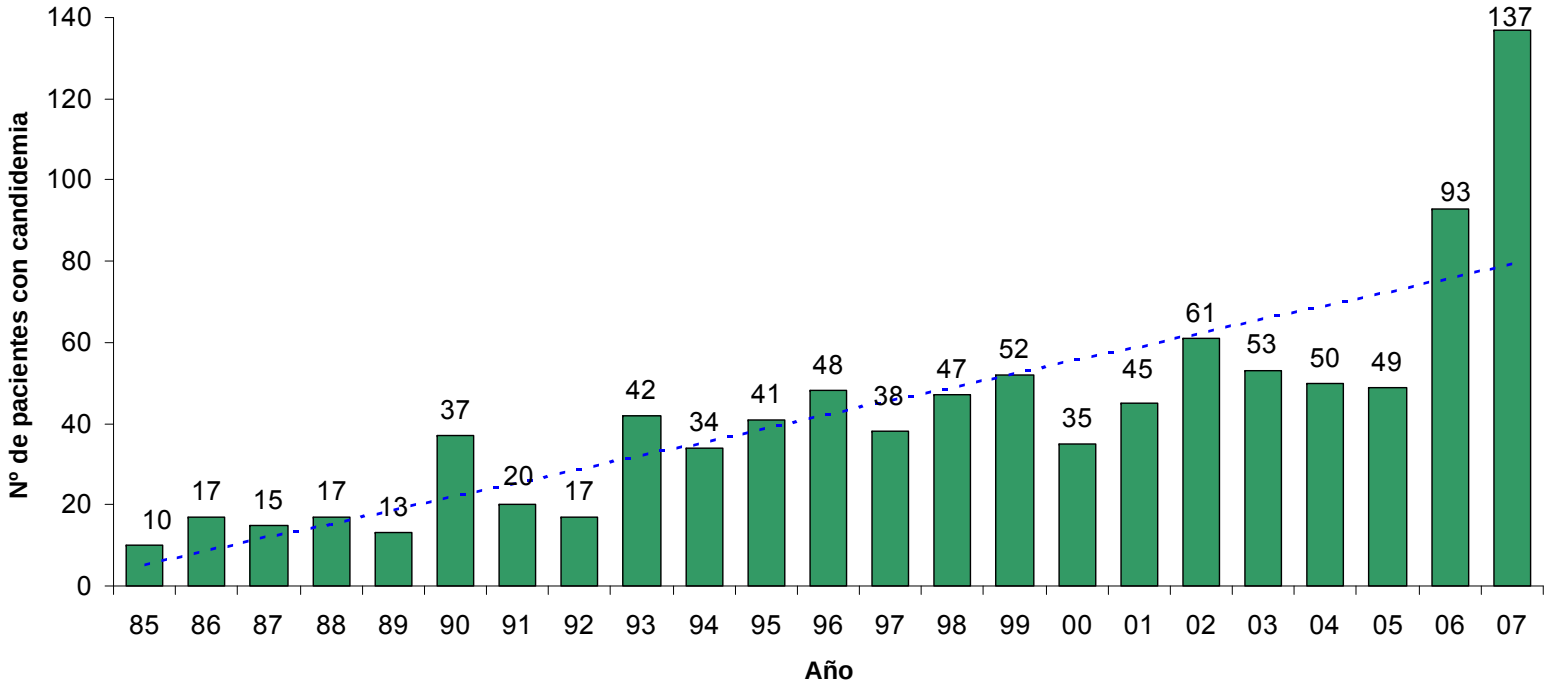


Fig.1. Evolución de episodios de candidemia en el Hospital Gregorio Marañon de Madrid, 1985-2007

Indicaciones:

Incidencia media de candidemia adquirida en UCI En 24 Unidades de Cuidados Intensivos (UCIs)		
Unidad	**Número de ingresos**	**Candidemia adquirida en UCI por 1.000 ingresos**
UCI Médica (N=12)	4.931	5,3
UCI quirúrgica (N=10)	2.745	7,3
Unidad Hematología (N=1)	702	8,5
Unidad Quemados (N=1)	131	38,2
Total	**8.509**	**6,7**
Adaptado de Bougnoux ME, et al. *Intensive Care Med.* 2008;34:292–299.		

Indicaciones:

	Tortorano (n=569) J Hosp Infect 2002	Trick (n=2759) CID 2002	Diekema (n=254) J Clin Microbiol 2002	Richet (n=377) CMI 2002	Pfaller (n=1134) J Clin Microbiol 2002	Marche (n=113 CID 2004
C.albicans	58,50%	59%	58%	53%	55%	66%
C.glabrata	12,80%	12%	20%	11%	15%	15%
C.parapsilosis	14,60%	11%	7%	16%	15%	1%
C.tropicalis	6,10%	10%	11%	9%	9%	9%
C.krusei	0,90%	1,20%	2%	4%	1%	2%
Miscellaneous	7,10%	7%	2%	6%	1%	7%

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Epidemiología:

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La resistencia a fluconazol en los aislados de candidemias causadas por Candida no-albicans es elevada en la mayor parte de los estudios publicados (C. glabrata)

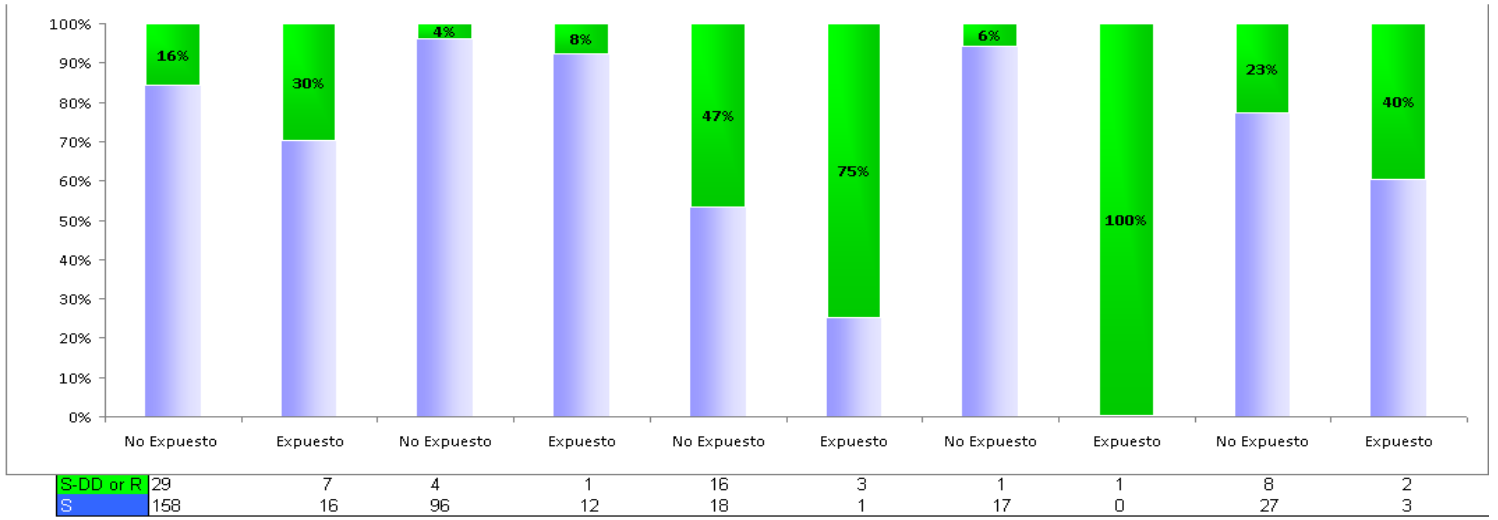


Figura 1: Sensibilidad in vitro a fluconazol de especies de Candida aisladas de pacientes sin tratamiento previo con azoles y de pacientes previamente expuestos a azoles. S= Sensible; S-DD: Sensible dosis dependiente; R= Resistente

Adaptado de Leroy O et al. Crit Care Med 2009; 37:1

Factores de riesgo:

Tabla 1. Factores de riesgo descritos que predisponen a los pacientes de UCI a las infecciones invasivas por Candida

Factores del huésped	Factores Yatrógenos
Neutropenia (especialmente >10 días)	Tratamiento inmunosupresor (corticoides)
Colonización por *Candida* (ej. Índice de colonización >0.5)	Terapia con antibióticos de amplio espectro,
Pancreatitis necrosante	Nutrición parenteral total
Perforación gastrointestinal	Catéter venoso central
Insuficiencia renal aguda	Ventilación mecánica
Sepsis bacteriana	Cirugía Mayor (ej : resección tumor abdominal)
Enfermedad hematológica maligna	Dehiscencia de anastomosis gastrointestinal
Índice APACHE II alto	Quimioterapia antineoplásica
Diabetes mellitus	Hemodiálisis
Mayor edad	

Epidemiology of Candidaemia in Europe: Results of 28-Month European Confederation of Medical Mycology (ECMM) Hospital-Based Surveillance Study

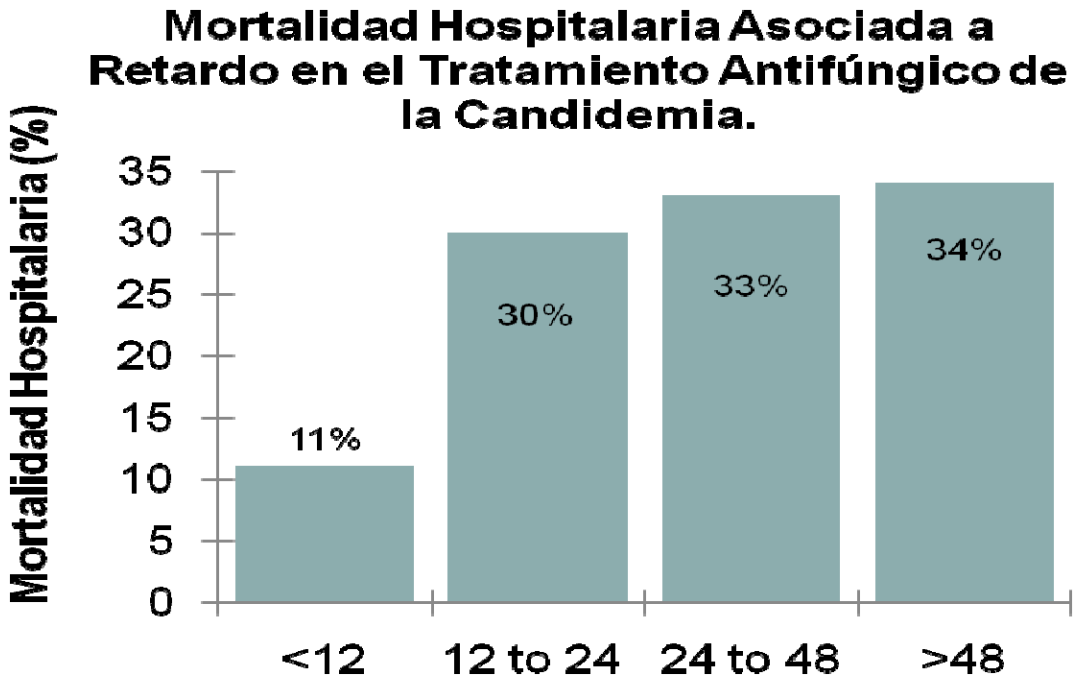
Underlying conditions[a,b]	No. (%) of
Surgery	933 (44.7)
Intensive care	839 (40.2)
Solid tumour	471 (22.5)
Haematological malignancy	257 (12.3)
Premature birth	125 (6.0)
Solid organ transplantation	74 (3.5)
HIV infection	63 (3.0)
Burns	29 (1.4)

Parameter	No. of episodes	Percent mortality	*P* value[a]
Aetiologic agent			
C. albicans	1,090	38.5	0.65
C. glabrata	269	45.0	0.02
C. parapsilosis	263	25.9	<0.001
C. tropicalis	140	41.4	0.42
Underlying condition			
Surgery	892	35.3	0.26
Intensive care	791	42.4	0.02
Solid tumor	442	49.2	<0.001
Haematological malignancy	247	44.9	0.03
HIV infection	61	23.4	0.03
Premature birth	123	26.8	0.02
Age group			
<1 y	142	26.0	0.006
1–19 y	148	22.3	<0.001
20–69 y	1,096	36.6	0.46
≥70 y	556	47.7	<0.001
Total	1,942	37.9	

[a]Calculated against overall crude mortality

Tortorano AM, Pemán J et al, Eur J Clin Infect Dis 2004; 23:317

Morrell et al. *Antimicrob Agents Chemother* 2005; 49: 3640.



Variable	OR Ajustada	IC 95%	P
APACHE II	1.24	1.18-1.31	<0.001
ATB previos	4.05	2.14-7.65	0.028
Retraso Antifúngicos	2.09	1.53-2.84	0.018

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Indicaciones:

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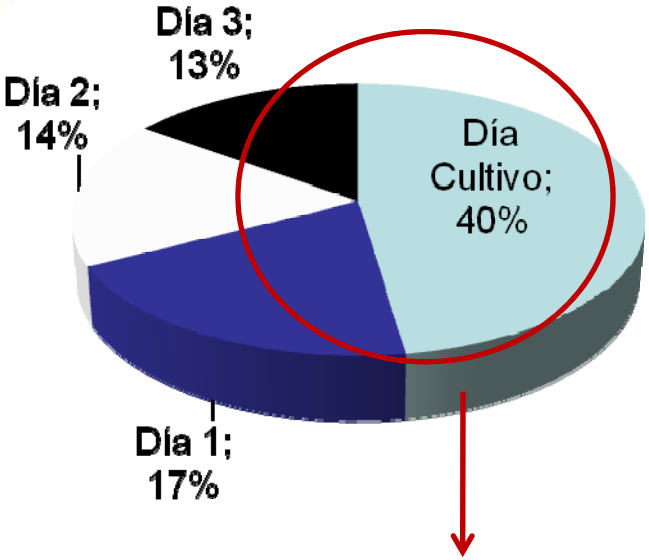
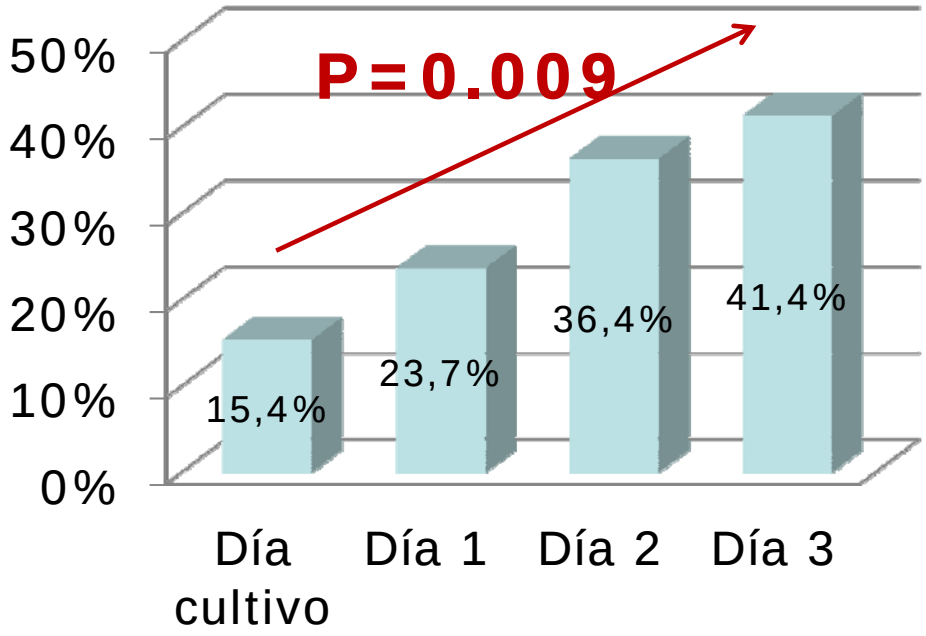
Inicio tratamiento antifúngico



Mortalidad Hospitalaria

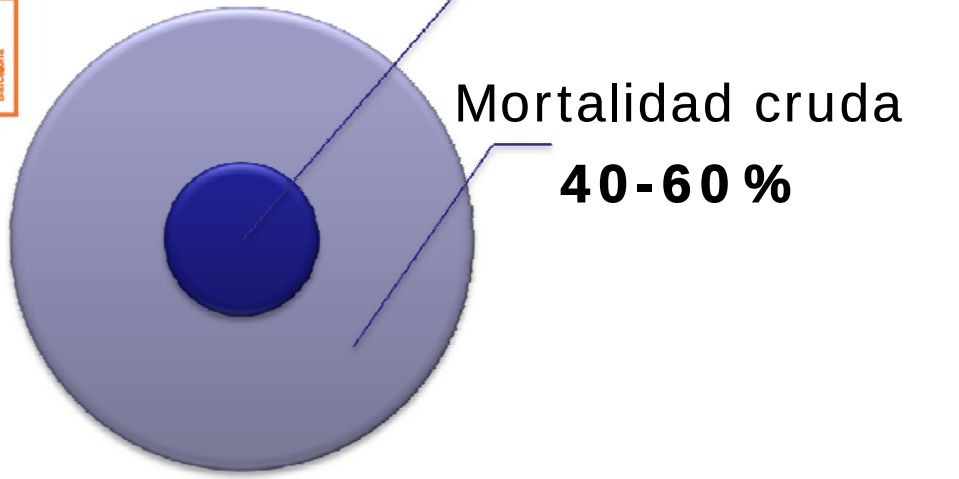


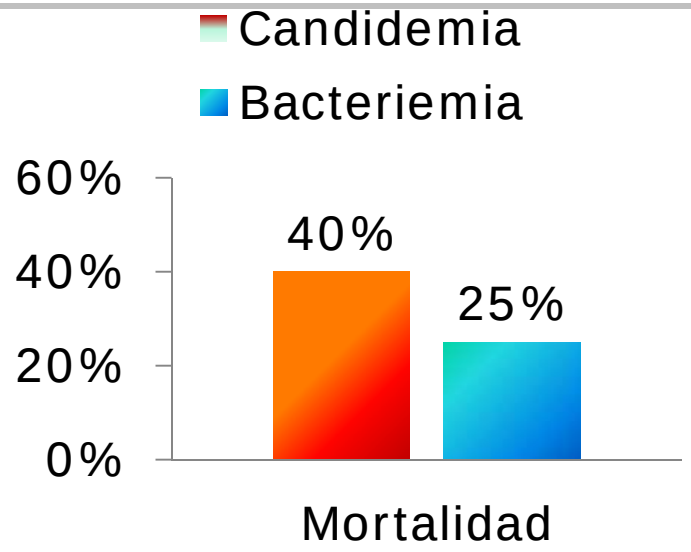
Variable	OR Ajustada	IC 95%	P
APACHE II	1.13	1.08-1.18	<0.001
Retraso Antifúngicos	1.5	1.09-2.09	<0.0138

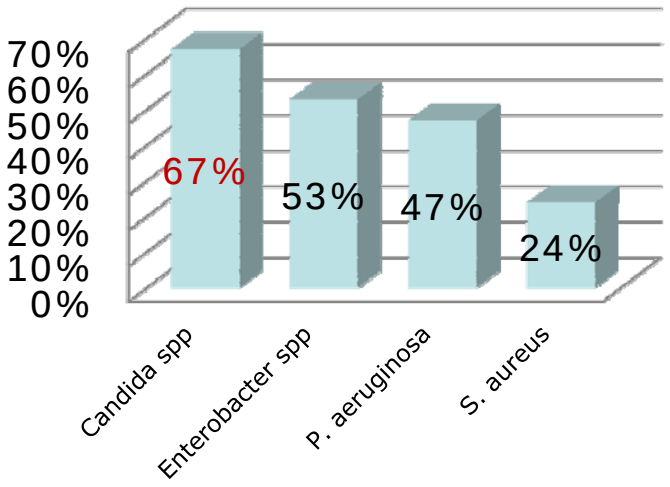
Garey et al. *Clin Infect Dis* 2006; 43: 25.

Indicaciones:

Pronóstico Candidemia:







Indicaciones:

Effects of Nosocomial Candidemia on Outcomes of Critically Ill Patients

Stijn I. Blot, MS, Koenraad H. Vandewoude, MD, Eric A. Hoste, MD, Francis A. Colardyn, MD

PURPOSE: To determine whether nosocomial candidemia is associated with increased mortality in intensive care unit (ICU) patients.

SUBJECTS AND METHODS: We performed a retrospective (1992 to 2000) cohort study of 73 ICU patients with candidemia and 146 matched controls. Controls were matched based on disease severity as measured by the Acute Physiology and Chronic Health Evaluation (APACHE) II score (± 1 point), diagnostic category, and length of ICU stay before onset of candidemia.

RESULTS: In comparison with the control group, patients with candidemia developed more acute respiratory failure (97% [n = 71] vs. 88% [n = 129], $P = 0.03$) during their ICU stay. They were mechanically ventilated for a longer period (29 ± 26 days vs. 19 ± 19 days, $P<0.01$) and had a longer stay in the ICU (36 ± 33 days vs. 25 ± 23 days, $P = 0.02$) as well as in the hospital (77 ± 81 days vs. 64 ± 69 days, $P = 0.04$). There was no difference in in-hospital mortality between the groups (48% [n = 35] vs. 43% [n = 62], $P = 0.44$), a difference of 5% (95% confidence interval [CI]: −8% to 19%). In a multivariate analysis, older age (hazard ratio [HR] = 1.13 per 10 years; 95% CI: 1.04 to 1.23; $P = 0.004$), acute renal failure (HR = 1.4; 95% CI: 1.1 to 2.0; $P = 0.02$), and unfavorable APACHE II scores (HR = 1.10 per 5 points; 95% CI: 1.00 to 1.20; $P = 0.05$) were independent predictors of mortality. Candidemia was not associated with mortality in a model that adjusted for these factors (HR = 0.9; 95% CI: 0.7 to 1.2; $P = 0.53$).

CONCLUSION: Nosocomial candidemia does not adversely affect the outcome in ICU patients in whom mortality is attributable to age, the severity of underlying disease, and acute illness. **Am J Med. 2002;113:480–485.**

González de Molina et al. Critical Care 2012, 16:R105
http://ccforum.com/content/16/3/R105

CRITICAL CARE

RESEARCH Open Access

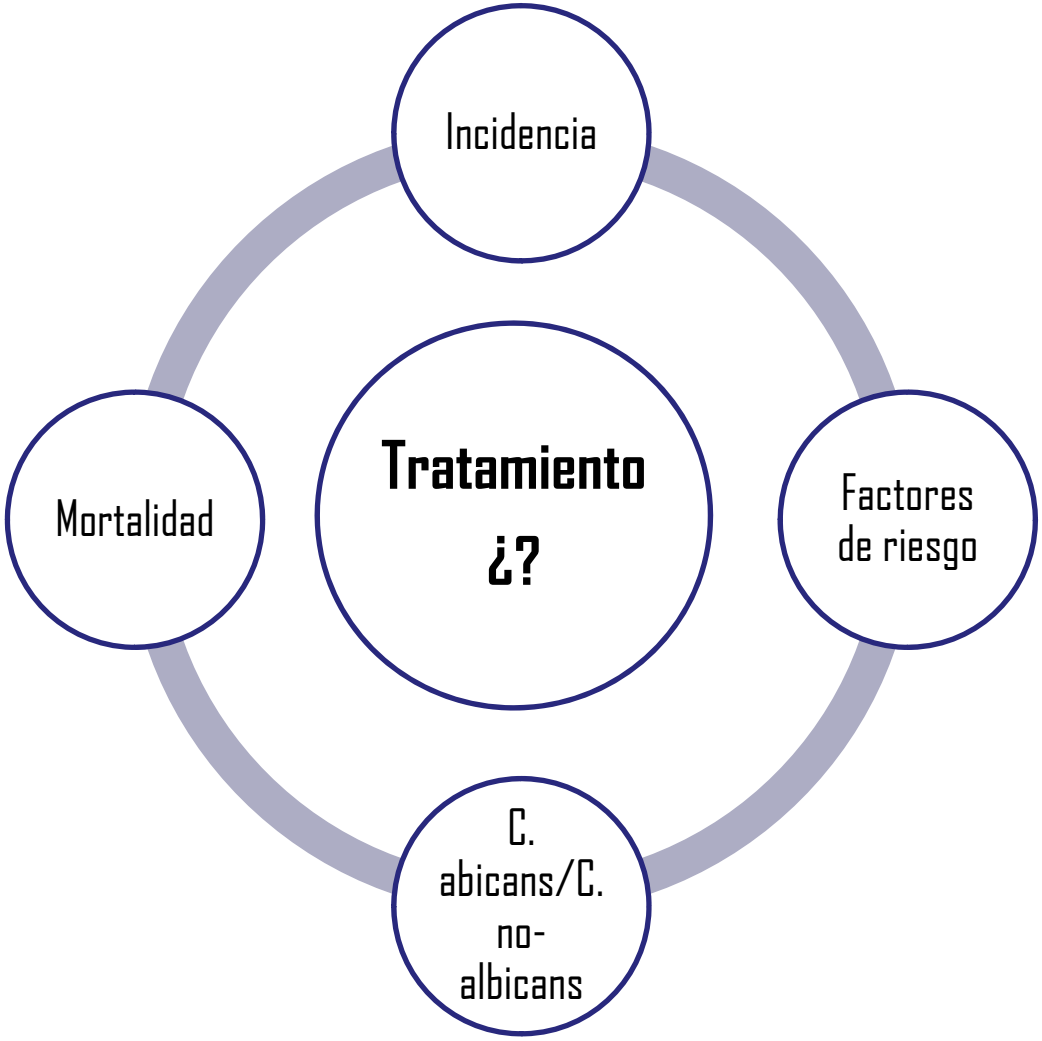
Assessment of candidemia-attributable mortality in critically ill patients using propensity score matching analysis

Francisco J González de Molina[1*], Cristóbal León[2], Sergio Ruiz-Santana[3] and Pedro Saavedra[4], for the CAVA I Study Group

Key messages

- Candidemia was not associated with an increase in either ICU or hospital mortality.
- The use of propensity score matching analysis to control for all potential confounding variables allowed the assessment of candidemia-attributable mortality in critically ill patients.
- Earlier treatment of bloodstream infection and better monitoring (surveillance sampling weekly), resulting in appropriate antifungal agent may contribute to increased survival.
- APACHE II at the time of diagnosis of candidemia was the only predictor of death in patients with candidemia.

Indicaciones:



Impact of Treatment Strategy on Outcomes in Patients with Candidemia and Other Forms of Invasive Candidiasis: A Patient-Level Quantitative Review of Randomized Trials

34 REUNIÓ SOCIETAT CATALANA Medicina Intensiva i Crítica

David R. Andes,[1] Nasia Safdar,[1] John W. Baddley,[2] Geoffrey Playford,[6] Annette C. Reboli,[3] John H. Rex,[4] Jack D. Sobel,[5] Peter G. Pappas,[2] and Bart Jan Kullberg[7] for the Mycoses Study Group[a]

[1]University of Wisconsin, Madison; [2]Univerity of Alabama at Birmingham; [3]Robert Wood Johnson Medical School, New Brunswick, New Jersey; [4]AstraZeneca, Wilmington, Delaware; [5]Wayne State University School of Medicine, Detroit, Michigan; [6]University of Queensland, Brisbane, Australia; and [7]Radboud University Nijmegen Medical Center, The Netherlands

CID 2012:54 (15 April)

Inclusión	Indentificar los ensayos clínicos randomizados que COMPARABAN diferentes tratamientos antifúngicos para Candidemias y Candidiasis Invasiva para cada especie de *Candida.*
Objetivos	Evalución de la mortalidad a los 30 días. Respuesta clínica y microbiológica al fin del tratamiento.
Antifúngicos	Los fármacos antifungicos a comparar: Polienos (anfotericina B). Triazoles (Fluconazol y Voriconazol). Equinocandinas (Anidulafungina, Caspofungina, Voriconazol).

Table 1. Characteristics of Randomized Controlled Candidemia Trials Fulfilling Criteria for Inclusion in Analysis

Reference (Patient No.; Enrollment Dates)	Drugs and Maintenance Regimens	Design	Inclusion	Host or Disease Factor Exclusion	Treatment Duration	Modified Intent-to-Treat Population	Primary Outcome	Secondary Outcome
Rex et al, 1994 [46] (237; 1989–1993)	Fluconazole 400 mg/d vs amphotericin B 0.5–0.6 mg/kg/d	Randomized, double blinded	Candidemia and fever or hypotension	Neutropenia, hematologic malignancy, HIV, transplant, pregnancy	≥14 d after last positive blood culture	Receipt of ≥1 d of antifungal drug	Clinical and microbiologic success at EOT	All-cause death at EOT
Mora-Duarte et al, 2002 [48] (239; 1997–2001)	Caspofungin 50 mg/d vs amphotericin B 0.6–0.7 mg/kg/d (0.7–1.0 for neutropenic patients)	Randomized, double blinded	Candidemia or invasive candidiasis	Endocarditis, osteomyelitis, meningitis	10 d intravenous and all therapy >14 d after last positive culture	Receipt of ≥1 d of antifungal drug	Clinical and microbiologic success and absence of toxicity-required change in therapy at EOT	All-cause death at EOT
Rex et al 2003 [45] (236; 1995–1999)	Fluconazole 800 mg/d vs amphotericin B 0.6–0.7 mg/kg/d and fluconazole 800 mg/d	Randomized, double blinded	Candidemia and fever or hypotension	Neutropenia, pregnancy, *Candida krusei*	≥14 d after last positive blood culture, amphotericin B component 5–8 d	Receipt of ≥1 d of antifungal drug	Clinical and microbiologic success at EOT	All-cause death at EOT
Kullberg et al 2005 [47] (422; 1998–2003)	Voriconazole 3 mg/kg every 12 h for 3 d, then possible switch to 200 mg oral twice daily vs amphotericin B 0.7–1.0 mg/kg/d followed by fluconazole 400 mg/d	Randomized, double blinded	Candidemia and fever or hypotension	Neutropenia, AIDS, chronic granulomatous disease, aplastic anemia, hepatic and renal dysfunction, pregnancy	≥14 d after last positive blood culture	Receipt of ≥1 d of antifungal drug	Clinical and microbiologic success at 12 wk and EOT	All-cause death at 30 d
Reboli et al 2007 [43] (245; 2003–2004)	Anidulafungin 100 mg/d vs fluconazole 400 mg/d	Randomized, double blinded	Candidemia or invasive candidiasis	Pregnancy	≥14 d after last positive blood culture	Receipt of ≥1 d of antifungal drug and document fungal infection	Clinical and microbiologic success at EOT	All-cause death within 30 d
Kuse et al 2007 [41] (264; 2003–2004)	Micafungin 100 mg/d vs liposomal amphotericin B 3 mg/kg/d	Randomized, double blinded	Candidemia or invasive candidiasis	Hepatic dysfunction	>14 d	Receipt of ≥1 d of antifungal drug	Clinical and microbiologic success at EOT	All-cause death within 30 d
Pappas et al 2007 [49] (595; 2004–2006)	Micafungin 100 or 150 mg/d for ≥10 d then possible switch to fluconazole 400 mg/d vs caspofungin 50 mg/d for ≥10 d then possible switch to fluconazole 400 mg/d	Randomized, double blinded	Candidemia or invasive candidiasis	Hepatic dysfunction, pregnancy, cyclosporin use, endocarditis, osteomyelitis, meningitis	≥14 d after last positive blood culture	Receipt of ≥1 d of antifungal drug and documentation of fungal infection	Clinical and microbiologic success at EOT	All-cause death within 30 d

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CID 2012:54 (15 April)

		Success		
	Factor	*P*	OR	95% CI
All organisms (n = 978)	APACHE II	.0001	0.94	.93–.96
	Echinocandin	.01	2.33	1.27–4.35
	CVC removed	.001	1.69	1.23–2.33
Candida albicans (n = 408)	APACHE II score	.005	0.92	.92–.99
	Echinocandin	.005	3.70	1.49–9.09
Candida glabrata (n = 104)	APACHE II score	.05	0.95	.90–.99
	Echinocandin	.05	2.63	1.10–625
Candida parapsilosis[c]	APACHE II score	.01	0.95	.90–.99
	Study	NS		

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Identifica dos factores asociados a un incremento en la supervivencia:

1. El uso de una equinocandina.
2. La retirada del CVC.

Impact of Treatment Strategy on Outcomes in Patients with Candidemia and Other Forms of Invasive Candidiasis: A Patient-Level Quantitative Review of Randomized Trials

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- Hasta la fecha se había demostrado la equivalencia o la no inferioridad de las equinocandinas frente al fluconazol o la anfotericina. De modo que sí se reportaba la mejor tolerancia de las candinas y menor incidencia de efectos adversos (tales como nefrotoxicidad) o interacciones pero sin impacto sobre la mortalidad.
- Ahora se establece finalmente la superioridad en terminos de supervicencia y eficacia de las candinas con respecto a los azoles o la anfotericina B.
- Y esto es así tanto para la *C. albicans* como para las no-albicans (C. parapsilosis (MIC>candinas). También en el estudio se analiza por quartiles del APACHE II y también la candina mejora la supervivencia en pacientes menos graves y pacientes graves (a excepción de cuando el APACHE II>24 que entonces no encuentra diferencias).

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CID 2012:54 (15 April)

EDITORIAL COMMENTARY

The End of an Era in Defining the Optimal Treatment of Invasive Candidiasis

Cornelius J. Clancy and M. Hong Nguyen
Department of Medicine, Division of Infectious Diseases, University of Pittsburgh, Pennsylvania

1. Son acordes a las actuales guía clínicas.
2. Equinocandinas como el tratamiento de primera elección en la mayoría de los pacientes
3. Resuelve la discusión sobre la retirada del CVC.

ESCMID PUBLICATIONS 10.1111/1469-0691.12039

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

O. A. Cornely[1†], M. Bassetti[2†], T. Calandra[3†], J. Garbino[4†], B. J. Kullberg[5†], O. Lortholary[6,7†], W. Meersseman[8†], M. Akova[9], M. C. Arendrup[10], S. Arikan-Akdagli[11], J. Bille[3], E. Castagnola[12], M. Cuenca-Estrella[13], J. P. Donnelly[5], A. H. Groll[4], R. Herbrecht[15], W. W. Hope[16], H. E. Jensen[17], C. Lass-Flörl[18], G. Petrikkos[19], M. D. Richardson[20], E. Roilides[21], P. E. Verweij[5], C. Viscoli[22] and A. J. Ullmann[23] for the ESCMID Fungal Infection Study Group (EFISG)

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ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

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Intervention	SoR	QoE	References	Comment
Anidulafungin 200/100 mg	A	I	[64]	Consider local epidemiology (*Candida parapsilosis*, *Candida krusei*), less drug–drug interactions than caspofungin
Caspofungin 70/50 mg	A	I	[67] [55] [63]	Consider local epidemiology (*C. parapsilosis*)
Micafungin 100 mg	A	I	[61] [63]	Consider local epidemiology (*C. parapsilosis*), less drug–drug interactions than caspofungin, consider EMA warning label
Amphotericin B liposomal 3 mg/kg	B	I	[61] [62]	Similar efficacy as micafungin, higher renal toxicity than micafungin
Voriconazole 6/3 mg/kg/day[a,b]	B	I	[43] [78] [77]	Limited spectrum compared to echinocandins, drug–drug interactions, limitation of IV formulation in renal impairment, consider therapeutic drug monitoring
Fluconazole 400–800 mg[a]	C	I	[165] [53] [74] [54] [64] [76] [75] [73] [72]	Limited spectrum, inferiority to anidulafungin (especially in the subgroup with high APACHE scores), may be better than echinocandins against *C. parapsilosis*
Amphotericin B lipid complex 5 mg/kg	C	II_a	[57] [58]	
Amphotericin B deoxycholate 0.7–1.0 mg/kg	D	I	[50]	Substantial renal and infusion-related toxicity

Se recomienda fuertemente el uso de equinocandinas para el tratamiento dirigido de un paciente con candidemia.

En esta situación se recomienda solo marginalmente el uso de fluconazol.

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

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Population	Intention	Intervention	SoR	QoE
Candidaemia with no organ involvement detected	To avoid organ involvement	Treat for 14 days after the end of candidaemia	B	II
		Take at least one blood culture per day until negative	B	III
	To detect organ involvement	Transoesophageal echocardiography	B	II_a
		Fundoscopy	B	II
		If CVC, PICC or intravascular devices, search for thrombus	B	III
Any	To simplify treatment	*Step-down to fluconazole after 10 days of IV, if species is susceptible, patient tolerates PO, and patient is stable	B	II

CVC, central venous catheter; PICC, peripherally inserted central catheter.
*If *C. parapsilosis* is identified, step-down to fluconazole may occur earlier.

La duración del tratamiento debe ser un mínimo de 14 días desde que el hemocultivo se negativiza.

Puede completarse el tratamiento por V.O. tras al menos 10 días de tratamiento I.V. si el paciente esta estable y la especie de Candida es plenamente sensible a azoles.

ESCMID* guideline for the diagnosis and management of *Candida* diseases 2012: non-neutropenic adult patients

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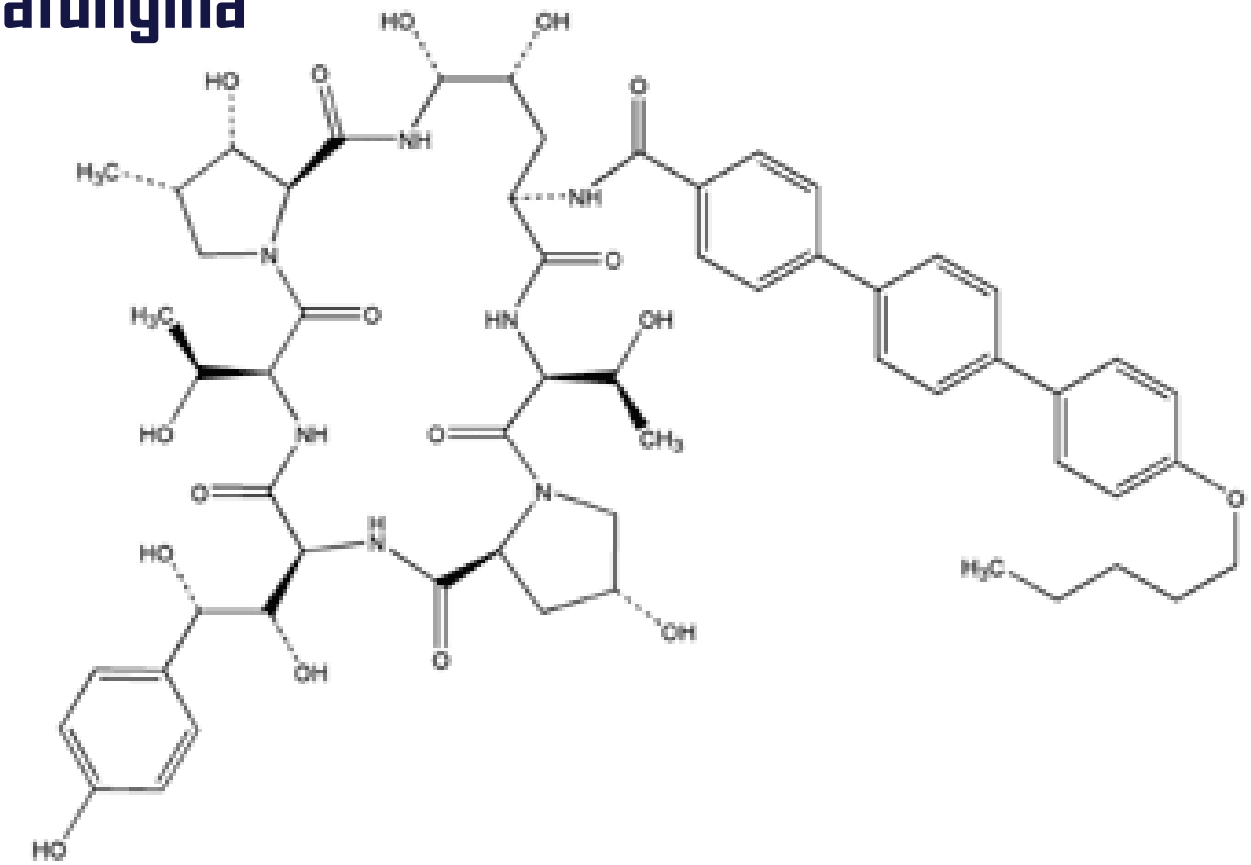
Population	Intervention	SoR	QoE
Central venous catheter can be removed	Remove indwelling lines (not over a guidewire)	A	II_r
Central venous catheter cannot be removed	Echinocandin, liposomal amphotericin B or amphotericin B lipid complex	B	II_r
	Azole or amphotericin B deoxycholate	D	II_r

Se recomienda siempre la retirada del CVC. Si no fuera posible, Utilizar una Candina a ANFBL.

Anidulafungina



Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

Anidulafungina:

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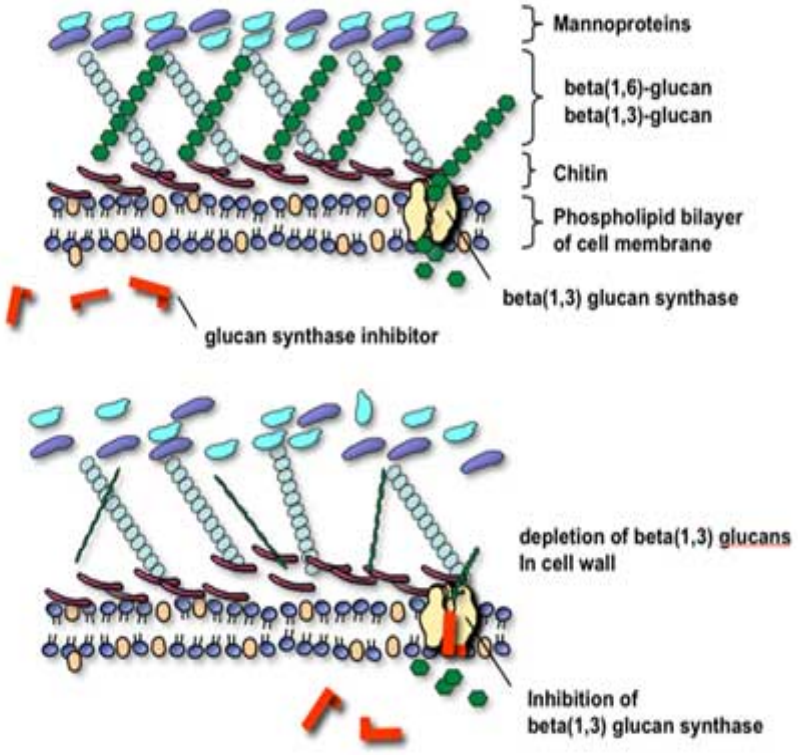
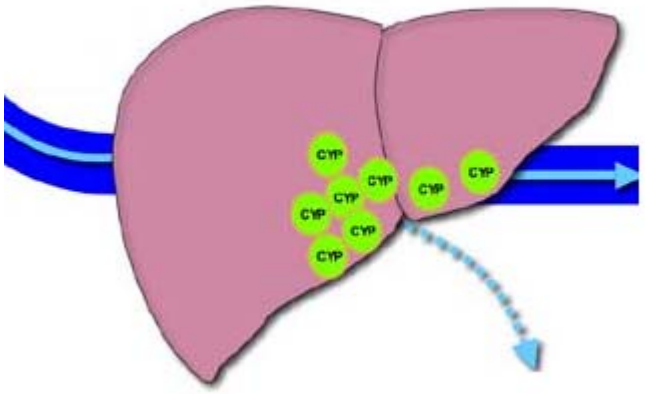
Mecanismo de acción:
Inhibidr no competitivo de Beta (1,3) beta-D-glucan synthase, enzoma responsable de la formación de polisacáridos de pared fúngica.

Farmacocinética:
No absorción oral.
No metabolismo hepático. Lenta degración química que es elimizada por heces (30% en 9 días).
Unión a proteinas:
Cmax, Cmin, and AUC
Cmax: 8.6 mcg/mL; AUC: 111.8 mcg/mL hr (200 mg carga, y 100mg/d en "steady state").
T1/2 : 52 hrs.
Distributción: Vd=30-50L. Baja penetración en SNC.
Dosis en disfunción hepática: For Child-Pugh class A, B, or C: sin cambios.
Dosis en insuficiencia renal: sin cambios.



Indicaciones:

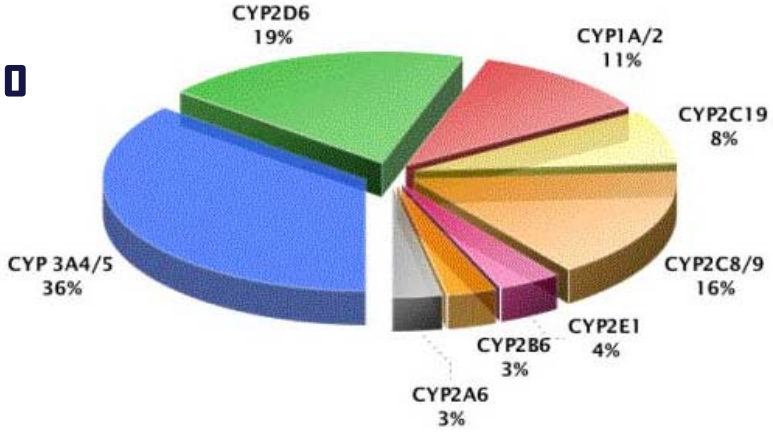
Caspofungina/Micafungina



Biodisponibilidad

Metabolismo

Azoles



Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

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	Caspofungina	Micafungina	Anidulafungina
Semivida ($t_{1/2}$)	9-11 h	15-17 h	26,5 h
Unión a proteínas	~ 97%	> 99%	99 %
Volumen de distribución	No determinado	0,39 l/kg	30-50 l
Metabolismo	Hepático vía hidrólisis y N-acetilación Degradación química espontánea a péptido de anillo abierto	Hepático vía arilsulfatasa y COMT, respectivamente, e hidroxilación vía CYP3A (vía menor)	Degradación química no enzimática lenta a péptido de anillo abierto (sin actividad antimicótica), que luego se convierte en productos de desecho peptídicos
Interacciones	Ciclosporina, tacrolimus, rifampicina, efavirenz, nevirapina, fenitoína, dexametasona, carbamazepina	Sirolimus, nifedipina, itraconazol	No conocidas
Ajuste de dosis en poblaciones especiales	Requeridos por peso[a] y en insuficiencia hepática (moderada)	No utilizar en pacientes con insuficiencia hepática grave[b]	No conocidas

COMT: catecol-O-metiltransferasa.
[a] En pacientes que pesen más de 80 kg, después de la dosis de carga inicial de 70 mg, se recomienda caspofungina 70 mg a diario.
[b] En la actualidad no se dispone de suficientes datos relativos al uso de micafungina en pacientes con insuficiencia hepática grave y, por tanto, no se recomienda su uso en dichos pacientes.

9. European Medicines Agency (EMEA). European public assessment report (EPAR) for caspofungin [consultado 24 Oct 2010]. Disponible en: http://www.ema.europa.eu/humandocs/PDFs/EPAR/cancidas/emea-combined-h379es.pdf
10. European Medicines Agency (EMEA). European public assessment report (EPAR) for micafungin [consultado 24 Oct 2010]. Disponible en: http://www.ema.europa.eu/humandocs/Humans/EPAR/mycamine/mycamine.htm
11. European Medicines Agency (EMEA). European public assessment report (EPAR) for anidulafungin [consultado 24 Oct 2010]. Disponible en: http://www.ema.europa.eu/humandocs/PDFs/EPAR/ecalta/emea-combined-h788es.pdf

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

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	Caspofungina (n=1013)	Micafungina (n= 870)	Anidulafungina (n= 575)
Fiebre (%)	5 – 21	1 – 3	0
Cefalea (%)	6-10	2.5	1
Flebitis (%)	4-16	2-4	1
Nauseas/Vómitos (%)	2-6	1.5-3	1
Diarrea (%)	4	2	4
Rash (%)	1-5	1.5-3	1-3

	Caspofungina (n=1013)	Micafungina (n= 870)	Anidulafungina (n= 575)
↑ AST/ALT (%)	4 – 13	1 – 3	2 – 3
↑ Bilirubina (%)	3 – 4	3	0
Fosfatasa alcalina (%)	8 – 11	2	2
Creatinina (%)	4	0	0
↓ Potasio (%)	4 – 10	2	3
↓ Hb/hematocrito (%)	11 – 12	0	0
↓ Plaquetas (%)	3	0	0
↓ Leucocitos (%)	6	1 – 3	1

Anidulafungin for Candidemia/Invasive Candidiasis in Intensive Care Unit Patients Postabdominal Surgery

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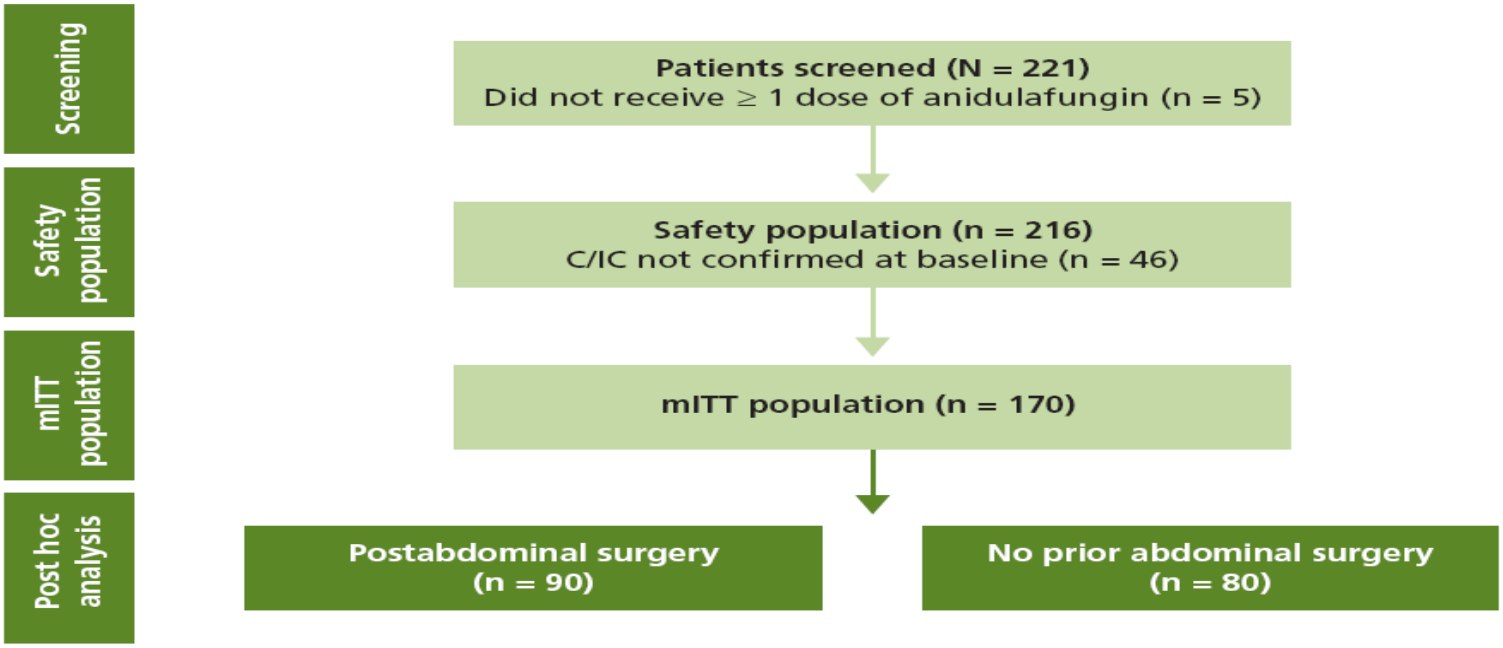
Objetivo:

1. Comparar la eficacia de Anidulafungina en pacientes con CI demostrada CON/SIN cirugía abdominal.
2. Supervivencia a 90 día.
3. Seguridad y tolerancia



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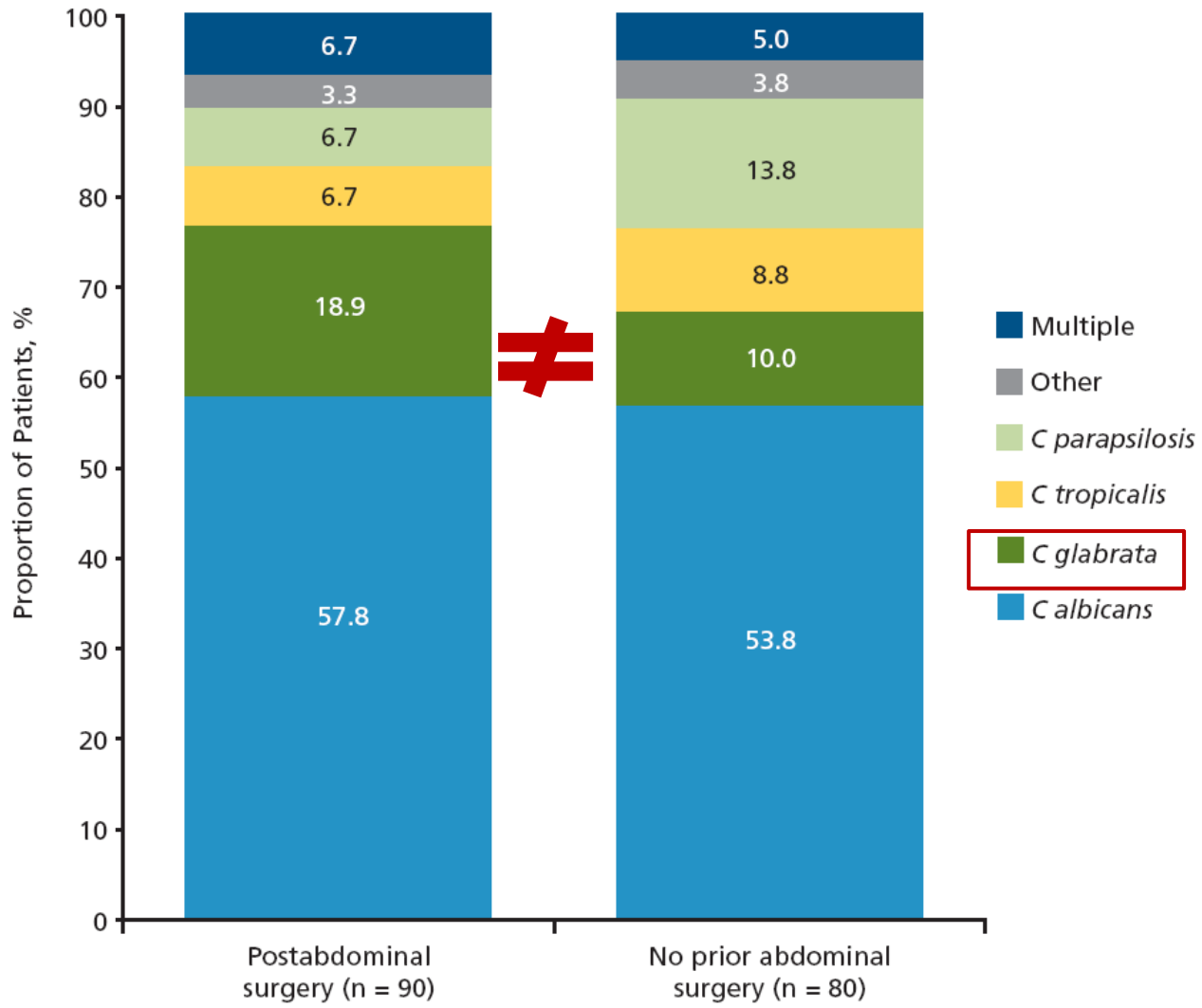

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Table 2. Global and Microbiologic Success Rates in Patients With and Without Prior Abdominal Surgery (mITT Population)

Patient Population	No. of Patients (%) [95% CI]			
	End of IV Therapy	EOT	2 Weeks Post-EOT	6 Weeks Post-EOT
Global success				
Postabdominal surgery	56/81 (69.1) [57.9-78.9]	54/79 (68.4) [56.9-78.4]	40/68 (58.8) [46.2-70.6]	34/63 (54.0) [40.9-66.6]
No prior abdominal surgery	55/76 (72.4) [60.9-82.0]	53/75 (70.7) [59.0-80.6]	37/60 (61.7) [48.2-73.9]	21/46 (45.7) [30.9-61.0]
P value	0.66	0.76	0.74	0.39
Microbiologic success				
Postabdominal surgery	57/82 (69.5) [58.4-79.2]	55/80 (68.8) [57.4-78.7]	40/68 (58.8) [46.2-70.6]	34/63 (54.0) [40.9-66.6]
No prior abdominal surgery	62/79 (78.5) [67.8-86.9]	60/78 (76.9) [66.0-85.7]	37/60 (61.7) [48.2-73.9]	21/46 (45.7) [30.9-61.0]
P value	0.20	0.25	0.74	0.39

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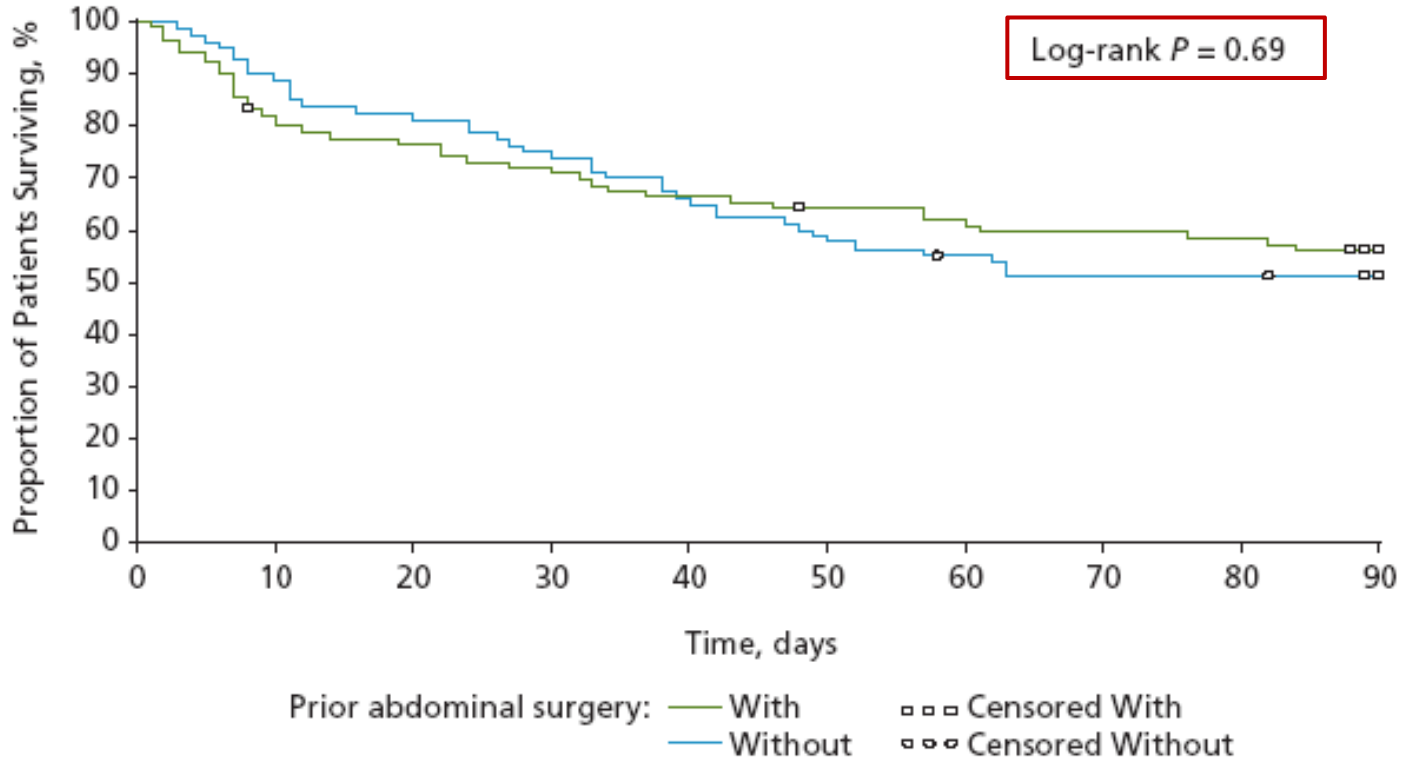

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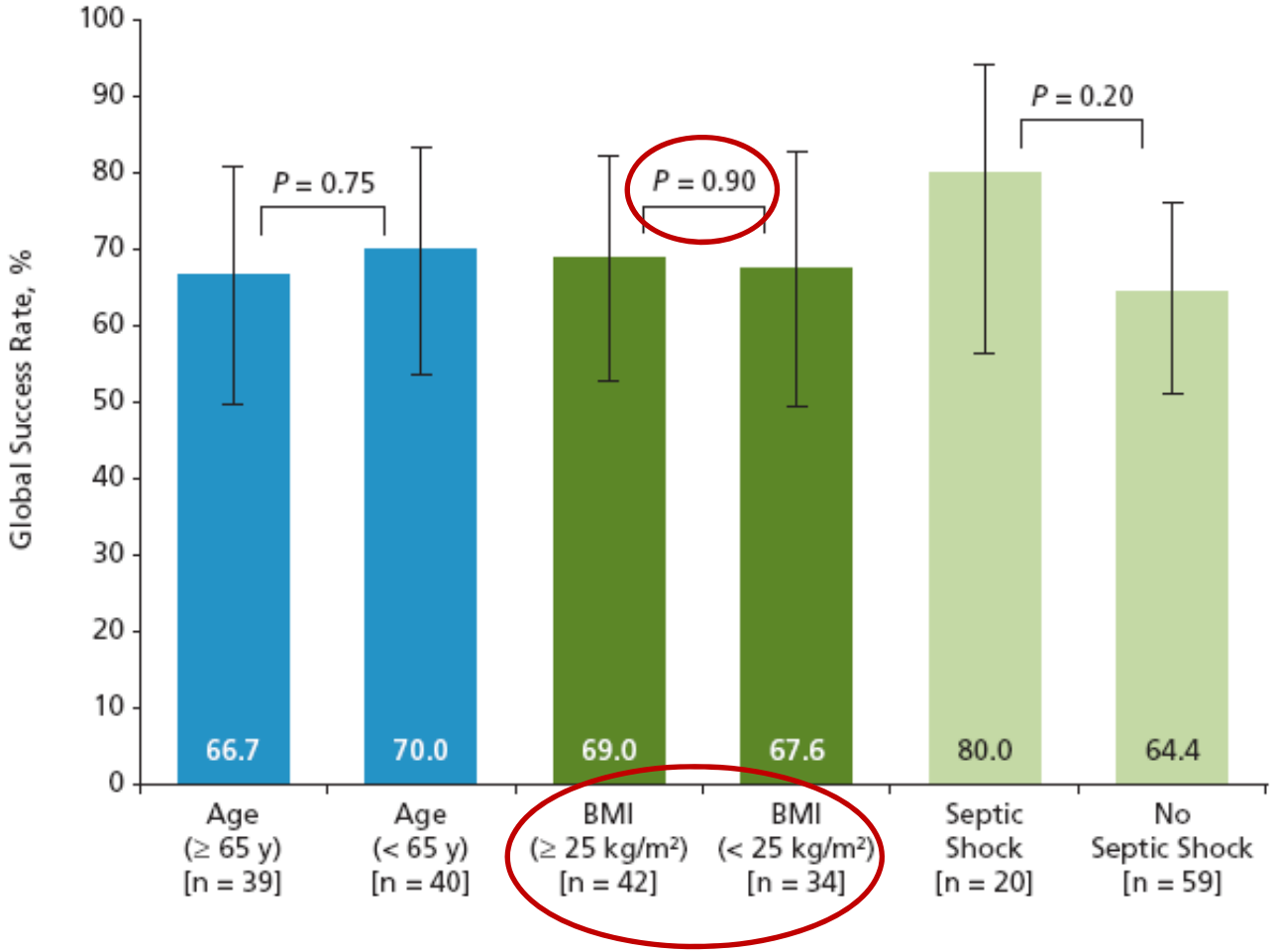

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CONCLUSIONS

- Anidulafungin was effective and safe for the treatment of C/IC in ICU patients who had undergone abdominal surgery.
  - The patients in this subpopulation had a particularly high incidence of deep-tissue infections (52%), and overall results support the efficacy of anidulafungin for invasive candidiasis as well as candidemia.
  - Postabdominal surgery patients also had a slightly elevated incidence of *C glabrata* infections, in keeping with recent observations suggesting that abdominal surgery is an independent risk factor for this pathogen.[9]

Efficacy of Anidulafungin in 105 Patients with Deep Tissue Candidiasis

U Conte,[1] H Schlamm,[1] P Biswas,[1] J Aram,[1] B J Kullberg,[2] M Ruhnke[3]

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Table 1. Patient Demographics

Number of patients, n (%)	105 (100.0)
Gender, n (%)	
Female	58 (55.2)
Male	47 (44.8)
Age, years, n (%)	
18–44	18 (17.1)
45–64	35 (33.3)
⩾65	52 (49.5)

Table 2. Baseline Characteristics

Number of patients, n (%)	105 (100.0)
APACHE II score, n (%)	
⩽20	86 (81.9)
>20	19 (18.1)
Risk factors for invasive candidiasis*, n (%)	
Mechanical ventilation	47 (46.1)
Use of broad spectrum antibiotics	89 (87.3)
Use of central venous catheter	78 (76.5)
Total parenteral nutrition (TPN)	48 (47.1)
Renal insufficiency / failure / dialysis	33 (32.4)
Surgery	67 (65.7)
Abdominal surgery	72 (70.6)
Solid organ transplant	7 (6.9)
Chemotherapy	5 (4.9)
Use of systemic steroids / other immunosuppressive	23 (22.5)
Length of intensive care unit stay ⩾4 days	50 (49.0)
Neutropenia	3 (2.9)

Table 4. Duration of Treatment and Switch to Oral Therapy

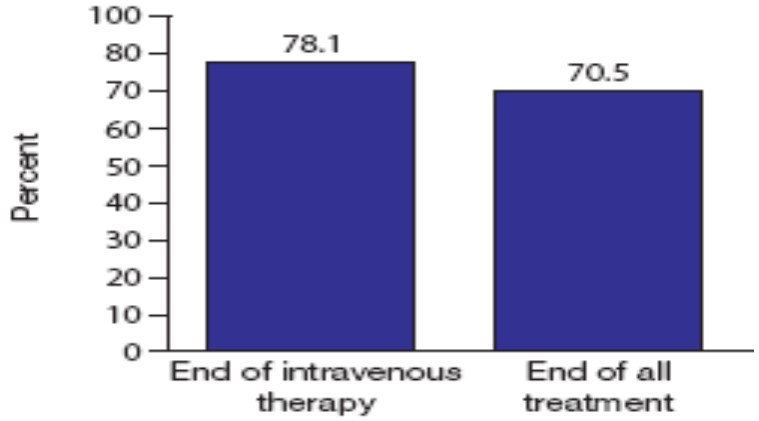
Mean duration of intravenous therapy	13.3 (1–42)
Number of subjects switched to oral therapy, n (%)	46 (43.8)
Mean time to switch to oral therapy (d)	12.0
Total duration (intravenous and oral) therapy, mean (range)	18.1 (1–56)

Table 5. Rate of All-Cause Mortality

	n/N	%
14-day all-cause mortality	19/105	18.1
28-day all-cause mortality	24/105	22.9

Modified intent-to-treat population

Figure 2. Global Response Rate



Safety of Anidulafungin in Solid Organ Transplant Recipients

LIVER TRANSPLANTATION 18:680-685, 2012

J.M. Aguado,[1] E. Varo,[2] P. Usetti,[3] J.C. Pozo,[4] A. Moreno,[5] M. Catalán,[1] O. Len,[6] M. Blanes,[7] A. Solé,[7] P. Muñoz,[8] M. Montejo,[9] and the TOSCANA Study Group

[1]12 de Octubre University Hospital, Madrid, Spain; [2]Central University Hospital, Santiago de Compostela, Spain; [3]Puerta de Hierro University Hospital, Madrid, Spain; [4]Reina Sofía University Hospital, Córdoba, Spain; [5]Hospital Clinic, Barcelona, Spain; [6]Vall d'Hebron University Hospital, Barcelona, Spain; [7]La Fe University Hospital, Valencia, Spain; [8]Gregorio Marañón University Hospital, Madrid, Spain; and [9]Cruces University Hospital, Bilbao, Spain

Evalua la seguridad de la anidulafungina en el trasplante de órgano sólido.
Son reclutados 86 pacientes (56 hepáticos, 20 pulmon, 8 riñon, 2 corazón).

No fue necesario la modificación de las dosis de los inmunosupresores
Ningún paciente interrumpió el tratamiento con anidulafungina por efecto adverso

In conclusion, the results of this study show that anidulafungin is well tolerated in SOT recipients who receive the drug as antifungal prophylaxis or for the treatment of IFIs.

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Transplantation Proceedings, 44, 1982–1985 (2012)

Anidulafungin—A New Therapeutic Option for Candida Infections in Liver Transplantation

G. Sganga, G. Pepe, V. Cozza, E. Nure, M.C. Lirosi, F. Frongillo, U. Grossi, G. Bianco, and S. Agnes

- Se incluyen 13 patientes receptores de trasplante hepático.
- No se observaron alteraciones de las enzimas hepáticas, indices de colestasis ni cambios en los niveles de inmunosupresores.

Conclusion. Anidulafungin was an effective, safe, and well-tolerated drug. There were neither toxic effects to the grafts or adverse interactions with immunosuppresants.

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Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

34 REUNIÓ SOCIETAT CATALANA Medicina Intensiva i Crítica

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Journal of Antimicrobial Chemotherapy

Multiple-dose pharmacokinetics of anidulafungin during continuous venovenous haemofiltration

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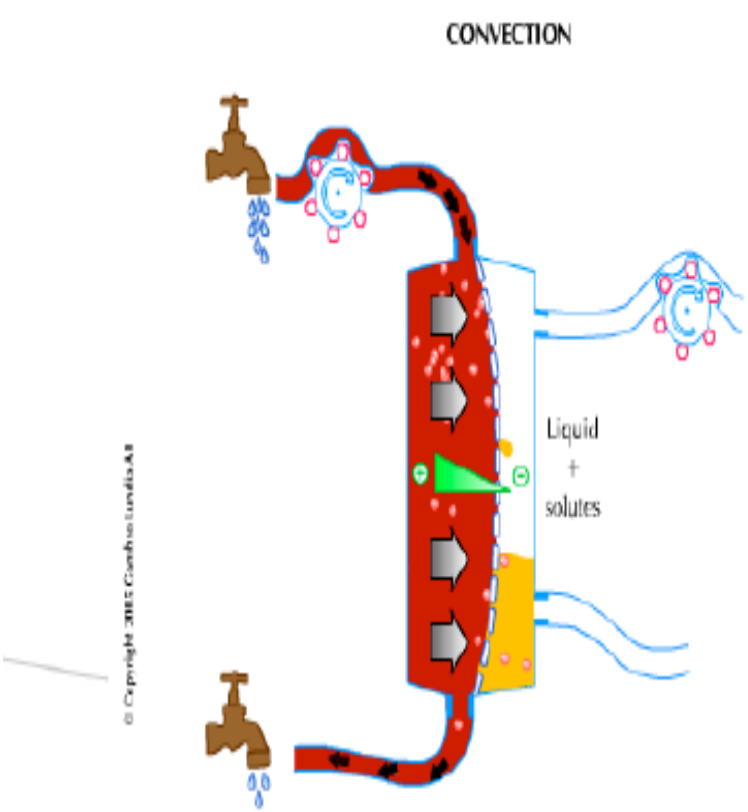
Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

34 REUNIÓ SOCIETAT CATALANA Medicina Intensiva i Crítica

1. **Farmacocinética de anidulafungina, administrada durante tres días, en 10 pacientes ingresados en UCI que fueron sometidos a HFVVC.**

2. **Los diez pacientes presentaban anuria, recibían ventilación mecánica y recibían anidulafungina a dosis estándar (200 mg. IV de carga y posteriormente 100 mg. cada 24 horas) por sospecha de candidiasis invasora (2 de ellos con candidiasis demostrada).**

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.



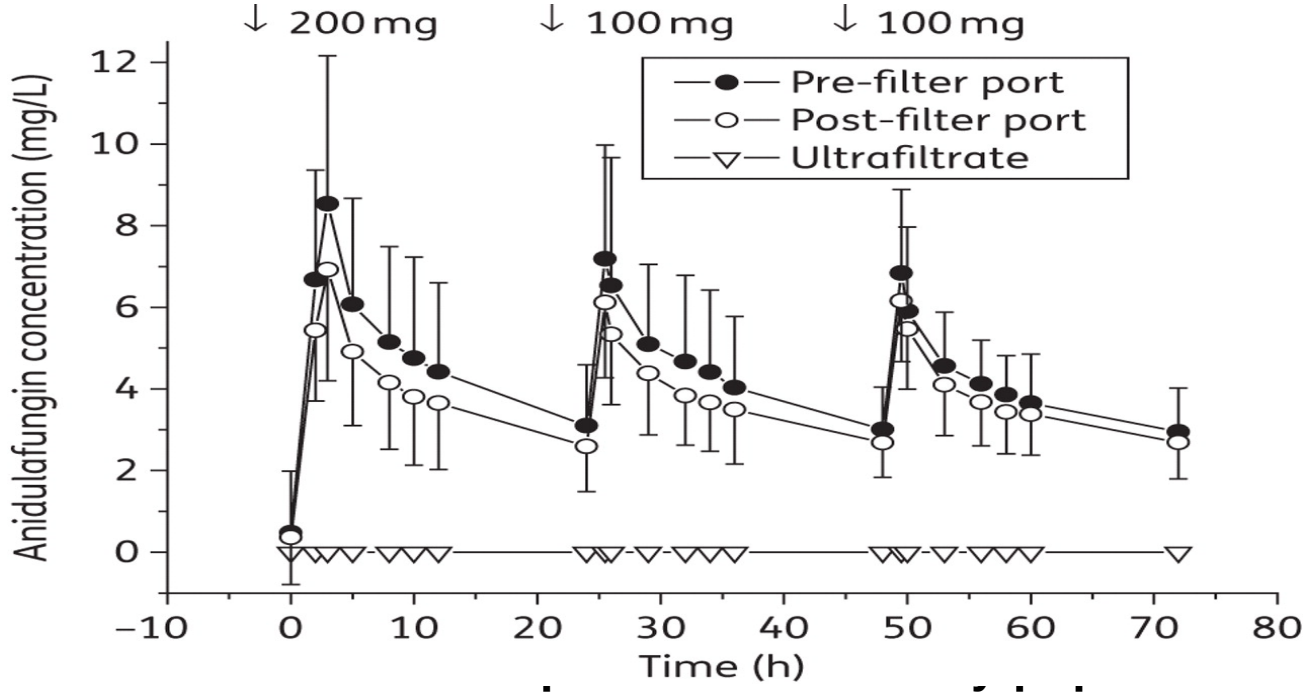
3. **Se tomaron muestras de sangre durante esos tres días tanto de la vía arterial como venosa del circuito extracorpóreo inmediatamente antes y después del final de la infusión de anidulafungina y posteriormente a las 2, 4, 6, 8 y 24 horas.**

4. **Al mismo tiempo se tomaron muestras del compartimiento externo del hemofiltro (ultrafiltrado).**

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

3. Se utilizó una membrana de polisulfona con una superficie de 1.2 m^2.(Aqua Max 12, Fresenius).
4. Se utilizaron flujos de sangre de 160-180 ml/min y una ultrafiltración de 25 ml/min (1500ml/h que para 75Kg= 20 ml/Kg/h). No se especifica lugar de reposición (pre vs post).

Avantatges d'Anidulafungina en el tratactament de les infeccions fúngiques en el pacient crític.

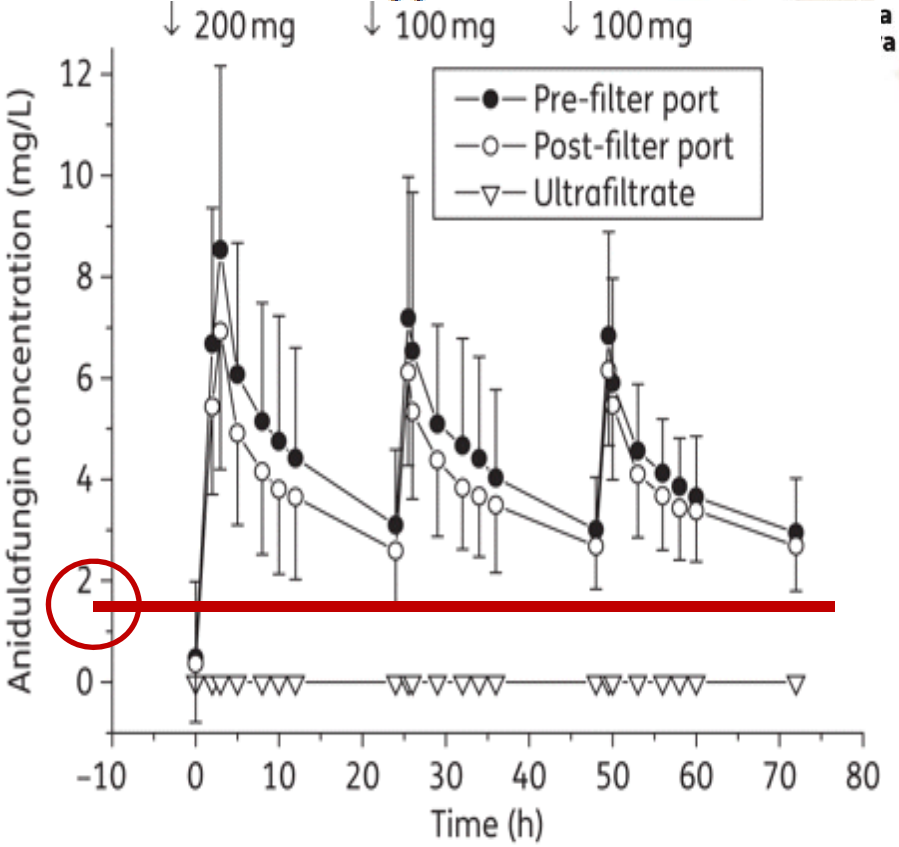


Patient	Dose (mg)	AUC_{0-24} (mg·h/L), arterial	AUC_{0-24} (mg·h/L), venous	Difference in AUC_{0-24} (mg·h/L)	CL_{tot} (L/h)	V (L)	$t_{1/2\beta}$ (h)
Mean ± SD	200 ± 0	109.9 ± 49.82	88.58 ± 36.02	20.44 ± 19.79	1.08 ± 0.41	41.97 ± 22.64	28.78 ± 10.40

MIC$_{50}$ and MIC$_{90}$ summary for the most common *Candida* spp.

Species (*n*)	AFG	
	50%	90%
C. albicans (733)	0.03	0.03
C. glabrata (458)	0.03	0.13
C. parapsilosis (391)	2	2
C. tropicalis (307)	0.03	0.13
C. krusei (50)	0.06	0.13
C. lusitaniae (20)	0.06	0.25
C. dubliniensis (18)	0.03	0.06

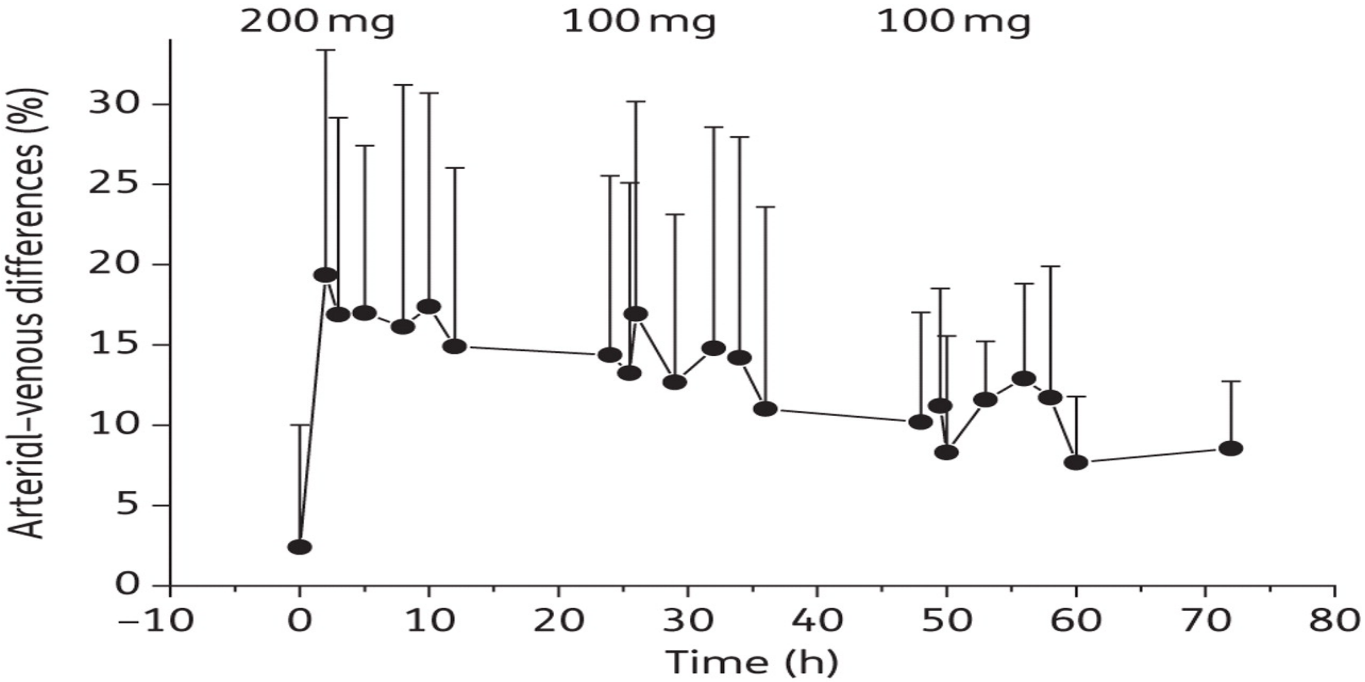
1,54 mg/L



Cmax/MIC y AUC$_{0-24}$/MIC

5. **Las concentraciones séricas se mantuvieron en todo momento en rangos elevados (la concentración mínima detectada fue de 1.54 mg/L), siempre por encima de las concentraciones mínimas inhibitorias (CMIs) de la mayoría de las especies de Candida sp.,**

Differences in anidulafungin concentration between the venous and arterial ports (AV differences).



6. **Maximas diferencias AV se presentaron 2 h (19±6%) y presentó un decremento progresivo 14±4% a 24 h, 10±2% a 48 h y 9±2% a 72 h.**

CONCLUSIONES

1. **A pesar de que la muestra del estudio es limitada, se puede concluir que, dadas las propiedades farmacológicas de anidulafungina, no es necesario un ajuste de dosis en pacientes críticos sometidos a HFVVC.**

2. **Dosis de carga, steady-tage 1d sobre un filtro nuevo de alta capacidad adsortiva.**

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Farmacoeconomía de la infección en la Unidad de Cuidados Intensivos

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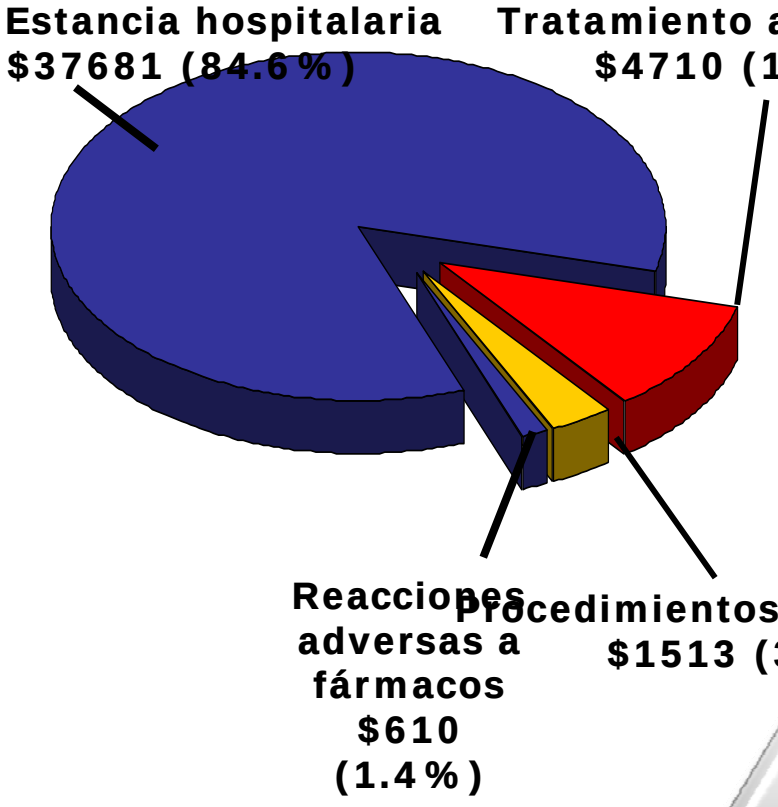
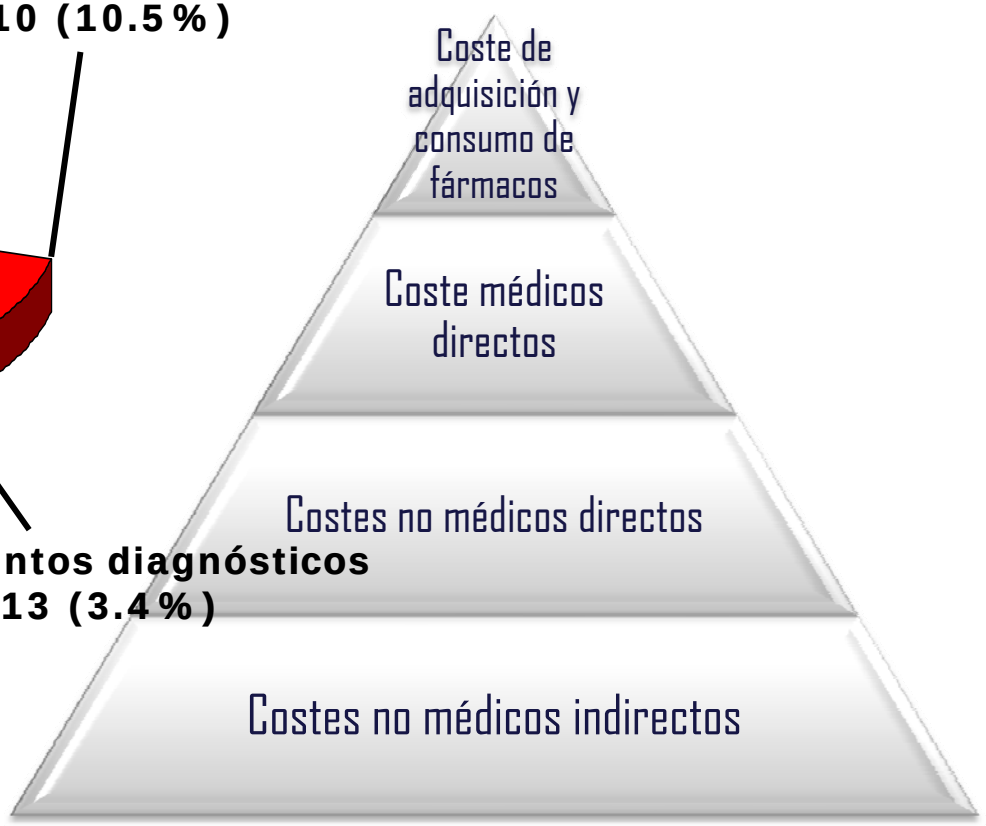
Rev Esp Quimioter 2008;21(Núm. Ext. 1):26-34





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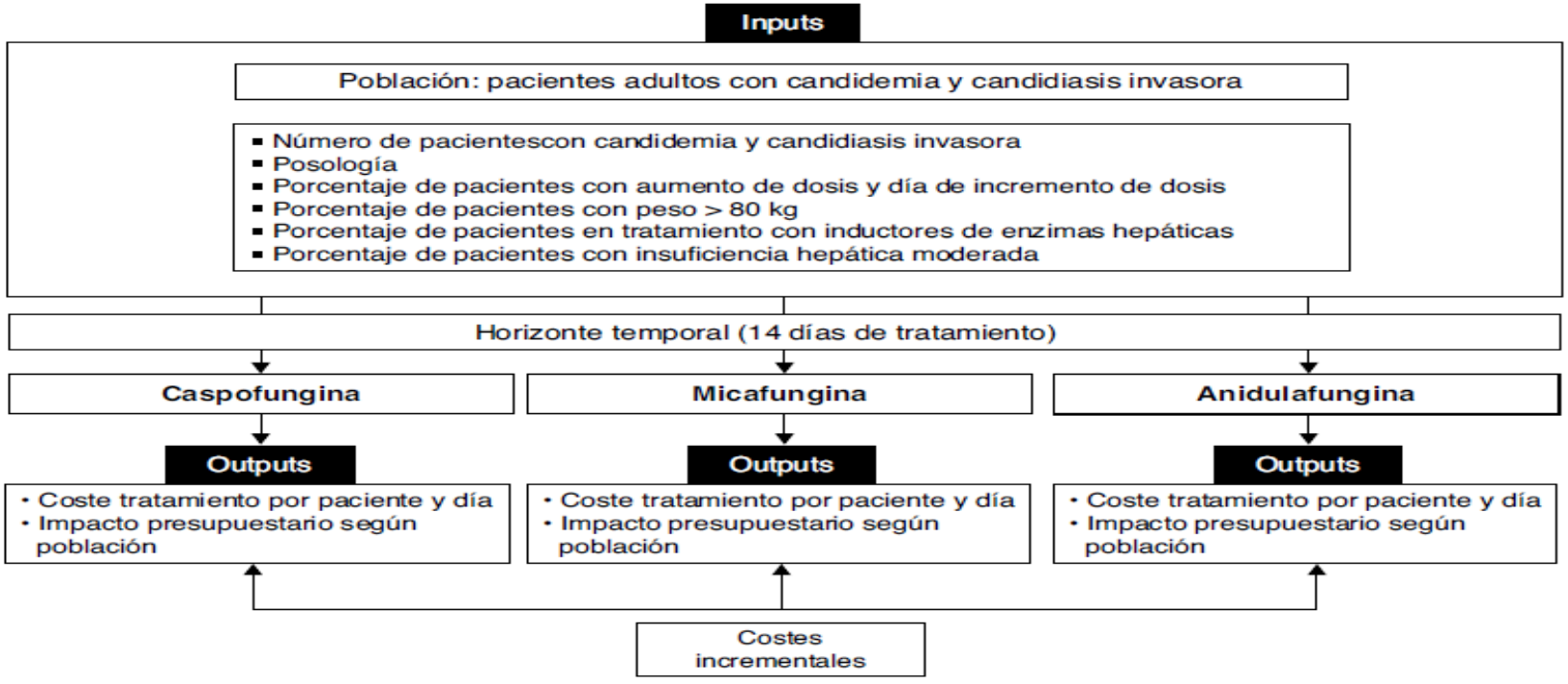
ORIGINAL

Análisis de costes de tres candinas en el tratamiento de la candidiasis invasora en pacientes adultos no neutropénicos en España

M. García-Vargas[a], M.A. Casado[b,*], N. Mir[c] y J.A. Barrueta[c]



Análisis de costes de tres candinas en el tratamiento de la candidiasis invasora en pacientes adultos no neutropénicos en España

Tratamiento y dosis	Dosis por día (mg)	Coste por día (€)
Caspofungina		
Dosis de carga	70	570,81
Dosis de mantenimiento (pacientes < 80 kg)	50	448,76
Dosis de mantenimiento (pacientes > 80 kg)[a]	70	570,81
Dosis de mantenimiento IHM (Child-Pugh 7-9)[b]	35	285,41
Micafungina		
Dosis inicial	100	428,57
Dosis de mantenimiento	100	428,57
Dosis de mantenimiento[c]	200	857,14
Anidulafungina		
Dosis de carga	200	720,00
Dosis de mantenimiento	100	360,00

Análisis de costes de tres candinas en el tratamiento de la candidiasis invasora en pacientes adultos no neutropénicos en España

Tabla 4 Coste total del tratamiento IV de primera línea con una candina durante 14 días (caso base; CB)[9–11] para un paciente adulto y para una cohorte de 100 pacientes adultos durante 14 días (CB), 12 días (análisis de sensibilidad; AS)[22] y 15 días (AS)[21] no neutropénicos con candidiasis invasora o candidemia con cada candina evaluada (€, 2010)

	1 paciente			100 pacientes	100 pacientes	100 pacientes
Horizonte temporal	CB 14 días			CB 14 días	AS 12 días	AS 15 días
Tratamiento	Peso < 80 kg	Peso > 80 kg	Puntuación Child-Pugh (7 – 9)[c]			
Caspofungina	**6.404,69**	**7.991,34**	**4.281,08**	**631.458,65**[b]	**543.092,86**[b]	**675.641,54**[b]
Día 1 (carga)	570,81	570,81	570,81			
Días 2 – 14 (mantenimiento)	5.833,88	7.420,53	3.710,27			
Micafungina (100 mg/día)	**5.999,98**	**5.999,98**	**5.999,98**	**632.997,89**[d]	**537.855,35**[d]	**680.569,16**[d]
Día 1 (inicial)	428,57	428,57	428,57			
Días 2 – 14 (mantenimiento)	5.571,41	5.571,41	5.571,41			
Micafungina (100 mg/día y respuesta inadecuada)	**8.999,97**	**8.999,97**	**8.999,97**			
Día 1 (inicial)	428,57	428,57	428,57			
Día 2 – 7 (mantenimiento)	2.571,42	2.571,42	2.571,42			
Días 8 – 14 (mantenimiento)[a]	5.999,98	5.999,98	5.999,98			
Anidulafungina	**5.400,00**	**5.400,00**	**5.400,00**	**540.000,00**	**468.000,00**	**576.000,00**
Día 1 (carga)	720,00	720,00	720,00			
Días 2 – 14 (mantenimiento)	4.680,00	4.680,00	4.680,00			

[a] En el modelo se asume que el aumento de dosis de micafungina (200 mg/día) se produce a mitad del tratamiento (día 7).
[b] Porcentaje de pacientes peso > 80 kg o en tratamiento con inductores de enzimas metabólicas: 10% (asunción).
[c] Porcentaje de pacientes con insuficiencia hepática moderada: 10,9%[20].
[d] Porcentaje de pacientes que requieren aumento de dosis de micafungina: 11%[21]. El aumento de dosis en el 11% de los pacientes se produce en el día 7.

ORIGINAL ARTICLE

Utilization and dosage pattern of echinocandins for treatment of fungal infections in US hospital practice*

Sheenu Chandwani[ab], Chuck Wentworth[c], Thomas A. Burke[b], Thomas F. Patterson[d]

CURRENT MEDICAL RESEARCH AND OPINION®
VOL. 25, NO. 2, 2009, 385–393

Records of 17 797 unique patient hospitalizations with use of only one echinocandin met the eligibility criteria. Of these, 708, 15 739, and 1350 received at least one dose of anidulafungin, caspofungin and micafungin,

Conclusions: In hospital practice, the mean dosages were consistent with the recommended loading and maintenance dosages for caspofungin and anidulafungin. Patients frequently received a loading dose of > 150 mg on day 1 of micafungin which was inconsistent with recommended dosing schedules. Micafungin maintenance dosages > 100 mg were also commonly used. Lack of information on reason for initiating echinocandin therapy was an important study limitation.

CMI
CLINICAL MICROBIOLOGY AND INFECTION

ESCMID

An evaluation of hospital length of stay in intensive care patients with invasive candidiasis treated with anidulafungin versus fluconazole

D. Kett, A. Reboli, C. Rotstein, A. Shorr, S. Gasper, H. Schlamm
(Miami, Camden, Washington, New York, US; Hamilton, CA)

Conclusion: In ICU patients with invasive candidiasis, ANID treatment was associated with shorter ICU and total hospital LOS compared with FLU treatment, and these differences were more pronounced in patients who survived for 2 weeks after EOT. These numerical differences in LOS will likely have financial implications given the expense associated with prolonged hospitalisation and ICU usage.

CMI
CLINICAL MICROBIOLOGY AND INFECTION

ESCMID

Cost-effectiveness of anidulafungin in confirmed candidaemia and other invasive *Candida* infections in Spain

S. Grau, M. García-Vargas, B. Martí, N. Mir (Barcelona, Alcobendas, Madrid, ES)*

Results: The percentage of successfully treated patients at the end of all therapy was higher for patients treated with anidulafungin than with fluconazole (74% vs. 57%). Treating with anidulafungin resulted in a higher antifungal drug costs (5,780€ vs. 2,082€); however, overall costs are lower for treatment with anidulafungin than for treatment with fluconazole (37,240€ vs. 37,327€) due to an offset in other medical costs. Univariate sensitivity analyses showed that anidulafungin remained the most cost-effective option.

Conclusions: Anidulafungin has demonstrated to improve the clinical efficacy versus standard of care in treating confirmed candidaemia. Despite an increase in drug costs, treating confirmed candidaemia with anidulafungin is a cost-effective strategy.

Conclusiones:

1. Epidemiología.
2. Mostalidad (atribuible).
3. Equinocandinas es la primera opción.
4. Anidulafungina
5. Coste-efectividad.

Gracias:

fgonzalez@mutuaterrass.es