V EDICIÓN JORNADA CIENTÍFICA

Gesitra-IC

ACTUALIZACIÓN EN LA PATOLOGÍA INFECCIOSA DE PACIENTES INMUNOCOMPROMETIDOS

5 Y 6 MARZO 2026

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Grupo de Estudio de Infección en el Trasplante y el Huésped Inmunocomprometido

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Actualización de tratamientos antifúngicos en el paciente inmunosuprimido

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Hospital Universitario Gregorio Marañón, Madrid
06 de marzo de 2026

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IiSGM
SaludMadrid
Hospital General Universitario Gregorio Marañón
Comunidad de Madrid

Uso de antifúngicos en pacientes inmunocomprometidos

POBLACIONES HETEROGÉNEAS

ALTA PROBABILIDAD DE IFI (profilaxis)

USO DE ANTIFÚNGICOS CONDICIONADO POR

- Tipo de infección fúngica
- Interacciones antifúngicos-inmunosupresores
- Entorno de creciente resistencia
- Nuevos antifúngicos

Nuevos antifúngicos y papel en inmunodeprimidos

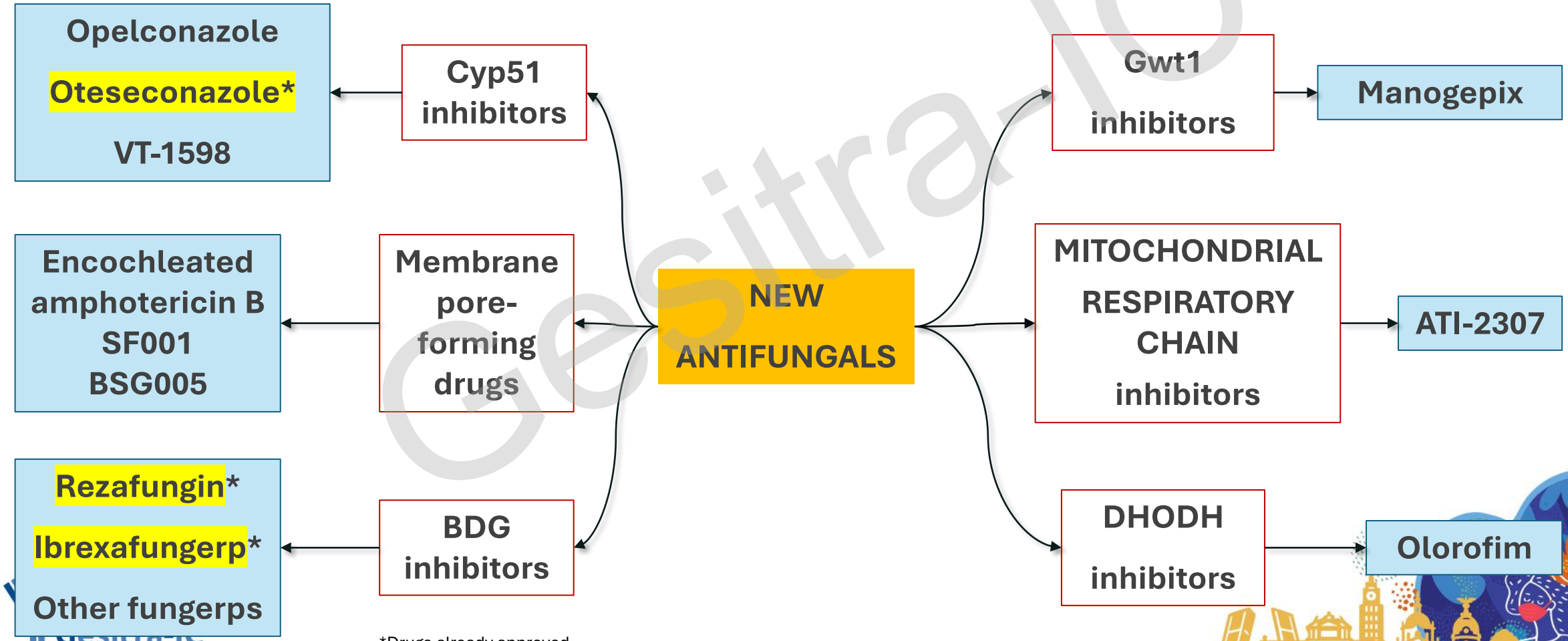
Nuevas equinocandinas (rezafungina)

Nuevos inhibidores de la BDG-sintasa (ibrexafungerp)

Nuevas familias (olorofima, fosmanogepix)

Nuevos azoles (opelconazol)

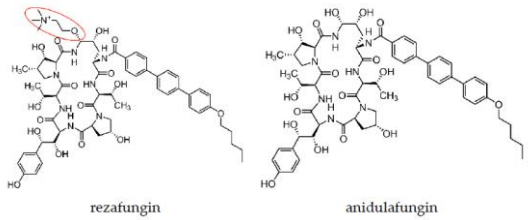
KNOWN MECHANISMS OF ACTION — NOVEL MECHANISMS OF ACTION



*Drugs already approved

Second generation echinocandin
Non-competitive inhibition of 1,3-B-D-glucan synthase enzyme complex
Derivative of anidulafungin (modification cyclic core)

(CD101, SP-3025, biafungin, **rezafungin**)



↑ Chemical stability
↑ Half-life

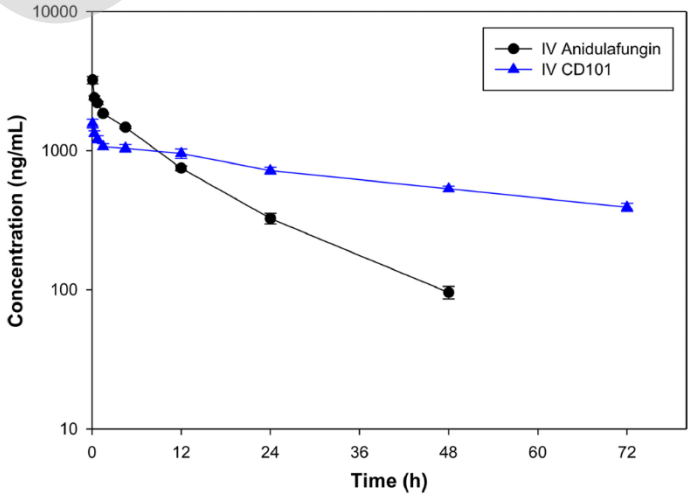
REZAFUNGIN

Less toxicity

↑ Drug exposure
1 dose a week

↑ Killing at the beginning of treatment
Prevention of FKS mutant emergence

Reza **130h** *vs* Anidula **24h**



Ref. Ong. AAC 2016; **Ref**. Boikov. JAC 2017; **Ref.** Krishnan. J Antibiot 2017; **Ref.** James. AAC 2017; **Ref.** Zhao. J Fungi 2020

	High activity	Partial activity	Poor activity
YEASTS FUNGICIDAL	*C. albicans* *C. glabrata* *C. tropicalis* *C. krusei* *C. dubliniensis* *C. lusitaniae* *C. auris*	*C. parapsilosis* complex *C. guilliermondii* complex *Sacharomyces cerevisiae* *Pneumocystis*	*Cryptococcus* *Rhodotorula* *Trichosporon*
MOULDS FUNGISTATIC		*Aspergillus* spp (covering cryptic species and azole resistance)	Mucorales *Scedosporium* *Fusarium*

SECONDARY RESISTANCE: Point mutations in hot spots *FKS* genes
FKS mutants similar rezafungin MICs to those of other echinocandins

Activity unaffected by the presence of azole resistance

Antibiofilm activity

EUCAST methodology implies the addition of Tween 20 into the broth

Which may result into artificially decreased MIC values

Ref. Wiederhold N. J Fungi 2022; **Ref**. Lepak A. AAC 2018; **Ref**. Pfaller M. AAC 2017; **Ref**. Hall D. DMID 2017; **Ref**. Tóth Z. JAC 2019

Protein binding	CYP450	Hepatotoxicity	Excretion	Tissue distribution	QT/QTc interval
98%	Minimal interactions	No signs	Biliary elimination	Wide (including liver abscesses)	Unaffected

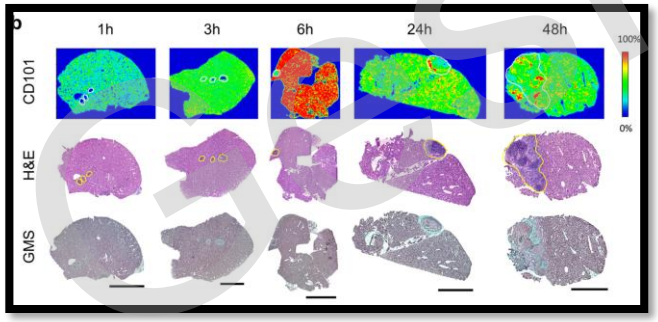
Administration		Penetration			Low drug-drug interactions expected	Dosage unaffected by	
Oral	IV	CNS	Eye	Urine		Haemofiltration	Liver disease
X	√	X	X	X	√	√	√

Ref. Ong. AAC 2016; **Ref**. Boikov JAC. 2017; **Ref.** Krishnan. J Antibiot 2017; **Ref.** James. AAC 2017; **Ref.** Sandison. AAC 2017; **Ref.** Flanagan. Clin Pharmacol Drug Develop 2019; **Ref.** Thompson. Lancet ID 2022

Antimicrobial Agents and Chemotherapy®

Unraveling Drug Penetration of Echinocandin Antifungals at the Site of Infection in an Intra-abdominal Abscess Model

Yanan Zhao,[a] Brendan Prideaux,[a] Yoji Nagasaki,[a] Min Hee Lee,[a] Pei-Yu Chen,[a] Landry Blanc,[a] Hsinpin Ho,[a] Cornelius J. Clancy,[b] Minh Hong Nguyen,[b] Véronique Dartois,[a] David S. Perlin[a]



MALDI-MSI

Ref. Zhao Y. AAC 2017

Blood Purification

Original Paper

Blood Purif 2018;46:214–219
DOI: 10.1159/000489212

Received: January 18, 2018
Accepted: April 12, 2018
Published online: June 14, 2018

Ex vivo Rezafungin Adsorption and Clearance During Continuous Renal Replacement Therapy

Soo Min Jang[a] Grayson Hough[b] Bruce A. Mueller[c]

tus was not observed for either hemodiafilter. ***Conclusion:*** Rezafungin is not removed by CVVH by membrane adsorption or via CL_{TM}. Ultrafiltrate flow rates and hemodiafilter types are unlikely to influence rezafungin CL_{TM}. No dosage adjustment of rezafungin is likely required for critically ill patients receiving CVVH.

Efficacy and safety of rezafungin and caspofungin in candidaemia and invasive candidiasis: pooled data from two prospective randomised controlled trials

George R Thompson III, Alex Soriano, Patrick M Honore, Matteo Bassetti, Oliver A Cornely, Marin Kollef, Bart Jan Kullberg, John Pullman, Maya Hites, Jesús Fortún, Juan P Horcajada, Anastasia Kotanidou, Anita F Das, Taylor Sandison, Jalal A Aram, Jose A Vazquez, Peter G Pappas

Lancet Infect Dis 2024; 24: 319–28

Published Online November 23, 2023 https://doi.org/10.1016/S1473-3099(23)00551-0

METODOLOGÍA

Estudios STRIVE y ReSTORE

- Ensayos clínicos doble ciegos, aleatorizados, multicéntricos e internacionales
- No inferioridad comparada con caspofungina
- Pacientes con candidemia o candidiasis invasora
- Régimen de tratamiento rezafungina:
  - Dosis de carga de 400 mg en día 0
  - Dosis de 200 mg en día 8
  - Opcional dosis de 200 mg en día 15 (ReSTORE) o día 22 (STRIVE)
- Régimen de tratamiento caspofungina:
  - Dosis de carga de 70 mg en día 0
  - Dosis de 50 mg / día desde día 1 a 21
- Pacientes estables en día 3 paso a vía oral:
  - Placebo en rezafungina
  - Fluconazol en caspofungina

VARIABLES A ESTUDIAR

Primario: mortalidad a los 30 días

Secundario: erradicación microbiológica en días 5 y 14

PACIENTES INCLUIDOS

294 mITT

17% (reza) y 19% (caspo) abandonaron tratamiento

Ambos grupos bien balanceados

70% pacientes sólo candidemia

En pacientes con CI, 70% eran intraabdominales

RESULTADOS

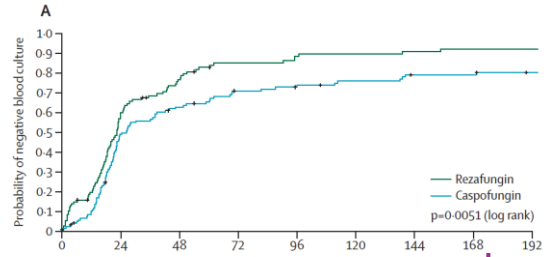
	Rezafungin (n=139)	Caspofungin (n=155)	Treatment difference (95% CI)
Primary pooled efficacy endpoint: day 30 all-cause mortality			
Deceased or unknown survival status	26 (19%)	30 (19%)	..
Known deceased	21 (15%)	25 (16%)	..
Unknown survival status	5 (4%)	5 (3%)	..
Alive	113 (81%)	125 (81%)	..
Death rate*	..	..	−1·5% (−10·7 to 7·7)
Secondary efficacy endpoints			
Day 5 mycological response			
Eradication	102 (73%)	100 (65%)	..
Failure or indeterminate	37 (27%)	55 (35%)	..
Eradication rate*	..	..	10·0% (−0·3 to 20·4)
Day 14 mycological response			
Eradication	100 (72%)	106 (68%)	..
Failure or indeterminate	39 (28%)	49 (32%)	..
Eradication rate*	..	..	4·3% (−6·2 to 14·7)
Exploratory efficacy endpoints			
Patients with negative blood culture†‡			
At 24 h	63/105 (60%)	57/116 (49%)	..
At 48 h	80/103 (78%)	73/115 (64%)	..
Day 14 global response§			
Cure	90 (65%)	97 (63%)	..
Failure	36 (26%)	48 (31%)	..
Indeterminate	13 (9%)	10 (6%)	..
Cure rate*	..	..	2·3% (−8·2 to 13·9)

EVALUACIÓN MORTALIDAD POR SUBGRUPOS DE PACIENTES

- >65 años (menor a favor de rezafungina)
- Enfermedad renal grave o moderada (menor a favor de rezafungina)
- No diferencias en pacientes sólo con candidemia, o CI, o por especies

EVALUACIÓN ACLARAMIENTO MICROBIOLÓGICO POR SUBGRUPOS DE PACIENTES

- En pacientes con candidemia sólo (mayor a favor de rezafungina)
- Diferencias significativas en día +5 pero no en +14
- No diferencias (ni en recaídas) al final del estudio



SEGURIDAD

- EA: rezafungina (91%) y caspofungina (83%)
- Más frecuentes en ambos brazos: fiebre, hipocalemia, y diarrea
- EA importantes relacionados con tratamiento 2% (rezafungina) y 3% (caspofungina)
- Algo más de pacientes con toxicidad renal y toxicidad hepática en pacientes caspofungina

FORTALEZAS Y APRENDIZAJES

- Rezafungina no inferior a caspofungina y parece tener un beneficio temprano
- Perfil de seguridad similar a caspofungina
- Mejor dosificación en pacientes críticos, obesos o con enf. hepática
- Erradicación inicial por mayor dosis de carga
- Dosificación semanal *vs* diaria

DEBILIDADES Y ASPECTOS NO RESUELTOS

- Beneficio temprano impacto en menor resistencia
- Mayor exposición tratamiento infecciones en santuarios biológicos
- Pocos casos de candidiasis intra-abdominal
- Formas excluidas en estos ensayos: infección de prótesis articular, osteomielitis, endocarditis, miocarditis, meningitis, endoftalmitis, infección SNC, candidiasis crónica diseminada, ITU
- Pacientes pediátricos excluidos

- Otra equinocandina pero PK peculiar
- Papel cuando tratamiento temprano tiene un impacto
- Pacientes con formas infrecuentes de candidiasis
- Papel en la prevención de IFI

Ensayos clínicos activos en pacientes inmunodeprimidos

☐ **NCT06774144** Enrolling by invitation

Rezafungin Prophylaxis in Liver Transplant

Conditions

Fungal Infection | Liver Transplant Infection

Locations

Pittsburgh, Pennsylvania, United States

☐ **NCT04368559** Active, not recruiting

Study of **Rezafungin** Compared to Standard Antimicrobial Regimen for Prevention of Invasive Fungal Diseases in Adults Undergoing Allogeneic Blood and Marrow Transplantation

Conditions

Aspergillus | Candidemia | Fungal Infection | Fungemia | Show 6 more conditions

Locations

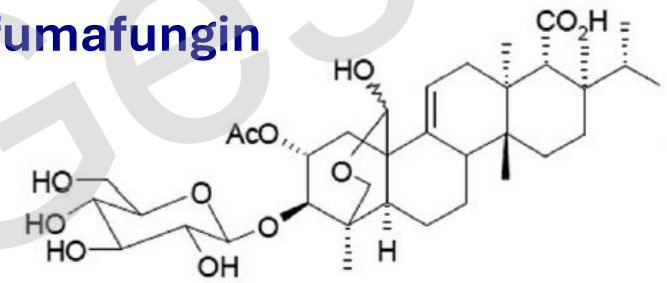
Birmingham, Alabama, United States
Los Angeles, California, United States
Stanford, California, United States
Augusta, Georgia, United States

Show all 53 locations

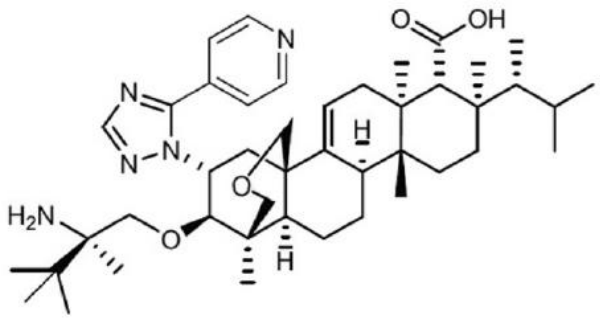
https://clinicaltrials.gov/search?intr=rezafungin

BDG inhibitors beyond the candins

- **Lipopeptides**
  - Echinocandins → Anidulafungin, Micafungin, Rezafungin
  - Pneumocandins → Caspofungin
- **Terpenoids**
  - **Enfumafungin**
  - **Semi-synthetic derivative** — **Ibrexafungerp**



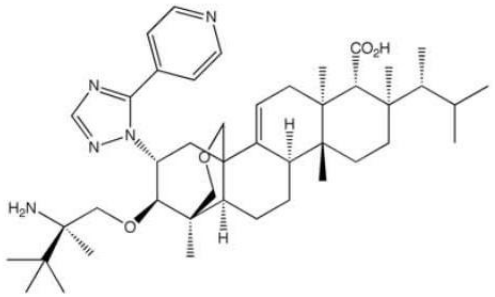
Enfumafungin



MK-3118

Ref: adapted from Romero M. Rev Esp Quimioter. 2005

Non-competitive inhibition of 1,3-B-D-glucan synthase enzyme complex



(MK-3118, SCY-078, **ibrexafungerp**)

Acts like a candin, but structurally different!!

IBREXAFUNGERP

- Different binding to FKS
- Limited cross resistance
- Orally administered
- High penetration in intra-abdominal lesions

	High activity	Partial activity	Poor activity
YEASTS FUNGICIDAL	*C. albicans* *C. glabrata* *C. parapsilosis* *C. tropicalis* *C. dubliniensis* *C. auris*	*C. krusei* *C. lusitaniae* *C. guilliermondii* complex *S. cerevisiae* *Pneumocystis*	*Cryptococcus* *Rhodotorula* *Trichosporon*
MOULDS FUNGISTATIC	*Aspergillus* (synergy in combination with vori or isa)	*Aspergillus* spp (covering cryptic species and azole resistance) *Scedosporium* *Paecylomyces variotii*	Mucorales *Fusarium*

Activity unaffected by the presence of azole resistance

SECONDARY RESISTANCE: Point mutations in hot spots *FKS* genes

In vitro* activity against some candin-resistant *C. glabrata

Antibiofilm activity

Ref. Diaz-García J. JAC 2022; **Ref**. Diaz-García J. AAC 2022; **Ref**. Wiederhold N. J Fungi 2022; **Ref**. Mesquida A. CMI 2022; **Ref**. Jiménez-Ortigosa C. AAC 2014; **Ref**. Jiménez-Ortigosa C. AAC 2017; **Ref**. Scorneaux B. AAC 2017; **Ref**. Shell W. AAC 2017; **Ref**. Ghannoum M. AAC 2018; **Ref**. Arendrup A. AAC 2020; **Ref**. Rivero-Menéndez O. J Fungi 2021; **Ref**. Lepak. AAC 2015

Protein binding	CYP450	Hepatotoxicity	Excretion	Tissue distribution	QT/QTc interval
99.8%	Interactions (low)	Non reported	Biliary elimination	Wide (including liver abscesses)	Unaffected

Administration		Penetration			Low drug-drug interactions expected	Dosage unaffected by	
Oral	IV	CNS	Eye	Urine		Haemofiltration	Liver disease
√	X	X	√ (uvea)	X	-/+	No data	Child-Pugh A and B Child-Pugh C (no data)

Ref. Wring. Clin Pharmacol Drug Develop 2019; Wring. AAC 2019

NCT03059992 Completed WITH RESULTS

Study to Evaluate the Efficacy and Safety of **Ibrexafungerp** in Patients With Fungal Diseases That Are Refractory to or Intolerant of Standard Antifungal Treatment

Conditions

Allergic Bronchopulmonary Aspergillosis | Blastomycosis | Chronic Pulmonary Aspergillosis | Coccidioidomycosis

Show 6 more conditions

Locations

Birmingham, Alabama, United States
Sacramento, California, United States
San Francisco, California, United States
Atlanta, Georgia, United States

Show all 37 locations

NCT05178862 Terminated

A Phase 3, Randomized, Double-blind Study for Patients With Invasive Candidiasis Treated With IV Echinocandin Followed by Either Oral **Ibrexafungerp** or Oral Fluconazole

Conditions

Candidemia | Candidiasis, Invasive

Locations

Birmingham, Alabama, United States
Tucson, Arizona, United States
Sacramento, California, United States
San Francisco, California, United States

Show all 101 locations

NCT03672292 Terminated WITH RESULTS

Evaluate Safety and Efficacy of the Coadministration of **Ibrexafungerp** With Voriconazole in Patients With Invasive Pulmonary Aspergillosis

Conditions

Invasive Pulmonary Aspergillosis

Locations

Boston, Massachusetts, United States
Ann Arbor, Michigan, United States
Winston-Salem, North Carolina, United States
Bruges, Belgium

Show all 8 locations

NCT03363841 Completed WITH RESULTS

Open-Label Study to Evaluate the Efficacy and Safety of Oral **Ibrexafungerp** (SCY-078) in Patients With Candidiasis Caused by Candida Auris (CARES)

Conditions

Candidemia | Candidiasis, Invasive

Locations

Jersey City, New Jersey, United States
Chandigarh, India
Bangalore, Karnataka, India
Kanayannur, Kochi, India

Show all 12 locations

https://clinicaltrials.gov/search?intr=ibrexafungerp

Antifungal susceptibility testing of SCY-247 against contemporary clinical yeast isolates

Carolyn Z. Grimes,[1] Maria Horne,[1] Katyna Borroto-Esoda,[2] David Angulo,[2] Luis Ostrosky-Zeichner,[1]
[1]The University of Texas Health Science Center at Houston, McGovern Medical School, Houston, TX, USA;
[2]SCYNEXIS, Inc. Jersey City, NJ, USA

P2909

Assessment of *in vitro* activity of the new triterpenoid antifungal, SCY-247, against a collection of yeasts causing fungaemia in patients admitted to a tertiary hospital in Madrid from 2014 to 2024

Pilar Escribano[1,2,3], Ana Gómez[1,2], Almudena Burillo[1,2,4], Patricia Muñoz[1,2,4,5], Jesús Guinea[1,2,3,5]
[1]Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Instituto de Investigación sanitaria Gregorio Marañón, Madrid, Spain; [3]Faculty of Health Science - HM Hospitals, Universidad Camilo José Cela, Madrid, Spain; [4]Medicine Department, Faculty of Medicine, Universidad Complutense de Madrid, Madrid, Spain; [5]CIBER Enfermedades Respiratorias - CIBERES (CB06/06/0058), Madrid, Spain

The new triterpenoid antifungal SCY-247 retained activity against most echinocandin and fluconazole-resistant *Candida* spp isolates: reduced susceptibility against *C. glabrata* isolates showing substitutions at the first amino acid in hotspot 1 *FKS2* gene

P2924

Spectrum of activity similar to ibrexafungerp

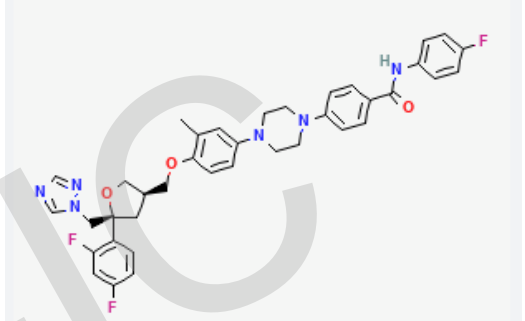
Improved PK profile (suitable for IV and oral formulations; Low propensity for DDIs; Tissue penetration)

Murine models role for the management of mucormycosis and *C. auris* infections

(PC945, **opelconazole**)

Synthetic triazole (designed for inhale administration)
inhibitor of *A. fumigatus* CYP51

Binding similar to that of posaconazole



Limitations of current azoles

PK variability
Drug-drug interactions
Toxicity
Insufficient lung penetration
Resistance

NO SYSTEMIC EFFECT

Administration		Penetration			Expected Low drug-drug interactions	Dosage unaffected by	
Oral	IV	CNS	Eye	Urine		Haemofiltration	Liver disease
X	X	X	X	X	√	√	√

Ref. Colley. AAC 2017; **Ref**. Murray. J Fungi 2020

NCT05037851 Completed

A Safety Study of PC945 (**Opelconazole**) Prophylaxis or Pre-emptive Therapy Against Pulmonary Aspergillosis in Lung Transplant Recipients (OPERA-S Study)

Conditions

Pulmonary Aspergillosis

Locations

Phoenix, Arizona, United States
Los Angeles, California, United States
La Jolla, California, United States
Jacksonville, Florida, United States

Show all 19 locations

NCT05238116 Terminated

Safety and Efficacy of PC945 (**Opelconazole**) in Combination With Other Antifungal Therapy for the Treatment of Refractory Invasive Pulmonary Aspergillosis (OPERA-T Study)

Conditions

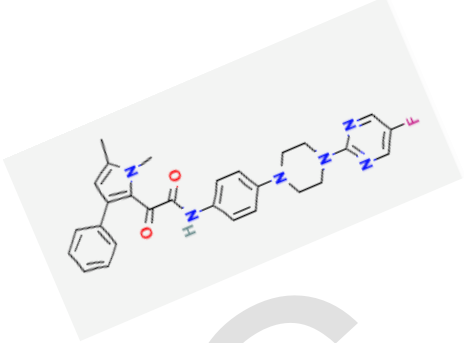
Refractory IPA

Locations

La Jolla, California, United States
Sacramento, California, United States
Los Angeles, California, United States (2)
Jacksonville, Florida, United States

Show all 83 locations

https://clinicaltrials.gov/search?intr=opelconazole



- **Orotomides (formerly F901318)**
- **New class: dihydroorotate dehydrogenase inhibitor (DHODH)**
- **New mechanism of action: Inhibition of pyrimidines synthesis (like cotrimoxazole)**
- **NO CROSS RESISTANCE WITH OTHER ANTIFUNGALS**


Clinical Microbiology and Infection

Research note

In vitro activity of olorofim against *Aspergillus fumigatus* sensu lato clinical isolates: activity is retained against isolates showing resistance to azoles and/or amphotericin B

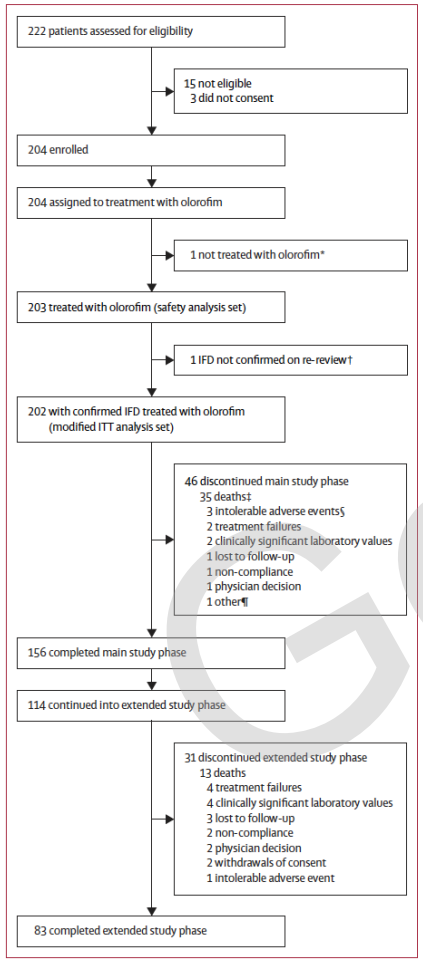
Pilar Escribano [1,2,**], Ana Gómez [1,2], Elena Reigadas [1,2], Patricia Muñoz [1,2,3,4], Jesús Guinea [1,2,3,*], on behalf of the ASPEIN Study Group

Candida and other yeasts	Mucorales	*Aspergillus*	*Scedosporium*	*Fusarium*
		Fungicidal		

Oral administration	Intravenous administration	CNS penetration	Eye penetration	No relevant DDI
√	√	√	??	√

Olorofim for the treatment of invasive fungal diseases in patients with few or no therapeutic options: a single-arm, open-label, phase 2b study

Johan A Maertens, George R Thompson III, Andrej Spec, Fariba M Donovan, Sarah P Hammond, Anke H W Bruns, Galia Rahav, Shmuel Shoham, Royce Johnson, Bart Rijnders, Joanna Schaenman, Martin Hoenigl, C Orla Morrissey, Sanjay R Mehta, Christopher H Heath, Philipp Koehler, David L Paterson, Monica A Slavin, Jesus Fortún, M Hong Nguyen, Thomas F Patterson, Olga Uspenskaya, Frank L Van de Veerdonk, Paul E Verweij, Mickael Aoun, Aspasia Georgala, Barbara D Alexander, Methee Chayakulkeeree, Varun Mehra, Marisa H Miceli, Monica K Sikka, Amparo Solé, Thomas J Walsh, Jose Maria Aguado, Steven M Holland, Mohamed Moussa, Riina Rautemaa-Richardson, Rohit Bazaz, Stefan Schwartz, Stephen R Walsh, Markus Plate, Dana Yehudai-Ofir, Roger J Brüggemann, Oliver A Cornely, Luis Ostrosky-Zeichner, Jose A Vazquez, P Lewis White, Karen Cornelissen, Geoffrey G Ross, Lesley Fitton, Aaron Dane, Daniela Zinzi, John H Rex, Sharon C-A Chen



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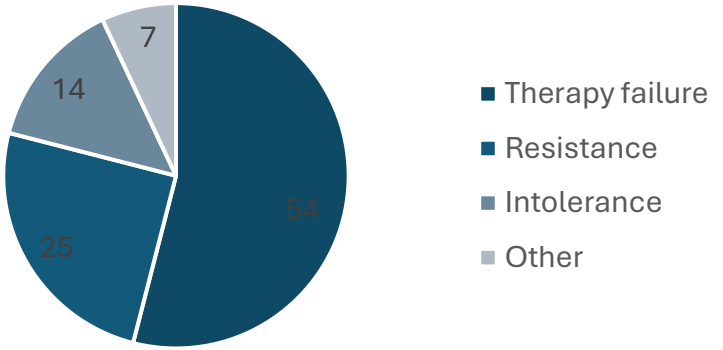
Eligible participants:

- ≥ 16 years proven/probable IFD caused by *Aspergillus* spp, *L. prolificans*, *Scedosporium* spp, or other olorofim-susceptible fungi
- Required to have at least one of the following: (1) infection caused by a pathogen with known or predicted **resistance** to licensed antifungal agents; (2) **failure to improve**, based on clinical–radiological assessment, after at least 7 days of standard antifungal therapy; (3) **intolerance** to licensed antifungal agents; (4) inability to manage **drug–drug interactions**; or (5) inability to achieve **therapeutic drug concentrations**



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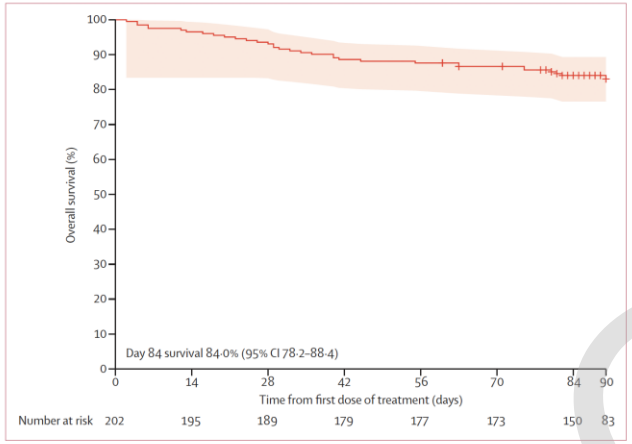

Figure 2: Kaplan–Meier curve for all-cause mortality from first dose of olorofim to day 90 in the modified ITT analysis set

	Successful global response rate: stable classified as failure*		Successful global response rate: stable classified as success†		All-cause mortality	
	Day 42	Day 84	Day 42	Day 84	Day 42	Day 84
Overall (n=202)	58 (28·7%, 22·6–35·5)	55 (27·2%, 21·2–33·9)	152 (75·2%, 68·7–81·0)	128 (63·4%, 56·3–70·0)	24 (11·9%, 7·8–17·2)	33 (16·3%, 11·5–22·2)
Aspergillus spp‡ (n=101)	35 (34·7%, 25·5–44·8)	34 (33·7%, 24·6–43·8)	65 (64·4%, 54·2–73·6)	55 (54·5%, 44·2–64·4)	19 (18·8%, 11·7–27·8)	26 (25·7%, 17·6–35·4)
Lomentospora prolificans‡ (n=26)	11 (42·3%, 23·4–63·1)	11 (42·3%, 23·4–63·1)	20 (76·9%, 56·4–91·0)	19 (73·1%, 52·2–88·4)	3 (11·5%, 2·4–30·2)	3 (11·5%, 2·4–30·2)
Scedosporium spp (n=22)	8 (36·4%, 17·2–59·3)	5 (22·7%, 7·9–45·4)	19 (86·4%, 65·1–97·1)	13 (59·1%, 36·4–79·3)	2 (9·1%, 1·1–29·2)	3 (13·6%, 2·9–34·9)
Other olorofim-susceptible fungi§ (n=12)	4 (33·3%, 9·9–65·1)	5 (41·7%, 15·2–72·3)	9 (75·0%, 42·8–94·5)	6 (50·0%, 21·1–78·9)	0 (0·0%, 0·0–26·5)	1 (8·3%, 0·2–38·5)
Coccidioides spp¶ (n=41)	0 (0·0%, 0·0–8·6)	0 (0·0%, 0·0–8·6)	39 (95·1%, 83·5–99·4)	35 (85·4%, 70·8–94·4)	0 (0·0%, 0·0–8·6)	0 (0·0%, 0·0–8·6)

Data are n (%, 95% CI). DRC=data review committee. ITT=intention to treat. MSG-EORTC=Mycoses Study Group and European Organization for Research and Treatment of Cancer consensus criteria.[26] *Successful global response rate includes complete responses and partial responses. †Successful global response rate includes complete responses, partial responses, and stable disease. ‡Patient groups with *Aspergillus* spp and *Lomentospora prolificans* each include one patient with proven *Scopulariopsis* spp co-infection. §Other olorofim-susceptible fungi were *Scopulariopsis* spp (n=4), *Fusarium* spp (n=3; *F solani*, *F fujikuroi* complex, and *F proliferatum*), *Blastomyces dermatitidis* (n=1), *Histoplasma capsulatum* (n=1), *Madurella mycetomatis* (n=1), *Phaeoacremonium* spp (n=1), and *Sporothrix schenckii* (n=1). ¶See text for a discussion of the response rate in coccidioidomycosis.

Table 2: **DRC-adjudicated MSG-EORTC global response rates and all-cause mortality at day 42 and day 84 in the modified ITT analysis set for the overall study population and by fungal subtype**

NCT03583164 Completed WITH RESULTS

Evaluate **F901318** (**Olorofim**) Treatment of Invasive Fungal Infections in Participants Lacking Treatment Options

Conditions

Invasive Fungal Infections

Locations

Bakersfield, California, United States
Sacramento, California, United States
San Diego, California, United States
Atlanta, Georgia, United States

Show all 82 locations

NCT05101187 Active, not recruiting

Olorofim Aspergillus Infection Study

Conditions

Invasive Aspergillosis

Locations

Birmingham, Alabama, United States
Duarte, California, United States
Sacramento, California, United States
San Francisco, California, United States

Show all 140 locations

https://clinicaltrials.gov/search?intr=olorofim

- **Glycosylphosphatidylinositol (GPI)-anchored proteins**
- **Essential function in fungi regeneration of fungal wall and adhesion**

	Candida	*Aspergillus*	*Cryptococcus*	Mucorales	*Scedosporium*	*Fusarium*
FOSMANOGEPIX	Fungistatic No *C. krusei*	Fungistatic			Fungistatic	Fungistatic

	Oral administration	Intravenous administration	CNS penetration	Eye penetration	No relevant DDI
FOSMANOGEPIX	√	√	Probable	√	√

Ref. Umemura M. J Biol Chem 2003;
Tsukahara K. Mol Microbiol 2003

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EXPERIMENTAL THERAPEUTICS

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Clinical Efficacy and Safety of a Novel Antifungal, Fosmanogepix, in Patients with Candidemia Caused by *Candida auris:* Results from a Phase 2 Trial

J Antimicrob Chemother 2023; **78**: 2471–2480
https://doi.org/10.1093/jac/dkad256 Advance Access publication 19 August 2023

Journal of Antimicrobial Chemotherapy

Clinical safety and efficacy of novel antifungal, fosmanogepix, for the treatment of candidaemia: results from a Phase 2 trial

Peter G. Pappas[1], Jose A. Vazquez[2], Ilana Oren[3]†, Galia Rahav[4,5], Mickael Aoun[6], Pierre Bulpa[7], Ronen Ben-Ami[5,8], Ricard Ferrer[9], Todd Mccarty[1], George R. Thompson III[10], Haran Schlamm[11], Paul A. Bien[12], Sara H. Barbat[11], Pamela Wedel[11], Iwona Oborska[11], Margaret Tawadrous[12]* and Michael R. Hodges[11]

Clinical Infectious Diseases

MAJOR ARTICLE

Infectious Diseases Society of America
HIV Medicine Association

OXFORD

Fosmanogepix for the Treatment of Invasive Mold Diseases Caused by *Aspergillus* Species and Rare Molds: A Phase 2, Open-Label Study (AEGIS)

Michael R. Hodges,[1,2] Margaret Tawadrous,[3,a] Oliver A. Cornely,[4,5,6] George R. Thompson III[7] Monica A. Slavin,[8] Johan A. Maertens,[9,10] Sanjeet S. Dadwal,[11] Galia Rahav,[12] Susan Hazel,[13,14] Mary Almas,[15] Abhijeet Jakate,[16] and Rienk Pypstra[3,a]

NCT04240886 **Terminated** WITH RESULTS

Open-label Study of APX001 for Treatment of Patients With Invasive Mold Infections Caused by Aspergillus or Rare Molds

Conditions

Invasive Fungal Infections

Locations

Duarte, California, United States (2)
Durham, North Carolina, United States (4)
Brussels, Belgium
Leuven, Belgium

Show all 15 locations

NCT06433128 **Available**

Expanded Access to **Fosmanogepix** for Patients With Serious or Life-threatening Invasive Fungal Infections

Conditions

Invasive Fungal Infections

Locations

Location not provided

NCT05421858 **Recruiting**

A Phase 3 Efficacy and Safety Study of **Fosmanogepix** for the Treatment of Adult Participants With Candidemia and/or Invasive Candidiasis.

Conditions

Candidemia
Candidiasis, Invasive

Locations

Birmingham, Alabama, United States
Duarte, California, United States
Los Angeles, California, United States
Sacramento, California, United States

Show all 122 locations

https://clinicaltrials.gov/search?intr=fosmanogepix

Conclusions

- New drugs, in old families or new groups
- New doors opened for immunosuppressed patients
- Treatment and prophylaxis
- Willing to look at new clinical data

Thanks to all my colleagues!

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