MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

Plan Nacional Resistencia Antibióticos

CoESAnt

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I Jornada del Comité Español del Antibiograma (COESANT)

Madrid 24 de noviembre de 2022

Puntos de corte de antifúngicos

Jesús Guinea
Servicio de Microbiología Clínica y Enfermedades Infecciosas
Hospital General Universitario Gregorio Marañón
Secretario Científico Steering Committee Antifungal Suceptibility Testing EUCAST

Implementación EUCAST en antifúngicos

- Procedimientos estandarizados metodología EUCAST para hongos filamentosos y hongos levaduriformes
- Acceso libre en https://www.eucast.org/ast_of_fungi
- Revisiones frecuentes de ECOFFs y puntos de corte
- Orientados a optimizar la terapia antifúngica
- Sistemas comerciales NO basados en metodología EUCAST
- Métodos disco-placa antifúngicos en metodología EUCAST INEXISTENTE

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

AST of fungi

- Organization
- Consultations
- EUCAST News
- New definitions of S, I and R
- Clinical breakpoints and dosing
- Rapid AST in blood cultures
- Expert rules and expected phenotypes
- Resistance mechanisms
- Guidance documents
- SOP
- MIC and zone distributions and ECOFFs
- AST of bacteria
- AST of mycobacteria
- **AST of fungi**
  - Breakpoints for antifungals
  - MIC distributions and ECOFFs
  - Methods in antifungal susceptibility te
  - QC AFST Tables
  - Rationale documents for antifungals
  - Publications in journals
  - Meetings, Minutes and Reports
  - Previous versions of documents
- AST of veterinary pathogens

Antifungal susceptibility testing (AFST)

Breakpoints and methods for susceptibility testing of yeasts, moulds and dermatophytes are developed and validated by the EUCAST subcommittee on AFST.

New and revised documents open for consultation will until accepted be published in the → **EUCAST News section** together with all other consultations from EUCAST.

Information on subcommittee organisation and members are available on the webpage describing the → **Organisation** of EUCAST.

Information for industry aiming to bring agents to EUCAST for review and revision of breakpoints or a new agent to EMA for registration is available at → **Information for industry**.

Development of new methods and validation and calibration of existing methods is performed at the EUCAST Development Laboratory for AFST:
→ **The EUCAST Development Laboratory for Antifungal Susceptibility Testing**
with the help of
→ **The EUCAST AFST Network Laboratories**

For **Copyright statement** and reference to EUCAST material, see the homepage of EUCAST.

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Clinical Data Coordinator Joseph Meletiadis (joseph.meletiadis[at]escmid.org)

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J Buil (The Netherlands)
M Castanheira (USCAST Representative, USA)
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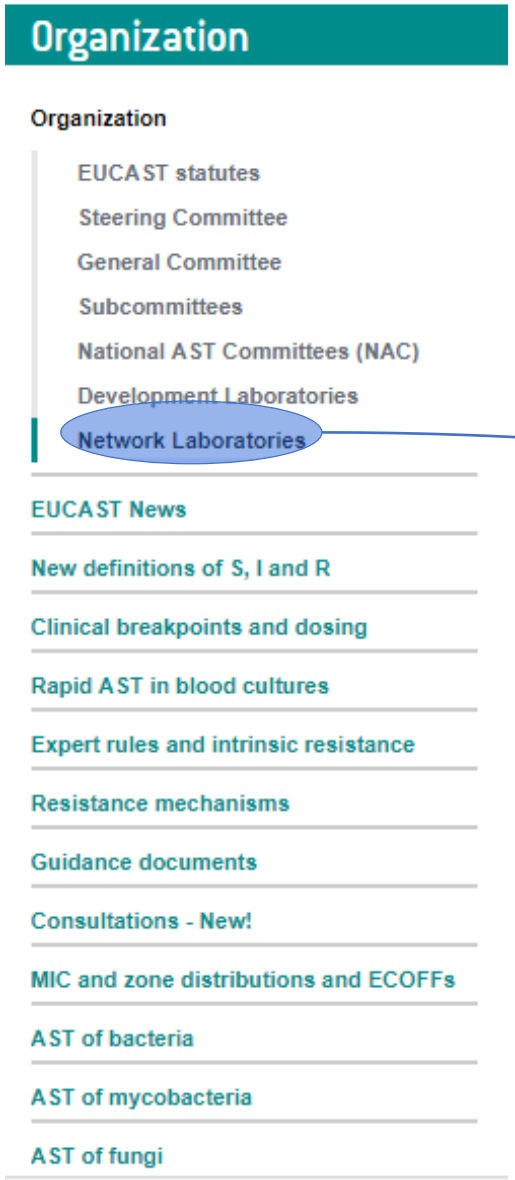
https://www.eucast.org/organization/subcommittees/eucast_afst



EUCAST AFST (yeasts and moulds) network laboratories

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- National Reference Centre for Invasive Mycoses , Germany (Contact - O Kurzai)
- Clinical Microbiology Laboratory, Athens, Greece (Contact - J Meletiadis)
- Mycology Reference Centre, Manchester, UK (Contact - C Moore)
- Erasmus MC - Department of Medical Microbiology and Infectious Diseases, Netherlands (Contact - W van de Sande)
- Mycology Research Laboratory & UOA/HCPF culture collection, Dept Microbiology, Medical School, National and Kapodistrian University of Athens, Greece (Contact - A Velegraki)
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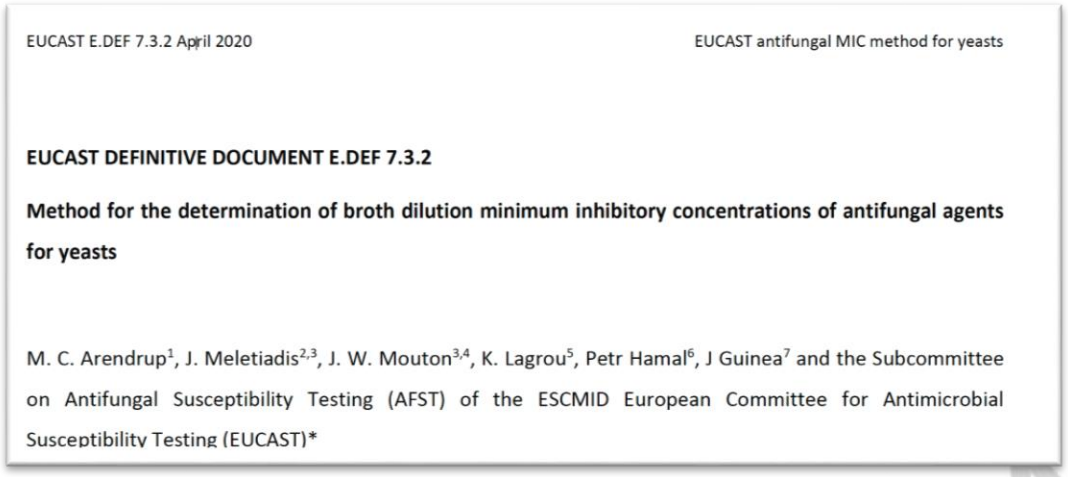
- Mycology and Aerobiology, Sciensano, Belgium (Contact - P Becker)

http://www.eucast.org/organization/network_laboratories/

Procedimientos EUCAST microdilución



EUCAST E.DEF 7.3.2 April 2020 EUCAST antifungal MIC method for yeasts

EUCAST DEFINITIVE DOCUMENT E.DEF 7.3.2

Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for yeasts

M. C. Arendrup[1], J. Meletiadis[2,3], J. W. Mouton[3,4], K. Lagrou[5], Petr Hamal[6], J Guinea[7] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)*

EUCAST E.DEF 9.4 March 2022 EUCAST antifungal microdilution method for moulds

Actualización lecturas de CMIs con el espectrofotómetro para azoles y AmB frente a *A. fumigatus*

J Guinea*[1,2,3], J Meletiadis*[4,5], S Arikan-Akdagli[6], K Muehlethaler[7], G Kahlmeter[8], M C Arendrup[9,10,11] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)**

*Both authors contributed equally

Clinical Microbiology and Infection 27 (2021) 55–60

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

How to: perform antifungal susceptibility testing of microconidia-forming dermatophytes following the new reference EUCAST method E.Def 11.0, exemplified by *Trichophyton*☆

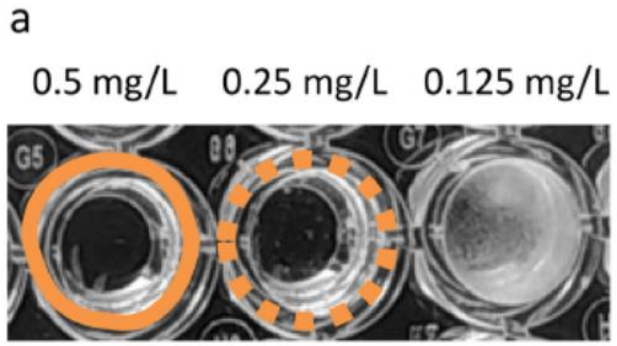
Maiken C. Arendrup [1, 2, 3, *], Gunnar Kahlmeter [4], Jesus Guinea [5, 6, 7, †], Joseph Meletiadis [8, 9, †], the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)

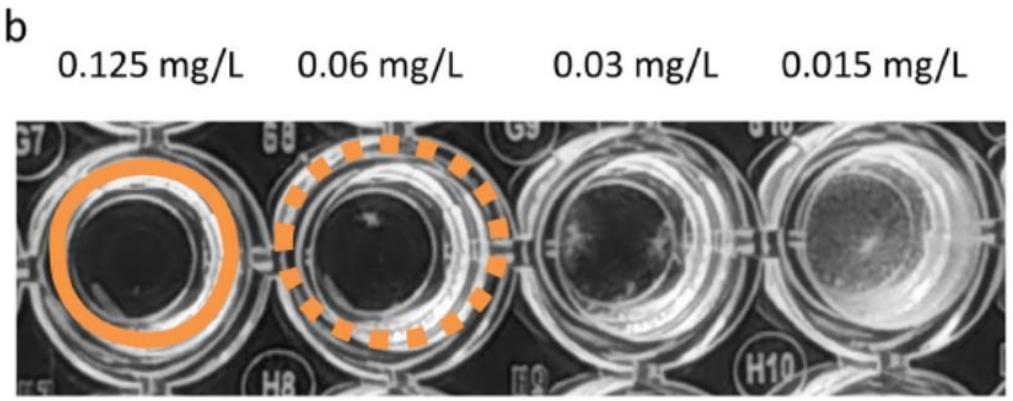
Azole and Amphotericin B MIC Values against *Aspergillus fumigatus*: High Agreement between Spectrophotometric and Visual Readings Using the EUCAST EDef 9.3.2 Procedure

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy®

Julia Serrano-Lobo,[a,b] Ana Gómez,[a,b] Waldo Sánchez-Yebra,[c] Miguel Fajardo,[d] Belén Lorenzo,[e] Ferrán Sánchez-Reus,[f] Inmaculada Vidal,[g] Marina Fernández-Torres,[h] Isabel Sánchez-Romero,[i] Carlos Ruiz de Alegría-Puig,[j] José Luis del Pozo,[k] Patricia Muñoz,[a,b,l,m] Pilar Escribano,[a,b] Jesús Guinea,[a,b,l] on behalf of the ASPEIN Study Group

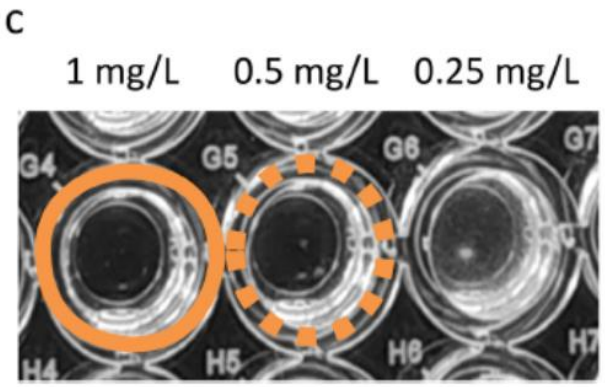
ITRA

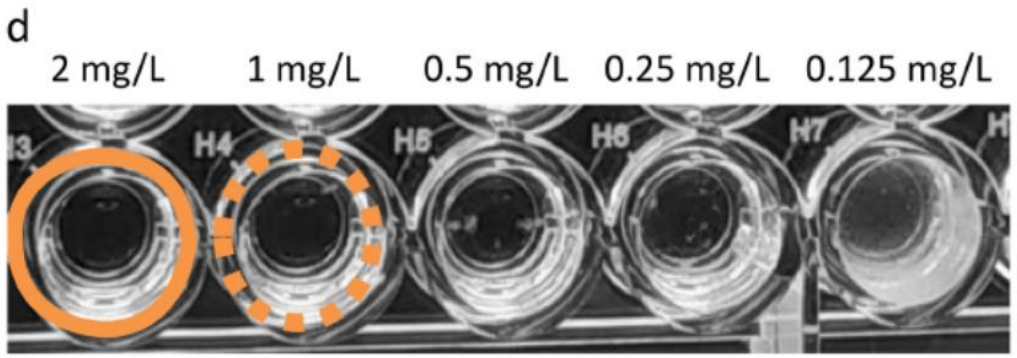




POSA

VORI



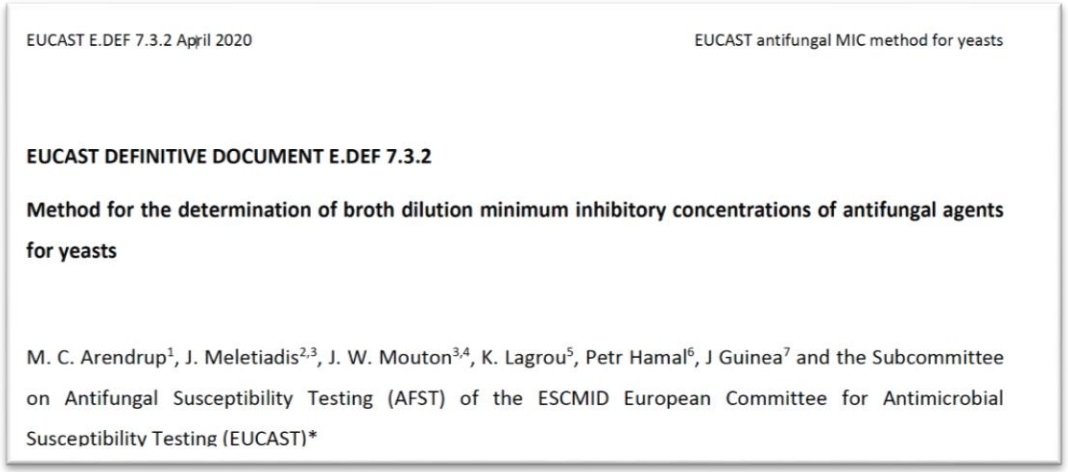


ISA

Itra: Itraconazol; **Vori:** voriconazol; **Posa:** posaconazol; **Isa:** isavuconazol.

Ref: Serrano-Lobo J *et al.* Antimicrobial Agents and Chemotherapy. 2021; January 1 e01693-20

Procedimientos EUCAST microdilución



EUCAST E.DEF 7.3.2 April 2020 EUCAST antifungal MIC method for yeasts

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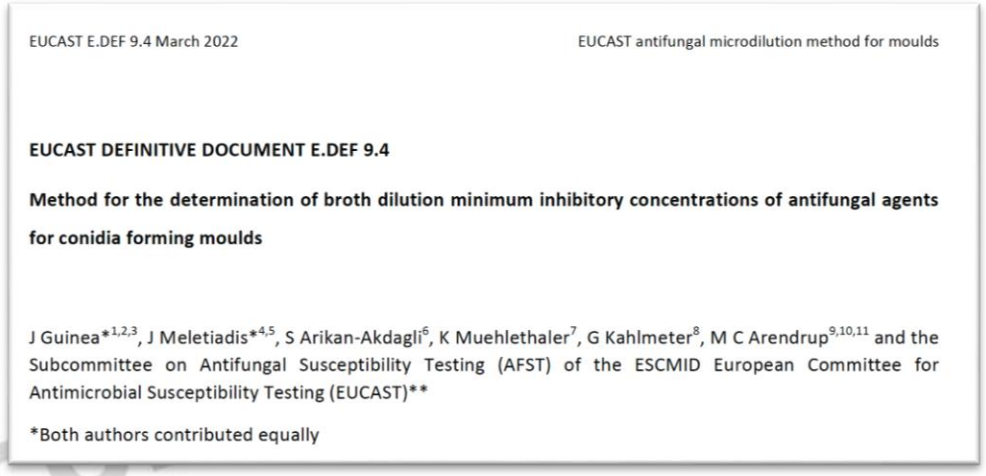
Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for yeasts

M. C. Arendrup[1], J. Meletiadis[2,3], J. W. Mouton[3,4], K. Lagrou[5], Petr Hamal[6], J Guinea[7] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)*



EUCAST E.DEF 9.4 March 2022 EUCAST antifungal microdilution method for moulds

EUCAST DEFINITIVE DOCUMENT E.DEF 9.4

Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for conidia forming moulds

J Guinea*[1,2,3], J Meletiadis*[4,5], S Arikan-Akdagli[6], K Muehlethaler[7], G Kahlmeter[8], M C Arendrup[9,10,11] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)**

*Both authors contributed equally

Clinical Microbiology and Infection 27 (2021) 55–60

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ELSEVIER

CMI CLINICAL MICROBIOLOGY AND INFECTION ESCMID

Narrative rev

How to: forming d E.Def 11.0, exemplified by *Trichophyton*

Maiken C. Arendrup [1, 2, 3, *], Gunnar Kahlmeter [4], Jesus Guinea [5, 6, 7, †], Joseph Meletiadis [8, 9, †], the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)

1ª Edición. Método específico para dermatofitos
Dirigido a detectar resistencia a terbinafina

Procedimientos EUCAST microdilución

EUCAST DEFINITIVE DOCUMENT E.Def 10.2

Screening method for the detection of azole and echinocandin resistance in *Aspergillus* using antifungal-containing agar plates, exemplified by *A. fumigatus*

J. Meletiadis[1,2], J Guinea[3,4,5], S. Arikan-Akdagli[6], N. Friberg[7], G. Kahlmeter[8], MC Arendrup[9,10,11] and the Subcommittee on Antifungal Susceptibility Testing (AFST) of the ESCMID European Committee for Antimicrobial Susceptibility Testing (EUCAST)*

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SUSCEPTIBILITY

Azole-Resistant *Aspergillus fumigatus* Clinical Isolate Screening in Azole-Containing Agar Plates (EUCAST E.Def 10.1): Low Impact of Plastic Trays Used and Poor Performance in Cryptic Species

Julia Serrano-Lobo,[a,b] Ana Gómez,[a,b] Belén Rodríguez-Sánchez,[a,b] Patricia Muñoz,[a,b,c,d] Pilar Escribano,[a,b] Jesús Guinea[a,b,c] on behalf of the ASPEIN Study Group

	Sensibilidad	Especificidad
Itraconazol	97%	96%
Voriconazol	79%	95%
Sospecha R azoles	100%	95%

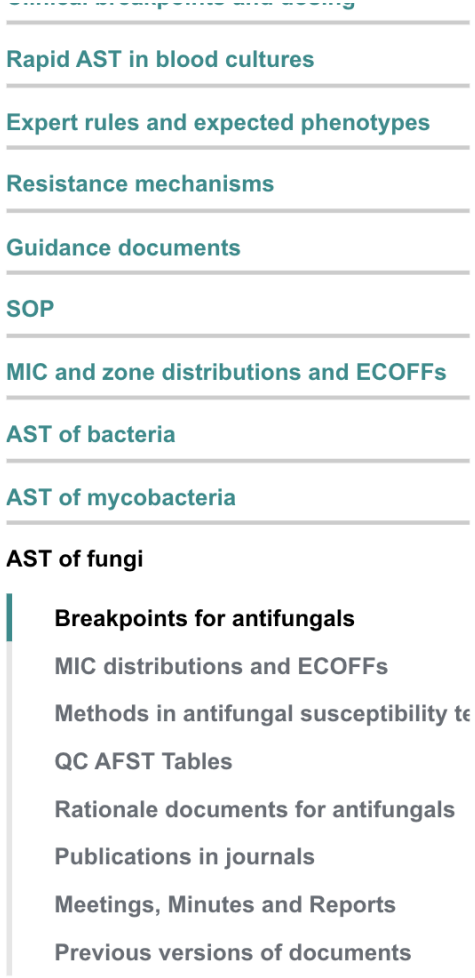
Aislados con TR_{34}-L98H, G54R y TR_{46}-Y121F-T289A detectados como **R**
Rendimiento pobre con especies crípticas

- Sospecha *TR_{46}-Y121F-T289A*: crecimiento voriconazol
- Sospecha *G54*: crecimiento en itraconazol y posaconazol
- Sospecha *TR_{34}-L98H*: crecimiento en itraconazol y voriconazol

Ref: Serrano-Lobo J *et al.* AAC 2021

Puntos de corte en antifúngicos EUCAST

- Solamente aplicables con microdilución EUCAST
- No intercambiables con CLSI
- NO SIRVEN PARA INTERPRETAR CMIS DE SYO O E-TEST



Clinical breakpoints for fungi (Candida and Aspergillus species)

March 20, 2019

- Clinical breakpoints for fungi v. 10.0 (PDF file for printing) - valid from 4 February 2020; links updated Sept 2020.
- Clinical breakpoints for fungi v. 10.0 (Excel file for screen) - valid from 4 February 2020;links updated Sept 2020.
- Overview of antifungal ECOFFs and clinical breakpoints for yeasts and moulds - valid from 18 January, 2022. (Previous version valid from 24 September, 2020)

Previous breakpoint tables

- Clinical breakpoints for fungi v 9.0 (pdf-file for printing) - valid from 12 February, 2018
- Clinical breakpoints for fungi v 9.0 (Excel file for screen) - valid from 12 February, 2018
- EUCAST guidance on "What to do when there are no breakpoints"

The EUCAST AFST subcommittee is currently reviewing breakpoint tables to introduce necessary changes to match the new EUCAST definitions of S, I and R.

https://www.eucast.org/astoffungi/clinicalbreakpointsforantifungals

New definitions of S, I and R

EUCAST has decided to change the definitions of susceptibility testing categories S, I and R as shown below. Results of several consultations on the new definitions are available on the EUCAST website under "Consultations".

- S - Susceptible, standard dosing regimen: A microorganism is categorised as "Susceptible, standard dosing regimen", when there is a high likelihood of therapeutic success using a standard dosing regimen of the agent.
- I – Susceptible, increased exposure*: A microorganism is categorised as "Susceptible, Increased exposure*" when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
- R - Resistant: A microorganism is categorised as "Resistant" when there is a high likelihood of therapeutic failure even when there is increased exposure.

*Exposure is a function of how the mode of administration, dose, dosing interval, infusion time, as well as distribution and excretion of the antimicrobial agent will influence the infecting organism at the site of infection.

EUCAST **explanatory video** (22 minutes) on the new definitions of S, I and R and on the use of the Area of Technical Uncertainty (ATU).
How to handle the ATU in clinical laboratories is described in a **EUCAST guidance document**.

http://www.eucast.org/newsiandr/

Revisados con las nuevas definiciones y la ATU

European Committee on Antimicrobial Susceptibility Testing

Antifungal Agents

Breakpoint tables for interpretation of MICs

Version 10.0, valid from 2020-02-04

This document should be cited as: "The European Committee on Antimicrobial Susceptibility Testing. Antifungal Agents. Breakpoint tables for interpretation of MICs, version 10.0, 2020. http://www.eucast.org/astoffungi/clinicalbreakpointsforantifungals/.

Modificaciones revisión 2020

- Revisión categoría "I" y conversión en "Sensible, exposición incrementada" o ATU (y su interpretación)
- Establecimiento puntos de corte para especies infrecuentes en base a *C. albicans* (para *Candida*) y *A. fumigatus* (para *Aspergillus*)
- Eliminación de "Intermedio" para equinocandinas y AmB

https://www.eucast.org/astoffungi/clinicalbreakpointsforantifungals

Puntos de corte disponibles

- *Aspergillus* y *Candida*
- *Cryptococcus* y anfotericina B
- No Mucorales, *Fusarium*, *Scedosporium/Lomentospora*
- No especies infrecuentes de *Candida*
- No levaduras no-Candida

https://www.eucast.org/astoffungi/clinicalbreakpointsforantifungals

Antifungal agent	MIC breakpoint (mg/L)																		Comments on the I category	Comments on the ATU
	Candida albicans			*Candida dubliniensis*		*Candida glabrata*		*Candida krusei*		*Candida parapsilosis*		*Candida tropicalis*		*Candida guilliermondii*		*Cryptococcus neoformans*		Non-species related breakpoints for *Candida*[1]		
	S ≤	R >	ATU	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	S ≤	R >	
Amphotericin B	1	1		1	1	1	1	1	1	1	1	1	1	IE	IE	1	1	IE	IE	No data to support an I category according to the new definitions	
Anidulafungin	0.03	0.03				0.06	0.06	0.06	0.06	4	4	0.06	0.06	IE[2]	IE[2]	-	-	IE	IE		
Caspofungin	Note[3]	Note[3]				Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	Note[3]	IE[2]	IE[2]	-	-	IE	IE		
Fluconazole	2	4		2	4	0.001[4]	16	-	-	2	4	2	4	IE[2]	IE[2]	IE	IE	2	4	See dosages table for appropriate dose	
Isavuconazole	IE	IE		IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE	IE		
Itraconazole	0.06	0.06		0.06	0.06	IE[2]	IE[2]	IE[2]	IE[2]	0.125	0.125	0.125	0.125	IE[2]	IE[2]	IE	IE	IE	IE		
Micafungin	0.016	0.016	0.03			0.03	0.03	IE[5]	IE[5]	2	2	IE[5]	IE[5]	IE[5]	IE[5]	-	-	IE	IE		If S to anidulafungin, report as S and add the following comment: "Isolates susceptible to anidulafungin with micafungin MIC of 0.03 mg/L do not harbour an *fks* mutation conferring resistance to the echinocandins". If not S to anidulafungin, report as R and refer to reference laboratory for *fks* sequencing and confirmation of MICs.
Posaconazole	0.06	0.06		0.06	0.06	IE[2]	IE[2]	IE[2]	IE[2]	0.06	0.06	0.06	0.06	IE[2]	IE[2]	IE	IE	IE	IE		
Voriconazole[6]	0.06[7]	0.25[7]		0.06[7]	0.25[7]	IE	IE	IE	IE	0.125[7]	0.25[7]	0.125[7]	0.25[7]	IE[2]	IE[2]	IE	IE	IE	IE	4 mg/kg iv twice daily	

9th Advances Against Aspergillosis and Mucormycosis
Palazzo dei Congressi Lugano, Lugano, Switzerland
27 – 29 February 2020

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Clinical *Aspergillus* isolates causing aspergillosis in the last 20 years: an overview of aetiology and antifungal resistance to azoles and amphotericin B

J. Serrano-Lobo[1,2], E. Reigadas[1,2], A. Vena[1,2], M. Machado[1,2], P. Muñoz[1,2,3,4], P. Escribano[1,2], J. Guinea[1,2,3,4]

[1] Clinical Microbiology and Infectious Diseases, Hospital General Universitario Gregorio Marañón, Madrid, Spain. [2] Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain. [3] CIBER Enfermedades Respiratorias-CIBERES (CB06/06/0058), Madrid, Spain. [4] Medicine Department, Faculty of Medicine, Universidad Complutense de Madrid

Table 1. Percentage of resistance (No. of isolates) of the 356 isolates against azoles and amphotericin B.

		Percentage of resistance (No. of isolates)									% of resistance/ non wild type
		0.03	0.06	0.125	0.25	0.5	1	2	4	≥8	
***A. fumigatus* SS (n=229)**	Amphotericin B	0	1	2	96	117	11	2	0	0	0 / 0.9
	Itraconazole	0	0	8	85	125	9	1	0	1	0.45 / 0.9
	Voriconazole	0	0	0	10	97	108	12	1	1	0.9 / 6
	Posaconazole	7	104	91	25	2	0	0	0	0	0.9 / 0.9
	Isavuconazole	0	0	0	14	122	82	9	0	2	5 / 0.9
Cryptic species (n=17)	Amphotericin B	0	0	0	0	1	1	7	5	3	47.5 / 88.2
	Itraconazole	0	0	0	1	5	4	5	0	2	12 / 41
	Voriconazole	0	0	0	0	0	1	11	3	2	29 / 94
	Posaconazole	0	0	5	9	2	1	0	0	0	18 / 17.6
	Isavuconazole	0	0	0	0	0	9	6	2	0	47 / 11.7

Numbers in bold indicate resistance; underlined numbers indicate non wild type isolates based on ECOFFs.

Code	*cyp51A*	AmB	ITC	VOR	POS	ISA
1	Wild type	0.5	0.5	1	0.125	2
2	Wild type	0.5	0.5	1	0.125	2
3	Wild type	0.25	0.5	2	0.125	2
4	Wild type	0.25	0.5	2	0.25	2
5	Wild type	0.125	0.5	2	0.125	2
6	G448S	0.5	2	≥16	0.5	8
7	Wild type	0.125	0.5	1	0.125	2
8	Wild type	0.25	0.5	2	0.25	2
9	Wild type	0.5	1	2	0.125	2
10	TR34L98H	0.25	≥16	4	0.5	8
11	Wild type	0.5	0.5	0.5	0.125	2

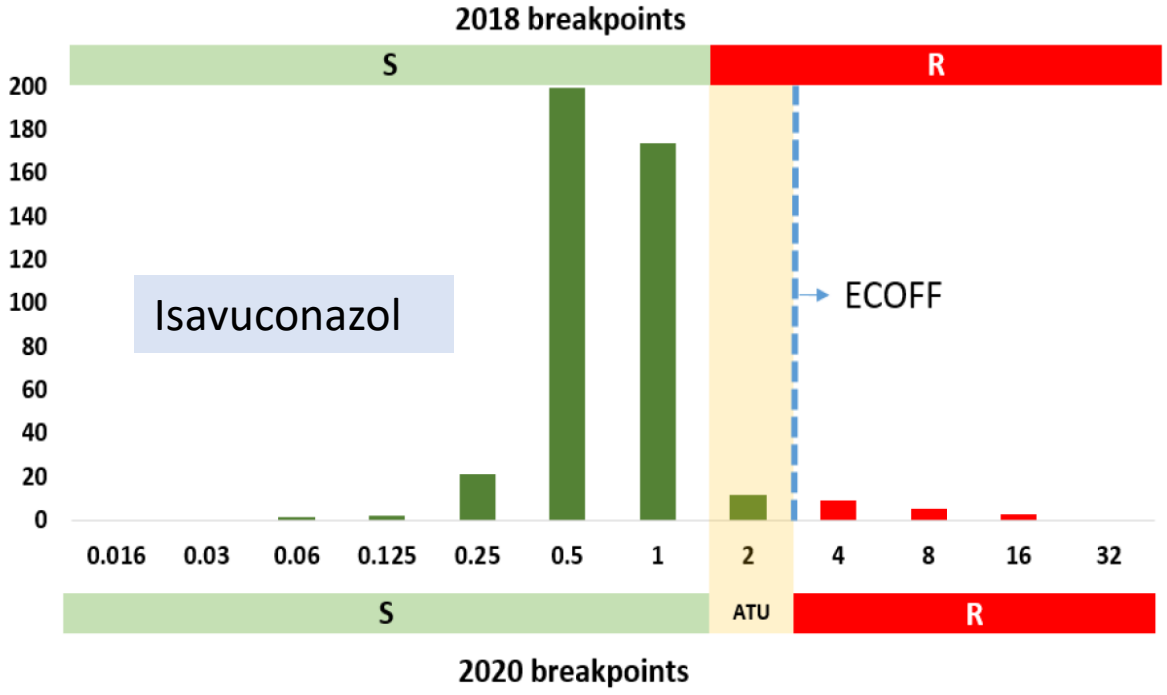
Journal of *Fungi*

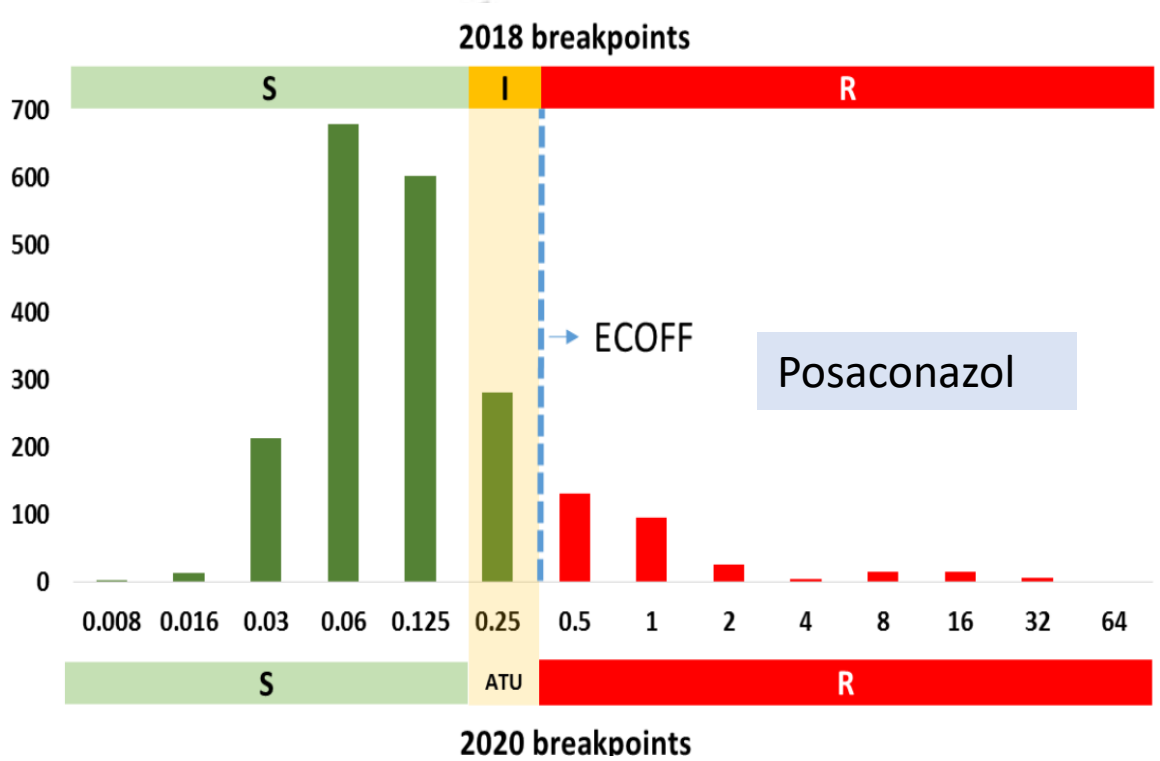
MDPI

Review

Updated EUCAST Clinical Breakpoints against *Aspergillus*, Implications for the Clinical Microbiology Laboratory

Jesús Guinea [1,2,3]

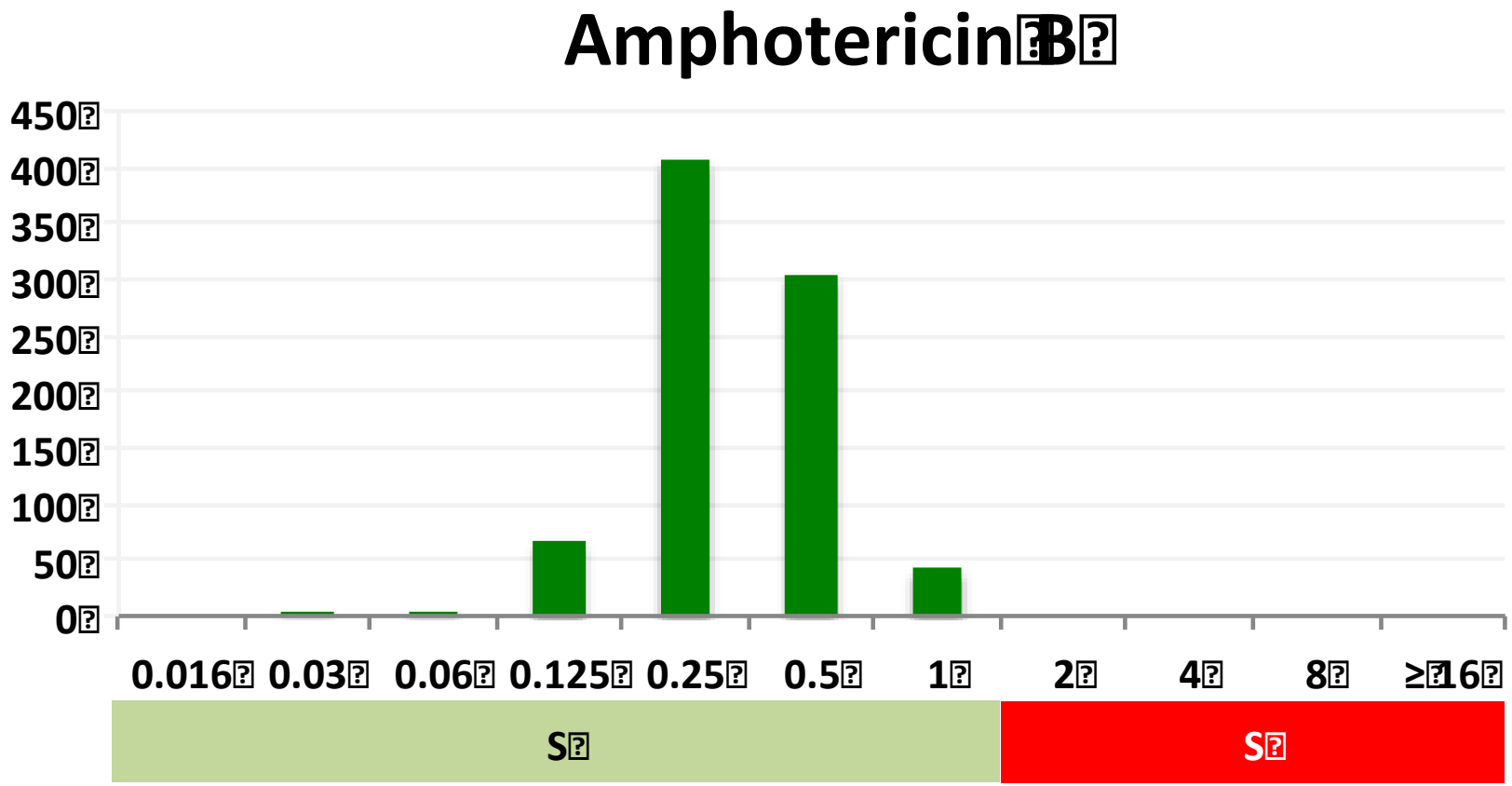




MIC distributions of isavuconazole y posaconazole obtained from https://www.eucast.org/astoffungi/rationale_documents_for_antifungals/

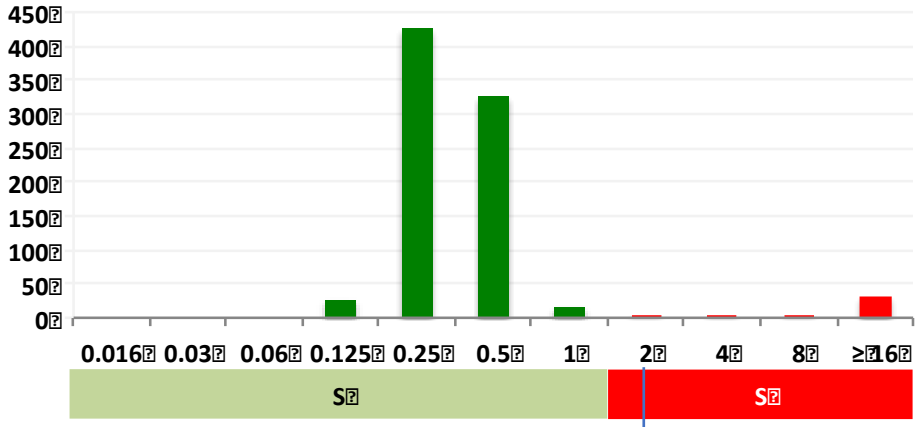
Ref: Guinea J. J. Fungi 2020, 6, 343

CMIs frente *A. fumigatus* sensu stricto (estudio ASPEIN)

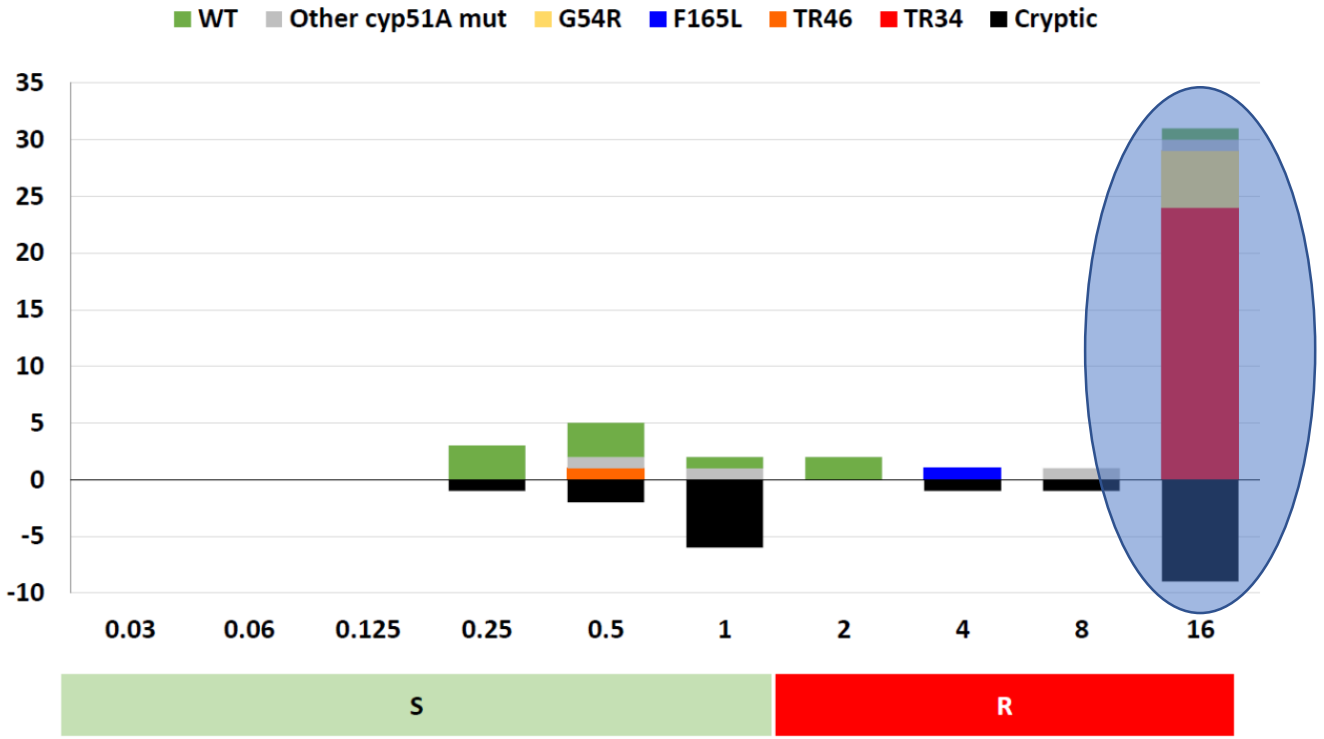


S, susceptible; **R**, resistant. **Ref:** Escribano P *et al.* Clin Microbiol infect. 2021 Aug;27(8):1170.e1-1170.e7

Itraconazol CMIs (*ASPE*IN)

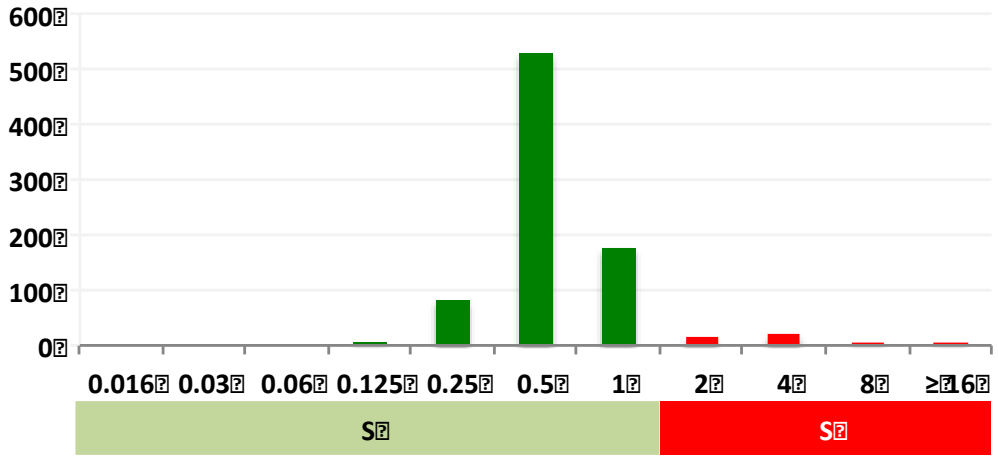


A. fumigatus sensu stricto resistant isolates and wild type *cyp51A* gene

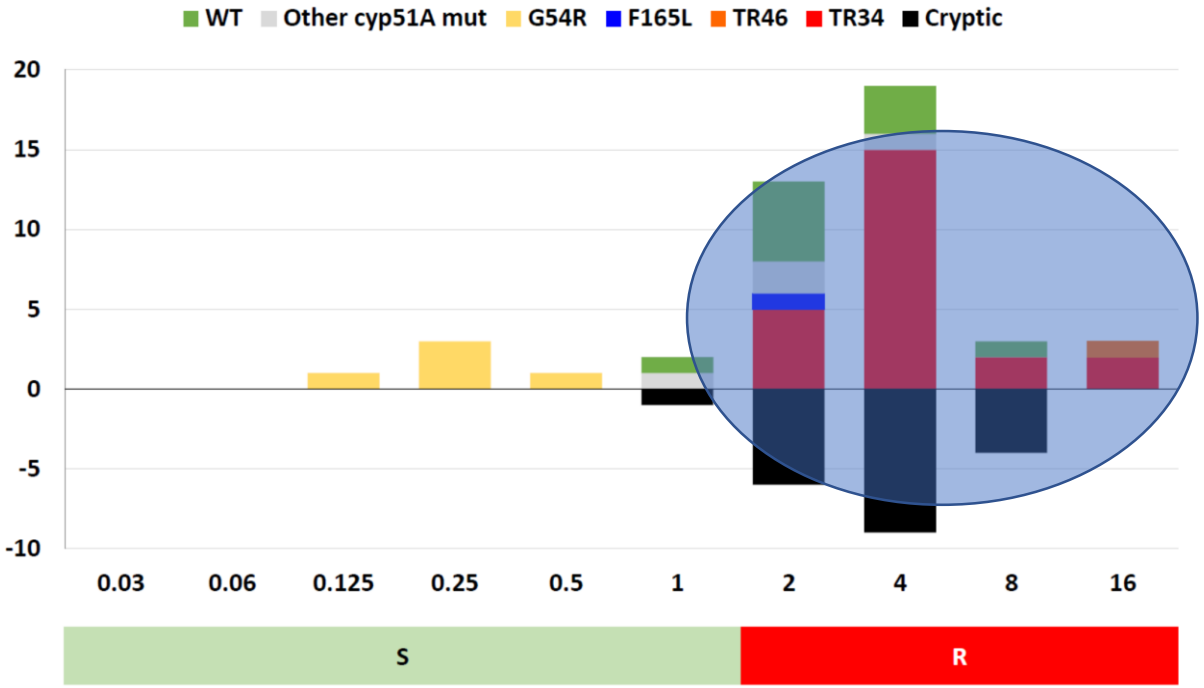


S, susceptible; **R**, resistant. **Ref:** Escribano P *et al.* Clin Microbiol infect. 2021 Aug;27(8):1170.e1-1170.e7

Voriconazol CMIs (*ASPE*IN)

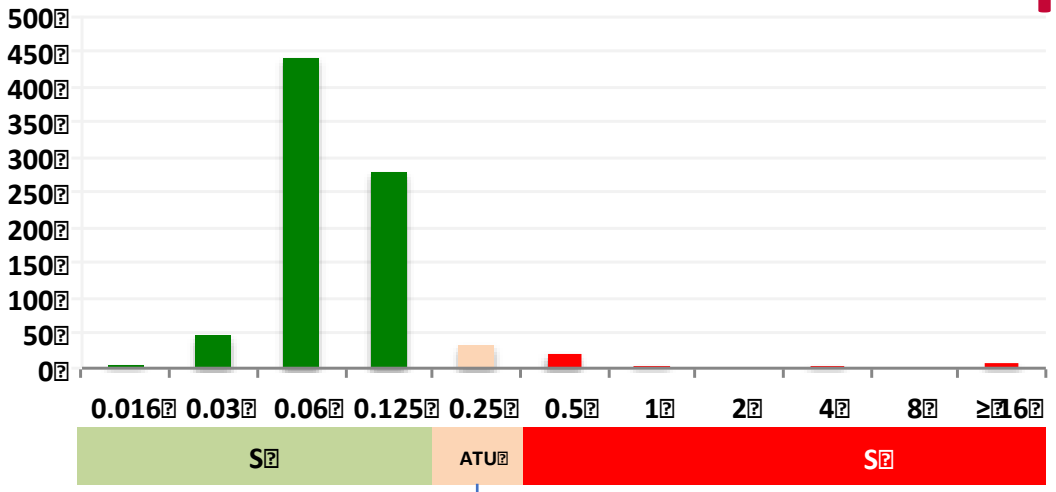


Resistant isolates (n=19) distributed as:
Cryptic species (n=6)
***A. fumigatus sensu stricto* (n=13) and *cyp51A* gene alterations:**
- F46Y/M172V/N248T/D255E/E427K (n=1)
- F46Y/M172V/N248T/D255E/E416Q/E427K (n=1)
- F165L (n=1)
- TR_{34}-L98H (n=5)
- Wild type (n=5)

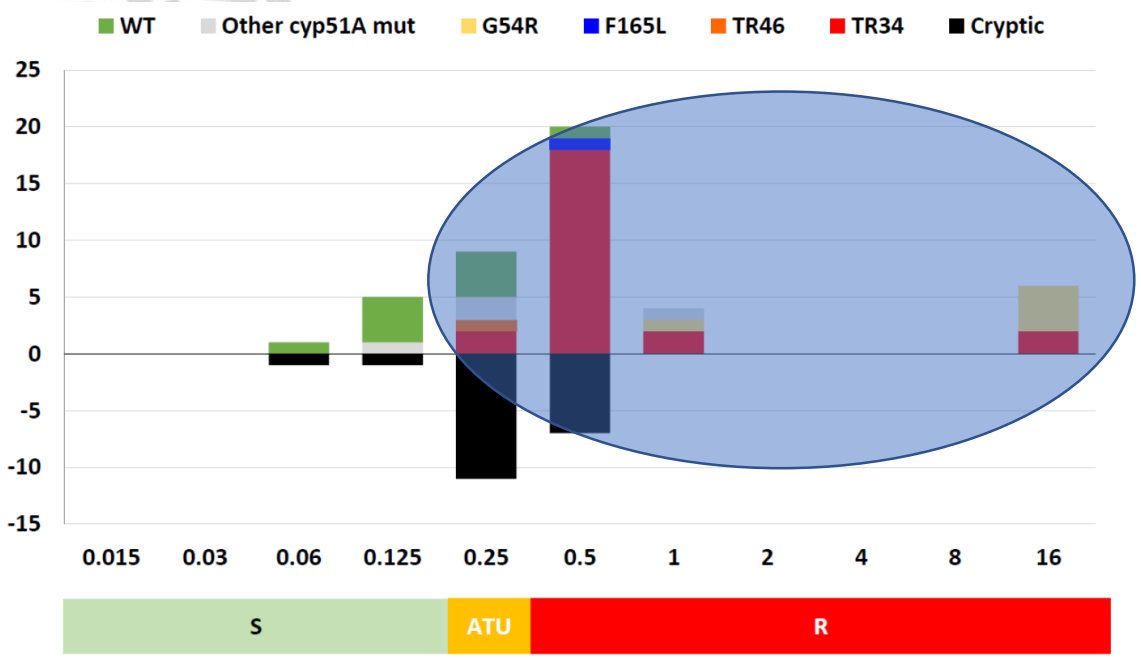


S, susceptible; **R**, resistant. **Ref:** Escribano P *et al.* Clin Microbiol infect. 2021 Aug;27(8):1170.e1-1170.e7

Posaconazol CMIs (*ASPE*IN)



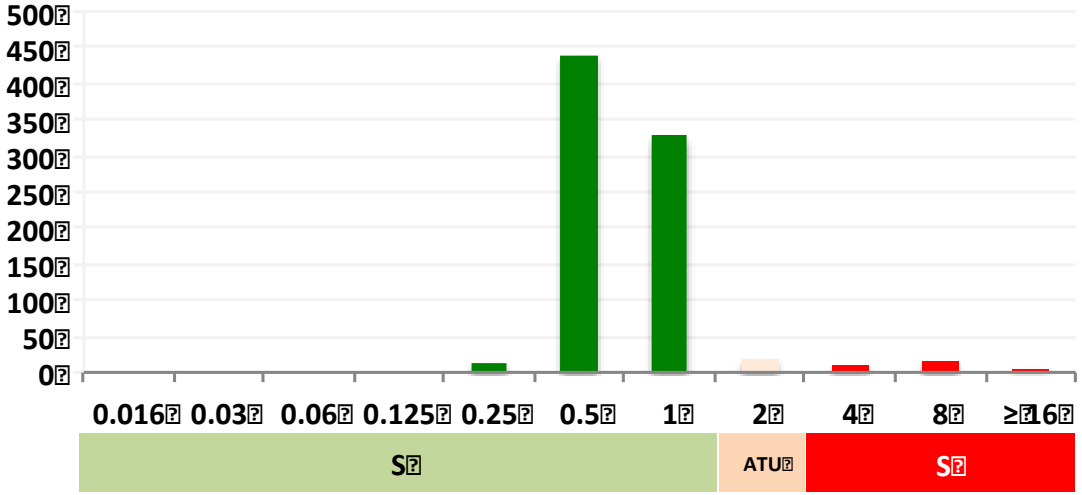
Resistant (n=9) distributed as:
Cryptic species (n=5)
***A. fumigatus sensu stricto* (n=4)**
and *cyp51A* gene alterations:
- S496L (n=1)
- TR_{34}-L98H (n=2)
- Wild type (n=1)



+ 23 aislados sensibles!!!

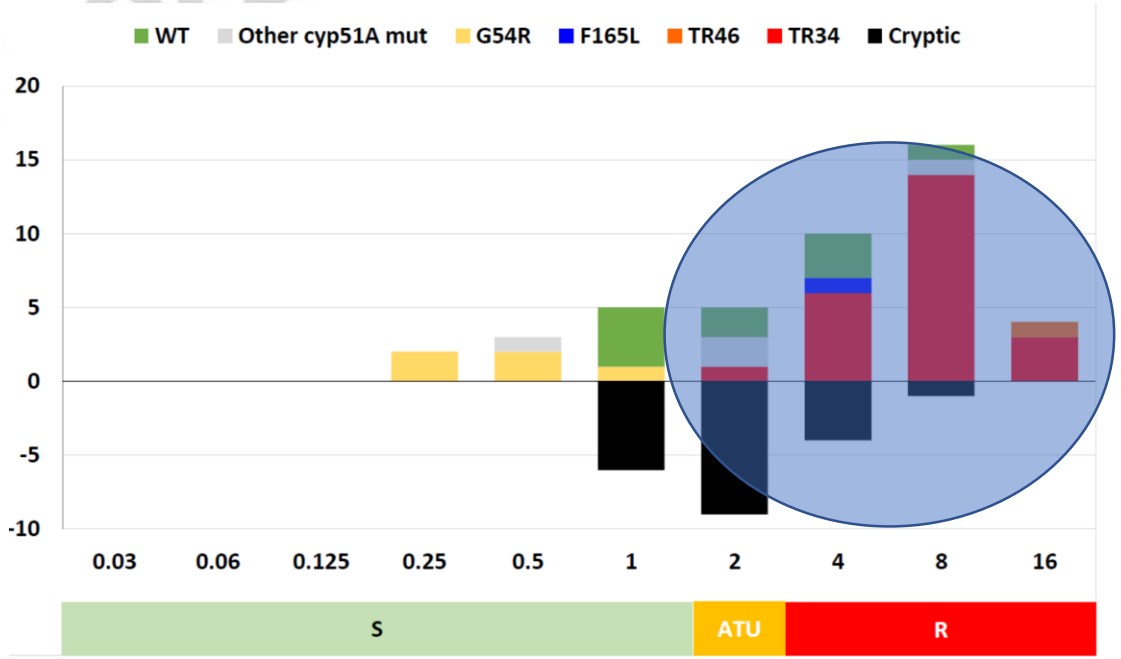
S, susceptible; **R**, resistant. **Ref:** Escribano P *et al.* Clin Microbiol infect. 2021 Aug;27(8):1170.e1-1170.e7

Isavuconazol CMIs (*ASPE*IN)



Resistant isolates (n=13) distributed as:
Cryptic species (n=8)
***A. fumigatus sensu stricto* (n=5)**
and *cyp51A* gene alterations:
- F46Y/M172V/N248T/D255E/E427K (n=1)
- F46Y/M172V/N248T/D255E/E416Q/E427K (n=1)
- TR_{34}-L98H (n=1)
- Wild type (n=2)

+ 13 aislados sensibles!!!



S, susceptible; **R**, resistant. **Ref:** Escribano P *et al.* Clin Microbiol infect. 2021 Aug;27(8):1170.e1-1170.e7

Antifungal agent	*A. fumigatus* MIC breakpoint (mg/L)						
	2018		2020			Comments on the I category	Comments on the ATU
	S ≤	R >	S ≤	R >	ATU		
Amphotericin B	1	2	1	1		No data to support an "I" category according to the new definition of "I"	
Isavuconazole	1	1	1	2	2	Isavuconazole MIC = 2 mg/L should not be interpreted as I but only followed up as an ATU	• If voriconazole wild-type (MIC ≤1 mg/L) report as S and add the following comment: *The MIC of 2 mg/L is one dilution above the S breakpoint but within the wild-type isavuconazole MIC range due to a stringent breakpoint susceptibility breakpoint*. • If voriconazole non wild-type report as R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs
Itraconazole	1	2	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) itraconazole can be used provided sufficient exposure is ensured*
Posaconazole	0.125	0.25	0.125	0.25	0.25	Posaconazole MIC = 0.25 mg/L should not be interpreted as I but only as ATU	• if S to itraconazole report as S and add the following comment: "The MIC is 0.25 mg/L and thus one dilution above the S breakpoint due to overlapping wt and non-wt populations". • If not S to itraconazole report as R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs.
Voriconazole	1	2	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) voriconazole can be used provided sufficient exposure is ensured*

Antifungal agent	*A. flavus* MIC breakpoint (mg/L)						
	2018		2020			Comments on the I category	Comments on the ATU
	S ≤	R >	S ≤	R >	ATU		
Amphotericin B	IE	IE	-	-		No data to support an "I" category according to the new definition of "I"	
Isavuconazole	IE	IE	1	2	2	Isavuconazole MIC = 2 mg/L should not be interpreted as I but only followed up as an ATU	• If voriconazole wild-type (MIC ≤1 mg/L) report as S and add the following comment: *The MIC of 2 mg/L is one dilution above the S breakpoint but within the wild-type isavuconazole MIC range due to a stringent breakpoint susceptibility breakpoint*. • If voriconazole non wild-type report as R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs
Itraconazole	1	2	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) itraconazole can be used provided sufficient exposure is ensured*
Posaconazole	IE	IE	IE	IE			
Voriconazole	IE	IE	IE	IE			

Antifungal agent	*A. nidulans* MIC breakpoint (mg/L)						
	2018		2020			Comments on the I category	Comments on the ATU
	S ≤	R >	S ≤	R >	ATU		
Amphotericin B	IE	IE	-	-		No data to support an "I" category according to the new definition of "I"	
Isavuconazole	0.25	0.25	0.25	0.25			
Itraconazole	1	2	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) itraconazole can be used provided sufficient exposure is ensured*
Posaconazole	IE	IE	IE	IE			
Voriconazole	IE	IE	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) voriconazole can be used provided sufficient exposure is ensured*

Antifungal agent	*A. niger* MIC breakpoint (mg/L)					
	2018		2020		Comments on the I category	Comments on the ATU
	S ≤	R >	S ≤	R >		
Amphotericin B	1	2	1	1	No data to support an "I" category according to the new definition of "I"	
Isavuconazole	IE	IE	IE	IE		
Itraconazole	IE	IE	IE	IE		
Posaconazole	IE	IE	IE	IE		
Voriconazole	IE	IE	IE	IE		

Antifungal agent	*A. terreus* MIC breakpoint (mg/L)						
	2018		2020			Comments on the I category	Comments on the ATU
	S ≤	R >	S ≤	R >	ATU		
Amphotericin B	-	-	-	-		No data to support an "I" category according to the new definition of "I"	
Isavuconazole	1	1	1	1			
Itraconazole	1	2	1	1	2		Report as R with the following comment: *In some clinical situations (non-invasive infections forms) itraconazole can be used provided sufficient exposure is ensured*
Posaconazole	0.125	0.25	0.125	0.25	0.25		• if S to itraconazole report as S and add the following comment: "The MIC is 0.25 mg/L and thus one dilution above the S breakpoint due to overlapping wt and non-wt populations". • If not S to itraconazole report as R and refer to reference laboratory for *CYP51A* sequencing and confirmation of MICs.
Voriconazole	IE	IE	IE	IE			

ORIGINAL ARTICLE

mycoses WILEY

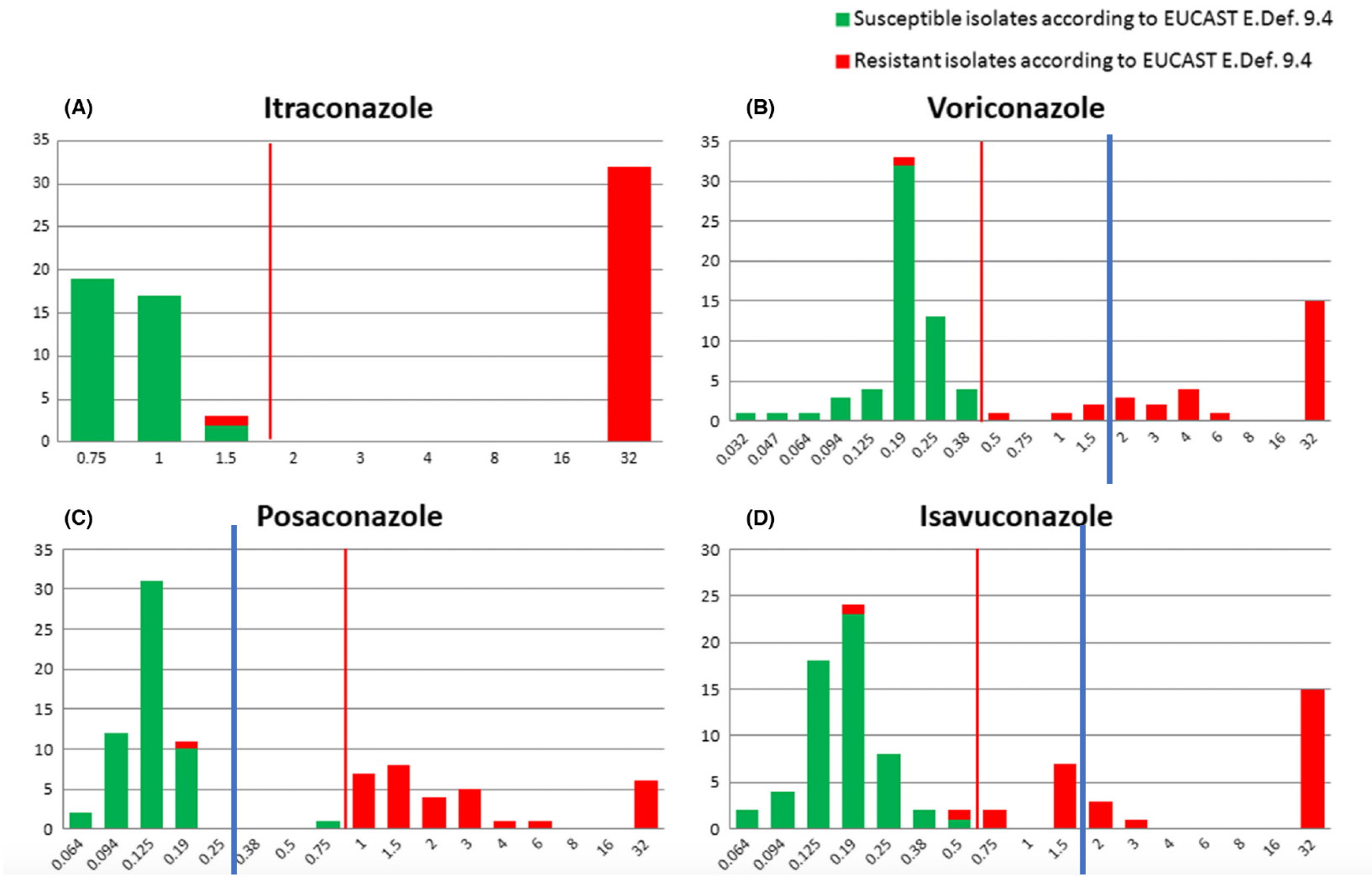
Gradient diffusion strips for detecting azole resistance in *Aspergillus fumigatus* sensu lato

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

- Sistemas comerciales testan cepas *sensibles*
- Insuficientemente validados con cepas *resistentes*
- Triazoles frente a *A. fumigatus* complex S y R a azoles

Ref: Serrano-Lobo J *et al.* Mycoses. 2022. En prensa

A. fumigatus sensu stricto

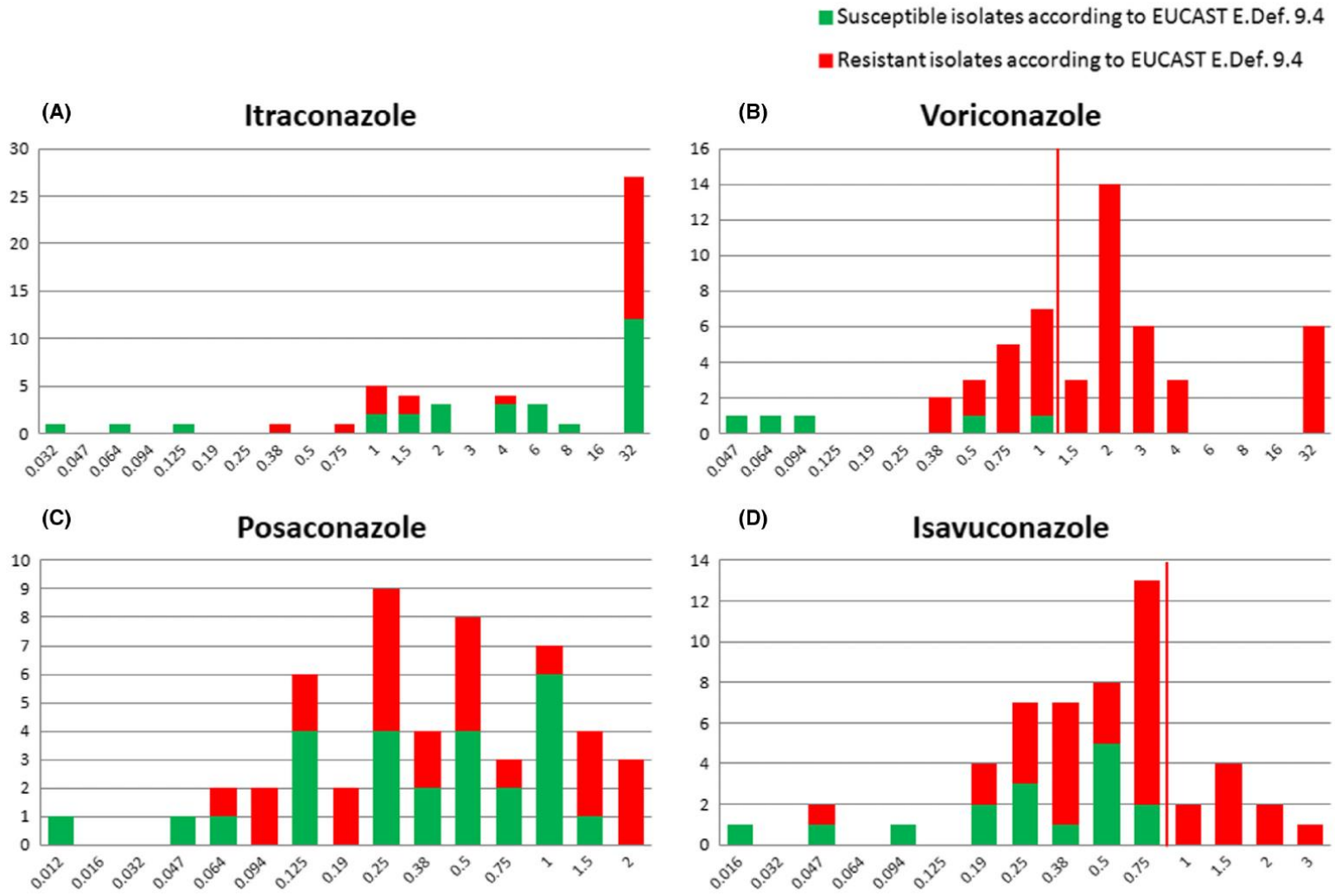


	Sensibilidad	Especificidad
Itra	97%	100%
Vori	97%	100%
Posa	97%	100%
Isa	93,3%	100%

Puntos de corte de EUCAST

Ref: Serrano-Lobo J *et al.* Mycoses. 2022. En prensa

Especies crípticas



Ref: Serrano-Lobo J *et al.* Mycoses. 2022. En prensa

Mensajes para llevar a casa

- Metodología EUCAST para antifúngicos difícil implementar en rutina
- Uso de agares (E.Def 10.2) *screening* resistencia a azoles y candinas
- No intercambiar puntos de corte/métodos!
- Más puntos de corte y ECOFFs

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING

European Society of Clinical Microbiology and Infectious Diseases

Antimicrobial susceptibility tests on groups of organisms or agents for which there are no EUCAST breakpoints

Updated 1 December 2021