EUCAST-AFST
Available breakpoints 2012

9th NSMM meeting
Göteborg, Sweden
October 25th
2012

EUCAST-AFST: MC Arendrup (Chair), WW Hope (Secretary), M Cuenca-Estrella & C Lass-Flörl

EUCAST-AFST documents

Reference Methods

- Yeast
  - **E.DEF 7.2 (2012)**
  - **TN- E.DEF 7.2 (CMI –epub July)**
  - E.DEF 7.1 (2008)
  - TN- E.DEF 7.1 (2008)
- Conidia forming moulds
  - E.DEF 9.1 (2008)
  - TN-E.DEF 9.1 (2008)

Breakpoints

Compound	*Candida*		*Aspergillus*	
	Rationale Doc	Techn. Note CMI	Rationale Doc	Techn. Note CMI
Amphotericin	2010	**2011**	**2012**	**epub July**
Anidulafungin	2010	**2011**		
Fluconazole	2007	2008	-	-
Itraconazole			**2012**	**epub July**
Posaconazole	2010	**2011**	**2012**	**epub July**
Voriconazole	2008	2008	**2012**	**In prep.**

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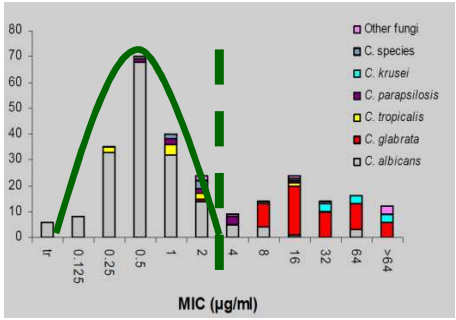
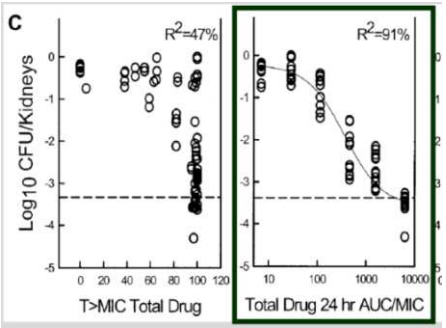
EUCAST BP establishing procedure

- MIC distributions
  - ➢ Per species
  - ➢ Several data sets
  - ➢ Epidemiological Cut Off Value (ECOFF)
- MIC-clinical outcome relationships
  - – Per species
  - – For wild type and non-wild type isolates
- PK/PD
  - – defining the important parameter and ratio (AUC/MIC, Peak/MIC, Time/MIC)
  - – are non wild type covered during standard dosing?
- ➢ BP never higher than ECOFF unless supported by data



MIC in mg/L	Candidaemia No. cure/Total	Candidaemia % response	OPC ≥ 100 mg/d No. cure/Total	OPC ≥ 100 mg/d % response	All % response
≤ 0.5	98/107	92	26/26	100	93
1	6/6	100	4/4	100	100
2	1/1	100	1/1	100	100
4	3/3	100	5/9	56	67
8	2/5	40	7/32	22	24
≥16	3/4	75	0/60	0	5



EUCAST *Candida* BPs

Breakpoints (BPs): S: ≤X / R: >Y

Antifungal agent	MIC breakpoint (mg/L)						
	C. albicans	***C. glabrata***	***C. krusei***	***C. parapsi-losis***	***C. tropicalis***	***C. guillier-mondii***	**Non-species related breakpoints**
Ampho. B	1/1	1/1	1/1	1/1	1/1	IE	IE
Anidulafungin	0.03/0.03	0.06/0.06	0.06/0.06	-*	0.06/0.06	IE[2]	IE
Fluconazole	2/4	IE*	-	2/4	2/4	IE	2/4
Posaconazole	0.06/0.06	IE[2]	IE[2]	0.06/0.06	0.06/0.06	IE[2]	IE
Voriconazole	0.125/0.125[4]	IE	IE	0.125/0.125[4]	0.125/0.125[4]	IE[2]	IE

[2] denotes the MICs for this species is generally higher than those for *C. albicans*
[4] denotes that voriconazole should be reserved for situations where fluconazole is not appropriate
- denotes the organism is regarded a poor target for the antimicrobial agent

Current revision proposals

* For *C. glabrata* and fluconazole it is proposed to categorise ≤ 32 mg/L as "I" and >32 mg/L as "R"
* For *C. parapsilosis* and anidulafungin it is proposed to categorise ≤ 2 mg/L as "I" and >2 mg/L as "R"

Breakpoints under development:

Micafungin and *Candida*

CLSI versus EUCAST

Breakpoints (BPs): S: ≤X; R: >Y Revised BPs

	CLSI M27-S3	CLSI revised (M27-S4)			EUCAST	
AMB	≤1	≤1			≤1; >1	
ANF	≤2	≤0.25;	>0.5	(alb, krus, trop)	≤0.032; >0.032	(alb)
		≤0.125;	>0.25	(glab)	≤0.06; >0.06	(glab, krus, trop)
		≤2; >4		(para, guillier)		(para poor target, guillier IE)
CSF	≤2				-	
MFG	≤2	≤0.25;	>0.5	(alb, krus, trop)	-	
		≤0.06;	>0.125	(glab)		
		≤2;	>4	(para, guillier)		
Fluco	≤8; >32	≤2;	>4	(alb, para, trop)	≤2; >4	(alb, trop, para)
		SDD ≤32;	>32	(glab)		(glab IE)
				(krus poor target)		(krus poor target)
Vori	≤1; >2	≤0.125;	>0.5	(alb, para, trop)	≤0.125; >0.125	(alb, trop, para)
		≤0.5;	>1	(krus)		(glab/krus IE)
				(glab IE)		
Itra	≤0.125; >0.5	≤0.125;	>0.5		-	
Posa	-	-			≤0.06; >0.06	(alb, trop, para)
						(glab/krus IE)

www.eucast.org; Pfaller Drug Resist Updat. 2010 & 2011

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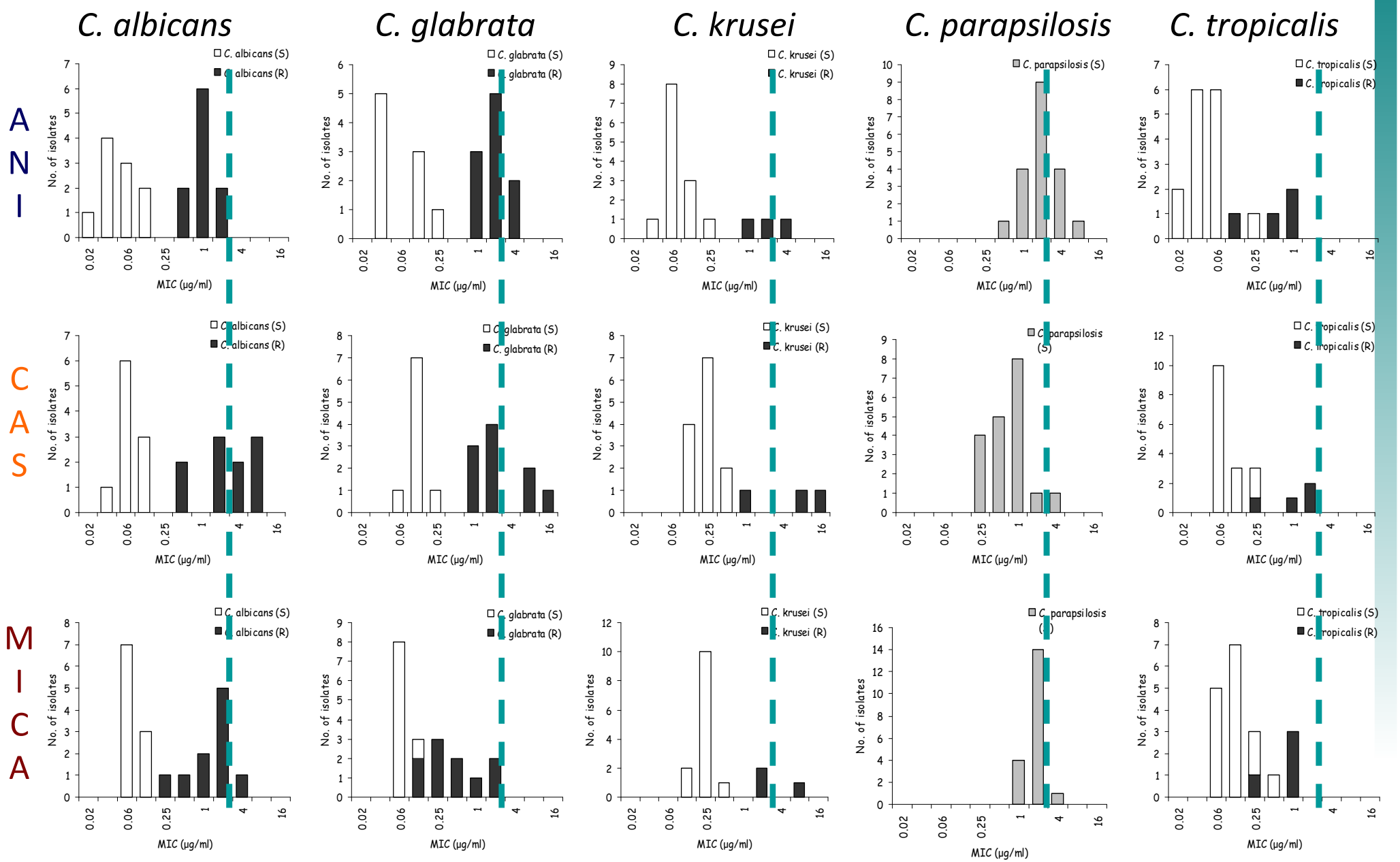
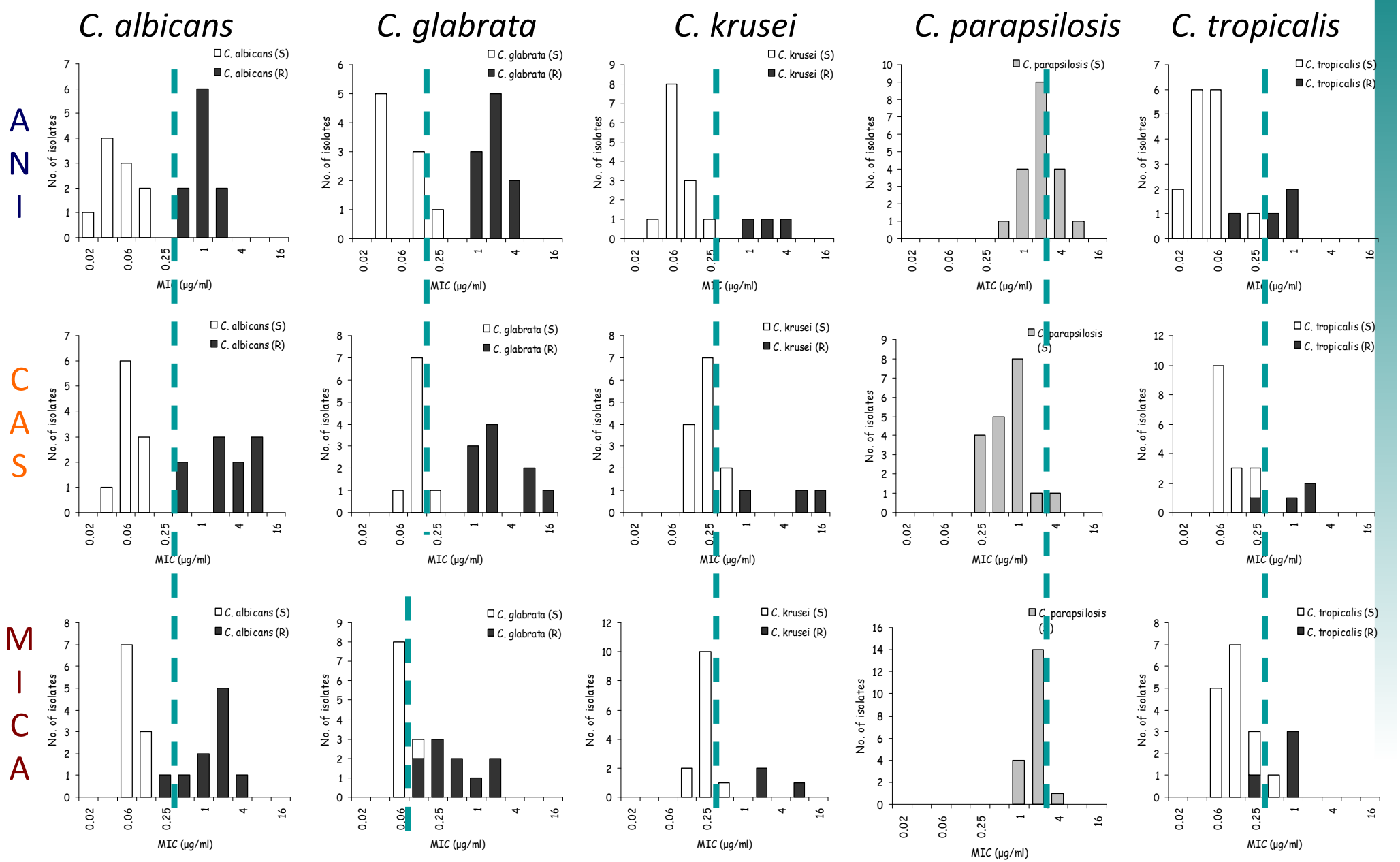
CLSI echinocandin MICs "M27-S3 BP"



Arendrup et al AAC 2010, CLSI M27-S3

EUCAST-AFST: MC Arendrup (Chair), WW Hope (Secretary), M Cuenca-Estrella & C Lass-Flörl

CLSI echinocandin testing – revised BP



Arendrup AAC 2010, Pfaller Drug Res Updates 2011, M27-S4

EUCAST & CLSI Anidulafungin MICs

Candida sp	0.002	0.004	0.008	0.016	0.032	0.064	0.125	0.25	0.5	1	2	4	8	>=16	ECOFF	BP
albicans EUCAST	284	576	314	427*	703*	14	25	4	3	4	0	0	0	4	0.03	**0.03**
albicans CLSI			338	1278	1542	896	216	12		1					0.125	**0.25**
glabrata EUCAST	55	43	64	177*	441*	111	28	11	5	3	3	1	2	0	0.06	**0.06**
glabrata CLSI				7	161	715	320	26	2	2	2	1			0.25	**0.125**
krusei EUCAST	2	1	13	26*	83*	34	8	4	0	0	0	0	0	0	0.06	**0.06**
krusei CLSI				4	159	91	14	1	1						0.125	**0.25**
parapsilosis EUCAST	0	3	1	0	4	6	2	36	78	171	96	13	7	2	4	-
parapsilosis CLSI				1	2	1	1	14	49	319	765	86			4	**2**
tropicalis EUCAST	18	34	17	47*	175*	24	7	6	3	1	0	0	0	2	0.06	**0.06**
tropicalis CLSI			41	254	493	173	24	7	1		3				0.125	**0.25**

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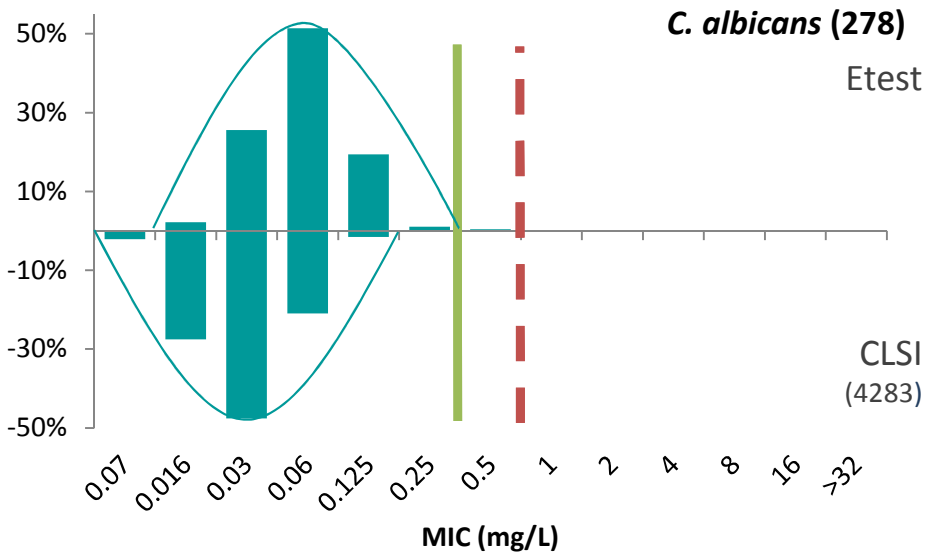
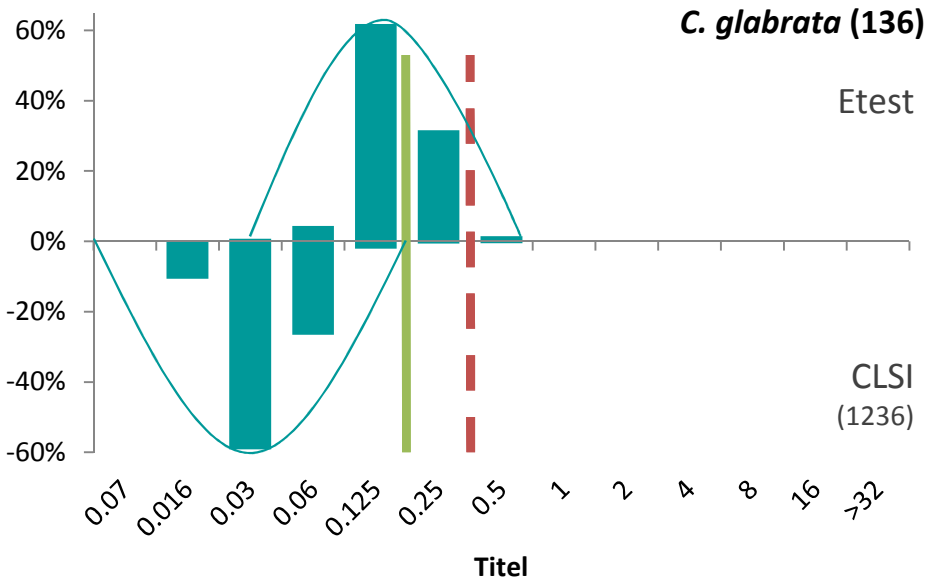
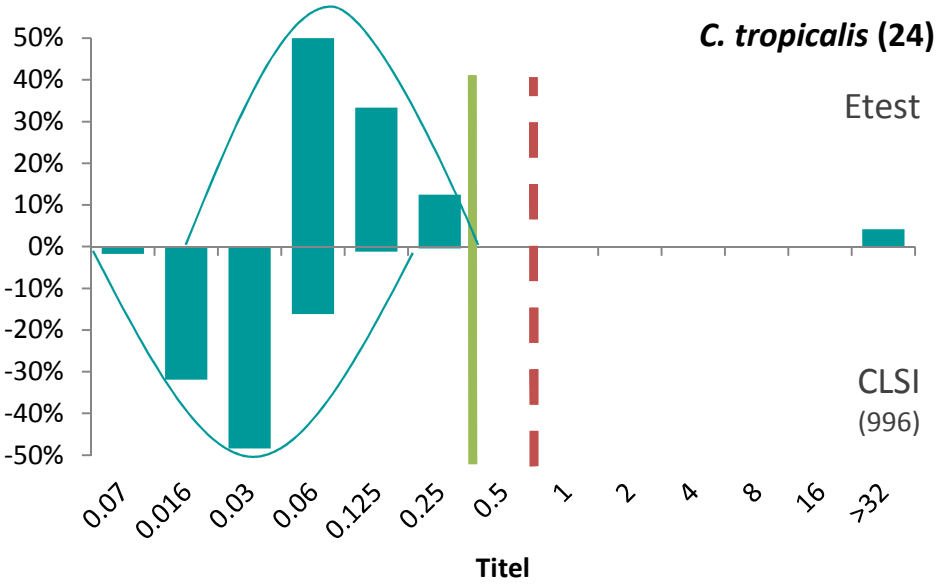
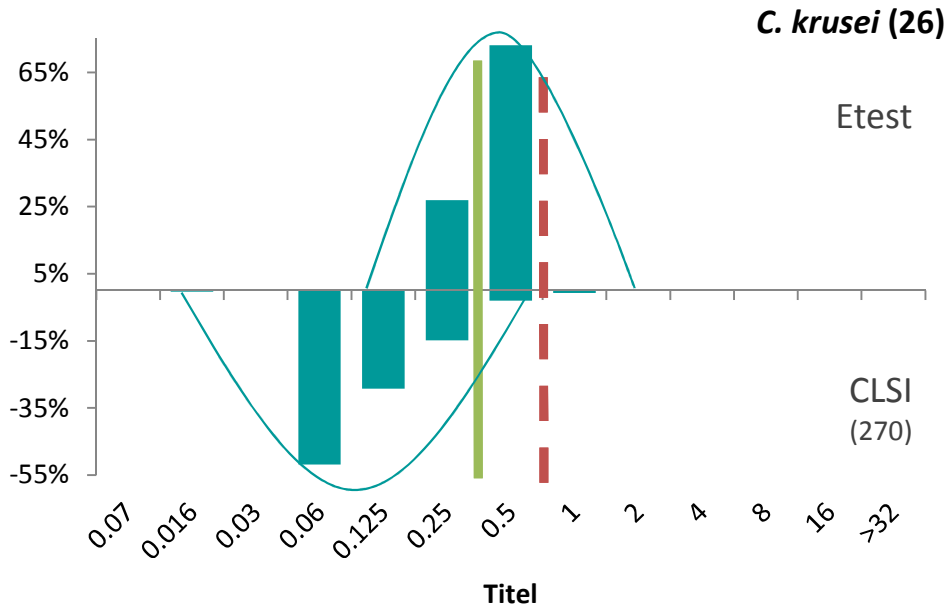
Etest: Caspofungin and CLSI BP









Arendrup & Pfaller AAC 2012

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EUCAST *Aspergillus* BPs 2012

BPs indicated as S ≤x / R >y

AF compound	*Aspergillus*				
	flavus	*fumigatus*	*nidulans*	*niger*	*terreus*
Amphotericin	IE*	1/2	Note	1/2	Poor Target
Itraconazole	1/2	1/2	1/2	IE*	1/2
Posaconazole	IE*	0.125/0.25**	IE*	IE*	Note
Voriconazole	Note	1/2	Note	Note	Note

* MICs are higher than for *A. fumigatus*
** provided sufficient levels can be achieved
Note: the MICs are similar to *A. fumigatus* but insufficient clinical data for BP setting

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www.eucast.org

- **Website update: the AFST tab**

May thanks for your attention

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C Lass-Flörl (Austria)
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