Traitement des candidémies en réanimation

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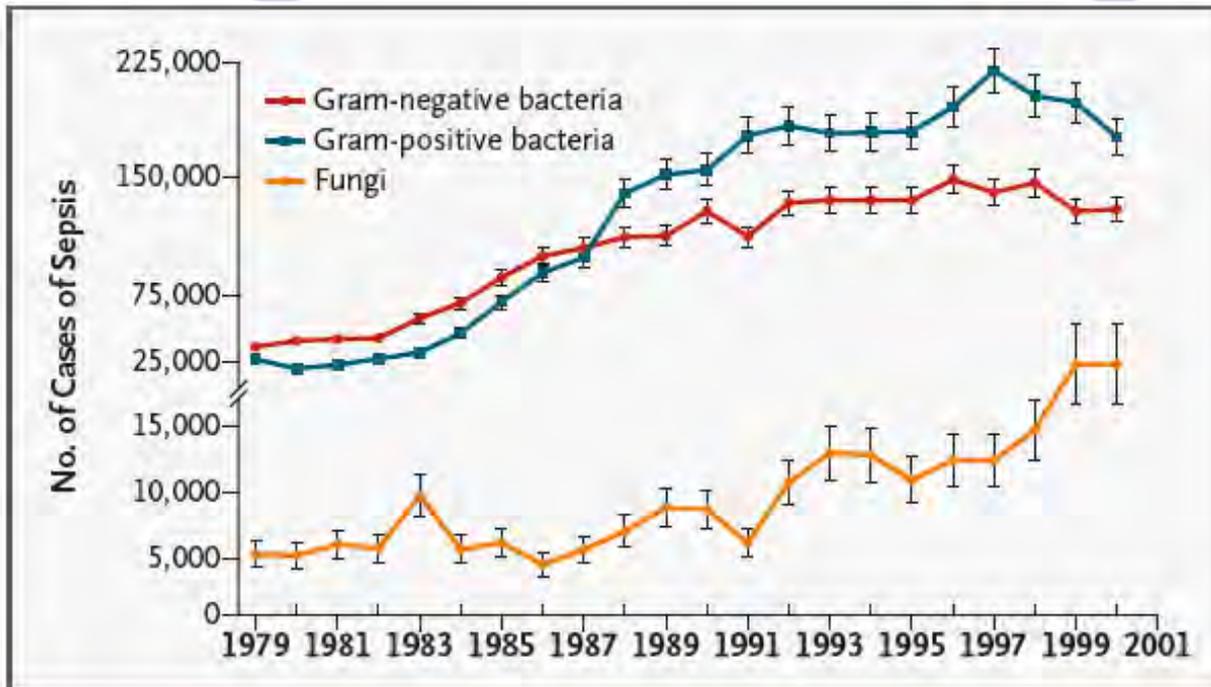
Candida spp et sepsis

Figure 3. Numbers of Cases of Sepsis in the United States, According to the Causative Organism, 1979–2000.

Points represent the number of cases for the given year, and I bars the standard error.

Martin GS *et al*. N Eng J Med 2004

Candidémies:
Incidence en réanimation

Isolated microorganisms	Incidence rate
Enterobacteriaceae	34.4%
Staphylococcus aureus	30.3%
Pseudomonas aeruginosa	28.7%
Coagulase-negative staphylococci	19.1%
Fungi	**17.1%**

Vincent *et al*. JAMA 1995

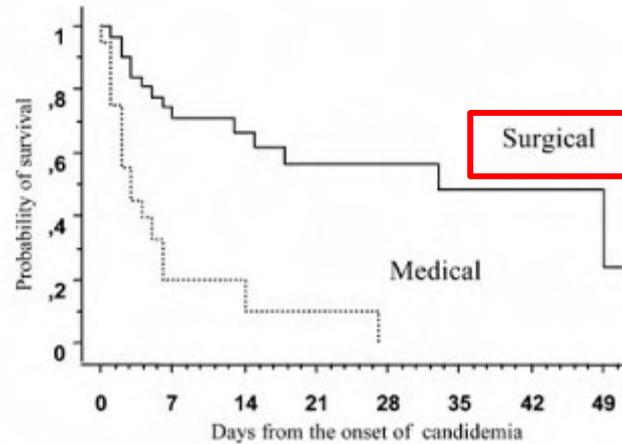| Pathogen	Bloodstream Infection (%) (n = 2971)
Coagulase-negative staphylococci	36
Enterococci	16
Staphylococcus aureus	13
Candida albicans	6
Klebsiella pneumoniae	4
Pseudomonas aeruginosa	3
Enterobacter	3
Other candida	3
Escherichia coli	3
Candida glabrata	2
Acinetobacter	2
Serratia marcescens	1
Other fungi	0.8
Citrobacter	0.5
Proteus	0.5
Aspergillus	0

Richards *et al*. Crit Care Med 1999
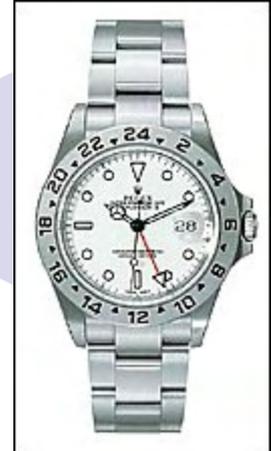
Candidémies : *impact*
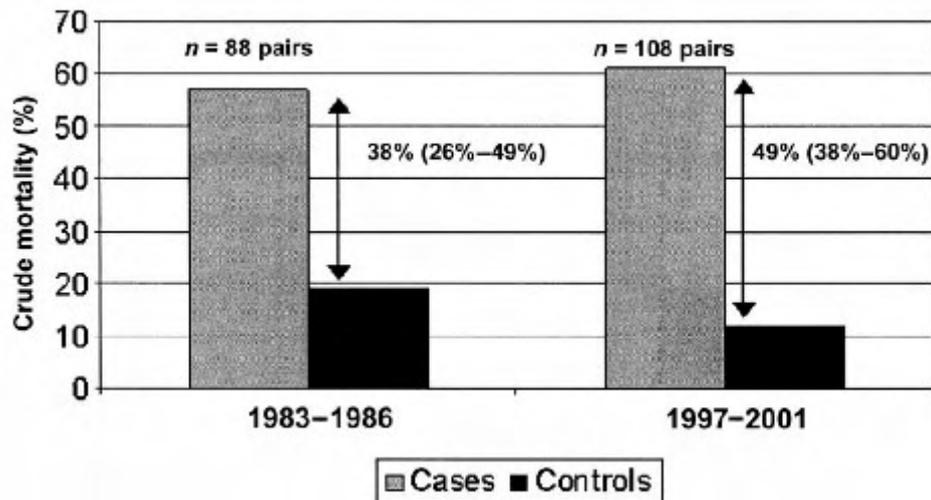
Characteristic	Patients with Candidemia (n = 73)	Controls (n = 146)	P Value
	Number (%), or Mean $\pm$ SD, Median (Interquartile Range)		
Age (years)	53 $\pm$ 18, 58 (41–68)	56 $\pm$ 18, 59 (47–69)	0.38
APACHE II score	25 $\pm$ 9, 25 (18–29)	25 $\pm$ 9, 25 (18–29)	0.99
Acute respiratory failure at ICU admission	69 (95)	126 (86)	0.07
Acute respiratory failure during ICU stay	71 (97)	129 (88)	0.03
Ventilator dependence (days)	29 $\pm$ 26, 22 (8–44)	19 $\pm$ 19, 16 (5–25)	<0.01
Acute renal failure at ICU admission	5 (7)	10 (7)	0.99
Acute renal failure during ICU stay	20 (27)	40 (27)	0.99
Hemodynamic instability at ICU admission	40 (55)	84 (58)	0.87
Hemodynamic instability during ICU stay	54 (76)	108 (74)	0.99
ICU stay (days)	36 $\pm$ 33, 25 (12–49)	25 $\pm$ 23, 21 (8–30)	0.02
Hospital stay (days)	77 $\pm$ 81, 54 (29–91)	64 $\pm$ 69, 38 (18–83)	0.04

Wey *et al*. Arch Int Med 1988

Blot *et al*. Am J Med 2002

Comment améliorer le *devenir*?

le prix du **retard**…

Morrel M *et al*, Antimicrobial Agents Chemother 2005
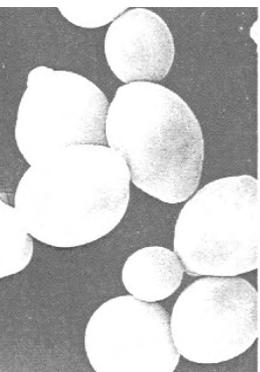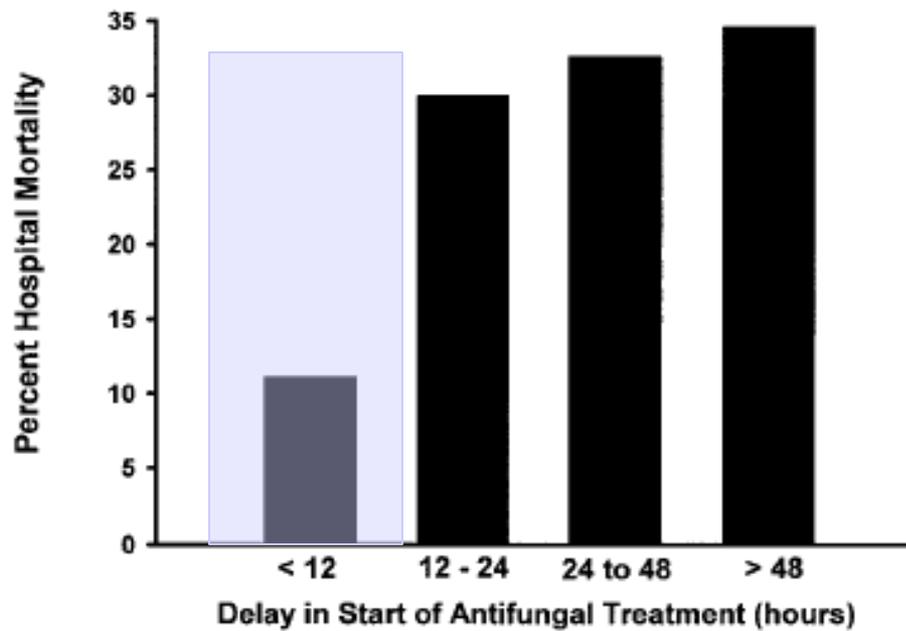
Les raisons du **retard**… (1)
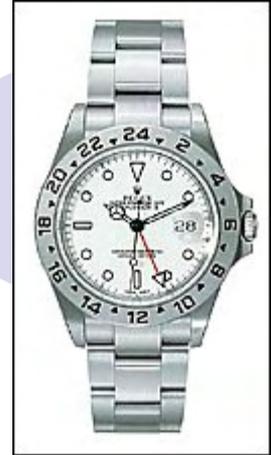
- **Hémocultures**:
  - Sensibilité
  - Délai de positivité
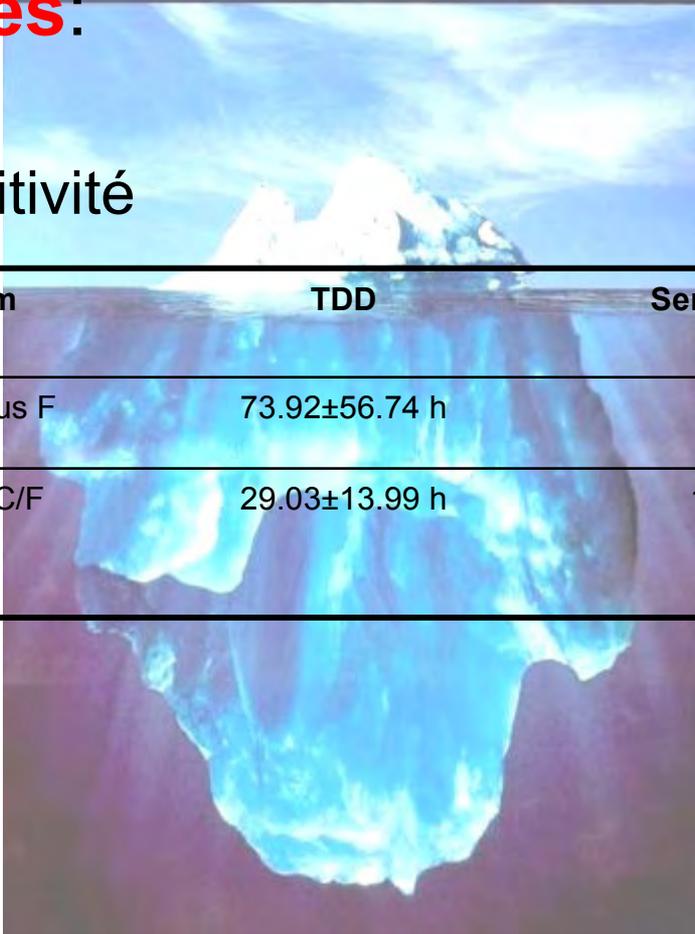
Medium	TDD	Sensibilité
Aerobic Plus F	73.92±56.74 h	45%
Mycosis IC/F	29.03±13.99 h	100%

Fricker-Hidalgo *et al*. Eur J Clin Microbiol Infect Dis 1998

Horvath *et al* J Clin Microbiol 2004

Les raisons du **retard**… (2)

- **Colonisation** Peau/**Muqueuses**
- **Adhésion**

- **Invasion** **Brèche** épithéliale
  - *Réelle* **SICU**
  - *Virtuelle* **MICU**

- **Candidémie**

- *Localisations secondaires*

Exogenous source   Endogenous source

Colonisation

Adhesion to mucosal surfaces

Invasion

Dissemination
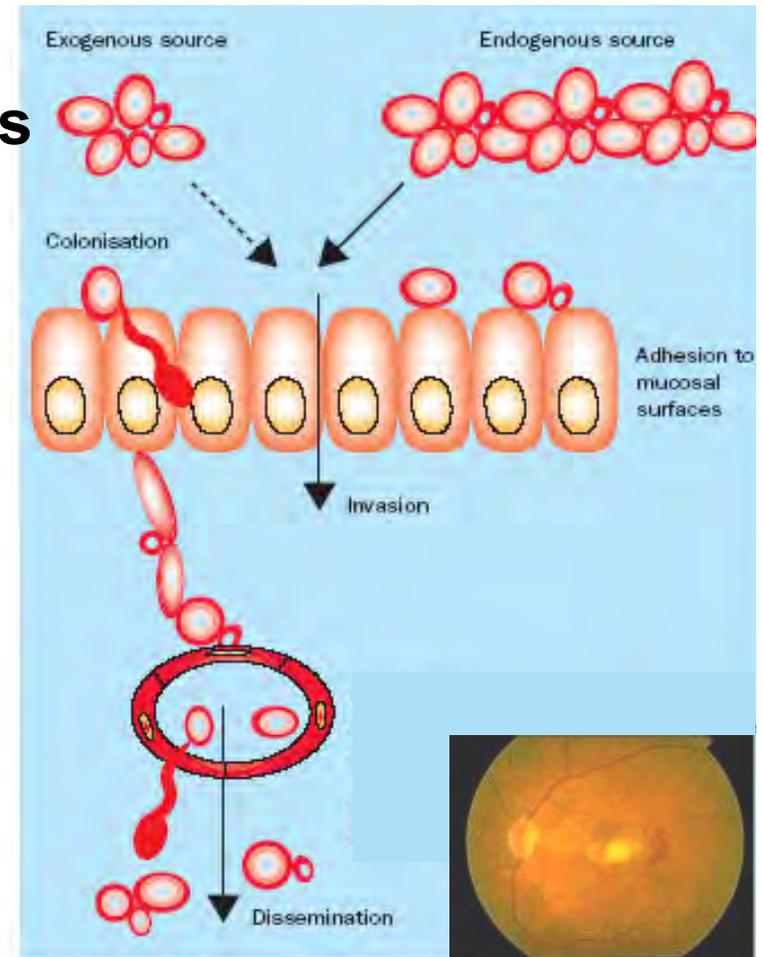
Candida chorioretinitis

Prise en Charge des Candidémies en Réanimation

1. Traiter tôt!

Comment *accélérer* le diagnostic?

- **Nouveaux outils**:
  - PCR
  - Sérologies
- **Nouvelles approches**:
  - Analyse des facteurs de risque
  - Scores cliniques

Facteurs de *risque*

Risk factors	Odd ratios	*p* value
N. of antibiotics	**1.73**	< 0.05
Hickman catheter	**7.23**	< 0.05
Hemodialysis	**18.13**	< 0.05
Candida sp. isolation from sites other than blood	**10.37**	< 0.05

Table 1. Multivariate analysis of risk factors for hospital acquired candidemia in 88 pairs of patients hospitalized between 1983 and 1986.

Table 7. Multivariate analyses of risk factors for candidal bloodstream infections in surgical intensive care unit (SICU) patients with and without prior surgery.

Model, risk factor	RR^a (95% CI)	P
Model 1[b]		
Antifungal medication	0.3 (0.1–0.6)	<.001
Acute renal failure	4.2 (2.1–8.3)	<.001
Parenteral nutrition	3.6 (1.8–7.5)	<.001
Any surgery	7.3 (1.0–53.8)	.05
Model 2[c]		
Antifungal medication	0.2 (0.1–0.5)	<.001
Acute renal failure	3.8 (1.9–7.4)	<.001
Parenteral nutrition	2.8 (1.3–5.8)	.01
Neurological surgery	0.2 (0.04–0.7)	.02
Ear/nose/throat surgery	0.3 (0.1–0.9)	.02
Triple-lumen catheter	5.4 (1.2–23.6)	.03

[a] Adjusted for all of the factors listed under each model and for the admission hospital with use of proportional hazards regression.
[b] A total of 4276 SICU patients.
[c] A total of 3201 SICU patients who had prior surgery.

Bross *et al*. Am J Med 1989

Blumberg *et al*. Clin Infect Dis 2001

CHIRURGIE

Table 2. Clinical characteristics, microbiological data, and outcome for surgery patients with intra-abdominal candidiasis or with colonization of the peritoneal fluid but no evidence of invasive disease.

Characteristic	Candidiasis ($n = 19$)	Candida colonization ($n = 30$)	P
Underlying surgical conditions			
Gastrointestinal perforation	9 (47)	19 (63)	NS
Recurrent gastrointestinal perforation	9 (47)	3 (10)	.005
Acute pancreatitis	9 (47)	1 (3)	<.001
Other abdominal conditions	2 (11)	10 (33)	.09
Emergency surgery	15 (79)	26 (87)	NS
Microbiological data[a]			
Candida growth in peritoneal fluid			
At surgery	15 (79)	13 (43)	.02
From drains	4 (21)	17 (57)	.02
Light vs. moderate or heavy growth on first culture	9 (47) vs. 10 (53)	26 (87) vs. 4 (13)	.008
Increasing in subsequent cultures	15 (79)	2 (7)	<.001
Outcome			
Failure of surgical drainage without antifungal treatment	16 (84)	0	<.001
Candida peritonitis	11 (58)	NA	
Intra-abdominal Candida abscess	5 (26)	NA	
Success with reintervention and antifungal therapy	9 (47)	NA	
Mortality			
Overall	12 (63)	3 (10)	<.001
Death due to infection	8 (42)	1 (3)	.001
Death due to fungal infection	7 (37)	NA	

Calandra *et al*. Lancet 1989

Perforations digestives *récidivantes*

	Fluconazole	Placebo	p Value
Number of patients	23	20	
Age	63 (21–82)	57 (33–78)	.44
Gender (male/female)	14/9	14/6	.75
APACHE II score	13 (4–24)	13 (6–24)	.69
Underlying surgical condition[a]			
Gastrointestinal cancer	9 (39%)	7 (35%)	>.99
Gastrointestinal (GI) perforation	14 (61%)	10 (50%)	.55
Upper GI tract	2	3	
Lower GI tract	12	7	
Pancreatitis	2 (9%)	2 (10%)	>.99
Number of surgical interventions	2 (1–7)	2 (2–4)	.93
Risk factors for fungal infection			
Antibiotic therapy	23 (100%)	20 (100%)	>.99
Number of antibiotics	2 (1–4)	2 (1–4)	.68
Antacid/H_2 antagonist use	15 (65%)	17 (85%)	.18
Parenteral nutrition	12 (52%)	9 (45%)	.76
Splenectomy	2 (9%)	4 (20%)	.39
Corticosteroid treatment	1 (5%)	1 (5%)	>.99
Diabetes	1 (5%)	1 (5%)	>.99
Malnutrition	0	1 (5%)	.47
Colonization with *Candida*	10 (44%)	7 (35%)	.75

[a] More than one condition/risk factor recorded for some patients. Values are median (range) unless specified otherwise.

Eggimann *et al*. Crit Care Med 1999
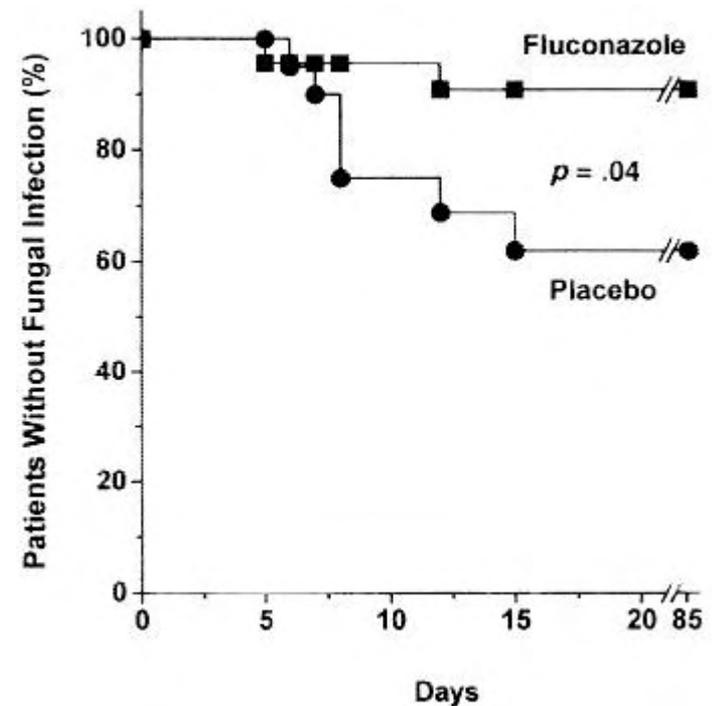
COLONISATION

	SICU ($n = 910$)		
	No. colonized	No. at risk for colonization	Incidence (%)
Candida albicans	183	690	26.5
Candida krusei	14	899	1.6
Candida lusitaniae	7	907	0.8
Candida parapsilosis	37	884	4.2
Candida tropicalis	38	892	4.0
Candida glabrata	63	821	7.7
Candida saitoana	8	906	0.9
Other *Candida* species	7	906	0.8
Any *Candida* species	312	628	49.7

Table 4. Incidence of colonization by *Candida* species as determined by culture of stool from initially culture-negative patients in surgical and neonatal intensive care units.
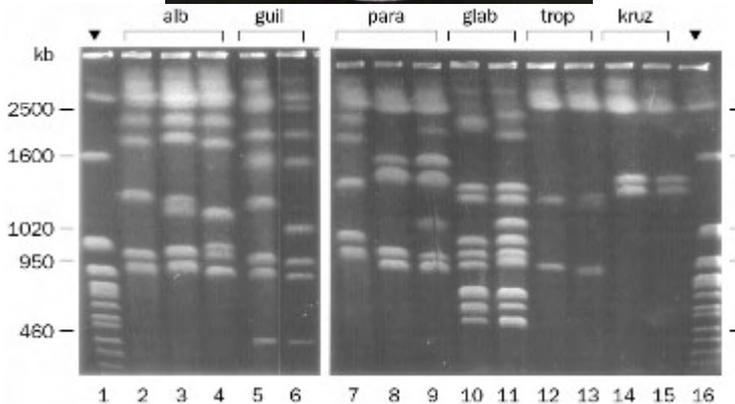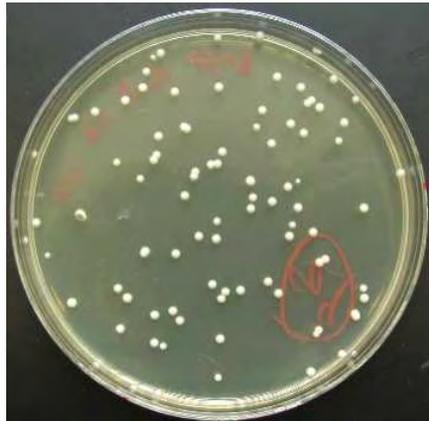
patients chirurgicaux

Table 2 *Candida* spp. colonization patterns (*CI* colonization index)

	ICU admission	ICU discharge or death
CI value	0.26 ± 0.26	0.35 ± 0.33*
Patients without colonization ($0.2\geq$ CI)	32 (34.8%)	33 (35.9%)
Patients with mild colonization ($0.5>$ CI >0.2)	39 (42.4%)	22 (23.9%)
Patients with heavy colonization (CI >0.5)	21 (22.8%)	37 (40.2%)*

*$p<0.05$

patients médicaux

Rangel-Frausto *et al*. Clin Infect Dis 1999

Charles *et al*. Intensive Care Med 2005

INTENSITE *de la colonisation*
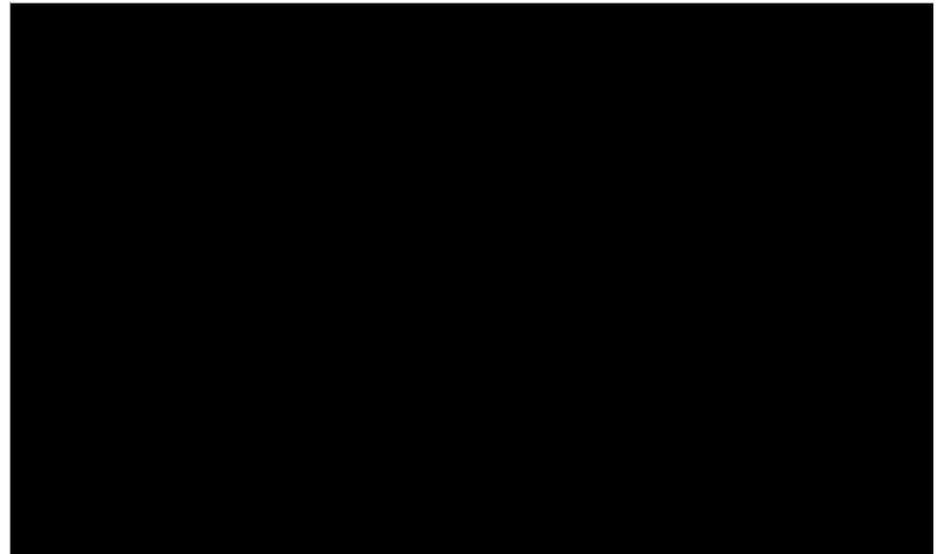
○	colonisation
●	infection

$$\text{Index de colonisation} = \frac{\text{N. de site(s) colonisé(s)}}{\text{N. de sites prélevés}}$$

Pittet *et al*. Ann Surg 1994

Patients *post-opératoires* SICU

Table 1. Characteristics of patients included during the two periods of the study

Characteristics of Patients	Retrospective Cohort n = 455	Prospective Cohort n = 478	p
Age, mean yrs ± SD	50.7 ± 19.6	52.0 ± 19.0	.33
SAPS II score, mean points ± SD	39.0 ± 15.0	43.2 ± 15.5	<.001
SICU stay, median day (interquartile range)	15 (9–23)	12 (7–21)	.001
Male/female ratio	295/160	331/147	.15
Number of antibiotics	2.8 ± 2.2	2.8 ± 2.0	.82
Antibiotherapy duration, mean days ± SD	9.4 ± 9.1	8.8 ± 7.3	.25
Receipt of anti-anaerobics/no receipt	259/196	385/93	<.001
Bacteremia, n (%)	55 (12.1)	49 (10.3)	.37
Underlying disorders, n (%)			
Abdominal surgery	94 (20.7)	109 (22.8)	.63
Vascular surgery	19 (4.2)	32 (6.7)	.09
Severe neurotrauma and trauma	197 (43.3)	197 (41.2)	.52
Neurosurgery	120 (26.4)	106 (22.2)	.13
Others	25 (5.5)	34 (7.1)	.31
Overall SICU mortality, n (%)	76 (16.7)	73 (15.3)	.55
Nonseptic conditions	47 (10.3)	49 (10.3)	.96
Septic conditions[a]	29 (6.4)	24 (5.0)	.37
Bacterial infections	8 (1.8)	6 (1.3)	.53
Candidiasis	7 (1.5)	2[b] (0.4)	.10
Aspergillosis	—	2 (0.4)	.49
Undocumented sepsis[c]	14 (3.1)	14 (2.9)	.89
Occurrence of proven candidiasis, n (%)	32 (7)	18 (3.8)	.03
Diagnosed at admittance (imported cases)	22 (4.8)	18 (3.8)	.42
SICU-acquired[d]	10 (2.2)	0	<.001

SAPS, Simplified Acute Physiology Score; SICU, surgical intensive care unit.
[a]Patients with sepsis (as defined by Ref. 17) at time of death; [b]imported candidiasis cases; [c]no isolation of pathogen from blood culture or a naturally sterile body site despite clinical features evoking infection; [d]diagnosed in SICU or during the month after SICU discharge.

Piarroux *et al*. Critical Care Med 2005

POIDS *de la colonisation*

Table 4. Calculation of the Candida score: Variables selected in the logistic regression model

Variable	Coefficient (β)	Standard Error	Wald χ^2	p Value
Multifocal *Candida* species colonization	1.112	.379	8.625	.003
Surgery on ICU admission	.997	.319	9.761	.002
Severe sepsis	2.038	.314	42.014	.000
Total parenteral nutrition	.908	.389	5.451	.020
Constant	−4.916	.485	102.732	.000

Leon *et al*. Crit Care Med 2006

Selection des patients à *haut risque*

Cutoff value	Sensitivity	False positive
1.055	.983	.653
1.509	.949	.495
1.963	.898	.426
2.069	.831	.312
2.074	.814	.301
2.528	.814	.259
2.982	.780	.231
3.026	.610	.132
3.093	.593	.130
3.547	.525	.092
4.001	.492	.077

A
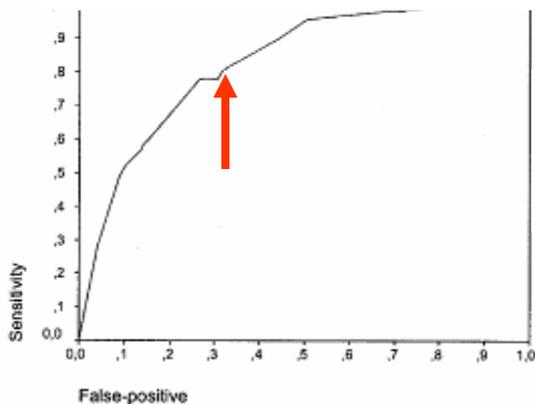
Candida score = .908 × (total parenteral nutrition) + .997 × (surgery) + 1.112 (multifocal *Candida* species colonization) + 2.038 (severe sepsis). Candida score (rounded) = 1 × (total parenteral nutrition) + 1 × (surgery) + 1 (multifocal *Candida* species colonization) + 2 × (severe sepsis). All variables coded as follows: absent, 0; present, 1.

Leon *et al*. Crit Care Med 2006
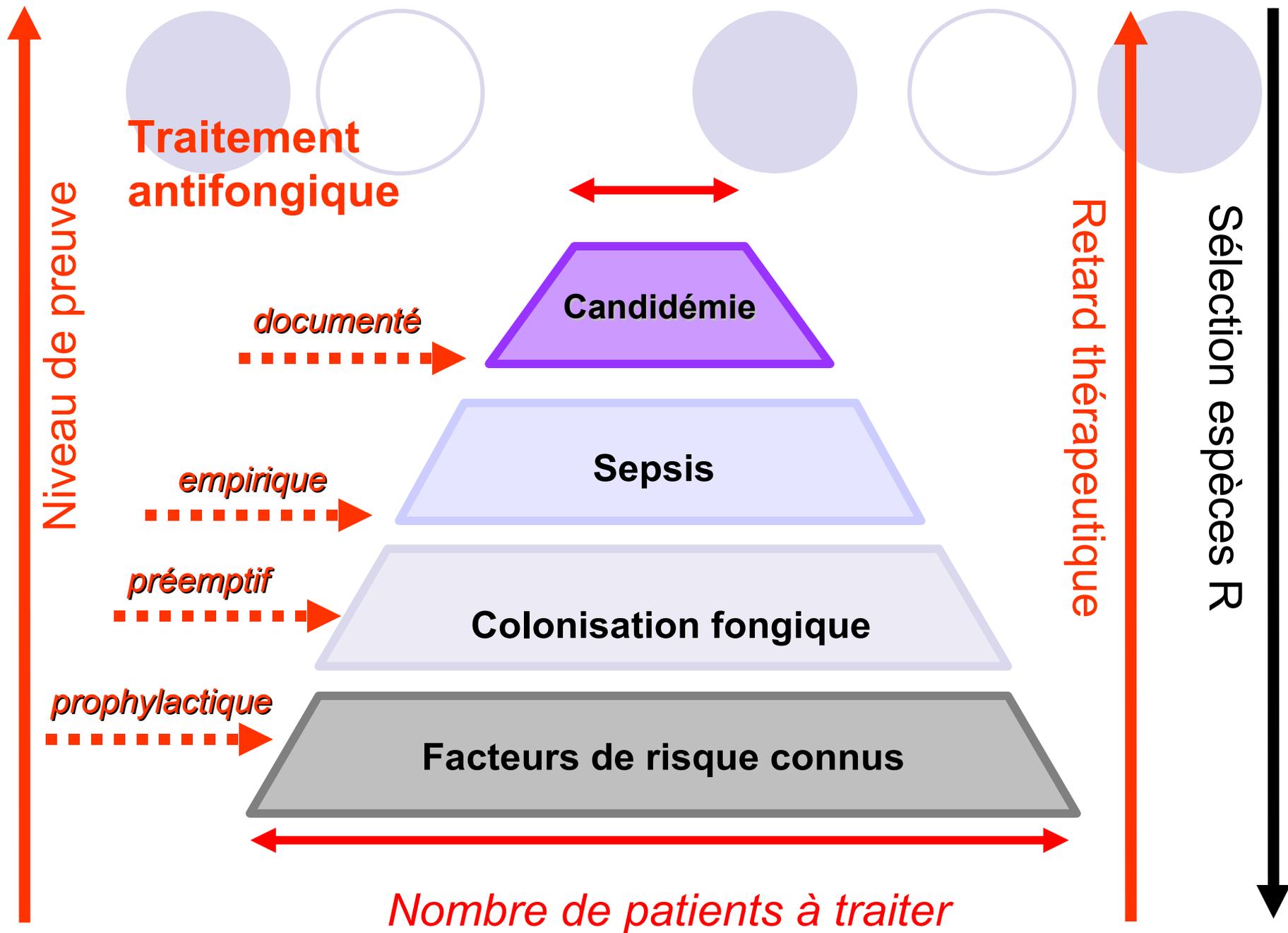
Prise en Charge des Candidémies en Réanimation

1. Traiter tôt!

2. Avec quelle molécule?

Spectre et tolérance

Table 1. Summarised susceptibilities of *Candida* spp to various antifungals

Species	Fluconazole	Itraconazole	Voriconazole	Posaconazole	Ravuconazole	Caspofungin	Flucytosine	Liposomal amphotericin B
C albicans	S	S	S	S	S	S	S	S
C tropicalis	S	S	S	S	S	S	S	S
C parapsilosis	S	S	S	S	S	S	S	S
C glabrata	S-DD to R	S-DD to R	S	S	S	S	S	S to I
C krusei	R	S-DD to R	S	S	S	S	I to R	S to I
C lusitaniae	S	S	S	S	S to R	S	S	S to R

Adapted from references 19–24. S=susceptible. S-DD=susceptible-dose dependent. I=intermediate. R=resistant

Toxicité	Hépatique
dose	800 mg/jour J1 400 mg/jour J+
Efficacité	Rex *et al*
Adapt. Poso.	CVVH

Hépatique « visuelle »
6 mg/kg/12h J1 4 mg/kg/12h J+
Kullberg *et al*
CVVH

Allergies
70 mg J1 50 mg J+
Mora-Duarte *et al*
Insuffisance hépatique

Réac. générales Rénale
3-5 mg/kg/jour
???
Insuffisance rénale

Adapté de Eggimann *et al*. Lancet Infect Dis 2003

Mécanismes d'action
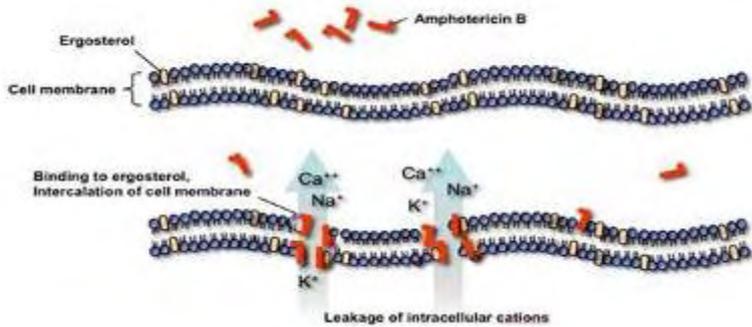
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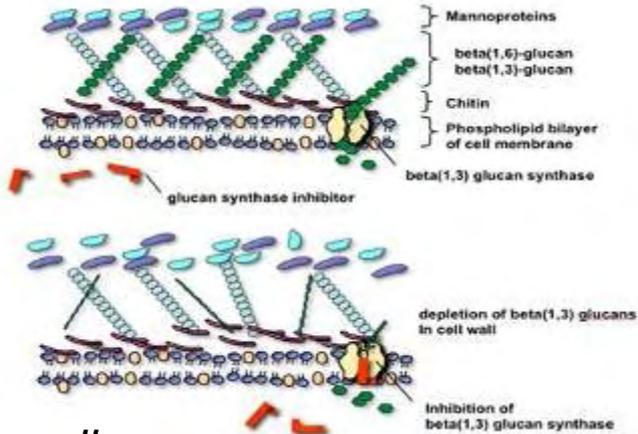
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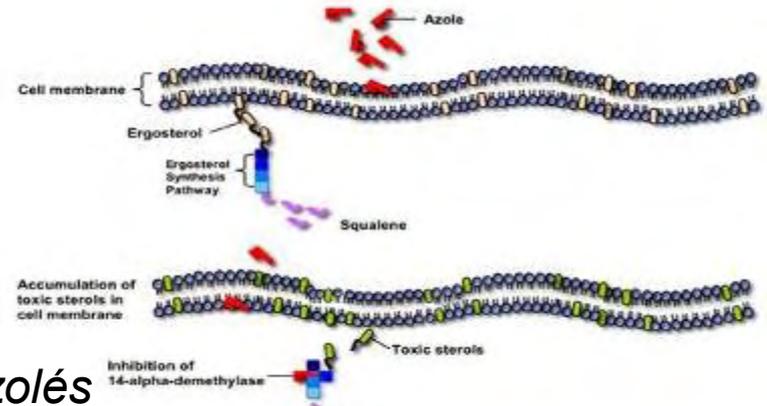
FONGISTATISME

Amphotéricine B *vs*. Fluconazole
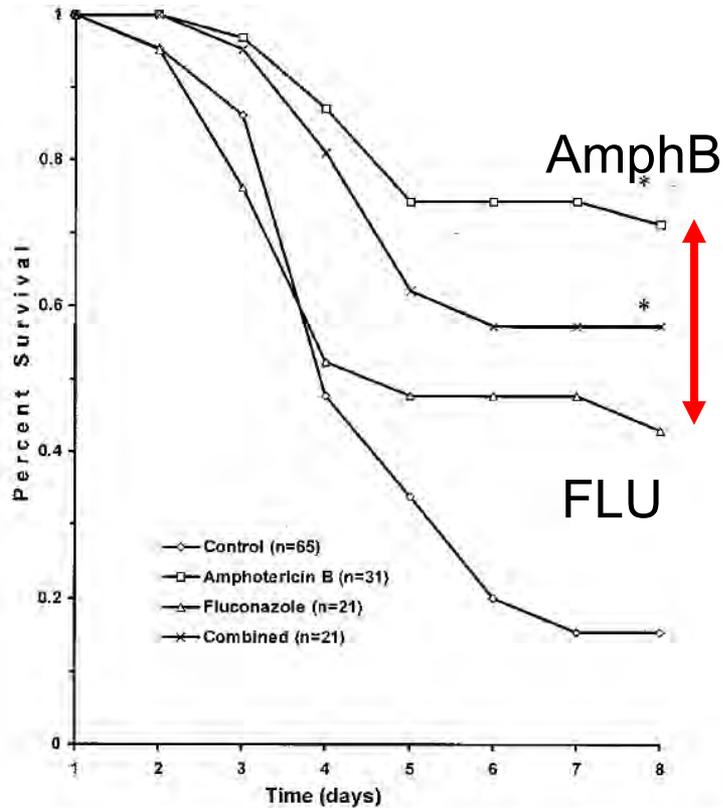
FIG. 1. Survival of neutropenic mice infected with *C. albicans* (10^3 CFU mouse). *, $P < 0.001$ versus controls.

TABLE 2. Concentration of *Candida* in cardiac vegetations of rabbits[a]

Treatment group	Mean colony count after treatment for:	
	7 Days (*n*)	14 Days (*n*)
Control	6.65 ± 0.37 (8)	6.61 ± 0.10 (7)
AmphB	4.34 ± 0.06^b (13)	4.36 ± 1.80^b (12)
FLU	6.23 ± 0.40 (9)	6.32 ± 0.54 (10)
Combined	5.10 ± 2.10^c (12)	4.90 ± 1.80^c (13)

Sanati *et al*. Antimicrob Agent Chemother 1997

A Randomized Trial Comparing Fluconazole with Amphotericin B for the Treatment of Candidemia in Patients without Neutropenia

John H. Rex, et al for The Candidemia Study Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group

Rex *et al*. N Eng J Med 1994
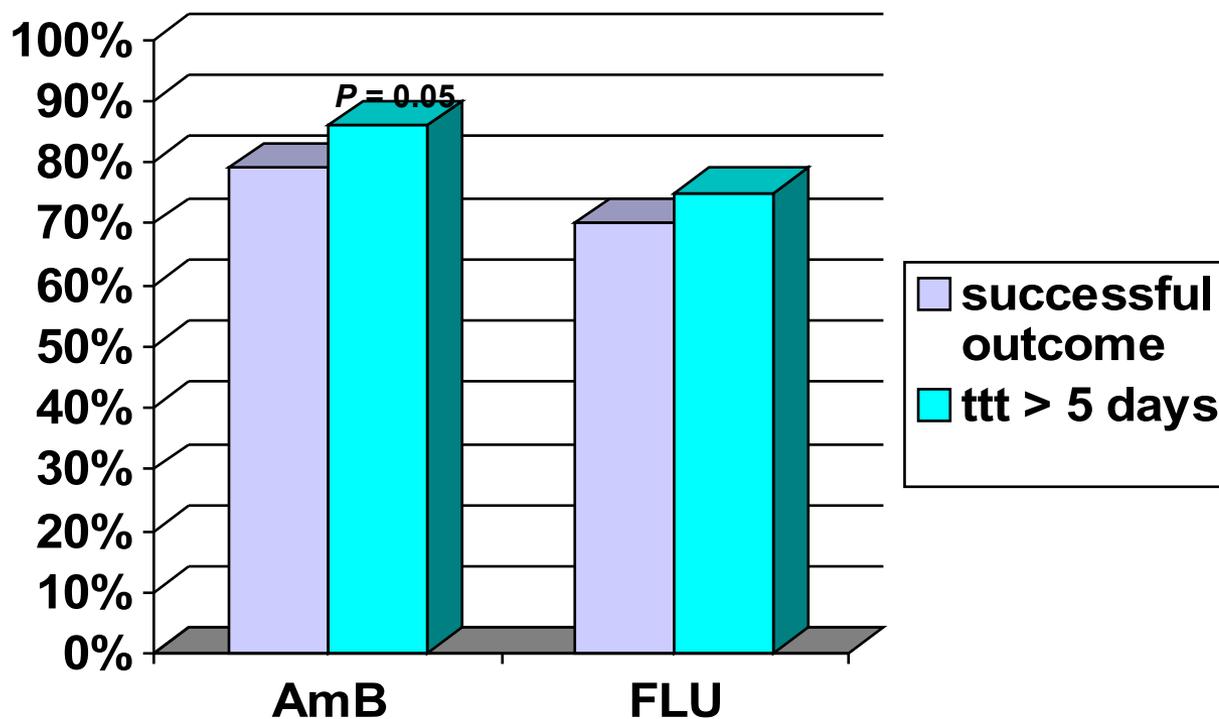
Pourquoi *ne pas utiliser* le fluconazole?

- Risque de **Fluco-R ou SDD**:
  - Acquise (*C. albicans*, *C. glabrata*):
    - Souche endogène
    - Souche exogène
  - Intrinsèque (*C. krusei*)
- Besoin d'être **fongicide**:
  - Immunodépression
  - Sévérité du tableau clinique

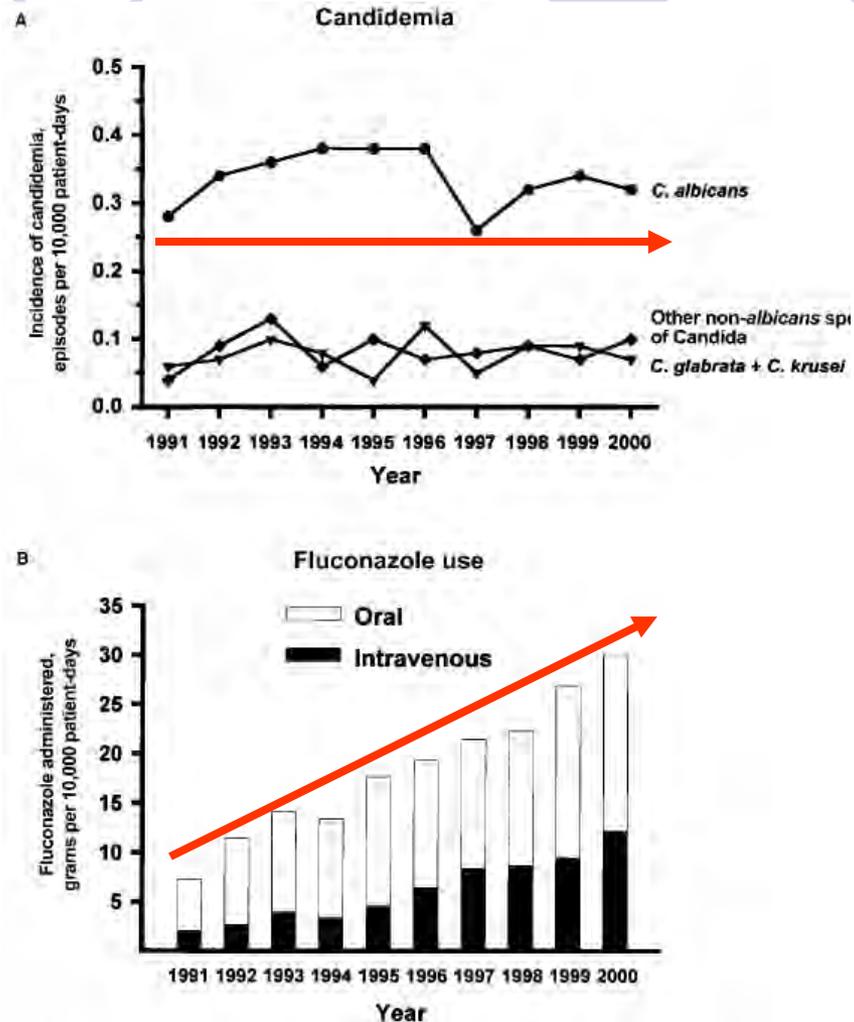# Espèces Fluco-R ou SDD: *corrélation CMI/efficacité?*

Rex *et al*. Antimicrob Agent Chemother 1995

Clancy *et al*. Antimicrob Agent Chemother 2005
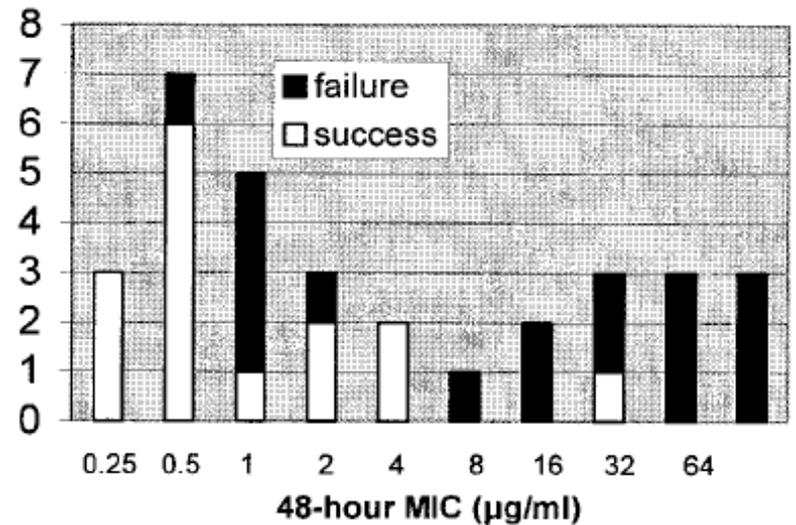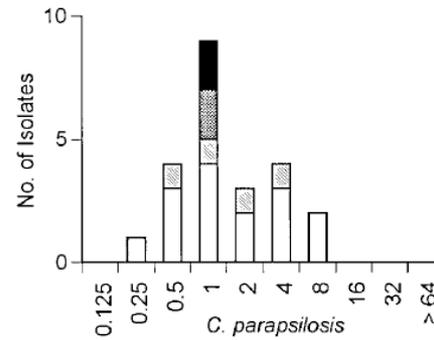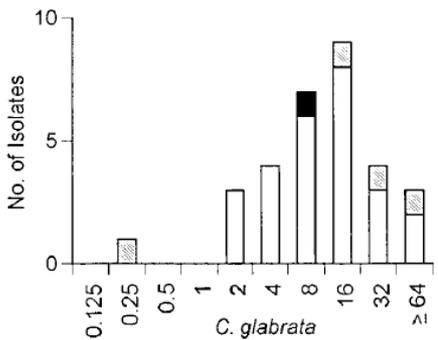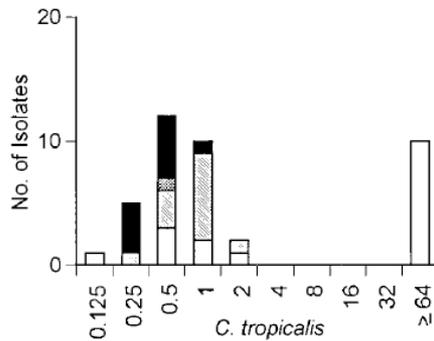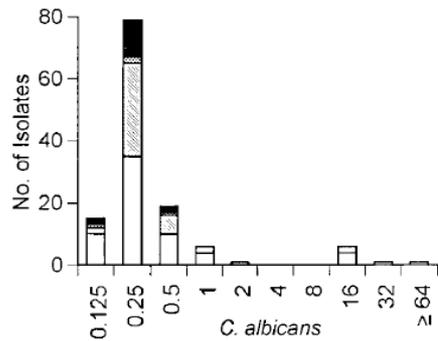
Espèces Fluco-R ou SDD : *réalité*

Table 1. Species distribution of candida bloodstream isolates by year: 1992–2001[a]

| Species | % of isolates by year | | | | | | | | | |
	1992	1993	1995	1996	1997	1998	1999	2000	2001	All years
No. tested	235	315	332	133	413	328	320	1236	2770	6082
C. albicans	44.3	45.4	53.3	52.6	54.0	55.2	54.7	54.4	59.8	55.9
C. glabrata	16.6	14.0	20.5	15.8	15.3	17.7	15.3	15.3	16.4	16.2
C. parapsilosis	21.7	24.4	9.0	10.5	18.9	14.3	10.3	13.8	10.7	13.1
C. tropicalis	11.9	12.4	11.4	15.8	7.0	8.5	11.9	11.8	7.9	9.6
C. krusei	2.6	1.3	4.2	3.0	1.7	1.2	2.8	2.5	2.7	2.5
C. lusitaniae	2.1	0.6	0.6	0.0	0.0	0.6	2.2	1.1	1.3	1.1
C. guilliermondii	0.4	1.3	0.4	0.0	1.9	2.1	0.9	0.4	0.6	0.8
Other spp.[b]	0.4	0.6	0.6	2.3	1.2	0.4	1.9	0.7	0.6	0.8

Risque de Fluco-R ou SDD

Bassetti *et al*. BMC Infect Dis 2006

Risque de Fluco-R ou SDD

Marchetti *et al*. Clin Infect Dis 2004

Risque de Fluco-R ou SDD

Pfaller *et al*. Clin Microbiol Rev 2006
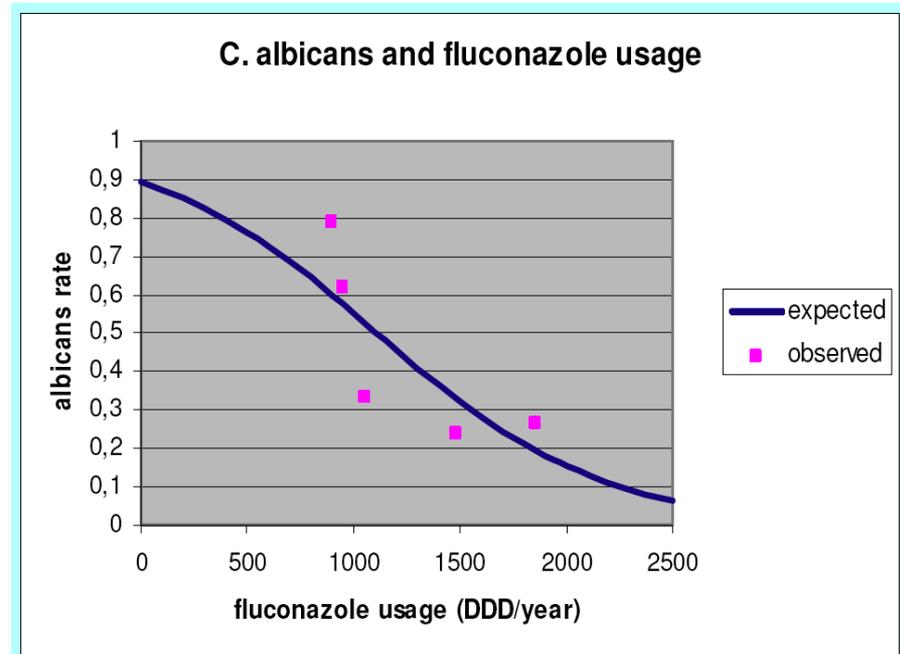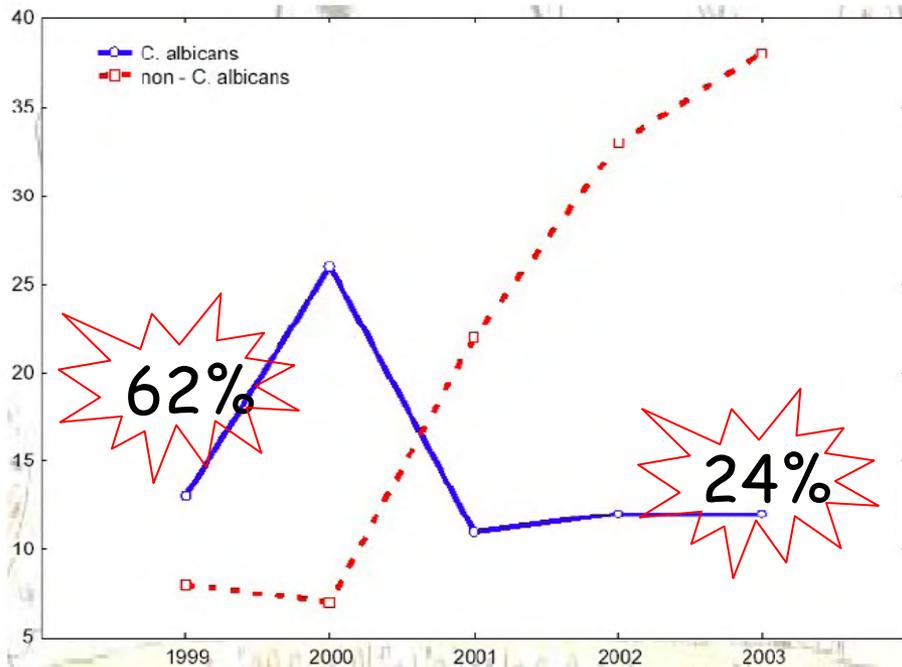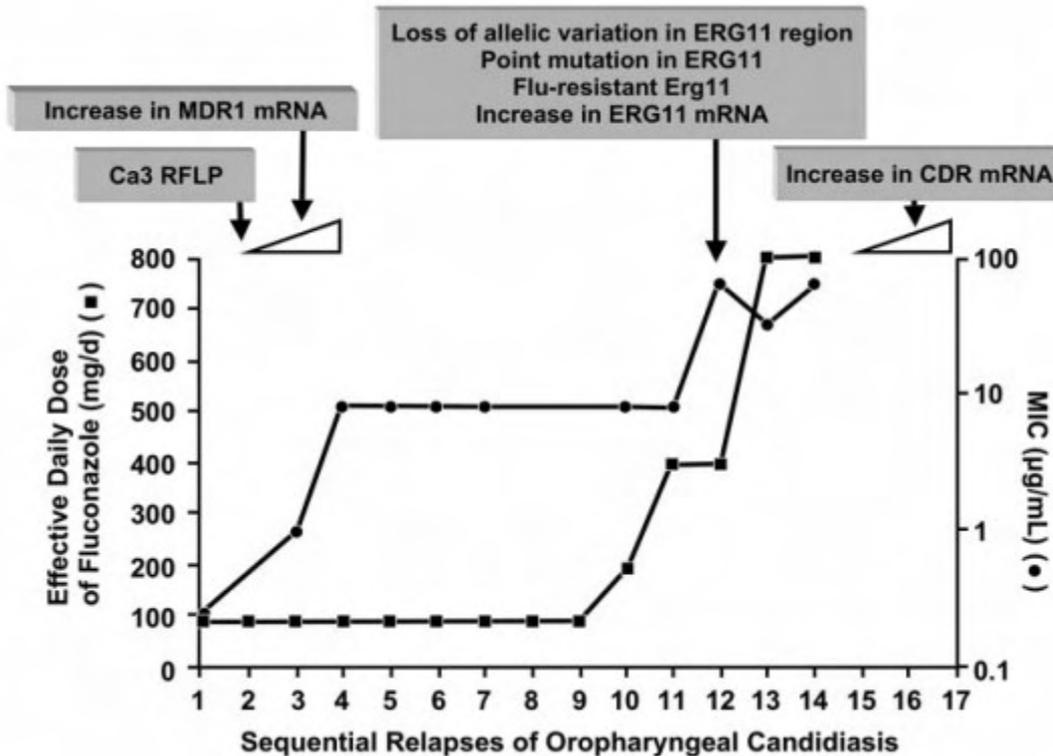
Conclusion:
faut-il craindre un *échec du fluconazole**?*

- Espèces Fluco-S ou SDD **dominantes**
- **Variations** selon les centres
- Peut-on la **prédire**?
  - Écologie locale
  - Écologie du patient
  - Exposition préalable
- Besoin d'être **fongicide**
  - Intérêt théorique et expérimental
  - Neutropénique
  - Patient « **instable** »

Quel antifongique choisir?

Alternatives au Fluconazole

COMPARISON OF CASPOFUNGIN AND AMPHOTERICIN B FOR INVASIVE CANDIDIASIS

Jorge Mora-Duarte, M.D., Robert Betts, M.D., Coleman Rotstein, M.D., Arnaldo Lopes Colombo, M.D., Luis Thompson-Moya, M.D., Juanita Smietana, B.S., Robert Lupinacci, M.S., Carole Sable, M.D., Nicholas Kartsonis, M.D., and John Perfect, M.D., for the Caspofungin Invasive Candidiasis Study Group*
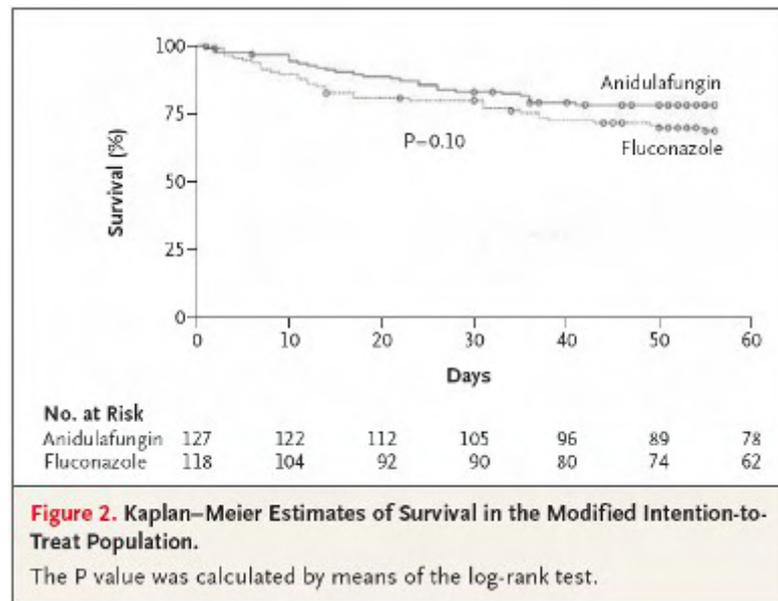
TABLE 4. Favorable Responses to Treatment.

Time Point	Modified Intention-to-Treat Analysis		Patients Who Met Criteria for Evaluation	
	Caspofungin (N=109)	Amphotericin B (N=115)	Caspofungin (N=88)	Amphotericin B (N=97)
	no. with a favorable response/total no. (%)			
End of intravenous therapy	80/109 (73.4)	71/115 (61.7)	71/88 (80.7)	63/97 (64.9)*
Absolute neutrophil count at enrollment				
<500/mm³	7/14 (50.0)	4/10 (40.0)	6/8 (75.0)	3/8 (37.5)
≥500/mm³	73/95 (76.8)	67/105 (63.8)	65/80 (81.2)	60/89 (67.4)
APACHE II score				
≤20	68/88 (77.3)	61/92 (66.3)	61/76 (80.3)	53/78 (67.9)
>20	12/21 (57.1)	10/23 (43.5)	10/12 (83.3)	10/19 (52.6)
Day 10 of intravenous therapy†	66/75 (88.0)	64/75 (85.3)	59/67 (88.1)	55/64 (85.9)
At end of all antifungal therapy	79/109 (72.5)	71/115 (61.7)	70/88 (79.5)	63/97 (64.9)‡
2 Weeks after treatment§	56/88 (63.6)	56/104 (53.8)	52/72 (72.2)	49/86 (57.0)
6–8 Weeks after treatment§	47/83 (56.6)	47/99 (47.5)	44/67 (65.7)	41/82 (50.0)
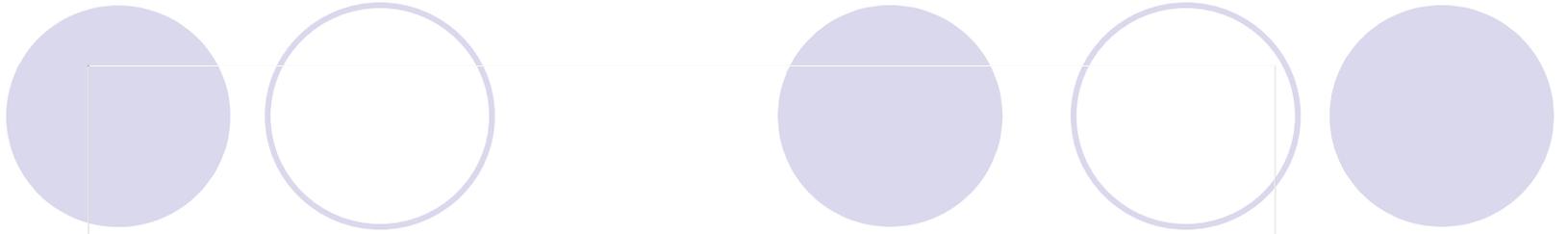
Mora-Duarte et al N Eng J Med 2002

Anidulafungin versus Fluconazole for Invasive Candidiasis

Annette C. Reboli, M.D., Coleman Rotstein, M.D., Peter G. Pappas, M.D., Stanley W. Chapman, M.D., Daniel H. Kett, M.D., Deepali Kumar, M.D., Robert Betts, M.D., Michele Wible, M.S., Beth P. Goldstein, Ph.D., Jennifer Schranz, M.D., David S. Krause, M.D., and Thomas J. Walsh, M.D., for the Anidulafungin Study Group
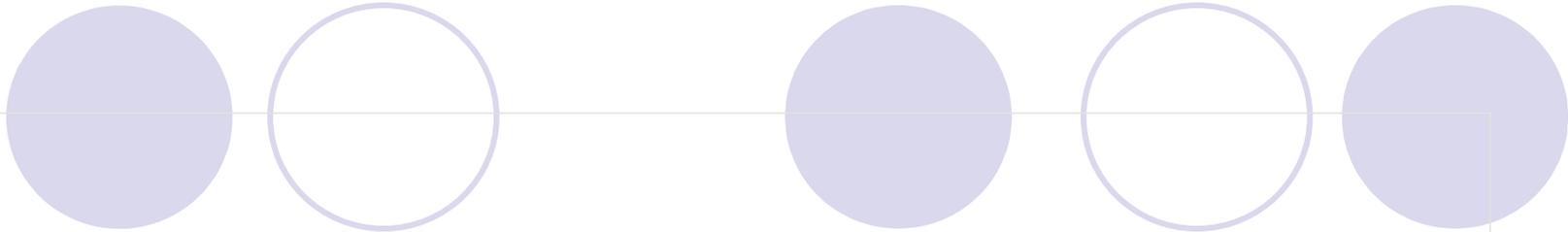
Figure 2. Kaplan–Meier Estimates of Survival in the Modified Intention-to-Treat Population.

The P value was calculated by means of the log-rank test.

Table 3. Microbiologic and Global Responses at the End of Intravenous Therapy in the Modified Intention-to-Treat Population.*

| Candida Pathogen	Successful Microbiologic Response			Successful Global Response†		
	Anidulafungin Group	Fluconazole Group	P Value	Anidulafungin Group	Fluconazole Group	P Value
	no. of isolates/total no. (%)			*no. of patients/total no. (%)*		
Candida albicans	77/81 (95)	57/70 (81)	0.01	60/74 (81)	38/61 (62)	0.02
C. glabrata	15/20 (75)	18/30 (60)	0.37	9/16 (56)	11/22 (50)	0.75
C. parapsilosis	9/13 (69)	14/16 (88)	0.36	7/11 (64)	10/12 (83)	0.37
C. tropicalis	13/15 (87)	7/11 (64)	0.35	13/14 (93)	4/8 (50)	0.04
Other candida species	5/6 (83)	3/3 (100)	1.00	3/4 (75)	2/3 (67)	1.00
All candida species	119/135 (88)	99/130 (76)	0.02	92/119 (77)	65/106 (61)	0.01

Activité sur le *biofilm*…

Candida species	Patients infected by biofilm-positive isolate		Patients infected by biofilm-negative isolate		OR (95% CI)	P^a
	Total no.	No. (%) who died	Total no.	No. (%) who died		
C. albicans	38	32 (84.2)	130	65 (50)	3.90 (1.72–8.83)	<0.001
C. parapsilosis	14	10 (71.4)	50	14 (28)	4.16 (1.46–11.82)	0.003
C. tropicalis	20	8 (40)	8	4 (50)	0.88 (0.54–1.45)	0.62
C. glabrata	6	4 (66.6)	20	11 (55)	1.46 (0.32–6.62)	0.61
Other[b]	2	2 (100)	6	4 (66.6)		0.34
Total	80	56 (70)	214	98 (45.7)	2.76 (1.55–5.00)	<0.001
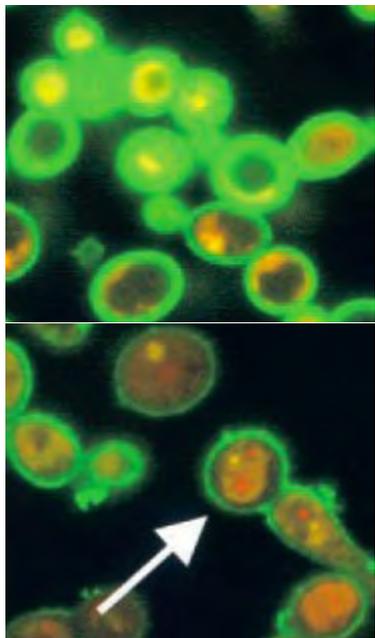
Casp

FLC
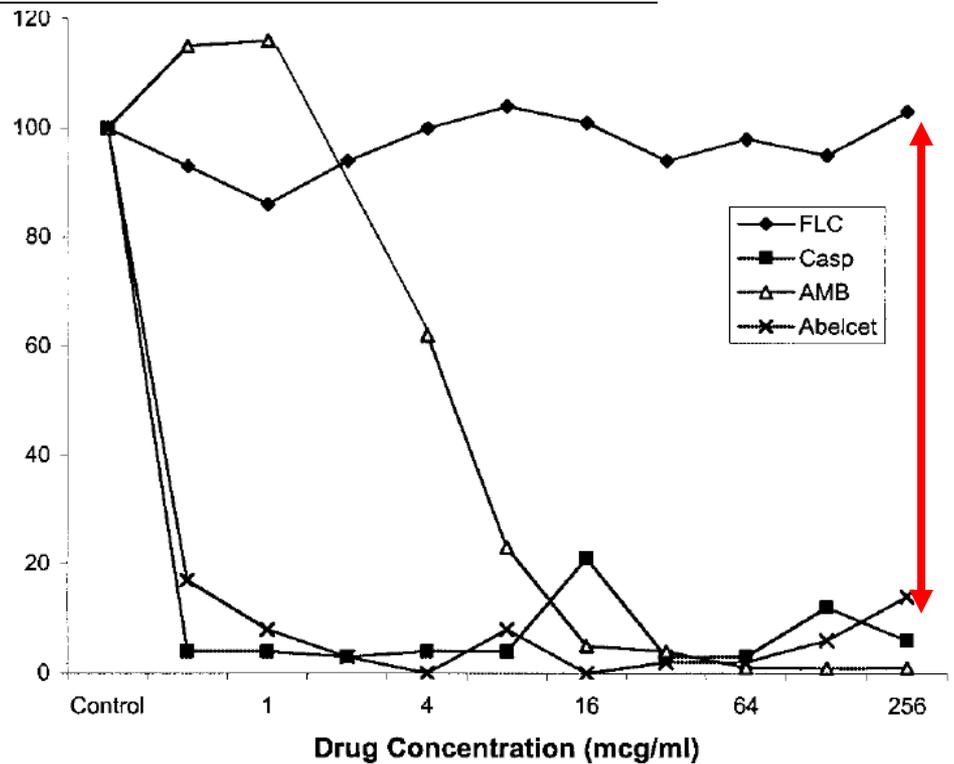
Voriconazole versus a regimen of amphotericin B followed by fluconazole for candidaemia in non-neutropenic patients: a randomised non-inferiority trial

B J Kullberg, J D Sobel, M Ruhnke, P G Pappas, C Viscoli, J H Rex, J D Cleary, E Rubinstein, L W P Church, J M Brown, H T Schlamm, I T Oborska,

Figure 2: Kaplan-Meier plot of time to first negative blood culture for modified intention-to-treat population with positive blood cultures on day 1
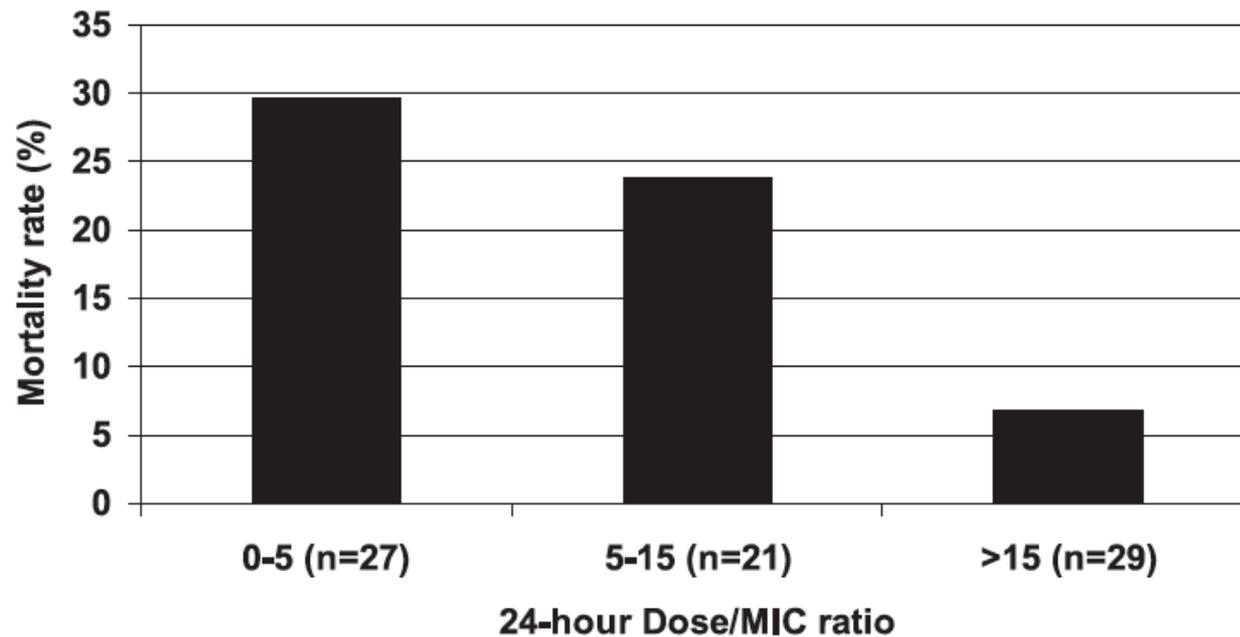
R croisées Fluco-Vorico
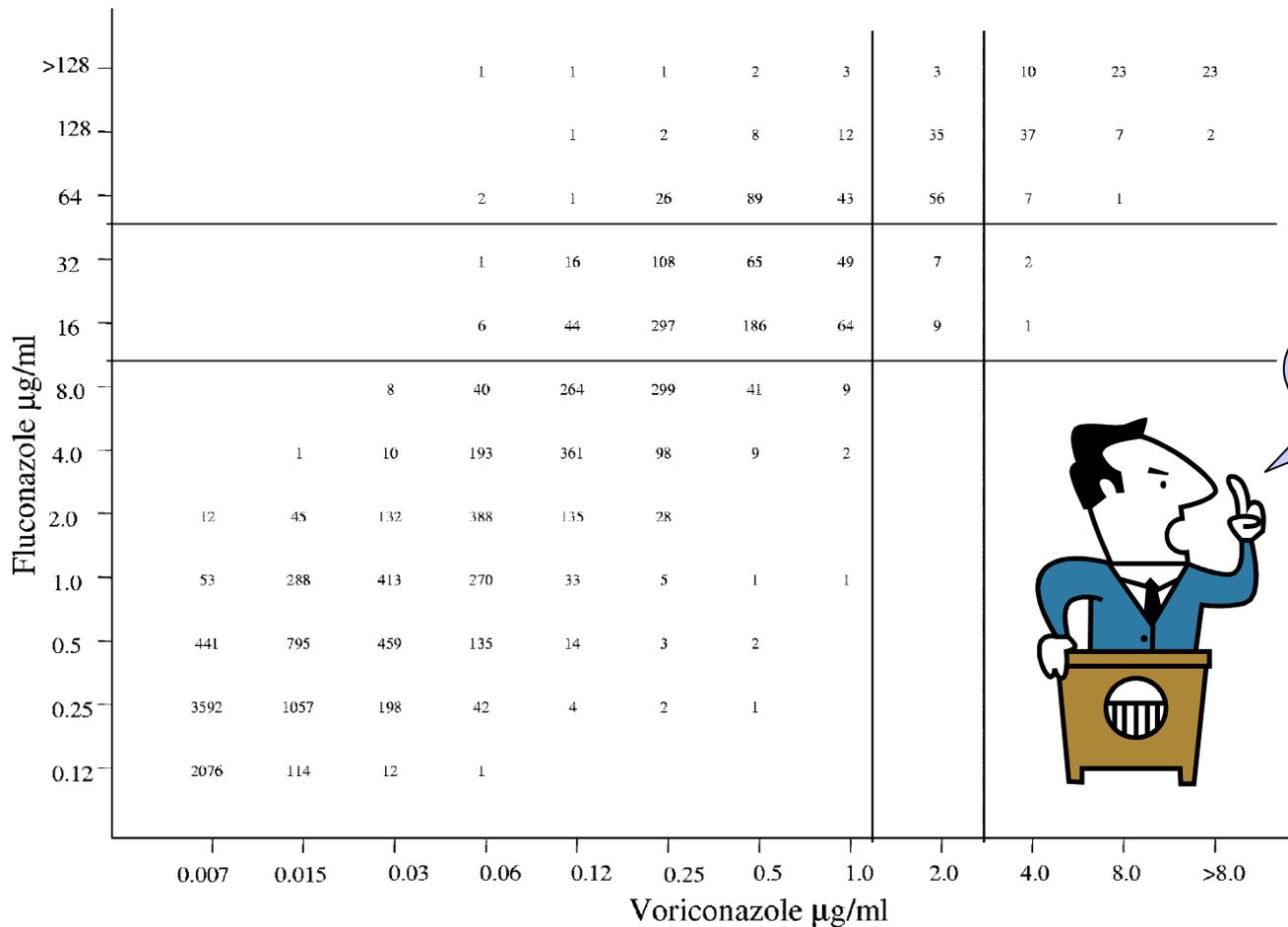
Association d'antifongiques

Table 2. Baseline characteristics of the study patients.

Variable	Fluconazole plus placebo group (n = 107)	Fluconazole plus AmB group (n = 112)
No. of male patients/no. of female patients	58/49	53/59
Age, mean years ± SE	57 ± 2	55 ± 2
APACHE II score, mean ± SE	16.8 ± 0.6	15.0 ± 0.7[a]
Organ transplantation stratum	1	4
Cancer	20	21
Receipt of long-term dialysis	10	10
HIV infection	0	4
Diabetes mellitus	37	33
Risk factor for candidemia[b]		
Recent use of broad-spectrum antibiotics	103	109
Recent use of central venous catheter	100	106
Recent hyperalimentation	65	61
Prior major surgery	53	41
Recent use of corticosteroids	29	26
Previous use of amphotericin B, mean mg/kg ± SE (no. of patients)	0.48 ± 0.08 (11)	0.50 ± 0.05 (17)
Previous use of fluconazole, mean mg/kg ± SE (no. of patients)	7.0 ± 0.4 (53)	7.2 ± 0.5 (58)

Rex et al Clin Infect Dis 2003
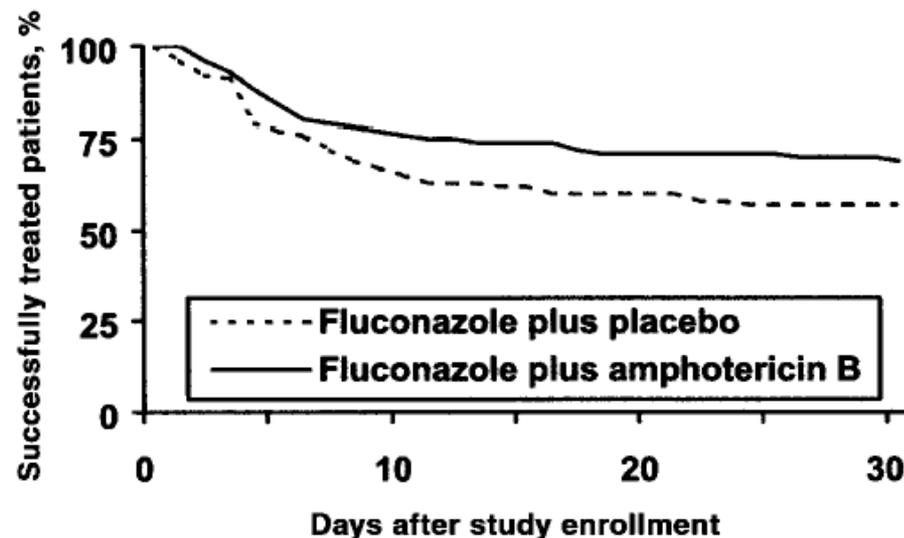
Fluco: relation *dose/efficacité*

Pai *et al*. Antimicrob Agent Chemother 2007

Fluco « *hautes doses* »

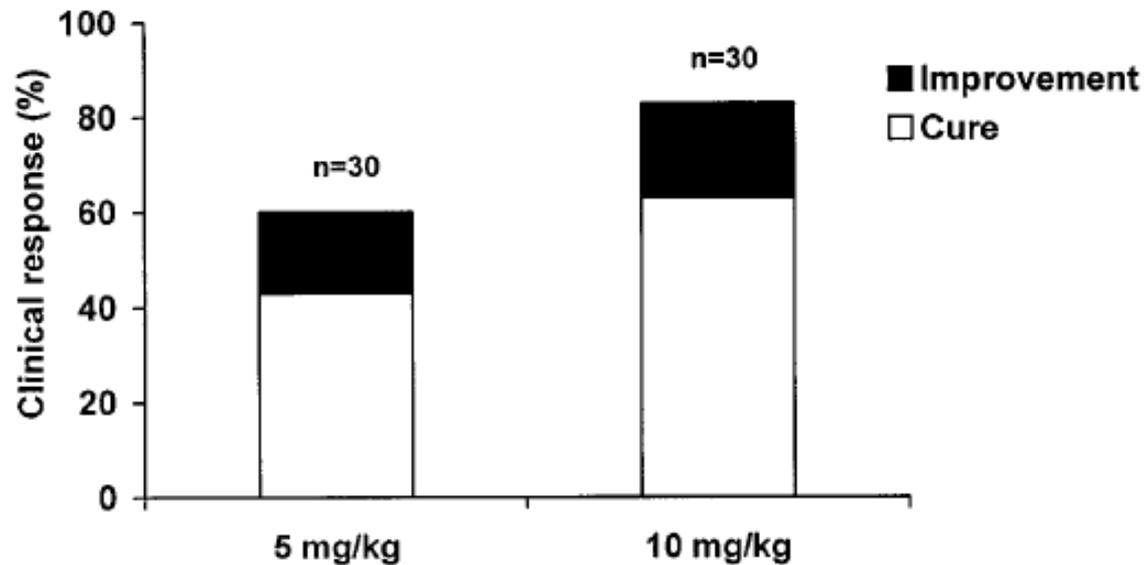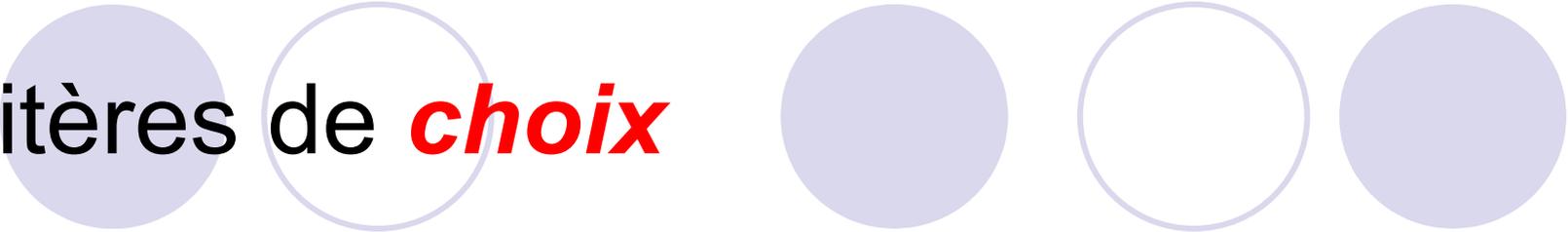**Figure 1** Dose-related clinical response to treatment with fluconazole in 60 evaluable patients with *Candida albicans* fungemia [54]

Graninger *et al*. J Infect 1993
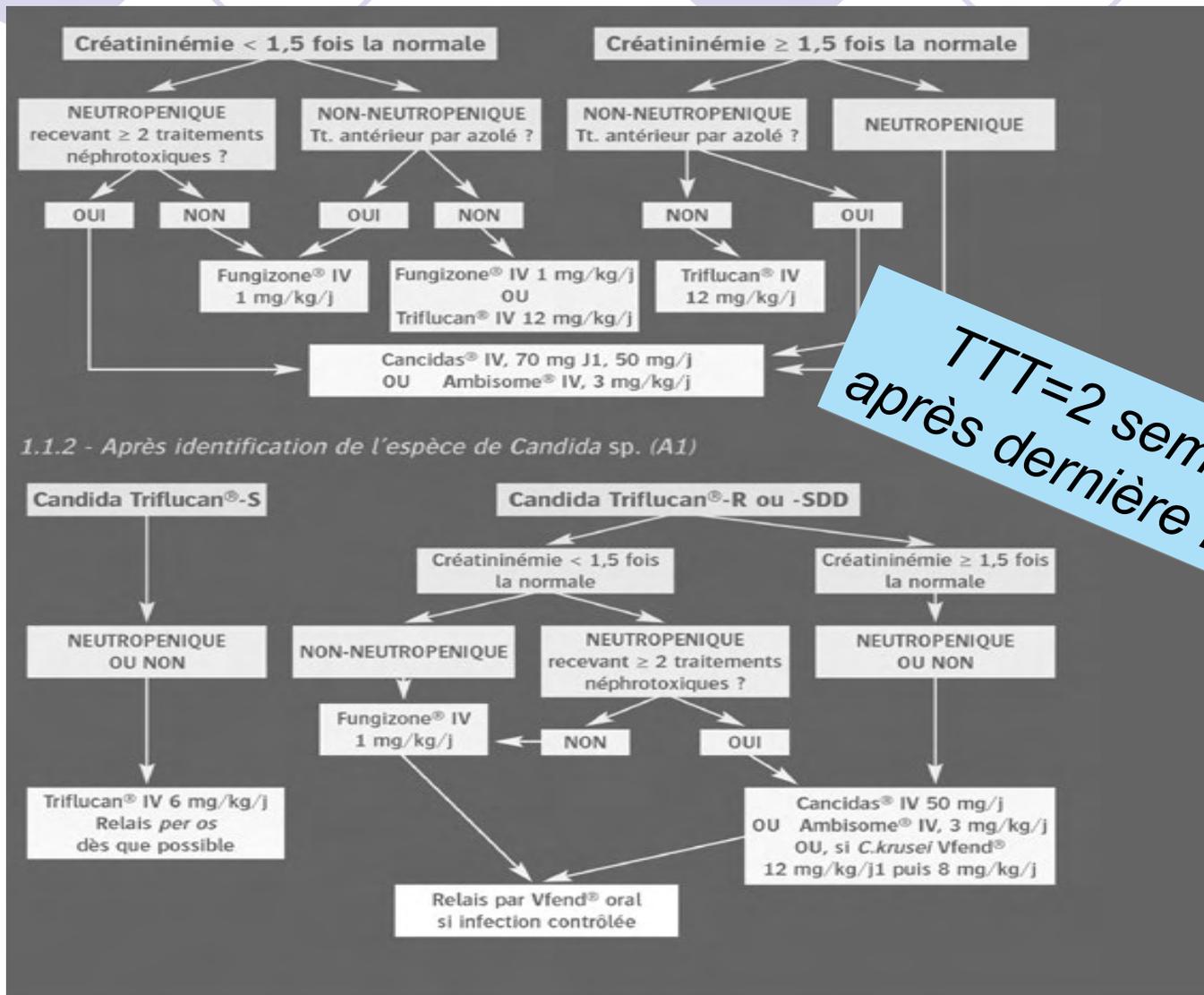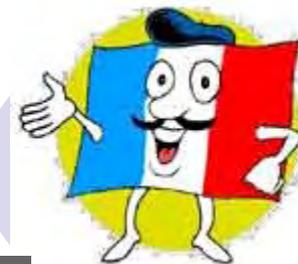
Quel antifongique choisir?

Recommandations

Critères de *choix*

- Risque d'espèce **fluco-R**
- **Sévérité** du patient:
  - Neutropénie
  - « instabilité » clinique
- **Tolérance** rénale
- *Tolérance hépatique*

Guidelines **SRLF** 2004

TTT=2 semaines après dernière hémoc+

Prise en Charge des Candidémies en Réanimation

1. Traiter tôt!

2. Avec quelle molécule?

3. Mesures associées

Contrôler la *source* de l'infection

- Rétablir la **barrière intestinale**:
  - Nutrition parentérale
 - *Antibiothérapie large spectre*
  - Stéroïdes
  - Etat de choc

- **Retrait KT** (biofilm)

- Contrôle chirurgical

Characteristic	Deaths (%)	Non-deaths (%)	Relative Risk (95% CI)	P value
Shock	22 (61)	29 (15)	5.5 (3.0–10.0)	<0.01
Renal failure	17 (46)	25 (13)	3.9 (2.2–6.7)	<0.01
Treatment with antifungal	25 (68)	188 (96)	0.2 (0.1–0.3)	<0.01
Catheter removal	20 (61)	142 (85)	0.4 (0.2–0.7)	<0.01
High severity of illness category	12 (41)	25 (19)	2.3 (1.2–4.4)	0.01
Catheter-related candidemia	5 (14)	62 (32)	0.4 (0.2–1.0)	0.03
Intubated	15 (43)	49 (25)	2.0 (1.1–3.6)	0.03
Age >65 yr	26 (68)	100 (50)	1.9 (1.0–3.7)	0.03
Neutropenia	8 (22)	19 (10)	2.1 (1.1–4.2)	0.04
Bacteria in incident culture	13 (34)	38 (19)	1.9 (1.0–3.4)	0.04
Hematologic malignancy	9 (24)	27 (13)	1.8 (0.9–3.4)	0.1

Contrôler les *localisations II*

- Retrait des cathéters

- Ablation d'une valve mécanique (EI)

- Traitement antifongique prolongé:
  - Localisations rétiniennes
  - Localisations viscérales
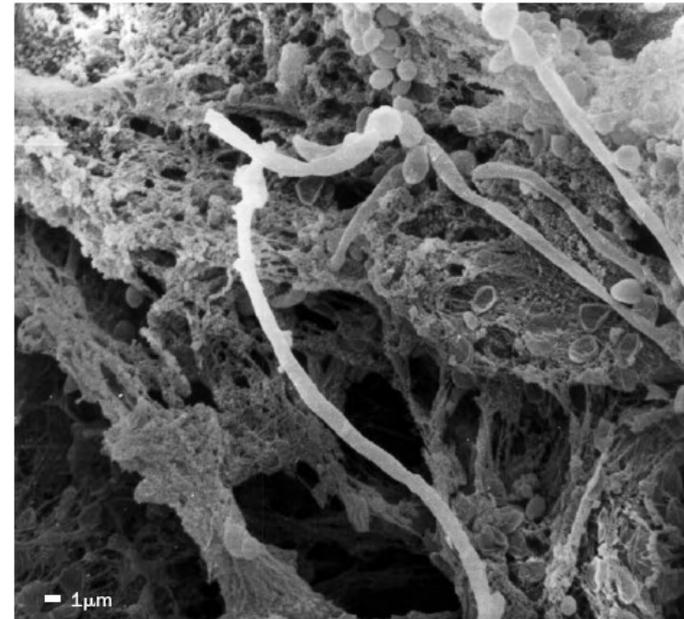
CONCLUSIONS
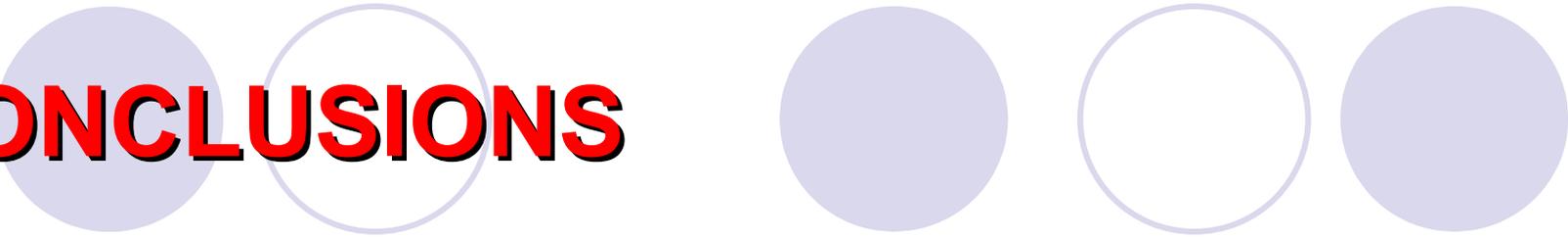
- **Reconnaissance** précoce des patients à risque
- Traitement **précoce**:
  - Prophylaxie?
  - Empirique+++
- **Choix** antifongique:
  - AmphoB = TTT de référence…?
  - Fluconazole = TTT de choîx…?
    - Evaluer risque d'espèce R
    - Sévérité clinique
    - « Déescalade »
  - Tolérance rénale et hépatique