



FIMUA

FEDERAZIONE ITALIANA MICOPATOLOGIA UMANA E ANIMALE

**XIV CONGRESSO
NAZIONALE
FIMUA**

PESARO

MERCURE HOTEL PESARO CRUISER

Viale Trieste 281

19-20 OTTOBRE 2018

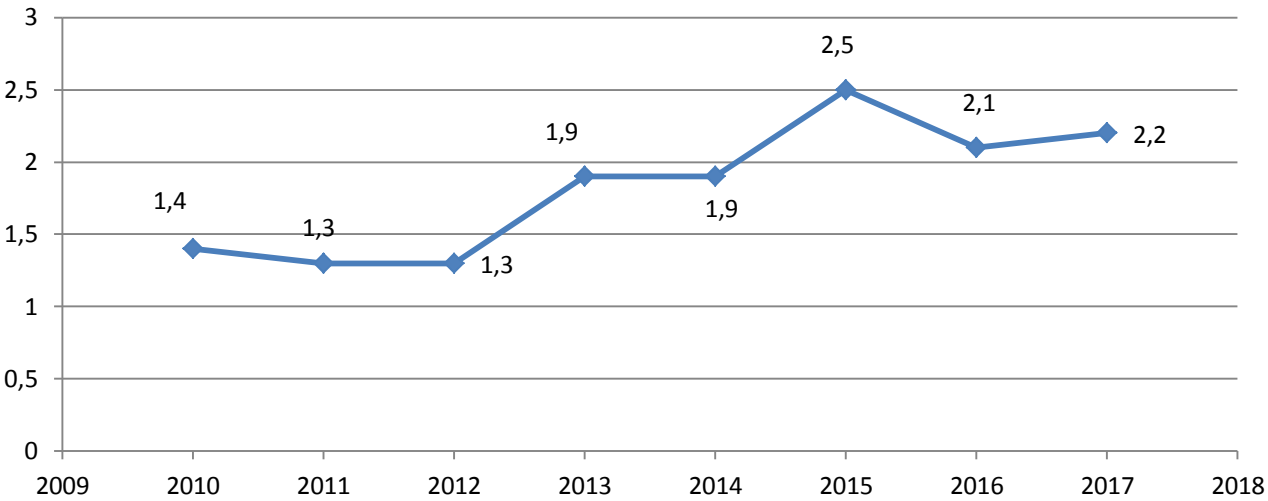
CANDIDEMIA E PAZIENTE CRITICO:QUALE TERAPIA?

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Risk factors for IC

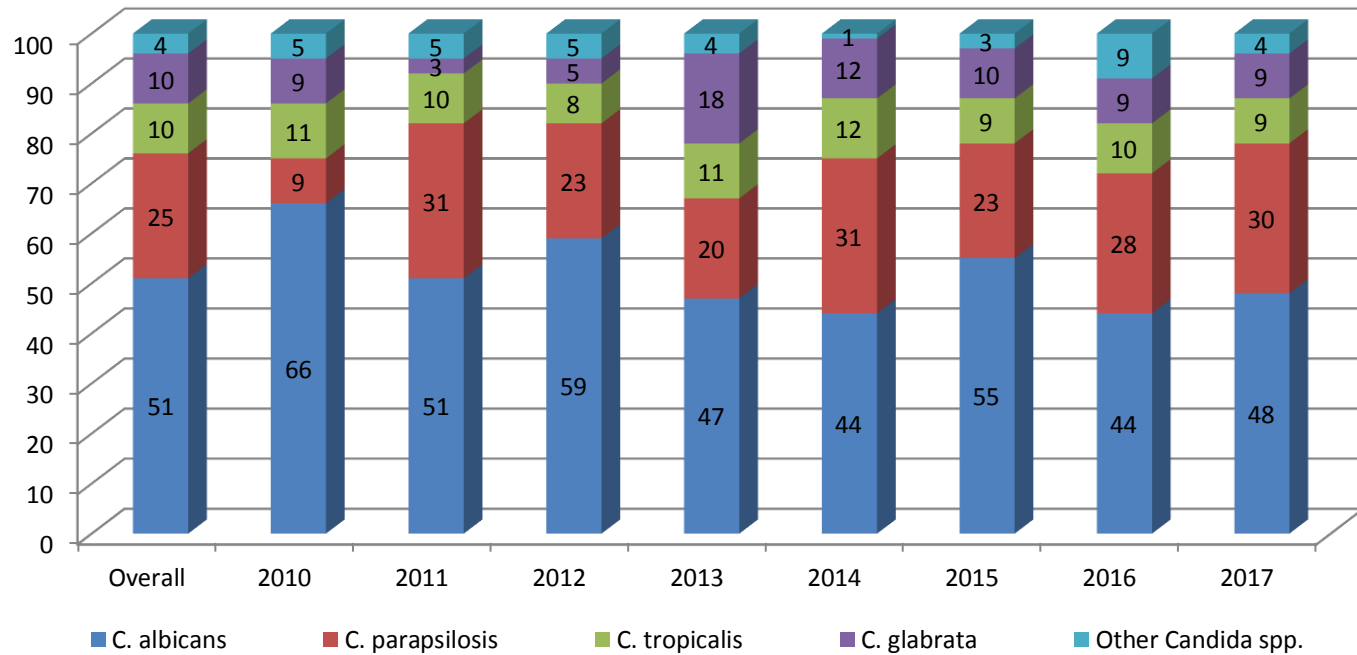
- Hospitalization in ICU
- Acute / chronic organ dysfunction requiring intensive care/invasive procedures
- Onco-haematological diseases and type, HSCT (ex. GVHD)
- SOT and type
- Immunosuppressive therapy
- Neutropenia
- Apache score
- Surgery (esp. abdominal), trauma, burns
- Age (neonatal / elderly patients)
- Renal failure requiring haemodialysis or hemofiltration
- Multiple site colonisation, previous history of *Candida* infection
- Duration of hospital stay
- TPN and use of indwelling catheters
- Diabetes mellitus
- Previous prolonged antibiotic therapy

incidenza



2010-2017
Tot = 420 candidemie

2010-2017
HM = 22 / 420 **5%**
No HM = 398 / 420 **95%**



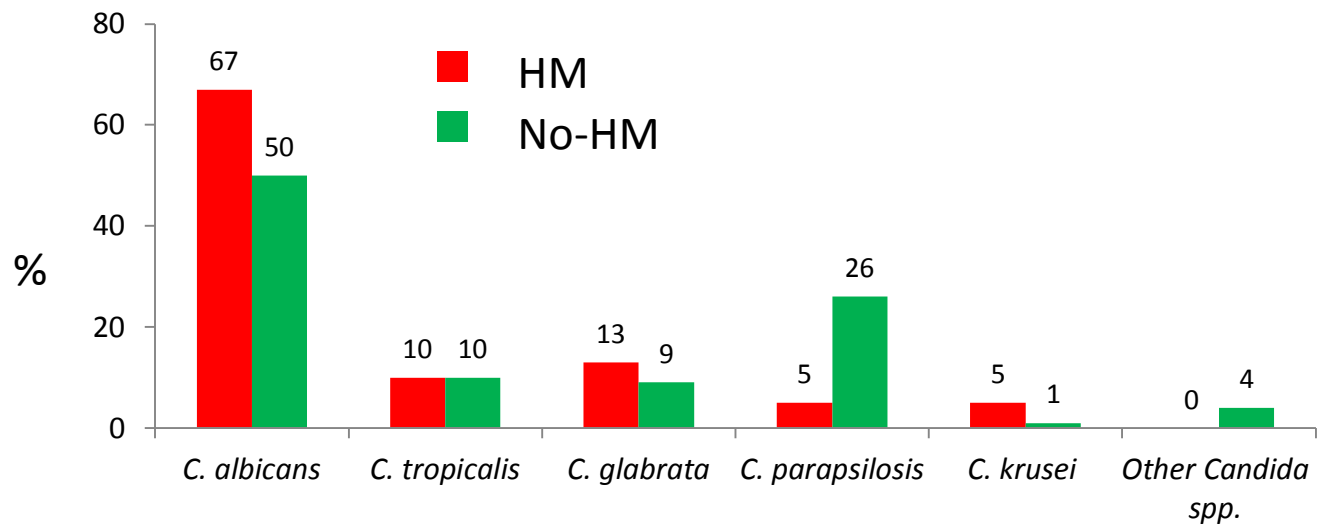


Table 4. Multivariate analysis of risk factors for 30-day mortality in the study cohort

Risk factors	Hazard ratio	CI 95%		<i>p</i> value
		Lower limit	Upper limit	
Ward	1.621	1.142	2.301	0.007
RRT	2.435	1.109	5.344	0.027
Neutropenia	8.976	2.052	39.269	0.004
Pneumonia	1.959	1.178	3.257	0.010
Septic shock	2.123	1.131	3.987	0.019

Tempi e modi della terapia antifungina nel paziente critico



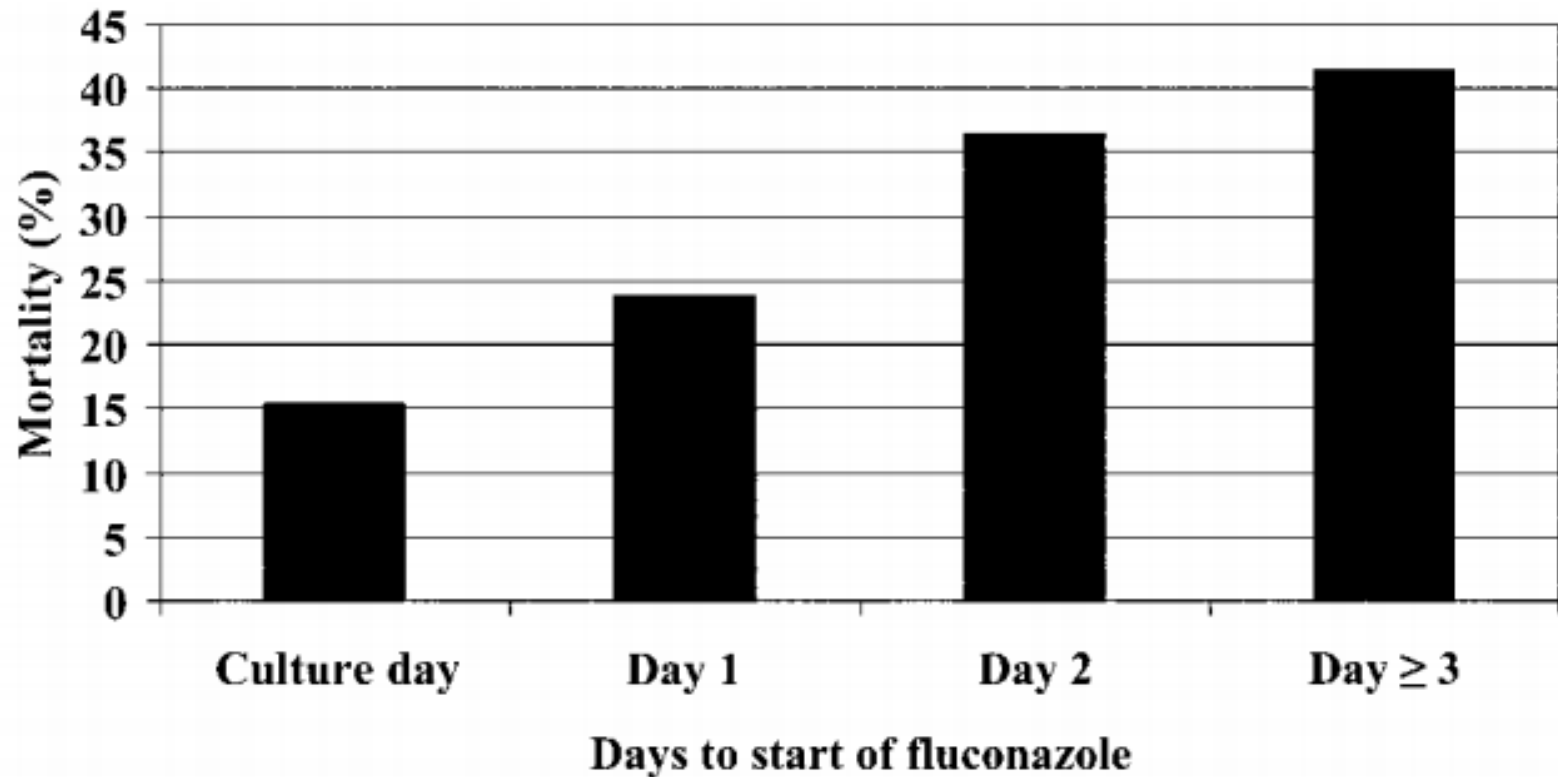
1. How soon?
2. How long?



Drug?

1. Target therapy
2. Empirical / preemptive / presumptive
3. Prophylaxis

Time to Initiation of Fluconazole Therapy Impacts Mortality in Patients with Candidemia: A Multi-Institutional Study



A multicentre study to evaluate the impact of timing of caspofungin administration on outcomes of invasive candidiasis in non-immunocompromised adult patients

Variables	EI, n=107	DI, n=62	P value
Overall response	82 (76.6%)	35 (56.5%)	0.006
All-cause mortality	24 (22.4%)	19 (30.6%)	0.27
Infection-related mortality	21 (19.6%)	18 (29.0%)	0.16
Total length of stay, days			
mean \pm SD	33.30 (40.016)	39.35 (23.082)	0.28
median, IQR	23 (12–37)	33 (23–50.25)	
Length of stay after isolation, days			
mean \pm SD	20.60 (17.068)	27.98 (16.517)	0.007
median, IQR	14 (9–26)	25 (16–33)	
Achieved vital sign stability	68 (63.6%)	38 (61.3%)	0.77
Time to vital sign stability, days			
mean \pm SD	7.0 (4.3)	16.2 (13.6)	<0.0001
median, IQR	6.5 (4–9)	13 (7–18.5)	



Recommendations on Initial Targeted Treatment of Candidaemia and Invasive Candidiasis in Adult Patients

Intervention	SoR	QoE	Reference	Comment
Anidulafungin 200/100 mg	A	I	[64]	Consider local epidemiology (<i>C. parapsilosis</i> , <i>C. krusei</i>), less drug-drug interactions than caspofungin
Caspofungin 70/50 mg	A	I	[67] [55] [63]	Consider local epidemiology (<i>C. parapsilosis</i>)
Micafungin 100 mg	A	I	[61] [63]	Consider local epidemiology (<i>C. parapsilosis</i>), less drug-drug interactions than caspofungin, consider EMA warning label
Amphotericin B liposomal 3 mg/kg	B	I	[61] [62]	Similar efficacy as micafungin, higher renal toxicity than micafungin
Voriconazole** 6/3 mg/kg/d	B	I	[43] [78] [77]	Limited spectrum compared to echinocandins, drug-drug interactions, limitation of IV formulation in renal impairment, consider therapeutic drug monitoring
Fluconazole* 400-800 mg	C	I	[165] [53] [74] [54] [64] [76] [75] [73] [72]	Limited spectrum, Inferiority to anidulafungin (especially in the subgroup with high APACHE scores), may be better than echinocandins against <i>C. parapsilosis</i>

ESCMID* Guideline for the Diagnosis and Management of *Candida* Diseases 2012:

Non-Neutropenic Adult Patients

5 RCT; 6 Open label studies; 2 Case reports

tot patients 2225 candidemia/IC

tot *parapsilosis* 347

tot *parapsilosis* treated with echinocandins 268

global response paraps/echinocandins 75% (200/268)

global response other *C. species*/echinocandins 77% (1186/1531)

P = 0.306



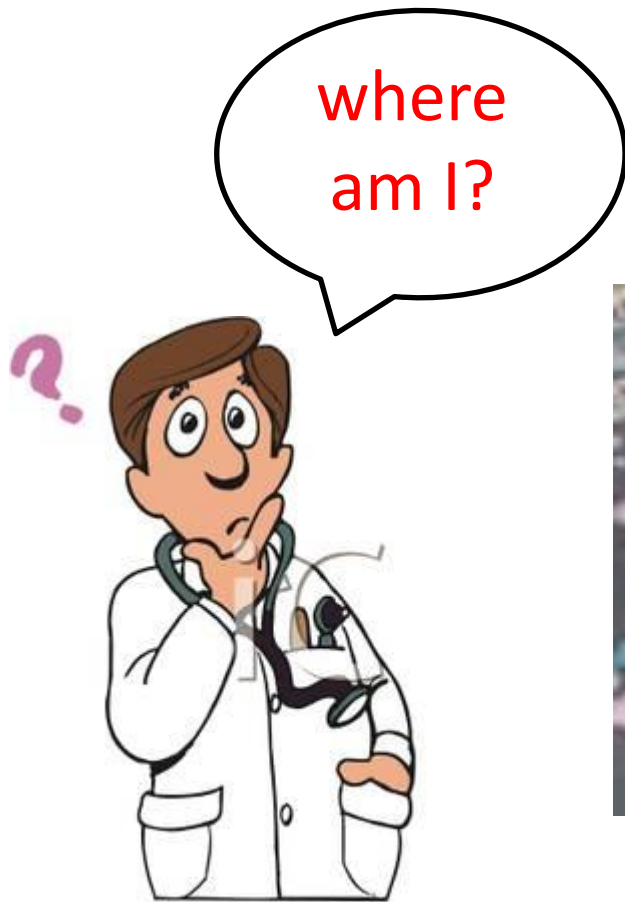
An Italian consensus for invasive candidiasis management (ITALIC)

- An *echinocandin* should be preferred as first line therapy in

Patients should be treated for at least 14 days after the last positive blood culture (this requires blood cultures to be performed daily until negativisation).

Voriconazole second

- Acceptable alternative in stable pts: *Fluconazole*
- De-escalation from an echinocandin to fluconazole to be considered in stable pts with FLU-S strain



Treatment Strategy	Certainty of Diagnosis	Risk Factors	Clinical signs	Biomarkers
Empirical	Possible	+	+	-
Pre-emptive	Probable	+	-	+
Presumptive	Probable	+	+	+

Recommendations on antifungal prophylaxis in ICU patients

Population	Dugs	SoR / QoE	Type of study
Recent abdominal surgery and recurrent gastrointestinal perforations or anastomotic leakages	<ul style="list-style-type: none"> • Fluconazole 400 • Caspofungin 70/50 	<ul style="list-style-type: none"> • BI • CII 	<ul style="list-style-type: none"> • Placebo (n=43) • Single arm (n=19)
Critically ill surgical patients with an expected length of ICU stay ≥ 3 days	<ul style="list-style-type: none"> • Fluconazole 400 	<ul style="list-style-type: none"> • CI 	<ul style="list-style-type: none"> • Placebo (n=260)
Ventilated for 48 h and expected to be ventilated for another ≥ 72 h	<ul style="list-style-type: none"> • Fluconazole 100 	<ul style="list-style-type: none"> • CI 	<ul style="list-style-type: none"> • Placebo (n=204)
Ventilated, hospitalized for ≥ 3 days, received antibiotics, CVC, and ≥ 1 of: parenteral nutrition, dialysis, major surgery, pancreatitis, systemic steroids, immunosuppression	<ul style="list-style-type: none"> • Caspofungin 50 	<ul style="list-style-type: none"> • CII 	<ul style="list-style-type: none"> • Placebo (n=186)

ESCMID* Guideline for the Diagnosis and Management of *Candida* Diseases 2012:

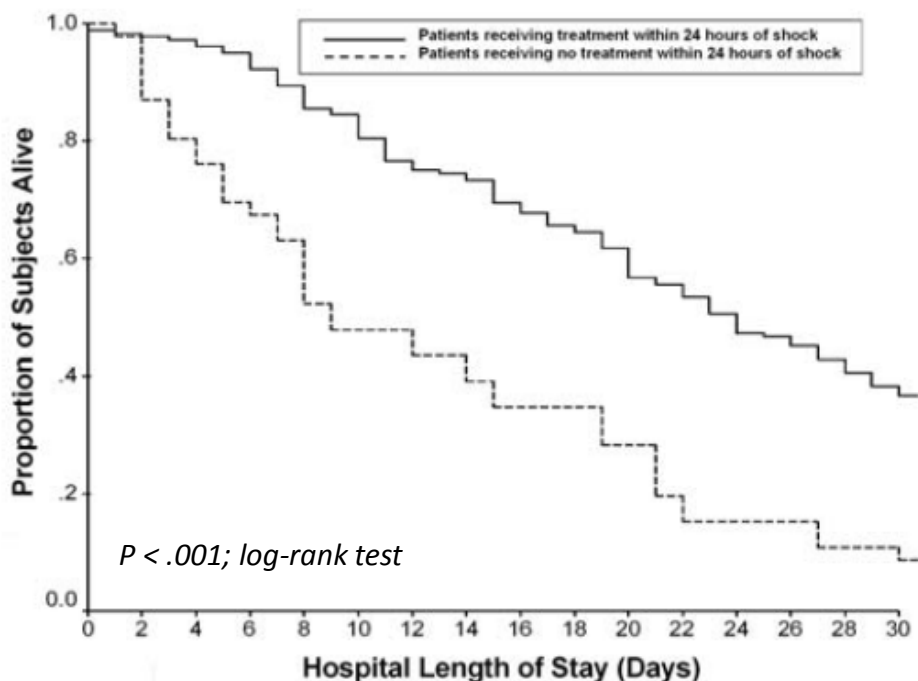
Non-Neutropenic Adult Patients

An Italian consensus for invasive candidiasis management (ITALIC)

Recommendation

1. Antifungal prophylaxis [28, 31, 94–104]:
 - Antifungal prophylaxis should not be administered in non-immunocompromised patients.

Septic Shock Attributed to *Candida* Infection: Importance of Empiric Therapy and Source Control



Multivariate Analysis of Risk Factors for Hospital Mortality

	AOR	95% CI	P value
Solid cell tumor with metastases	6.01	2.98–12.10	.010
Class IV congestive heart failure	4.95	2.53–9.68	.017
APACHE II Score (1-point increments)	1.37	1.26–1.48	<.001
Inadequate source control	77.40	21.52–278.38	.001
Red blood cell transfusion	6.49	4.06–10.38	<.001
Serum albumin (1 g/dL increments)	0.42	0.30–0.59	.012
Delayed antifungal treatment ^b	33.75	9.65–118.04	.005

Factors Related to Outcome of Bloodstream Infections due to *Candida parapsilosis* complex

Table 2: Multivariate model of risk factors for outcome of 63 patients considered in this study

Risk factors	95% CI			P value ^a
	HR	LL	UL	
Early CVC removal ^b	0.019	0.003	0.114	<0.0001
Cardiovascular diseases ^c	3.632	1.251	10.547	0.018
Acute events ^d	3.723	1.019	13.597	0.047

^aCox's regression analysis

^b Early removal was considered occurring within 48 h from blood cultures drawing

^cCardiovascular diseases include heart failure, ischemic heart disease, endocarditis and arrhythmia

^dAny acute event (i.e.: cardiovascular events, pneumonia, intestinal perforation, septic shock, acute renal failure etc.) occurring during the episode of BSI

Conclusioni

- Individuare i pazienti a «rischio»
- Iniziare una terapia antifungina il più precocemente possibile
- Iniziare con un farmaco fungicida
- Source Control

GRAZIE
PER L'ATTENZIONE