

# Evaluation of the safety and tolerance of micafungin vs other antifungals in patients with pre-existing child B or C liver disease

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## BACKGROUND

- Incidence of invasive fungal infection (IFI) in end stage liver disease patients (ESLD) ranges from 1% to 10% and development of IFI has a profound effect on patient's outcome.
- Echinocandins are generally safe and well-tolerated in ESLD patients. However, micafungin is the only echinocandin not approved in these patients, because of an EMA warning on the potential development of liver tumors, based on studies in rats.
- Our **objective** was to analyze the association between exposure to micafungin, other echinocandins, or azoles and the development of short-term liver injury (STLI) or LTLI in a population of patients with pre-existing Child-Pugh B or C ESLD

## RESULTS

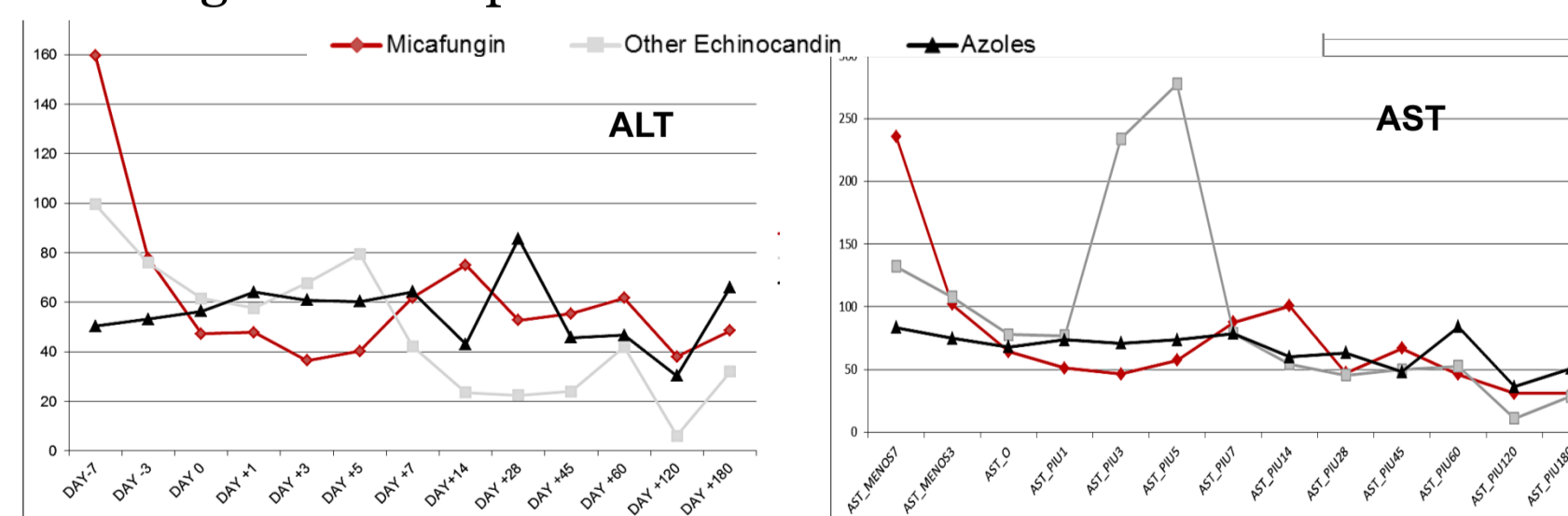
- During the study period, 2,335 ESLD patients were admitted to the 6 hospitals in the study. Of these, 20 with Child-Pugh B or C ESLD received micafungin for  $\geq 72$  hours (0.85%).
- Demographics and baseline characteristics of the 3 groups are shown in **Table 1**.

CHARACTERISTICS	Total N=60	Micafungin n=20	Other echinocandins n=20	Azoles n=20	p
Age, years (mean $\pm$ SD)	58.2 $\pm$ 14.5	61.2 $\pm$ 11.2	52.8 $\pm$ 9.6	60.6 $\pm$ 20.1	0.13
Male sex	45 (75.0)	15 (75.0)	15 (75.0)	15 (75.0)	1
Pre-existing liver disease					
HCV-associated cirrhosis	26 (43.3)	7 (35.0)	12 (60.0)	7 (35.0)	0.64
HBV-associated cirrhosis	7 (11.6)	3 (15.0)	1 (5.0)	3 (15.0)	0.11
Alcohol-associated cirrhosis	18 (30.0)	7 (35.0)	5 (25.0)	6 (30.0)	0.52
Cryptogenic cirrhosis	4 (6.6)	0	1 (5.0)	3 (15.0)	0.78
Hepatocellular carcinoma	8 (13.3)	2 (10.0)	4 (20.0)	2 (20.0)	0.15
Other causes*	7 (11.6)	3 (15.0)	3 (15.0)	1 (5.0)	0.56
Baseline Child-Pugh Class B	35 (58.3)	12 (60.0)	8 (40.0)	15 (75.0)	0.08
Baseline Child-Pugh Class C	25 (41.6)	8 (40.0)	12 (60.0)	5 (25.0)	0.08

## MATERIAL AND METHODS

- **Study design.** Retrospective multicenter, case-control study performed in 6 hospitals in Spain and Italy.
- **Cases:** pts with Child-Pugh B or C ESLD receiving micafungin at 100 mg daily  $\geq 72$  hours.
- **Controls:** pts with other echinocandins or 1 azole at about the same time as the case and with the same indication.
- **Primary outcome:** Incidence of short- or long-term toxicity. **Secondary outcomes:** incidence of 1) pts stopping AF due to hepatotoxicity, 2) needing transplantation due to hepatotoxicity and 3) episodes of ascitic decompensation, gastrointestinal bleeding and re-admission in the following year.
- **STLI** was defined as: 1) an increase in transaminase level to  $>3$  times the ULN range for patients who started treatment with normal liver function; or 2) a doubling of the initial transaminase level when AF treatment was started in patients with abnormal baseline transaminase levels.
- LTLI was defined as the development of any type of liver tumour during the follow-up period

- Exposure to antifungal treatment is reported in **Table 2**.
- **Figure 1** shows how ALT and AST changed over time
- Follow-up data was available for 30 pts until a median of 1.3 y.
- No differences were observed between groups with respect to secondary outcomes.
- Only **1 patient, in the azole group**, experienced LTLI with a new diagnosis of hepatocellular carcinoma.



## CONCLUSIONS

- The administration of micafungin therapy to patients with ESLD was safe and did not imply a higher risk of developing short nor long term liver injury.

CHARACTERISTICS	Total N=60	Micafungin n=20	Other echinocandins n=20	Azoles n=20	P
Reason for starting AF					
Empirical therapy	24 (40.0)	10 (50.0)	9 (45.0)	5 (25.0)	0.23
Targeted therapy	36 (60.0)	10 (50.0)	11 (55.0)	15 (75.0)	
Length of AF (median, range)	14.1 $\pm$ 8.0	12.3 $\pm$ 6.5	10.9 $\pm$ 5.6	19.2 $\pm$ 9.1	<0.001
IFI					
Bloodstream infection	20 (33.3)	5 (50.0)	6 (54.5)	9 (60.0)	0.88
Abdominal infection	5 (8.3)	2 (20.0)	0	3 (20)	0.13
Urinary tract	6 (10.0)	2 (20.0)	2 (18.9)	2 (13.3)	0.89
Lung	2 (3.3)	0	1 (9.1)	1 (6.7)	0.64
Other <sup>&amp;</sup>	3 (5.0)	1 (10.0)	2 (18.9)	0	0.24
Septic shock	17 (28.3)	7 (35.0)	10 (50.0)	0	0.22
SOFA score (mean $\pm$ SD)	6.8 $\pm$ 3.2	6.5 $\pm$ 3.2	8.1 $\pm$ 2.8	5.8 $\pm$ 3.2	0.06
Development of STLI	<b>6 (10.0)</b>	<b>2 (10.0)</b>	<b>2 (10.0)</b>	<b>2 (10.0)</b>	<b>1</b>