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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: Micafungin is the only echinocandin not approved in patients with end-stage liver disease because of an EMA warning on potential development of liver tumors based on preclinical studies in rats. The aim of our study was to determine the association between exposure to micafungin, or other antifungals (AF) with development of short (STLI) or long term liver injury (LTLI) in patients with child B or C liver disease.

Material/methods: This is a multicenter study including patients with Child-Pugh B or C liver disease who received antifungals ≥ 72 hours (January 2009-December 2015) in 6 Spanish and Italian hospitals. All micafungin patients were randomly matched with 1 patient who received other echinocandin and 1 patient with azole treatment. STLI was defined as: 1) an increase in transaminase level to >3 times the upper limit of normal 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.

Results: Overall, 20/2,500 (0.08%) patients with a chronic liver disease admitted to the 6 centers were found to have child B or C liver disease and received micafungin for ≥ 72 hours. Patients treated with micafungin were older (61.2 vs 52.8, p=0.01) but required less ICU admission (5% vs 40%, p=0.02) than patients treated with other echinocandins. When compared with patients treated with azoles, micafungin patients had higher MELD (18.6 vs 14.9, p=0.29) and Child-Pugh score (9.1 vs 8.6, p=0.15), and more septic shock (35% vs 0%, p=0.08). Etiology and complications of liver disease and AF indication were similar. During AF treatment, we observed a similar rate of STLI (2/20 patients in each group). Most cases were asymptomatic and AF switch to another class of AF was required in only two patients (1 micafungin and 1 azole). No patient developed acute liver insufficiency requiring ICU admission or transplantation. All patients normalized transaminase levels after AF withdrawal. No death related to hepatotoxicity was reported. Follow-up (median of 1.3 year) was available in 30 patients. No differences between groups were observed regarding rate of re-hospitalization, ascitic decompensation or gastrointestinal bleeding. However, patients treated with micafungin required less frequently the administration of a new AF within the subsequent year. A new diagnosis of liver tumor was obtained in 1 patient only, who was previously treated with azoles.

Conclusions: Our study suggests that the administration of micafungin therapy to patients with ESLD does not imply a higher risk of developing short nor long term liver injury.