EV0759
ePoster Viewing
Diagnostic mycology (incl molecular)

Screening with serum galactomannan (sGM) in haematological patients on micafungin prophylaxis: does the test remain useful for diagnosis of invasive aspergillosis?

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Background: Invasive aspergillosis (IA) remains a significant cause of morbidity and mortality in hematological patients. In order to achieve an early diagnosis, systematic screening with sGM is performed in many hematology departments. However, recent studies have shown that posaconazole prophylaxis reduces very significantly the positive predictive value of GM (11%) (Duarte et al, 2014), leading to many unnecessary CTs and antifungal therapies. Micafungin is also used for active anti-mould prophylaxis, especially in patients with mucositis. Our aim was to investigate the diagnostic performance of sGM assay in high risk hematology patients receiving micafungin prophylaxis.

Material/methods: Retrospective 5-year study including hematological patients who received micafungin prophylaxis during high-risk episodes. Indication of sGM testing was classified as: prompted by clinical suspicion ("diagnostic driven") or twice weekly screening in afebrile patients ("surveillance GM"). The clinical situation oft he patients was classified as follows: **True positive-TP** (positive GM test results in the context of breakthrough IA), **False positive-FP** (positive GM test in patients who remained on micafungin prophylaxis and had no evidence of IA), **True negative-TN** (episodes with all consecutive GM tests negative and no diagnostic features of IA), **False negative-FN** (negative GM test results in the context of breakthrough IA) and **non-evaluable** (patients received antifungal treatment and IA could not be excluded or confirmed with certainty).

Results: During the study period, 149 patients (60.4% male) with a median age of 43 years (range,5-76), underwent micafungin prophylaxis during 208 episodes at risk of IA (40 AML chemotherapy, 129 allogeneic HCT, and 39 GVHD). A total of 1617 serum GM tests were performed in these patients,

with a median of 8 GM tests per risk episode (range, 2–40). Of these, 1405 samples were negative, and 212 serum GM tests (13.1%) were positive, corresponding to 54 episodes (27.9%). Overall, 62 (29.7%) episodes were not evaluable because patients received antifungal treatment for other fungal infections (3 episodes) or due to persistent fever (59 episodes). Of the remaining 146 episodes, 4 corresponded to TP GM test results in the context of breakthrough probable IA (incidence of breakthrough IA under micafungin prophylaxis 2.7%). Among the remaining episodes, 111 (76%) were considered as TN and 31 (21.2%) as FP. No FN episodes were detected. All except one episode of FP result occurred among surveillance GM tests, leading to high-resolution CT scans in 25% of them, all of which were negative. PPV/NPV of GM test used in surveillance or diagnostic driven approaches were 3.1% /100% and 75% and 100%, respectively.

Conclusions: GM surveillance of asymptomatic patients receiving micafungin prophylaxis is not recommended, because all results will be either negative or false positive. However, sGM may still be helpful for the diagnosis of breakthrough IA in symptomatic patients during prophylaxis.