

O426

1-hour Oral Session

Challenges in antifungal treatment

**Retrospective analysis of 1mg/kg/day dose of liposomal amphotericin for empirical treatment of potential invasive mould disease in at-risk adult haematology patients whilst awaiting further results**

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**Background:** Standard dosing of liposomal amphotericin B formulation (AmBisome®) in neutropenic patients with fever unresponsive to broad-spectrum antibacterials is 3mg/kg/day. There is absence of evidence that this dose is superior to 1mg/kg/day. Local guidelines for anti-fungal agents in Adult Haematology patients, currently suggests routinely starting at 1mg/kg/day of AmBisome®; & then reviewing the dose / use of an intravenous antifungal in light of chest high resolution CT scan (HRCT) / serum galactomannan result(s) *et al*, with these investigations being requested at time of initiating AmBisome® if not previously. This retrospective analysis evaluated this strategy – namely the number / proportion of patients who were started on AmBisome® at 1mg/kg/day & the subsequent outcomes – *i.e.* relative proportions of recipients who were switched to 3mg/kg/day or to an alternative agent, & likelihood that they had an invasive mould infection at the time, and survival.

**Material/methods:** Patients who received AmBisome® were identified by interrogating pharmacy records. 347 patients were initially identified during the study period Jan 2009 to May 2011- which was reduced to 326 after de-duplication / exclusion of non-eligible cases. Relevant mycological results were collated for these 326 – *i.e.* any mould growth from specimen(s) and galactomannan results (both blood & broncho-alveolar lavage (BAL) fluid). The results of chest HRCT scans and of other relevant imaging; and the ultimate outcome were collated from electronic records for cases who had at least one positive mycological result.

**Results:** 43 patients had  $\geq$  one positive mycological result for a mould (as defined by EORTC/MSG Consensus Group for invasive fungal disease, De Pauw 2008); of which 16 had  $\geq$  two positive tests (either same or different modality). Two of these cases' results were from samples collected elsewhere and therefore excluded. Six patients had "borderline" positive mycological results (galactomannan in BAL  $> 0.5$  but  $< 1.0$ ). 22 patients had at least one respiratory sample culture positive for *Aspergillus* spp (usually *A. fumigatus*) – no other mould was grown. Of these 41 patients, six didn't have HRCT scans in the requisite time-frame, eight didn't have any relevant abnormalities detected on concurrent HRCT; 15 had „non-specific“ changes, and 12 had changes consistent with EORTC / MSG diagnostic criteria. Eleven patients are still alive, 10 died over 90 days after the positive result(s) whereas eleven

died within 30 days and seven died between 30 & 90 days later. Of the 12 patients meeting EORTC / MSG radiological criteria, only two died within 30 days, and five are still alive.

**Conclusions:** Preliminary analysis suggests use of 1mg/kg/day liposomal amphotericin B dose in a semi-empirical setting, whilst awaiting further results, is safe w.r.t efficacy; and clearly cost saving compared to conventional 3mg/kg/day regimen.