16.1. Safety and Efficacy of Anidulafungin in the Treatment of Invasive Candidiasis in Children

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Background. Treatment with an echinocandin is recommended as first-line therapy of patients with invasive candidiasis including candidemia. Little is known about the efficacy and safety of anidulafungin (ANID) for the management of ICC in children.

Methods. Subjects aged 1 months to 17 years with ICC were enrolled into a prospective, open-label, non-comparative, multi-center, global study (NCCT00716267) to receive ANID 10 mg/kg on days 1, 1.5 mg/kg on day 2, and 1 mg/kg thereafter. An interim analysis was completed in children 2–17 years. Subjects were to receive ANID for at least 10 days up to 35 days. A central venous catheter suspected as a site of infection was to be removed. A switch to oral fluconazole could be made after day 10. Treatment was required for at least 14 days after two negative cultures separated by 24 hours. Efficacy, based on a determination of global response (combination of clinical and microbiological response), was assessed at end of IV treatment (EOIVT), end of treatment (EOT), 2- and 6-week follow-up. Safety was assessed through 6-week follow-up.

Results. In total, 42 subjects (18, 2, to 5-year-olds, 5-17 years) received at least 1 dose of ANID (mean 11 days; range 1–35 days) and were assessed for safety. Forty-seven subjects had microbiologically confirmed ICC and were evaluated for efficacy. The most common baseline pathogens were C. albicans (38%) and C. parapsilosis (26%). Forty-four (93.6%) subjects had candidemia only. Global response success rates at EOIVT and EOT were 72.3 and 74.5%, respectively. All subjects reported at least one treatment emergent adverse event (AE) with diarrhea (22.9%), vomiting (22.9%), and pyrexia (18.8%) being most frequent. Five subjects discontinued treatment due to the AEs, four of which four [increased cardiovascular (2), vomiting, pyrexia, or anaphylaxis] were considered related to ANID. All-cause mortality by the 2- and 6-week follow-up visit was 12.5 and 14.6%, respectively. Of the seven deaths during the study, one was considered related to ICC; two were related to disease progression (Ewing's sarcoma, medulloblastoma); the remaining were related to other conditions (intracranial hemorrhage, sepsis/septic shock, and respiratory failure).

Conclusion. Anidulafungin was effective with an acceptable tolerability and safety profile in children aged 2–17 years diagnosed with ICC.

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16.2. Invasive Mold Infections (IMIs) of the Central Nervous System (CNS) in Patients with Hematologic Cancer (HC) (2000–2016): Uncommon but Deadly

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Background. There is paucity of data regarding IMIs of the CNS in patients with HC or stem cell transplantation (SCT).

Methods. Review of the charts of patients with HC and/or SCT recipients who were diagnosed with CNS IMIs at MD Anderson Cancer Center (1/1/2000–5/31/2016). IMIs were classified as proven or probable (EORTC/MSG criteria). We excluded patients with mixed CNS infections. Risk factors for survival at day 42 post diagnosis (dx) were assessed. A multivariate logistic regression analysis was performed to identify independent predictors of mortality.

Results. We identified 40 patients (16 proven; 40%). Most patients were white (29%; 73%) and male (33; 83%). Median age was 58 years. The most common HC was acute leukemia (23; 58%). Seventeen patients (43%; 13 (76%) had GVHD. Most patients had active HC and neutropenia at dx (58; 95% and 21; 53%, respectively). Twenty-seven patients (68%) were in the ICU at dx. Aspergillus sp; (13; 33%) and Mucorales (8; 20%) accounted for >50% of cases. CNS IMIs were deemed to be secondary to direct extension or hematogenous spread in 9 (23) and 31 (77%) patients, respectively. In the latter group, 28/31 (90%) had fungal pneumonia. Of the 27 and 9 patients who had Aspergillus galactomannan antigen tested from serum and CSF, respectively, 18 had positivity in serum (66%) and 3 in CSF (33%). Most patients (30; 75%) had exposure to mold-active agents within 30 dx. Most patients (34; 85%) received antifungals. Immune response in pathology, steroid tapering and possibly treatment with micafungin therapy. Risk factors for candidemia identified in this study are consistent with previously published literature. These findings highlight the need for more precise predictors could promote judicious use of empiric echinocandins. Ultimately, this could decrease antifungal exposure, development of resistance, and associated costs.

Conclusion. CNS IMIs occur in patients with HC who are often pre-exposed to antifungals. Immune response in pathology, steroid tapering and possibly surgical drainage are associated with improved outcome.

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163. Risk Factors for Candidemia as Compared with Patients with Negative Blood Cultures Placed on Empiric Micafungin

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Background. Numerous risk factors have been linked to invasive candidiasis; however, they are non-specific. We sought to identify factors that may trigger empiric antifungal therapy in a large number of patients. Identification of more precise predictors could promote judicious use of empiric echinocandins. Ultimately, this could decrease antifungal use, development of resistance, and associated costs.

Methods. This was a retrospective review of patients admitted to Baylor University Medical Center from 10/1/14 to 10/25/16. Patients with positive blood cultures for Candida spp were compared with a randomly selected cohort of patients on empiric micafungin for 3 or more days and with blood cultures negative for Candida spp. This study excluded patients on prophylactic antifungals and patients with positive blood cultures but negative blood cultures for Candida spp. Data was analyzed using the χ² test, t-test comparing means, and logistic regression as applicable.

Results. There were 127 patients with candidemia and 134 patients without candidemia on empiric micafungin. Factors associated with candidemia included positive 1,3-β-glucan assay in patients without multifocal antifungal therapy (26.0% vs. 15.7%, P = 0.001) and more likely to receive antibacterial therapy in the previous 10 days (55.9% vs. 79.9%, P = 0.001) and more likely to have imaging suggestive of an invasive fungal infection (11.0% vs. 30.6%, P < 0.001). There was no difference in mean length of stay (25.5 days vs. 27.3 days, P = 0.631) or 30-day all-cause mortality (32.3% vs. 23.9%, P = 0.131) between patients with candidemia and patients on empiric micafungin, respectively.

Conclusion. A negative 1,3-β-glucan assay in patients without multifocal Candida colonization or receiving TPN was inversely correlated with invasive candidiasis, as defined by candidemia. Therefore, the absence of these factors may be useful to deescalate empiric micafungin therapy. Risk factors for candidemia identified in this study were consistent with previously published literature. These findings highlight the opportunity to improve empiric micafungin prescribing patterns at our institution.

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