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## Safety and Tolerability of Combination Anidulafungin (ANID) and Liposomal Amphotericin B (LAmB) for the Treatment of Invasive Aspergillosis (IA)

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**Background:** Response rates with existing monotherapy for IA remain suboptimal, and mortality remains unacceptably high. Anidulafungin is a novel echinocandin (EC) in late stage development with potent *in vitro* activity that is additive or synergistic with amphotericin B (AmB) against *Aspergillus* spp. ANID's distinct PK characteristics and favorable safety profile support development as a first-line therapeutic agent. AmB has efficacy for IA but has unacceptable toxicity. Combination of ANID and LAmB may offer improved outcome with no excessive toxicity. The safety of combination ANID plus LAmB was evaluated.

**Methods:** Pts  $\geq 18$  yrs with proven or probable IA (per EORTC, MSG criteria) and life expectancy  $> 72$  hrs were enrolled into an open-label, non-comparative study. Exclusion criteria included receipt of more than 5 days of antifungal therapy (unless treatment failure) and AST/ALT  $> 5 \times$  ULN. ANID was given as 200 mg IV loading dose day 1 with 100 mg daily maintenance (200/100mg); LAmB was given daily up to 5 mg/kg/day. Treatment continued until resolution of signs/symptoms up to 90 days. Clinical assessments were done on therapy, end of therapy (EOT) and at 4 weeks post EOT (FU). Safety labs and ECGs were performed.

**Results:** Data on 17 of 30 enrolled patients are presented. Mean age was 55 (range 21-79). The majority of pts had pulmonary IA (12); other sites included CNS (2), cutaneous, hepatic and bone (1 each). Risk factors for IA were steroid use (3); AML (3); ALL (1); other malignancies (2); aplastic anemia (1), other acquired immunodeficiency (2); allogeneic BMT (3); heart (1) or liver transplant (1). 12 of 17 patients had at least 1 drug-related adverse event (DRAE). Of these pts, 7 and 3 had an AE expected with LAmB and with LAmB and/or ANID, respectively. DRAEs reported in  $\geq 2$  pts were hypokalemia, increased transaminases, increased ALP, hypomagnesemia and flushing. 14 pts had a total of 22 serious AEs; only 2 were drug related (renal failure, an expected event for LAmB; abnormal LFTs). There were 9 deaths during the 90 day study period; none considered related to study drug. No trends attributable to ANID/LAmB were seen for post-baseline hematology or chemistry results.

**Conclusions:** The patterns of AEs and laboratory abnormalities were not unexpected for this ill population. No untoward safety findings were found. Based upon available data, ANID and LAmB can be safely co-administered.