
SAFETY AND EFFICACY OF AMBISOME IN PATIENTS WITH FUNGAL INFECTIONS. A POST MARKETING MULTICENTRE SURVEILLANCE STUDY IN TURKEY.

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Methods: From October 1997 through January 2003, a total of 550 case report forms from patients treated with AmBisome were collected.

The objective was to prospectively evaluate of the safety and efficacy of AmBisome in patients with suspected fungal infections where toxicity precludes the use of conventional amphotericin B (CAB). Fifty-six sites actively participated. Information on demographics, underlying disease, indications for use of AmBisome together with the dose, duration of therapy, evaluation of safety and treatment outcome were collected.

Results: Two hundred sixty adults, 242 children (<15 years), and 43 neonates (< 2 months) were included. Forty-one percent of the study population was female. The average age was 14.6 yrs (7 days – 78.5 yrs). The median weight was of 43 kg for adults, 21.5 kg for children , and 2 kg for neonates. In 78.2% of the patients, haematological malignancy was the underlying disease. BMT was described in 33 patients (6.4%). In 157 of 270 patients with a suspected fungal infection, the diagnosis was considered confirmed: 124 patients with *Candida* (21 were neonates), 29 with *Aspergillus*, one *Cryptococcus*, two *Mucor* and one *Trichosporon* infections. Forty- eight *Candida* infections were identified as *C. albicans*, in 21 patients a non-*albicans* species was identified, and in 55 patients no species was mentioned. *Aspergillus fumigatus* was mentioned for 9 patients, *A. flavus* for 5 patients, and no specification for 15 *Aspergillus* infections.

The baseline clinical diagnosis indicated: 210 patients (43.6%) had FUO, 170 patients (35.3%) had pulmonary symptoms, 123 patients (25.5%) had symptoms of haematological disease, 21 patients (4.4%) had signs of hepatic disease and 10 (2.1%) patients had symptoms of CNS disease. One or more antifungal treatments were applied to 256 (52%) patients before administration of AmBisome, primarily CAB (146 patients) and fluconazole (150 patients).

The overall AmBisome median daily dose was 1.16 mg/kg for a median duration of 14 days (2 to 185 days). The median highest dose was 1.25 mg/kg/day and given for 13 days. Of the three age groups studied, neonates on average were given the highest daily dose and for a longer period of time. The median dose in neonates was 2.0 mg/kg/day (0.1-21.4) and was given for a median of 16 days (3-28). In adults, this dose was 1.0 mg/kg/day (0.3 – 5.5) for 12 days (2 -185) and in children, 1.5 mg/kg/day (0.1-21.4) for 13 days (2 – 122).

One hundred seven side effects were described in 100 patients (18.2%). The most frequent adverse event was hypokalaemia in 49 patients (8.9%). Fever was reported in 26 patients (4.7%). The investigators considered 98 adverse events as “mild” or “moderate”, 6 events were described as “severe” and 3 as “life-threatening” . for 23 events no severity was described.

For 540 patients, information on the outcome of therapy was available: 56.5% were cured, and clinical improvement was reported for 20.9% of patients (CR + PR= 77.4%). Ninety-eight patients (18.1%) expired; in 86 (15.9%) of these patients, the underlying disease was the cause of death. Treatment failure was reported for 31 patients (22 fungal deaths, 4%).

Conclusion: AmBisome can be considered as an effective and safe treatment, with few side effects, similar to the existing literature.