ABSTRACT

BACKGROUND:

Sleeping sickness (human African trypanosomiasis [HAT]) is a neglected tropical disease with limited treatment options that currently require parenteral administration. In previous studies, orally administered pafuramidine was well tolerated in healthy patients (for up to 21 days) and stage 1 HAT patients (for up to 10 days), and demonstrated efficacy comparable to pentamidine.

METHODS:

This was a Phase 3, multi-center, randomized, open-label, parallel-group, active control study where 273 male and female patients with first stage Trypanosoma brucei gambiense HAT were treated at six sites: one trypanosomiasis reference center in Angola, one hospital in South Sudan, and four hospitals in the Democratic Republic of the Congo between August 2005 and September 2009 to support the registration of pafuramidine for treatment of first stage HAT in collaboration with the United States Food and Drug Administration. Patients were treated with either 100 mg of pafuramidine orally twice a day for 10 days or 4 mg/kg pentamidine intramuscularly once daily for 7 days to assess the efficacy and safety of pafuramidine versus pentamidine. Pregnant and lactating women as well as adolescents were included. The primary efficacy endpoint was the combined rate of clinical and parasitological cure at 12 months. The primary safety outcome was the frequency and severity of adverse events. The study was registered on the International Clinical Trials Registry Platform at www.clinicaltrials.gov with the number ISRCTN85534673.
FINDINGS/CONCLUSIONS:

The overall cure rate at 12 months was 89% in the pafuramidine group and 95% in the pentamidine group; pafuramidine was non-inferior to pentamidine as the upper bound of the 95% confidence interval did not exceed 15%. The safety profile of pafuramidine was superior to pentamidine; however, 3 patients in the pafuramidine group had glomerulonephritis or nephropathy approximately 8 weeks post-treatment. Two of these events were judged as possibly related to pafuramidine. Despite good tolerability observed in preceding studies, the development program for pafuramidine was discontinued due to delayed post-treatment toxicity.


Links: