

IN VITRO AND IN VIVO ACTIVITY OF ALBACONAZOLE

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Albaconazole (ALBA, UR-9825) is a new, broad-spectrum triazole antifungal agent presently under clinical investigation. We have studied the *in vitro* and *in vivo* activity of ALBA compared to that of other azole compounds.

In vitro activity: MICs of ALBA, fluconazole (FLU), itraconazole (ITR), voriconazole (VOR) and ravuconazole (RAV) were determined in several studies by the NCCLS microbroth dilution method against clinical yeasts (255 isolates for ALBA and VOR, 158 isolates for RAV and 97 isolates for FLU and ITR). ALBA was the most active compound with a MIC₅₀ of 0.03 µg/ml, which was slightly lower than the MIC₅₀ obtained for VOR and RAV (0.06 µg/ml for both drugs) and clearly lower than ITR (MIC₅₀ 0.5 µg/ml) and FLU (MIC₅₀ 2 µg/ml). The *in vitro* activity of ALBA against 30 isolates of filamentous fungi including *Aspergillus ssp* and dermatophytes was comparable to that of VOR and ITR and higher than FLU. Geometric means of MICs were 0.31 µg/ml for ALBA, 0.29 µg/ml for VOR, 0.41 µg/ml for ITR and 22.6 µg/ml for FLU.

In vivo activity: ALBA administered orally showed potent anti-*Candida* and anti-*Aspergillus* activity *in vivo*. It reduced dose-dependently (0.5-20 mg/kg/day) *Candida albicans* burdens in the kidneys and lungs of infected rabbits with a potency about 25-fold that of FLU. ALBA showed similar efficacy compared to FLU in a model of systemic candidosis in rats. ALBA also demonstrated good *in vivo* activity in a systemic aspergillosis (*A. fumigatus*) model in immunosuppressed rats, reducing significantly the fungal burden in the livers of the animals in a clear dose-dependent manner (1-50 mg/kg, bid). At the highest dose tested ALBA eradicated the fungus from the liver. Other investigators have reported ALBA to be also very active in animal models of Cryptococcosis, Scedosporiosis and Chagas' disease.

Conclusion: ALBA shows a very high *in vitro* and *in vivo* activity against a wide variety of pathogenic fungi. These results suggest that albaconazole may be clinically effective in the treatment of human fungal infections. Clinical trials are in progress.