

CLINICAL EXPERIENCE OF CASPOFUNGIN AND CYCLOSPORIN A (CsA) IN PATIENTS TREATED IN CASPOFUNGIN CLINICAL TRIALS

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Objective: In a Phase I study in healthy subjects, mild transient elevations in ALT had been seen in 5 of 12 subjects after a single day of concomitant dosing with caspofungin and CsA. As a result of this finding, use of CsA with caspofungin is not recommended unless the benefit to the patient outweighs the potential risk. The caspofungin salvage invasive aspergillosis (IA) protocol and compassionate use protocol (CUP) were amended in 2001 to obtain additional data on use of caspofungin and CsA in patients treated in a setting with appropriate risk-benefit.

Methods: The caspofungin salvage IA study and CUP enrolled patients with documented invasive fungal infections (IFI) who were refractory to or intolerant of standard antifungal therapies. Patients who were receiving CsA could be enrolled in the study provided their AST and ALT were < 3 times normal at study entry. Liver enzymes (ALT, AST, alkaline phosphatase) were to be monitored every other day for the first 14 days of caspofungin plus CsA therapy and twice weekly thereafter. The dosing regimen for patients on CsA was caspofungin 35 mg daily, after a loading dose of 70 mg on day 1.

Results: Data on 6 patients who received concomitant CsA and caspofungin are available. The patients were all adults with mean age of 48 years. Five had undergone allogeneic hematopoietic stem cell transplants and one had received a kidney transplant. All had IA (5 with pulmonary and 1 with sinus involvement); 5 were refractory to at least 1 other antifungal agent. Patients received concomitant therapy with caspofungin and CsA for 2 to 56 days. Five patients were receiving CsA in the prestudy period prior to the onset of caspofungin therapy; one patient was started on CsA while receiving caspofungin. During careful monitoring, none of the patients had elevations in serum transaminases on caspofungin plus CsA therapy, and no patient had concomitant therapy discontinued or interrupted due to a drug-related adverse event.