Safety and Pharmacokinetics of Single and Multiple Doses of CD101 IV: Results from Two Phase 1 Dose-Escalation Studies

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ABSTRACT
Introduction: CD101 (formerly known as CR001) is a novel antimicrobial in development for once-daily, intravenous treatment of invasive fungal infections. CD101 has potent in vitro activity against Candida spp., Aspergillus spp., and other fungal pathogens. CD101 is a novel once-daily intravenous (IV) fungal therapeutic for invasive fungal infections.

Methods: Sequential cohorts of 8 healthy subjects (n=6, active; n=2, placebo) received single (50, 100, 200, 300, 400 mg) or multiple (180 mg/200 mg dose cohorts) on Days 1, 8, and 15. Safety, tolerability, pharmacokinetics, and pharmacodynamics were assessed by adverse events (AEs), vital signs, physical exams, electrocardiograms (ECGs), and safety laboratory values up to 21 days post dosing.

Results: Overall incidence of AEs in the CD101 IV and placebo groups were similar. The majority of AEs were mild, and all events resolved. The 400 mg 3-day group of the multiple dose study had slightly higher incidences of AEs and related treatment emergent adverse events (TEAEs). In this study, there were no clinically meaningful changes in laboratory values, physical exams, and no deaths. Serious AEs, severe AEs, or withdrawals due to AEs were not observed. Plasma exposures were dose dependent. CD101 IV demonstrated linear pharmacokinetics that may improve treatment outcomes and is a potential therapeutic for treatment of invasive fungal infections.

INTRODUCTION
CD101 is a novel antimicrobial being developed for treatment of invasive fungal infections as a once-daily, intravenous therapy that provides high efficacy and safety profile. CD101 has potent in vitro activity against Candida spp. and Aspergillus spp. and demonstrated high efficacy and safety profile in multiple animal studies.

Methods: Sequential cohorts of 8 healthy subjects (n=6, active; n=2, placebo) received single (50, 100, 200, 300, 400 mg) or multiple (180 mg/200 mg dose cohorts) on Days 1, 8, and 15. Safety, tolerability, pharmacokinetics, and pharmacodynamics were assessed by adverse events (AEs), vital signs, physical exams, electrocardiograms (ECGs), and safety laboratory values up to 21 days post dosing. CD101 IV demonstrated high plasma exposures that may improve treatment outcomes and is a potential therapeutic for treatment of invasive fungal infections.

RESULTS
Safety
Adverse Events
No SAEs, severe AEs, study withdrawals due to an AE, or deaths in either study
No dose-response trends in treatment-emergent AEs (TEAEs) or TEAEs related to study drug or placebo (blinded phase I trial).
Relatively higher incidence of TEAEs observed in the group receiving 400 mg x 3 doses.

Pharmacokinetics
CD101 IV demonstrated dose proportional increases in AUC and Cmax values that are consistent with the dose of 400 mg and 180 mg/200 mg with the second dose of 150 mg, resolved within minutes of infusions without sequelae or interdependence of infusions.

ACKNOWLEDGEMENTS
These Phase 2 studies established the safety and PK profile of single- and multiple-dose of CD101 IV in healthy subjects.

CD101 IV x 400 mg once daily for 3 weeks is safe and well tolerated.

Overall incidence of AEs were similar between CD101 IV and placebo groups.

There were no clinically significant trends in vital signs, physical exam, or lab findings.

CD101 IV demonstrated doserelated proportional PK with a long half-life, plasma concentrations through 408 hours after the last dose.

These data support the continued development of CD101 IV for treatment of candidia infections and candidate in the essential and outpatient settings.

REFERENCES
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