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Poster Session VI

PK/PD of antifungals and miscellaneous antibacterials

Pharmacokinetics of 100 mg/d of micafungin in patients with severe burn injuries

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Introduction: Micafungin (MCF) is an echinocandin agent with broad activity against *Candida* spp., which are frequently isolated in blood and eschar cultures of burn patients who have different pharmacokinetic characteristics of drugs given the high volume of distribution and increased renal clearance. The aim of this study was to investigate the pharmacokinetics of micafungin in plasma and burn eschar.

Methods: Prospective observational pharmacokinetic study of MCF performed during a 6 months period in eight consecutive critically ill burn patients (6 men and 2 women; aged 18 to 57 years). Median total body surface area (TBSA) burned of 50% (23-80) and median full thickness (FT) 37.5% (12 to 70). MCF 100 mg/d by intravenous infusion over 1-h during 5 days.

In plasma concentrations were obtained: at the end of the infusion (C_{max} or peak) on day 1, immediately before next dosing (C_{min} or trough) on day 2 and C_{max} and C_{min} on days 4 and 5 of therapy.

The burn eschar tissue concentrations were obtained on day 5 of therapy 1-3 hours after MCF administration.

MCF concentrations in plasma and burn eschar were measured by a validated HPLC method.

Results: Clinical and pharmacokinetic characteristics are summarized in the table.

Conclusions: This is the first study of MCF administered at a fixed dose of 100 mg/d that investigates their pharmacokinetics in plasma and penetration into burn eschar tissue in critically ill burn patients. After the initial and repeated administration of MCF, the concentrations achieved in plasma and burn eschar tissue were higher than the reported MIC₉₀ against clinically important *Candida* species in all patients.

| Patient 1-8 TBSA (FT)% | ABSI at admission | SOFA At the first MCF administration | MCF mg/kg weight | Plasma concentration (mcg/ml) | | | | Eschar tissue (mcg/g) |
|---------------------------|----------------------|---|---------------------|-------------------------------|----------------|------------------------------|------------------------------|--------------------------|
| | | | | Cmax Dose 1 | Cmin Dose 2 | Cmin Dose 4 / Cmax Dose 4 | Cmin Dose 5 / Cmax Dose 5 | |
| 35 (20) | 9 | 1 | 1.33 | 8.62 | 0.76 | 0.78/8.64 | 1.00/7.44 | 2.32 |
| 40 (35) | 8 | 6 | 2.0 | 8.54 | 1.10 | 2.05/8.98 | 1.84/9.39 | 0.14 |
| 23 (16) | 8 | 2 | 1.25 | 6.44 | 0.83 | 1.12/5.82 | 1.21/10.31 | 0.10 |
| 70 (40) | 12 | 6 | 1.11 | 3.93 | 0.52 | 1.24/7.53 | 0.83/4.53 | 0.43 |
| 23 (12) | 7 | 5 | 1.25 | 7.47 | 1.82 | 1.37/7.01 | 1.43/7.95 | 0.58 |
| 70 (60) | 11 | 5 | 1.17 | 3.37 | 0.51 | 0.61/6.51 | 0.85/4.95 | 1.47 |
| 80 (70) | 12 | 5 | 1.05 | 3.78 | 0.39 | 0.85/3.40 | 0.38/4.02 | 0.25 |
| 60 (50) | 10 | 2 | 1.42 | 4.78 | 0.53 | 0.82/4.49 | 1.05/4.27 | 0.23 |