Analysis of early outcomes in the STRIVE Trial of rezafungin once-weekly treatment of candidaemia and invasive candidiasis

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Background: Front-loading of antimicrobials (ie, achieving and maintaining high drug exposure early in therapy) has been shown to be a pharmacometric determinant of efficacy. Rezafungin is a novel echinocandin that demonstrates a long half-life and front-loaded plasma exposures. The Phase 2 STRIVE trial (NCT02734862) evaluated the safety and efficacy of rezafungin once weekly (QWk) compared with once daily (QD) caspofungin in the treatment of candidaemia and/or IC. Secondary efficacy endpoints were evaluated to assess treatment response throughout the course of therapy, including at Day 5, by which point patients had either received one dose of QWk rezafungin or 5 doses of QD caspofungin.

Materials/methods: Adults (≥18 y) with systemic signs and mycological confirmation of candidemia and/or IC were randomized to receive rezafungin 400 mg QWk, rezafungin 400 mg on Week 1 followed by 200 mg (400 mg/200 mg) QWk, or caspofungin 70 mg on Day 1 followed by 50 mg QD for ≥14 days. Overall response (resolution of clinical signs of infection + mycological eradication) at Day 5 and time to negative blood culture were determined for rezafungin (pooled), as both groups received 400 mg in Week 1 versus caspofungin.

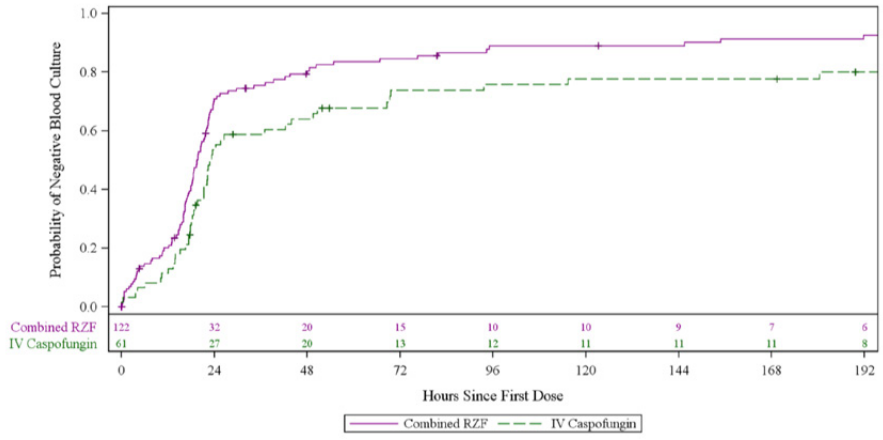
Results: At Day 5, the rate of overall success was 62.3% (76/122) for rezafungin and 55.7% (34/61) for caspofungin (Table). Rates of mycological cure at Day 5 were 69.7% and 62.3%, respectively. Rezafungin-treated patients demonstrated a shorter time to negative blood culture (median: 19.5 hours versus 22.8 hours for caspofungin, log-rank p=0.02) (Figure). While small differences favoring rezafungin were noted initially, the probability of a negative blood culture reached its maximum difference about 24 hours after the first dose.

Conclusions: Early efficacy of rezafungin was demonstrated based on outcomes of overall success, mycological success and time to negative blood culture. These findings support front-loaded plasma exposure as a pharmacometric determinant of efficacy and the development of rezafungin for treatment of candidaemia and IC.

Table. Efficacy Outcomes at Day 5 in the STRIVE Phase 2 Trial

Outcome at Day 5	Rezafungin 400 mg/400 mg QWk N= 76	Rezafungin 400 mg/200 mg QWk N= 46	Rezafungin QWk Pooled N=122	Caspofungin 70 mg/50 mg QD N= 61
	n (%)			
Overall success	42 (55.3)	34 (73.9)	76 (62.3)	34 (55.7)
Mycological Cure	50 (65.8)	35 (76.1)	85 (69.7)	38 (62.3)

Figure. Time to Negative Blood Culture following Treatment with Rezafungin vs Caspofungin



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