Rezafungin Treatment of Candidemia and Invasive Infections: Outcomes Stratified by Baseline Renal Function – Analysis of the Phase 2 + Phase 3 Trials

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INTRODUCTION

- Rezafungin is a next-generation echinocandin in development for the treatment of candidemia and invasive candidiasis (IC) and for the prevention of invasive fungal disease caused by Candida, Aspergillus, and Pneumocystis spp. in patients undergoing bone and marrow transplantation.
- Rezafungin once weekly (QWk) was compared with caspofungin once daily (QD) in two double-blind, randomized, controlled trials of candidemia and/or IC: STRIVE (Phase 2, NCT02734862; primary endpoint: overall cure [defined as resolution of clinical signs of candidemia/IC and mycological eradication]) and ReSTORE (Phase 3, NCT03667690; primary endpoint: US – all-cause mortality at Day 30; EU – global cure [defined as clinical and radiological cure and mycological eradication]) at Day 14.1,3
- In a previous analysis from the STRIVE study, the pharmacokinetics of rezafungin were unchanged by renal function (creatinine clearance rate [CrCL] <60 mL/min vs. ≥60 mL/min).4
- Here we report the patient-level meta-analyses of efficacy and safety data from both STRIVE and ReSTORE in which outcomes were stratified by renal function at baseline.

METHODS

- STRIVE and ReSTORE methods were previously described.1,3,5 This analysis of data from both trials compared patients who received rezafungin QWk (400 mg on Week 1, then 200 mg) with those who received caspofungin QD (70 mg on Day 1 followed by 50 mg with optional step-down to oral fluconazole) for ≥14 days (up to 4 weeks).
- Data were stratified by renal function at baseline according to CrCl ≥60 mL/min (normal/mild impairment) and CrCl <60 mL/min (moderate/severe impairment).
- Outcomes included in the integrated analysis were mycological eradication at Day 5 and Day 14, 30-day all-cause mortality and incidence of treatment-emergent adverse events (TEAEs). Differences were evaluated between the CrCl categories and treatment groups.

RESULTS

Patient Demographics

- Demographics and baseline characteristics were comparable in the rezafungin (N=139) and caspofungin (N=155) groups in the pooled analysis (Table 1).
- The proportions of patients with normal/mild and moderate/severe renal function were comparable between treatment groups (Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Rezafungin (N=139)</th>
<th>Caspofungin (N=155)</th>
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</thead>
<tbody>
<tr>
<td>Age, mean years ± SD, (range)</td>
<td>59.8 ± 15.7 (19, 91)</td>
<td>60.8 ± 15.0 (20, 93)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>49 (35.3)</td>
<td>65 (41.9)</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td>100 (71.9)</td>
<td>115 (74.2)</td>
</tr>
<tr>
<td>Invasive candidiasis</td>
<td>39 (28.1)</td>
<td>40 (25.8)</td>
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<tr>
<td>Baseline renal function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal/mild (CrCl ≥60 mL/min)</td>
<td>75 (55.4)</td>
<td>83 (53.5)</td>
</tr>
<tr>
<td>Moderate/severe (CrCl &lt;60 mL/min)</td>
<td>54 (38.8)</td>
<td>59 (38.1)</td>
</tr>
</tbody>
</table>

*All patients who received any amount of study drug and with documented Candida infection. mITT=modified intent-to-treat.

Mycological Eradication

- The proportion of patients achieving mycological eradication with rezafungin was comparable in patients with normal/mild vs. moderate/severe renal impairment at Day 5 and Day 14 (Figure 1).
- Eradication rates with rezafungin vs. caspofungin were comparable in patients with normal/mild renal impairment but were higher with rezafungin in the moderate/severe category.

All-Cause Mortality at Day 30

- All-cause mortality at Day 30 in rezafungin-treated patients was lower in those with moderate/severe compared with normal/mild renal impairment (Figure 2).
- Conversely, for the caspofungin treatment group, all-cause mortality was higher for moderate/severe vs. normal/mild impairment.
- All-cause mortality was lower for rezafungin vs. caspofungin in patients with moderate/severe renal impairment.

Adverse Events

- Rates of TEAEs were generally higher for patients with moderate/severe vs. normal/mild renal impairment; these differences were observed for both rezafungin and caspofungin (Table 2).

CONCLUSIONS

- The efficacy of rezafungin was comparable in patients with normal/mild vs. moderate/severe impairment in baseline renal function.
- In patients with moderate/severe renal impairment who received rezafungin, mycological eradication was higher, and 30-day all-cause mortality was lower, compared with caspofungin-treated patients with moderate/severe renal impairment.
- Further analyses are needed to evaluate the observed differences between treatment groups.

REFERENCES


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