The Safety of Iclaprim among Diabetic Patients for the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSI): Pooled REVIVE Studies

D.B. Huang, T.L. Holland, W. O’Riordan, T. Lodise, L. Berne

INTRODUCTION

• Diabetes is a risk factor for ABSSSI.
  • Patients with diabetes have worse outcomes with increased clinical failures and longer hospitalizations than patients without diabetes [1, 2].
  • In two Phase 3 trials (REVIVE-1 and REVIVE-2) iclaprim has shown clinical response comparable to vancomycin among patients treated for ABSSSI [3,4].
  • The objective of this post-hoc analysis was to determine the safety of iclaprim versus vancomycin in the treatment of ABSSSI among patients with diabetes.

METHODS

• A pooled analysis from two Phase 3, randomized, double-blind studies (REVIVE-1 and REVIVE-2) that evaluated the safety and efficacy of intravenous iclaprim versus vancomycin in the treatment of ABSSSI suspected or confirmed to be due to Gram-positive pathogens was conducted.
  • All patients with diabetes were evaluated for safety on the basis of medical history and physical examinations, routine electrocardiography, laboratory tests, urinalysis and reports of clinical adverse events (AEs).
  • While blinded to treatment assignment, the investigator categorized the severity of each AE and the relationship to study drug.
  • Baseline renal impairment was determined by Cockcroft-Gault formula.

RESULTS

11% (127/1198) of ITT patients in the REVIVE studies had diabetes.
  • Slightly more patients with diabetes were treated with vancomycin (n=71) than with iclaprim (n=56).
  • Renal impairment was common among patients with diabetes in the pooled REVIVE ITT population.
  • Mild, or moderate to severe renal impairment was reported in 22/56 (39.2%) of diabetic patients in the iclaprim group and 26/71 (36.6%) in the vancomycin group. (Table 1).

Table 1. Baseline renal function of ABSSSI patients with diabetes (ITT population).

<table>
<thead>
<tr>
<th>Creatinine Clearance, n (%)</th>
<th>REVIVE-1</th>
<th>REVIVE-2</th>
<th>Pooled REVIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iclaprim (n=20)</td>
<td>VAN (n=34)</td>
<td>Iclaprim (n=36)</td>
<td>VAN (n=36)</td>
</tr>
<tr>
<td>≥ 90 ml/min</td>
<td>11 (55.0)</td>
<td>20 (57.1)</td>
<td>22 (61.1)</td>
</tr>
<tr>
<td>60-89 ml/min</td>
<td>8 (40.0)</td>
<td>7 (20.0)</td>
<td>8 (22.2)</td>
</tr>
<tr>
<td>15-59 ml/min</td>
<td>1 (5.0)</td>
<td>6 (17.1)</td>
<td>5 (13.8)</td>
</tr>
</tbody>
</table>

Overall, AEs were numerically lower in the iclaprim group compared with the vancomycin group (Table 2).

• Three patients with diabetes who were treated with vancomycin developed acute kidney injury/increased blood creatinine levels, whereas no patients treated with iclaprim developed these renal AEs in the REVIVE studies.
• Discontinuation of study drug due to an AE was reported in 3.6% (2/56) of patients treated with iclaprim versus 10.0% (7/70) of patients treated with vancomycin.

CONCLUSIONS

• Renal impairment was common among patients with diabetes in the ITT population of the REVIVE studies (37.8%).
  • Overall, there were numerically lower AEs in the diabetic patients treated with iclaprim (48.2%) compared with vancomycin (52.9%).
  • Lower numbers of treatment-related AEs were reported in those treated with iclaprim compared with vancomycin (8.9% vs 15.7%).
  • Diabetic patients, particularly those with renal impairment, may be vulnerable to vancomycin related AEs, including nephrotoxicity.
  • Further evaluation is warranted, given the frequent occurrence of diabetes among hospitalized ABSSSI patients, and the broad use of vancomycin in hospital settings.

REFERENCES

CONTACT
David B. Huang, MD, PhD
Motif BioSciences Inc.
5 Independence Way, Suite 300
Princeton, NJ 08540
David.huang@motifbio.com