**Abstract**

Oritavancin (ORI) is a lipoglycopeptide antibiotic characterized by rapid, concentration-dependent bactericidal activity against gram-positive bacteria including methicillin-resistant Staphylococcus aureus (MRSA). The efficacy and safety of ORI have been assessed in over 3000 patients and healthy volunteers. The current study was designed to generate cardiac safety data for ORI in healthy volunteers.

**Methods**

The current study was designed to generate cardiac safety data for ORI in healthy volunteers. A total of 21 healthy subjects enrolled in each arm of the dose escalation phase of the study. Systolic blood pressure and heart rate were monitored continuously. ECGs were obtained at 0.5, 3, 3.5, 4, 5, 6, 7, 9, 11, 15, 24, and 24+ hours after the start of the infusion.

**Results**

The cardiac safety of oritavancin was previously evaluated in a Phase I, double-blind, randomized, placebo-controlled, parallel design study with an open label positive control (moxifloxacin) to evaluate the safety and tolerability of oritavancin at doses of 350 mg every 12 hours. A total of 21 subjects were randomized to one of the following: ORI 150 mg, 300 mg, 600 mg, 1200 mg, or placebo. Twelve ECGs were obtained from each subject in the ORI group (500 mg, 1000 mg, 1200 mg, 1500 mg, 1800 mg) every 12 hours after the start of the infusion.

**Conclusions**

The current study was designed to generate cardiac safety data for oritavancin (ORI) in healthy volunteers. A total of 21 subjects enrolled in each arm of the dose escalation phase of the study. Systolic blood pressure and heart rate were monitored continuously. ECGs were obtained at 0.5, 3, 3.5, 4, 5, 6, 7, 9, 11, 15, 24, and 24+ hours after the start of the infusion.

The cardiac safety of oritavancin was previously evaluated in a Phase I, double-blind, randomized, placebo-controlled, parallel design study with an open label positive control (moxifloxacin) to evaluate the safety and tolerability of oritavancin at doses of 350 mg every 12 hours. A total of 21 subjects were randomized to one of the following: ORI 150 mg, 300 mg, 600 mg, 1200 mg, or placebo. Twelve ECGs were obtained from each subject in the ORI group (500 mg, 1000 mg, 1200 mg, 1500 mg, 1800 mg) every 12 hours after the start of the infusion.

**Drug Exposure**

Mean ± (SD) plasma oritavancin concentration-time profile

**ECG Parameters (Pharmacokinetic Population)**

| Parameter | ORI (mg) | Placebo
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (g/L)</td>
<td>2.53 ± 0.85</td>
<td>0.20 ± 0.18</td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>2.02 ± 0.58</td>
<td>1.50 ± 0.50</td>
</tr>
<tr>
<td>CL (L/hr)</td>
<td>1.02 ± 0.18</td>
<td>0.67 ± 0.12</td>
</tr>
<tr>
<td>Vss (L)</td>
<td>2.02 ± 0.58</td>
<td>1.50 ± 0.50</td>
</tr>
</tbody>
</table>

**EFGIS (mg) (Oritavancin)**

| Parameter | ORI (mg) | Placebo
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (g/L)</td>
<td>2.53 ± 0.85</td>
<td>0.20 ± 0.18</td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>2.02 ± 0.58</td>
<td>1.50 ± 0.50</td>
</tr>
<tr>
<td>CL (L/hr)</td>
<td>1.02 ± 0.18</td>
<td>0.67 ± 0.12</td>
</tr>
<tr>
<td>Vss (L)</td>
<td>2.02 ± 0.58</td>
<td>1.50 ± 0.50</td>
</tr>
</tbody>
</table>

**Safety**

Oritavancin administered as a single infusion at a supratherapeutic dose of 1500 mg was well tolerated. A higher percentage of adverse events was reported in the oritavancin group compared to the placebo group. The most common adverse events were nausea (41.7%), vomiting (21.7%), and headache (19.4%). There were no significant changes in vital signs, laboratory tests, or electrocardiographic parameters.

**References**