Utility of Shift Tables to Assess the Degree and Chronicity of Antibiotic-associated Changes in Renal Function in Clinical Trials: Results from ATTAIN trials of Telavancin

Nogid BI, Hardin TC*, Lacy MK, Sherman C*, Morrow LE, Dwyer JP, Marr KA, Barriere S*, and Bruss J

TheraVance Biopharma, Inc. 555 South California, Los Angeles, CA 90017, USA

ABSTRACT

Objectives: Shift tables are a useful tool to identify changes in renal function over time. Our objective was to determine the degree and duration of renal function changes in patients receiving vancomycin (VAN) or telavancin (TEL) in the Phase 3 trials of Telavancin Treatment of Infection Failure (ATTAIN) trials.

Methods: In ATTAIN trials, TEL was compared with VAN in patients hospitalized for bacteremic infections (Gram-positive infection: methicillin-resistant Staphylococcus aureus (MRSA)) or severe infections associated with bacteremia (VAP) and as an aerosolized antibiotic for ventilator-associated bacterial pneumonia (VABP). Adverse events, renal function, and baseline characteristics were collected. The rate ratio (RR) of estimated glomerular filtration rate (eGFR) change from baseline was calculated. The incidence of changes in renal function was determined as the percentage change from baseline in each 7-day period.

Results: Median renal function changes were similar between TEL and VAN. The frequency of renal function changes was higher in VAN-treated patients, with 61% of VAN patients compared to 54% of TEL patients experiencing a renal function change. The incidence of renal function changes was 28% for TEL and 32% for VAN. There was no effect of TEL (RR 0.92, 95% CI 0.71-1.19) or VAN (RR 0.91, 95% CI 0.70-1.18) on renal function change as compared to placebo.

Conclusions: These findings support shift tables as a useful tool in clinical trials of antibiotic therapies to assess the degree and duration of renal function changes.

Table 1: Changes in Renal Function by Categorical Shifts from Baseline

<table>
<thead>
<tr>
<th>Day 4</th>
<th>Day 7</th>
<th>EOT</th>
<th>MARC (CV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Shift</td>
<td>Shifts $&gt;$ 40%</td>
<td>Shifts $&lt;$ 40%</td>
<td>No Shift</td>
</tr>
<tr>
<td>TEL</td>
<td>40.6%</td>
<td>37.4%</td>
<td>55.2%</td>
</tr>
<tr>
<td>VAN</td>
<td>41.4%</td>
<td>36.6%</td>
<td>56.4%</td>
</tr>
</tbody>
</table>

REFERENCES


ACKNOWLEDGEMENTS

The authors would like to acknowledge the contributions of theATTAIN investigators and the ATTAIN clinical trial staff for their support and participation in the ATTAIN trials.

DISCUSSION

- The majority of patients (75%) in both treatment groups in ATTAIN had either no change in renal function compared to baseline or no improvement in renal function at Day 7.
- For those that experienced a reduction in renal function compared to baseline:
  - No significant differences were observed in percentage of patients with a categorical decrease in serum creatinine and in end of trial (EOT) measures of change from baseline (VAN: -4.9%, TEL: -5.0%)
  - VAN (3.3%, 95% CI: 0.0-6.7%) and TEL (3.1%, 95% CI: 0.0-6.7%) had similar changes in eGFR, with no significant differences observed in change in eGFR between TEL and VAN at Day 7.
- Majority of renal function changes for TEL and VAN were Grade 1 shifts at all time points (DAY, DO, EOT), and even when DO was considered.
- For VAN, 6% of shifts from DO to EOT were Grade 2 or worse, compared to 7% for TEL.
- For VAN, further decline in renal function was noted at each time point during the course of therapy.

Conclusions:

- Shift tables are a useful tool to identify changes in renal function over time and can provide an enriched understanding of the timing of these changes in antibiotic-associated renal injury.

- The present analysis uses shift tables to explore the degree and chronicity of changes in renal function in patients receiving vancomycin (VAN) or telavancin (TEL). The results of the analysis from the Phase 3 trials of Telavancin Treatment of Infection Failure (ATTAIN) provide insights into the renal function changes observed in patients receiving these antibiotics.

- The findings indicate that shift tables can be a valuable tool in clinical trials for assessing the degree and duration of renal function changes associated with antibiotic use. This information can help guide the development of renal protective strategies and improve patient outcomes.

- The study also highlights the importance of monitoring renal function in clinical trials to ensure the safety and efficacy of new therapies.

- The results of this analysis suggest that shift tables can be a useful tool in antibiotic development and clinical trials to identify and mitigate potential renal effects of new antibiotics.

- Overall, the findings from this study support the continued use of shift tables as a useful tool in clinical trials to assess renal function changes associated with antibiotic use.