Dalbavancin is a lipoglycopeptide antibiotic with activity against Gram-positive pathogens and a long half-life allowing for weekly dosing. Dalbavancin was designed to reflect vancomycin (VAN) with option to switch to oral linezolid for the treatment of ABSSSI. We evaluated outcomes of ABSSSI in patients treated with VAN by dosing regimen utilized and serum trough concentrations for VAN.

**METHODS**

Both trials were double-blind, double dummy, pharmacist-unblinded randomized trials in which patients with ABSSSI were randomized to receive dalbavancin 1g IV on Day 1 and 500 mg on Day 8 or VAN 1g (or 15mg/kg) IV every 12 hours (q12h) for at least 3 days with an option to extend oral dosing of up to 800 mg q12h to complete 14 days of therapy. The primary endpoint was measured at 48-72 hours of therapy with success requiring cessation of spread of the infection and absence of fever for at least 2 days after stop of treatment. Outcomes by fixed versus weight-based dosing regimens of VAN and outcomes by serum VAN trough concentrations were analyzed.

**RESULTS**

Clinical response rates for patients with ABSSSI were similar in patients treated with a fixed-dose regimen or weight-based dosing regimen of vancomycin. No association was observed between serum vancomycin trough concentrations and efficacy outcomes at the 48-72 hour time point or at EOT.

**CONCLUSIONS**

• The majority of patients in the vancomycin treatment group received a fixed-dose regimen of 1 gram IV twice daily, consistent with medical practice outside of the US.

• The weight-based dosing regimen of vancomycin was more frequently used in North America, where most patients were treated in the outpatient setting.

• Baseline patient characteristics of age, gender, race and BMI were similar among patients in the fixed-dose regimen and weight-based dosing subgroup regimens.

• No association was observed between the sub-type of infection and the choice of either weight-based or fixed vancomycin dosing regimens.

• Adverse events rates were similar with each dosing approach.

• No association with either safety or efficacy outcomes was observed for patients with vancomycin trough levels ≤ 10 µg/ml; note that most patients were dosed for < 10 days with vancomycin.

• Fixed dose administration of vancomycin was associated with higher rates of nephrotoxicity.

• Weight based dosing was associated with a lower incidence of elevations in creatinine.

**DISCUSSION**

Phase 3 Program Trial Design

- Primary Efficacy Measure: Clinical response at completion of therapy
- Secondary Efficacy Measures:
  - Clinical success at 48-72 hours
  - Clinical success at 14 days
  - Absence of fever at 3 consecutive recordings q6h
- Duration of Therapy:
  - Fixed-dose regimen: 1g IV on Day 1 and 500 mg IV on Day 8
  - Weight-based regimen: 1g IV on Day 1 and 500 mg IV on Days 1, 8, 15, and every 2 weeks thereafter

**METHODS**

- Vancomycin dosing approach was performed according to the local standard of care
- Weight-based dosing was associated with a lower incidence of elevations of serum creatinine

**CONCLUSIONS**

- Clinical response rates for patients with ABSSSI were similar in patients treated with either a fixed-dose or weight-based dosing regimen of vancomycin.

- Clinical success outcomes at the 48-72 hour time point were not statistically different between the two dosing regimens.

- No association was observed between a serum vancomycin trough concentration < or ≥ 10 µg/ml and either safety or efficacy outcomes.

- In these studies, weight based dosing was associated with less renal toxicity in patients treated with vancomycin.