Efficacy and Safety of High-Dose Daptomycin versus Linezolid for the Treatment of Vancomycin-Resistant Enterococcus (VRE) Bacteremias: A Retrospective Study

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BACKGROUND
- Vancomycin-resistant Enterococcus (VRE) bacteremia has become a major concern in the nosocomial setting
- Currently, daptomycin and linezolid are two common options to treat VRE bacteremia infections with resistance to ampicillin
- Studies suggest linezolid and standard dose daptomycin (6 mg/kg) have similar clinical outcomes for treatment of VRE bacteremia
- A comparison of high-dose (HD) daptomycin (>6 mg/kg) to linezolid may provide insight into another treatment option
- To our knowledge, there are currently no published studies that evaluate the efficacy and safety of high-dose daptomycin compared to linezolid for the treatment of VRE bacteremia

OBJECTIVE

To compare the efficacy and safety of high-dose daptomycin to linezolid for the treatment of VRE bacteremia

MATERIALS AND METHODS

Study Design & Data Collection
- This is a retrospective health outcomes study utilizing electronic medical chart review of eligible patients admitted to New York Methodist Hospital
- The primary investigator screened microbiology reports containing positive enterococcal blood cultures from January 2011 to March 2015 for potential patients to be included in this analysis
- Pertinent information of patients were obtained from Cerne® including baseline demographics and clinical characteristics
- To promote the efficacy and safety of high-dose daptomycin compared to linezolid for the treatment of VRE bacteremia

Primary Efficacy Endpoints
- Microbiological clearance: At least one negative blood culture for VRE after targeted treatment initiation and remains negative while on targeted therapy
- Clinical response (needs to meet all three criteria):
  1. Resolution or improvement of baseline signs & symptoms
  2. Blood cultures remain negative at the end of targeted therapy
  3. No additional anti-VRE antibiotics were given for treatment of VRE bacteremia due to lack of clinical response

Secondary Efficacy Endpoints
- 10-Day Mortality
- Infection Related Mortality
- Overall Mortality
- 30-Day Readmission
- Time to First Negative Culture from Initiation of Targeted Therapy
- Length of Hospital Stay from Initiation of Targeted Therapy
- Overall Hospital Length of Stay

Safety Endpoints
- Adverse Event Profile
- Anemia (Hb < 13 g/dL for males and <12 g/dL for females)
- Thrombocytopenia (platelets < 100,000/mm³)
- Neutropenia (absolute neutrophil count [ANC] < 1000)
- Elevated Creatine Phosphokinase (>120 µL/L)
- Hypomagnesemia
- Renal Insufficiency
- Discontinuation due to an Adverse Drug Event

RESULTS

Table 1. Baseline Demographics
- **Characteristics**: HD Daptomycin (n = 25) vs. Linezolid (n = 25)
- **p-value**: 0.95, 0.22, 0.75, 0.55
- **Demographics**:
  - Age: 64.9 (± 9.2) vs. 74.1 (± 9.5)
  - Gender ratio: Male (73.3%) vs. 61.5% (± 32.2%)
  - Height (in): 67.2 (± 4.8) vs. 67.2 (± 4.8)
  - BMI (kg/m²): 24.9 (± 4.8) vs. 24.9 (± 4.8)
- **Location Prior to Hospital Admission**:
  - Home: 64.5% vs. 64.5%
  - Nursing Home: 43.6% vs. 43.6%
  - VAE: 0% vs. 0%
  - Hospital: 19% (± 24%) vs. 37.5% (± 24%)
- **Comorbidity Index**:
  - CCI: 7.8 (± 4.2) vs. 7.3 (± 4.2)

Table 2. Microbiological Susceptibilities
- **Enterococcus species**:
  - faecalis: 3 (12%) vs. 6 (24%)
  - faecium: 12 (75%) vs. 19 (76%)
  - Clindamycin: 1 (6.3%) vs. 0 (0%)

Table 3. Microbiology
- **Microbiology**:
  - HD Daptomycin (n = 25): 6.67 vs. Linezolid (n = 25): 203.6

Table 4. Secondary Efficacy Endpoints
- **Secondary Endpoints**: HD Daptomycin (n = 25) vs. Linezolid (n = 25)
- **p-value**: 0.1, 0.34, 0.22
- **Other Hematologic**: Neutropenia (0%) vs. 0%
- **Drug Feasibility**: Quinupristin/Dalfopristin (%): 6 (3%) vs. 0%
- **Adverse Drug Event**: Non-severe 46.4% after initiation of Targeted Therapy

Table 5. Safety Endpoints
- **Adverse Drug Events**:
  - HD Daptomycin (n = 25): 46.4% vs. Linezolid (n = 25): 0%
- **p-value**: 0.34, 0.22, 0.75

Table 6. Microbiological Cleanout
- **Clinical Response**: 8/16 (50%) vs. 13/25 (52%)
- **Microbiological Cleanout**: 4/15 (26%) vs. 12/15 (80%)

STRENGTHS
- Clearly defined endpoints to minimize potential bias
- Examined clinically relevant adverse effects commonly associated with linezolid and daptomycin

LIMITATIONS
- Retrospective study
- Small sample size

CONCLUSIONS
- This retrospective analysis suggests the clinical response and microbiological clearance rates of high-dose daptomycin were similar to linezolid for the treatment of VRE bacteremias
- A large, randomized, prospective study comparing high-dose daptomycin and linezolid for the treatment of VRE bacteremias would provide additional insight on whether there is a difference between both therapies

DISCLOSURES
- Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
  - All authors: Nothing to disclose