No strings attached: Long-acting lipoglycopeptides considerations for gram positive infections in high-risk patients

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- ACPE requires active learning and most prefer real-time participation rather than a graded post-test
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  - PollEverywhere app: Download app and join ushp presentation
  - Text Messaging: Text ushp to 22333
- We recommend the PollEverywhere app or web browser as they are easier to respond
- For each question, you can click on the correct answer in Web Browser or App or text correct answer to 22333

Disclosure

- Relevant Financial Conflicts of Interest
  - CE Presenter, Stephani Halloran, PharmD: University of Utah Health
  - CE mentor, Ashley Cline, PharmD, BCPS: University of Utah Health
  - CE co-mentor, Karen Fong, PharmD, BCIDP, AAHIVP: University of Utah Health
- Off-Label Uses of Medications
  - Dalbavancin
  - Oritavancin
Learning Objectives - Pharmacists

- Explain: Explain the mechanism of action and pharmacokinetics of long acting lipoglycopeptides
- Evaluate: Evaluate literature for utilization of long acting lipoglycopeptides
- Identify: Identify high-risk patient characteristics who may benefit from long acting lipoglycopeptides
- Describe: Describe the pros and cons of long acting lipoglycopeptide use for treatment

Learning Objectives - Technicians

- Describe: Describe the compounding process for long acting lipoglycopeptides
- Apply: Apply beyond-use-dating requirements to compounded long acting lipoglycopeptides
- Assess: Assess the cost associated with long acting lipoglycopeptides

Patient Case

- CC: right arm pain, redness, erythema, fevers
- HPI: TJ 29-year-old male with PMH of IVDU, homelessness, and psychiatric disorders admitted for IV antibiotic therapy due to a purulent skin and soft tissue infection complicated by right arm osteomyelitis cause by methicillin-resistant S. Aureus
Background

- More than 13 million people inject drugs worldwide
- Approximately 6.5 million have injected drugs in the United States
- People who inject drugs (PWID) are 16 times more likely to develop invasive methicillin-resistant Staphylococcus aureus (MRSA) infections
- There were nearly 5 times the number of overdose deaths in 2018 compared to 2010
- More than 115,000 Americans died from overdoses related to heroin from 1999 to 2018

Injection drug use increases the risk for

- Viral, bacterial, and fungal infections
- Recurrent infections due to relapse
- Multidrug-resistant (MDR) infections
- Incomplete treatment regimens
- Frequent contact with healthcare systems

Bacterial infections in substance use disorder

- Common pathogens: *Staphylococcus aureus, streptococcus* species

<table>
<thead>
<tr>
<th>Type</th>
<th>Rate (%)</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscesses</td>
<td>59.1</td>
<td>30,064</td>
</tr>
<tr>
<td>Skin and soft tissue</td>
<td>53.8</td>
<td>10,254</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>72.4</td>
<td>33,610</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>60.4</td>
<td>22,607</td>
</tr>
</tbody>
</table>

Mechanism for developing infections

- Direct inoculation of bacteria present in the injection drug
- Introduction of commensal flora into circulation
- Transmission of pathogens via needle sharing
- Suppression of immunity
- Unsafe sexual practices
- Poverty, poor hygiene, homelessness
Summary

- Increased infection risk
- Increased morbidity and mortality

Strategies for outpatient treatment (oral and OPAT)

Long-acting Lipoglycopeptides

Clinical Considerations for Dalbavancin and Oritavancin

Cost considerations

Addiction Medicine Consult Considerations

Patient Case

What outpatient treatment options are available for TJ?

Strategies to facilitate outpatient treatment

- Transition to outpatient oral antibiotics
- Transition to outpatient parenteral antibiotics therapy (OPAT)
Limitations to oral antibiotic therapy

- Ability to adhere to dosing intervals
- Lower bioavailability of select antibiotics
- Risk of subtherapeutic concentrations

Limitations to outpatient parenteral antibiotics

- Need for IV access
- Maintenance for line care
- Knowledge of medication administration techniques
- Need for stable housing
- Risk of IV-line contamination
- Risk of IV-line misuse
- Proper medication storage
- Insurance coverage

Barriers to current strategies

- Poor candidates for outpatient oral or parenteral antibiotic therapy
- Prevents hospital discharge
- Prolonged hospital admission for parenteral antibiotic course
- Increase healthcare costs, unnecessary hospital exposure

- Psychiatric disorders
- Poor physical health
- Homelessness
- Incarceration
- Poor health insurance

Barriers to current strategies

- Psychiatric disorders
- Poor physical health
- Homelessness
- Incarceration
- Poor health insurance
New therapeutic approaches are warranted to facilitate safe and effective hospital discharge strategies for vulnerable patients.

Long-acting lipoglycopeptides may be useful antibiotics to transition patients into an outpatient setting.

Summary

- Increased infection risk
- Increased morbidity and mortality
- Many limitations to optimal management
- PWID are often poor candidates for standard outpatient therapy
- Leads to prolonged hospitalizations

Knowledge check

What high-risk characteristics contribute to prolonging length of hospitalization stays?

- Psychiatric disorders
- Poor physical health
- Homelessness
- Intravenous drug use
- All the above

Patient Case

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>Staphylococcus aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daptomycin</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>Resistant</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>Resistant</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>Pending</td>
</tr>
<tr>
<td>Dalbavancin</td>
<td>Pending</td>
</tr>
</tbody>
</table>

Susceptibility

- Daptomycin
- Linezolid
- Oxacillin
- Rifampin
- Sulfamethoxazole
- Vancomycin
- Oritavancin
- Dalbavancin
Long-acting Lipoglycopeptides

- Agents:
  - Oritavancin
  - Dalbavancin

- Semisynthetic derivatives of naturally occurring glycopeptides

- Contain lipophilic side chain on heptapeptide core which contributes to prolongs half-life

**Mechanism of action**

- Increased affinity to the D-ala-D-ala binding site
- Dimerize and stabilize binding to the peptidoglycan cell wall
- Anchor to the membrane via hydrophobic substituents
- Disrupts bacterial membrane potential (Oritavancin)

**Properties**

<table>
<thead>
<tr>
<th>Properties</th>
<th>Oritavancin (Orbactiv)</th>
<th>Dalbavancin (Dalvance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity</td>
<td>Concentration-dependent bactericidal activity</td>
<td>Concentration-dependent bactericidal activity</td>
</tr>
<tr>
<td>FDA indications</td>
<td>ABSSTI</td>
<td>ABSSTI</td>
</tr>
<tr>
<td>Dose</td>
<td>1,200 mg once</td>
<td>1,000 mg IV, then 500 mg IV a week later</td>
</tr>
<tr>
<td>Renal Adjustments</td>
<td>CrCl&lt;30 mL/min</td>
<td>None</td>
</tr>
<tr>
<td>Administration</td>
<td>3-hour IV infusion</td>
<td>30-minute IV infusion</td>
</tr>
<tr>
<td>Half-life</td>
<td>10 days</td>
<td>14 days</td>
</tr>
<tr>
<td>Warnings</td>
<td>Artificially prolong aPTT, increase warfarin exposure</td>
<td>LFT elevation</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>Headache, Nausea, Vomiting, ALT elevations</td>
<td>Nausea, Vomiting, ALT elevations</td>
</tr>
<tr>
<td>Drug Interactions</td>
<td>CYP2C9, CYP2C19 inhibitor</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>CYP3A4, CYP2D6 inducer</td>
<td>None</td>
</tr>
<tr>
<td>Contraindication</td>
<td>UFH for 5 days after use</td>
<td>None</td>
</tr>
</tbody>
</table>
## Properties

<table>
<thead>
<tr>
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<td>UFH for 5 days after use</td>
<td>None</td>
</tr>
</tbody>
</table>

## FDA Indications

- ABSSTI

## Dose

- **1,200 mg once**
- **1,000 mg IV, then 500 mg IV a week later**
- **1125 mg IV, then 750 mg a week later**

## Renal Adjustments CrCl<30 mL/min

- **None**
- **None**

## Administration

- **3-hour IV infusion**
- **30-minute IV infusion**

## Half-life

- **10 days**
- **14 days**

## Warnings

- **Artificially prolong aPTT, increase warfarin exposure**
- **LFT elevation**

## Adverse effects

- **Headache, Nausea, Vomiting, ALT elevations**
- **Nausea, Vomiting, ALT elevations**

## Drug Interactions

- **CYP2C9, CYP2C19 inhibitor CYP3A4, CYP2D6 inducer**
- **None**

## Contraindication

- **UFH for 5 days after use**
- **None**
Spectrum of Activity

<table>
<thead>
<tr>
<th>Microbiology</th>
<th>Oritavancin</th>
<th>Dalbavancin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vancomycin-resistant enterococci (VRE)</td>
<td>✓ (VanA and VanB)</td>
<td>✓ (VanB only)</td>
</tr>
<tr>
<td>Vancomycin-intermediate S. aureus (VISA)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Vancomycin-resistant S. aureus (VRSA)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Gram-positive aerobes</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Gram-positive anaerobes</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

CLSI Breakpoints

<table>
<thead>
<tr>
<th>MIC</th>
<th>Oritavancin</th>
<th>Dalbavancin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus spp.</td>
<td>≤0.12</td>
<td>≤0.25</td>
</tr>
<tr>
<td>Enterococcus faecalis (vancomycin-susceptible)</td>
<td>≤0.12</td>
<td>≤0.25</td>
</tr>
<tr>
<td>Vancomycin-resistant S. aureus</td>
<td>≤0.25</td>
<td>≤0.25</td>
</tr>
</tbody>
</table>

Compounding Oritavancin

- **Reconstitution**: Add 40 mL of SWFI to 3 vials.
- **Dilution**: Withdraw 120 mL from a 1000 mL bag of D5W (ONLY).
- **Storage**: Room Temperature: use within 6 hours. Refrigerator: use within 12 hours.

Compounding Dalbavancin

- **Reconstitution**: Add 25 mL of SWFI or D5W to each vial.
- **Dilution**: Transfer dose to IV bag of D5W (ONLY).
- **Storage**: Total time from reconstitution to dilution BUD: 48 hours. Store at room temperature or in the refrigerator.
Cost

**Oritavancin**
- 400 mg vial: $1,194.80
- Non-formulary

**Dalbavancin**
- 500 mg vial: $1,896.89
- Non-formulary

Summary

- Increased infection risk
- Increased morbidity and mortality
- IVDU
- Many limitations to optimal management
- PWID are often poor candidates for outpatient therapy
- Leads to prolonged hospitalizations

Patient Case

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<td>Resistant</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Sensitive</td>
</tr>
<tr>
<td><strong>Oritavancin</strong></td>
<td>No interpretation</td>
</tr>
<tr>
<td><strong>Dalbavancin</strong></td>
<td>Sensitive MIC &lt;0.25</td>
</tr>
</tbody>
</table>

Knowledge Check

What pharmacokinetic properties contribute to long-acting lipoglycopeptides prolonged duration of action?

- Increased affinity and potency
- Dimerize and stabilize binding to the peptidoglycan cell wall
- Dimers anchor to the bacterial membrane by means of their hydrophobic substituents
- Increased binding affinity to the D-ala-D-ala site
- All the above
Patient Case

Would you consider dalbavancin for management of TJ’s infection?

Let’s look at the evidence!

Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Bacteria</th>
<th>Dalbavancin</th>
<th>Standard of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>4 (5%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td>MSSA</td>
<td>38 (54%)</td>
<td>5 (50%)</td>
<td></td>
</tr>
<tr>
<td>CoNS</td>
<td>14 (20%)</td>
<td>2 (20%)</td>
<td></td>
</tr>
<tr>
<td>E. Faecalis</td>
<td>7 (10%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td>E. Faecium</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Strep spp.</td>
<td>3 (4%)</td>
<td>1 (10%)</td>
<td></td>
</tr>
<tr>
<td>Anaerobes</td>
<td>9 (10%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Population</th>
<th>Number</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, yr)</td>
<td>49 (26-79)</td>
<td>n=70</td>
<td>Dalbavancin 1,500 mg on day 1 and day 8, Standard of care twice daily for 4 to 6 weeks</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP (mean)</td>
<td>43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR (mean)</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed Infection</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debridement</td>
<td>70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety

#### mITT Primary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin (n=67)</th>
<th>Standard of Care (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure at day 42</td>
<td>65/67 (97%)</td>
<td>7/8 (87.5%)</td>
</tr>
</tbody>
</table>

#### Secondary Outcomes

| Clinical Improvement at day 21    | 63/67 (94%)        | 5/8 (62.5%)            |
| Clinical Cure at 6 months         | 63/67 (94%)        | 7/8 (87.5%)            |
| Clinical Cure at 1 year           | 63/67 (94%)        | 5/8 (62.5%)            |

#### Microbiological mITT Primary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin (n=67)</th>
<th>Standard of Care (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure at day 42</td>
<td>60/62 (96.8%)</td>
<td>7/8 (87.5%)</td>
</tr>
</tbody>
</table>

#### Secondary Outcomes

| Susceptible to treatment          | 62/62 (100%)       | 8/8 (100%)             |
| Clinical Failure                  | 0 (0%)             | 7/8 (87.5%)            |
| Clinical cure at 1 year           | 63/67 (94%)        | 5/8 (62.5%)            |

### Baseline Gram-Positive Bacteremia

<table>
<thead>
<tr>
<th>Organism</th>
<th>Dalbavancin (n=4)</th>
<th>Standard of Care (n=0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSSA</td>
<td>2 (50%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>CoNS</td>
<td>2 (50%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

### Clearance of bacteremia

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance of bacteremia</td>
<td>4 (100%)</td>
</tr>
</tbody>
</table>
Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety

All patients had elevated CRP in both treatment groups

CRP decreased in all patients by day 28

Pharmacoeconomic Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin (n=67)</th>
<th>Standard of Care (n=8)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (mean, days)</td>
<td>15.8 ± 7.1</td>
<td>33.3 ± 14.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>IV infusion (mean, hours)</td>
<td>1 ± 0.02</td>
<td>101.3 ± 20.8</td>
<td>-</td>
</tr>
<tr>
<td>Treatment duration (mean, days)</td>
<td>2.0 ± 0</td>
<td>31.6 ± 7.0</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion

• Demonstrated positive clinical efficacy rates on both the mITT and micro-mITT analyses
• Achieved clearance of blood cultures in patients with gram-positive bacteremia
• Displayed mild adverse effect profile and medication tolerance
• Identified statistically significant shorter length of stay in the dalbavancin group
• Estimates shorter total IV-infusion time and active days on therapy

Limitations

Single center study design, small sample size, descriptive, open-label and non-blinded, limited to primary osteomyelitis
Treatment of Acute Osteomyelitis with Once-Weekly Oritavancin: A Two-Year, Multicenter, Retrospective Study

Pathogens isolated (n=128)

- MRSA 92 (77%)
- MSSA 25 (21%)
- VRE 7 (5%)
- VISA 2 (1%)
- VRE (daptomycin MIC > 4) 2 (1%)

Primary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>ETE (n=134)</th>
<th>PTE (n=130)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical success</td>
<td>118 (88.1%)</td>
<td>80 (80.0%)</td>
</tr>
</tbody>
</table>

Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>ETE (n=134)</th>
<th>PTE (n=130)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical failure</td>
<td>9 (6.7%)</td>
<td>4 (3.0%)</td>
</tr>
</tbody>
</table>

Subgroups evaluated at ETE

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>4-dose regimen (n=118)</th>
<th>5-dose regimen (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical success</td>
<td>107 (90.7%)</td>
<td>11 (68.8%)</td>
</tr>
</tbody>
</table>

Baseline Gram-Positive Bacteremia

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Oritavancin (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clearance of bacteremia</td>
<td>9 (100%)</td>
</tr>
</tbody>
</table>

Conclusion

- Demonstrated low failure rates in both the ETE and PTE analysis
- Showed clinical success while including patients with co-morbidities
- Achieved clearance of blood cultures in patients with gram-positive bacteremia
- Displayed mild adverse effect profile and medication tolerance
- Included patients with all ranges of renal function without high rates of adverse effects
- A five-dose regimen may not provide additional benefit in clinical success rates

Limitations

- Retrospective, observational, non-comparative methodology

ETE: assessment 7-10 days after the end of the last dose
PTE: assessment 3 and 6 months after the end of last dose
Clinical success: resolution of symptoms or improvement in symptoms, no further need for treatment
Clinical failure: lack of improvement, need of additional antibiotics for osteomyelitis, admission to hospital for osteomyelitis, or loss to follow-up
DALBACEN cohort: dalbavancin as consolidation therapy in patients with endocarditis and/or bloodstream infection produced by gram-positive cocci

Multicenter, observational, retrospective study from 2016 to December 2017.

Population
- Patients > 18 years of age with gram-positive cocci infective endocarditis or bloodstream infection

Number
- n=83

Intervention
- Patients received at least 1 dose of dalbavancin

Characteristics
- Male: 61 (73.5%)
- Age, median (range): 73 (53-77)
- Bacteremia: 49 (59%)
- Infective Endocarditis: 34 (41%)
- Mean Charleston Index Score: 2
- DBV-covered days: 14

IE Baseline Microbiology
- CoNS: 15 (43%)
- MSSA: 7 (20%)
- MRSA: 3 (8%)
- Strep spp.: 7 (20%)
- E. faecalis: 3 (8%)

BSI Baseline Microbiology
- CoNS: 17 (34.7%)
- MSSA: 15 (30.6%)
- MRSA: 9 (18.4%)
- Strep spp.: 2 (4.1%)
- E. faecalis: 2 (4.1%)
- E. Facium: 2 (4.1%)

Primary Outcome
- Infective Endocarditis (n=34)
  - Outcomes
    - Dalbavancin
      - Clinical cure: 33 (97%)
      - Clinical failure: 1 (3%)

Secondary Outcome
- Infective Endocarditis (n=34)
  - Outcomes
    - Dalbavancin
      - 90-day relapse: 0 (0%)
      - Clinical cure at 12-months: 33 (85%)
      - Negative follow-up blood cultures (n=17): 17 (100%)

- Dalbavancin as consolidation therapy in patients with endocarditis and/or bloodstream infection produced by gram-positive cocci

Primary Outcome - Infective Endocarditis (n=34)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical cure</td>
<td>33 (97%)</td>
</tr>
<tr>
<td>Clinical failure</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

Secondary Outcome - Infective Endocarditis (n=34)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-day relapse</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Clinical cure at 12-months</td>
<td>33 (85%)</td>
</tr>
<tr>
<td>Negative follow-up blood cultures (n=17)</td>
<td>17 (100%)</td>
</tr>
</tbody>
</table>

- Clinical cure: recovery without relapse of IE due to the same microorganism within 3 months
- Clinical failure: persistent or breakthrough BSI during the IE treatment or when the same microorganism was isolated in the blood culture of a patient with IE requiring surgery after completing antibiotic therapy

- 3 deaths unrelated to DBV treatment
- 2 patients with new episodes of endocarditis due to different organisms

- Clinical cure: recovery without repeat positive blood cultures due to the same microorganism
- Failure: persistent or breakthrough BSI during the IE treatment or when the same microorganism was isolated in the blood culture of a patient with IE requiring surgery after completing antibiotic therapy

- Reduction in length of stay (mean, days): 14 days
- Negative follow-up blood cultures (n=36): 35 (97.2%)
DALBACEN cohort: dalbavancin as consolidation therapy in patients with endocarditis and/or bloodstream infection produced by gram-positive cocci

Estimated Pharmacoeconomic Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Dalbavancin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in hospital stay for BSI (sum, days)</td>
<td>636</td>
</tr>
<tr>
<td>Reduction in hospital stay for IE (sum, days)</td>
<td>557</td>
</tr>
<tr>
<td>Early Discharges (sum, patients)</td>
<td>71</td>
</tr>
<tr>
<td>Cost savings for BSI (sum, Euro)</td>
<td>315,424.20€</td>
</tr>
<tr>
<td>Cost savings for IE (sum, Euro)</td>
<td>263,187.46€</td>
</tr>
</tbody>
</table>

Conclusions
• Demonstrated low failure rates in patients with IE or BSI
• Achieved clearance of blood cultures in patients with gram-positive bacteremia
• Displayed mild adverse effect profile and medication tolerance
• Showed low relapse rates of infections due to the same pathogen

Limitations
Small sample size, no comparator group, retrospective descriptive study design, multiple dosing regimens

Knowledge Check
Based on the Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety trial, what were the clinical observations found with Dalbavancin?
- Positive clinical efficacy
- Clearance of blood cultures
- Mild adverse effect
- Shorter length of stay
- Shorter total IV-infusion time
- All the above

Strategies for outpatient treatment (oral and OPAT)
- Broad spectrum of activity for gram-positive pathogens
- Potentially favorable due to the addition of a lipophilic side chain
- Demonstrates coverage of Enterococci and Staphylococci
- Oritavancin covers VanA and VanB isolates of VRE

Clinical and Cost Considerations for Dalbavancin and Oritavancin
- Demonstrated low failure rates in patients with osteomyelitis, endocarditis, and bacteremia
- Achieved clearance of blood cultures in patients with gram-positive bacteremia
- Displayed mild adverse effect profile and medication tolerance
- Reduced length of stay, decrease total IV-infusion time, and reduced healthcare expenses
Patient Case

- Dalbavancin was considered as an alternative antibiotic agent for TJ
- Uncontrolled psychiatric illness and substance use disorder
- Addiction and psychiatry consultation
- Continued vancomycin for 6 weeks of IV therapy

Knowledge Check

What are the potential benefits of initiating a long-acting lipoglycopeptide in a high-risk PWID?

- No PICC required
- Potential health care cost savings
- No level monitoring
- Convenient dosing regimen
- All the above

Addiction Medicine Considerations

Addiction Medicine Consultations Reduce Readmission Rates for Patients With Serious Infections From Opioid Use Disorder

Retrospective chart review from January 2016 and January 2018

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Addiction Consult (n=38)</th>
<th>Non-Addiction Consult (n=87)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>21 (55%)</td>
<td>46 (52%)</td>
</tr>
<tr>
<td>Age, yr, median (range)</td>
<td>36 (19-63)</td>
<td>35 (19-67)</td>
</tr>
<tr>
<td>IV heroin use</td>
<td>37 (97%)</td>
<td>81 (93)</td>
</tr>
<tr>
<td>Bipolar Disorder</td>
<td>2 (5%)</td>
<td>6 (7%)</td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>7 (18%)</td>
<td>19 (22%)</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>9 (24%)</td>
<td>21 (24%)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>25 (66%)</td>
<td>43 (49%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (5%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>HDV</td>
<td>25 (66%)</td>
<td>34 (38%)</td>
</tr>
</tbody>
</table>

OFID. 2020. 1-4
Addiction Medicine Consultations Reduce Readmission Rates for Patients With Serious Infections From Opioid Use Disorder

Primary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Addiction Consult (n=38)</th>
<th>No Addiction Consult (n=87)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication-assisted</td>
<td>33 (87%)</td>
<td>15 (17%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic completion</td>
<td>30 (78.9%)</td>
<td>35 (40.2%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Elopements/AMA</td>
<td>6 (15.8%)</td>
<td>43 (49.4%)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

90-day Readmission

Addiction medicine consultation reduced readmissions within 90 days of discharge (HR 0.378; 95% CI 0.21-0.69)

Conclusions

- Demonstrated statistically significant improvements in receiving MAT therapy
- Achieved statistically significant rates of antibiotic completion
- Displayed statistically significant few patients who elope or leave AMA
- Showed significantly fewer readmissions within 90 days after discharge

Limitations

Small sample size, single center, retrospective study design, section bias,  
treatment/consult refusal

Addiction Medicine Consult Consultations in PWID

- Growing evidence suggest improved care in patients who are admitted for serious infections requiring prolonged antibiotic therapy and hospitalization

Summary

- Increased infection risk
- Increased mortality and mortality
- Strategies for outpatient treatment (oral and OPAT)
- Many limitations to optimal management
- PWID are often poor candidates for outpatient therapy
- Leads to prolonged hospitalization
- Broad spectrum of activity for gram-positive pathogens
- Prolonged half-life due to the addition of a lipophilic side chain
- Oritavancin covers Enterococci and non-fermentative gram-negative bacilli
- Oritavancin regimens are typically 2 or 3 weeks
- Reduced readmission rates
- Improved likelihood of antimicrobial completion
- Reduced healthcare expenses
- Identification of potential benefit to shorten length of stay, decrease total IV-infusion time, and reduced healthcare expenses
- Demonstrated low failure rates in patients with osteomyelitis, endocarditis, and bactereamic
- Achieved clearance of blood cultures in patients with gram-positive bacilli
- Demonstrated-ideal adverse effect profile and medication tolerance
- Bolstered by broad spectrum of activity for gram-negative bacilli
- Bolstered by prolonged half-life due to the addition of a lipophilic side chain
Knowledge check
If dalbavancin was ordered for TJ in the outpatient setting, what IV solution must dalbavancin be compounded in?

- Normal Saline
- Dextrose 5% Water
- Sterile water for injection

Knowledge Check
How long would TJ’s dalbavancin product be stable for if kept in the fridge?

- 24 hours
- 12 hours
- 6 hours
- 48 hours

Knowledge Check
Dalbavancin was ordered in clinical for treatment of osteomyelitis. Based on the Dalbavancin for the Treatment of Osteomyelitis in Adult Patients: A Randomized Clinical Trial of Efficacy and Safety trial, the dose studied was 1500 mg on day 1 and day 8. Approximately how much will total treatment cost in dollar amount?

- $11,300.00
- $7,700.00
- $15,900.00
- $21,100.00

Dalbavancin 500 mg vial: $1,897

Pros
- Safety profile
- PICC not required for use
- No drug-level monitoring
- Convenient dosing regimen

Cons
- Evidence growing for use in non-ABSSSI
- Oritavancin contraindicated with heparin for 5 days
- Only compatible in D5W
- Expensive!!
Limited evidence demonstrates that long-acting lipoglycopeptides may be a beneficial alternative to oral and IV-treatment for osteomyelitis, bacteremia, and endocarditis for specific patients.

Use may avoid the need for PICC-line placement, risk of line-associated infections, or line misuse.

Potential beneficial option to consider to maintain parenteral antibiotic therapy and avoid oral regimens with lower bioavailability's.

Once weekly dosing regimens may a patient-centered regimen to avoid the complexity of home infusions.

Evidence shows mild adverse event profiles long-acting lipoglycopeptides.

Summary

Long-acting lipoglycopeptides use may facilitate earlier discharges into outpatient settings.

Earlier transitions to outpatient settings may lead to decreased health care costs.

Outpatient management may limit time spent in hospital and exposure to nosocomial pathogens.

Addiction consult services significantly improved patient care outcomes in receiving MAT therapy, completing antibiotic treatment and lower 90-readmission rates for patients with opioid use disorder.

Large, randomized comparator clinical trials are warranted to compare of long-acting lipoglycopeptides to standards of care.

References