Impact of the BacT/Virtuo® Blood Culture System on Time to Clearance of *Staphylococcus aureus* Bacteremia

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Disclosure Statement

These individuals have nothing to disclose concerning possible financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation:

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• Jonathan Grey
• Christopher Fronczek
• Kerry Marr
Presentation Objective

To describe the effect of a new resin-based blood culture system on the time to *Staphylococcus aureus* bacteremia clearance and related antibiotic utilization
**Background**

**Treatment of *Staphylococcus aureus***

- IDSA MRSA guidelines published in 2011
  - Recommendation for early vancomycin therapy
  - Streamlining based on rapid diagnostic tests results
  - 7 days of therapy before initiating changes in therapy

**Importance of Early Detection**

- Also referred to as Time to Positivity (TTP)
- *S. aureus* is a very common organism in bacteremia
  - High mortality rate (20%)
- Resin based culture media, BacT/ALERT® Plus, neutralize antibiotics effectively and increase sensitivity vs. charcoal-based culture media, VersaTREK™

## Combination Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilworth, et al. 2014</td>
<td>80</td>
<td>• Eradication: 96% CG vs. 80% VG (p = 0.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mortality rate: 8% CG vs. 13.3% VG (p = 0.45)</td>
</tr>
<tr>
<td>Casapao, et al. 2015</td>
<td>97</td>
<td>• Clinical failure rate: 24.6% CG vs. 30% VG (p = 0.55)</td>
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<tr>
<td></td>
<td></td>
<td>• Duration of bacteremia: 3 days CG vs. 4 days VG (p = 0.048)</td>
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<tr>
<td></td>
<td></td>
<td>• Length of stay: 14.5 days CG vs. 13.5 days VG (p = 0.15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mortality rate: 21.1% CG vs. 15% VG (p = 0.60)</td>
</tr>
<tr>
<td>Truong, et al. 2018</td>
<td>99</td>
<td>• Duration of bacteremia of 3 days in both groups (p = 0.96)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Length of stay: 15 days CG vs. 12 days VG (p = 0.59)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mortality rate: 15% CG vs. 14.9% VG (p = 1.00)</td>
</tr>
<tr>
<td>Dilworth, et al. 2019</td>
<td>156</td>
<td>• Persistent bacteremia: 26.7% CG vs. 43.9% VG (p = 0.03)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mortality rate: 15.6% CG vs. 13.6% VG (p = 0.82)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Adverse events: 18.9% CG vs. 7.6% VG (p = 0.06)</td>
</tr>
</tbody>
</table>

*CG – combination group; VG – vancomycin alone group*
Duration of MRSA Bacteremia

Definition of persistent MRSA bacteremia differs amongst literature
- 3, 5, and 7 days

Minejima, et al. 2020

BacT/ALERT® Plus Media

Detecting more infections

Decreased time to detection

Increased TTC

Providers are using time to clearance as a primary surrogate marker for treatment success or failure
Study Group
- 195 patients in charcoal-based (CB) media cohort vs. 99 patients in resin-based (RB) media cohort
- Baseline characteristics similar among groups

Primary Outcome
- TTC of MSSA bacteremia

Results
- TTC in median days: 2.5 CB vs. 3.7 RB, p < 0.001
- TTP in median hours: 15 CB vs. 14 RB, p = 0.01
- Length of stay (LOS) in median days: 26 CB vs. 22 RB, p = 0.1
- Median days of IV antibiotics: 27 CB vs. 29 RB, p = 0.2

Conclusions
- Duration of MSSA bacteremia was 1.2 days longer when using RB media compared to CB media
- Duration of *S. aureus* bacteremia in other studies could be influenced by the type of blood culture media used
To evaluate the effect of a new, more sensitive blood culture system on the time to *Staphylococcus aureus* bacteremia clearance and related antibiotic utilization
Multi-Center Study Design

Mease Countryside Hospital
- Beds: 311
- ER Visits: 61,916
- Discharges: 17,760

St. Joseph’s Hospital
- Beds: 465
- ER Visits: 98,731
- Discharges: 25,549

Morton Plant Hospital
- Beds: 599
- ER Visits: 97,791
- Discharges: 25,549
Study Design

Retrospective Cohort Analysis

January 9th 2018 – June 30th 2018
Pre-implementation cohort VersaTREK™

January 2019
Introduction of BacT/Virtuo® blood culture system

January 9th 2019 – June 30th 2019
Post-implementation cohort BacT/ALERT® Plus
Methods

Data Collection
• Patient data extracted from Cerner® electronic medical record (EMR) and Theradoc©

Inclusion Criteria
• Adult inpatients (≥ 18 years of age)
• Staphylococcus aureus bacteremia

Exclusion Criteria
• Death within 48 hours
• No documentation of bacteremia clearance
• Polymicrobial bacteremia
Outcomes

Primary Outcome

• Time to bacteremia clearance

Secondary Outcomes

• Time to positivity
• Duration of positivity
• Length of stay
• 30-day all-cause mortality
• 30-day all-cause readmission
• 30-day recurrence
• Antibiotic days of therapy per 100 patient days
• Appropriateness of escalation of therapy
• Incidence of escalation of therapy

Appropriate defined as:
• After 7 days of adequate therapy at an effective dose
• Lack of improvement or worsening of clinical signs:
  • Temperature
  • WBC
  • PCT
  • Etc.
• Decline in clinical status upon provider’s clinical judgement
Statistics

Power Calculation

• Sample size
  • 170 patients total to detect a difference of 1.5 days
  • Power ($\beta$) = 0.80
  • Alpha ($\alpha$) = 0.05

Statistical Analysis

• Categorical Data
  • Chi-squared or Fisher’s exact

• Continuous Data
  • Mann-Whitney test for non-parametric
  • 2-sample Poisson rate test for DOT
Results

Screened
N=371

Excluded
N=97

Group 1
VersaTREK™
N=127

Group 2
BacT/Alert® Plus
N=147

<table>
<thead>
<tr>
<th>Reason</th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No follow-up culture</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>*13 due to death</td>
<td></td>
<td>*18 due to death</td>
</tr>
<tr>
<td>Polymicrobial</td>
<td>13</td>
<td>26</td>
</tr>
</tbody>
</table>
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>VersaTREK™ N=127</th>
<th>Bact/ALERT® Plus N=147</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>61.2 (49.4-69.5)</td>
<td>64.5 (48.6-76.6)</td>
<td>0.08</td>
</tr>
<tr>
<td>Male Sex, N (%)</td>
<td>78 (61.4)</td>
<td>87 (59.2)</td>
<td>0.71</td>
</tr>
<tr>
<td>Central Venous Line, N (%)</td>
<td>35 (27.6)</td>
<td>45 (30.6)</td>
<td>0.58</td>
</tr>
<tr>
<td>Intravenous Drug User, N (%)</td>
<td>21 (16.5)</td>
<td>32 (21.8)</td>
<td>0.27</td>
</tr>
<tr>
<td>Vascular Implants, N (%)</td>
<td>37 (29.1)</td>
<td>48 (32.7)</td>
<td>0.53</td>
</tr>
<tr>
<td>Orthopedic Implants, N (%)</td>
<td>24 (18.9)</td>
<td>34 (23.1)</td>
<td>0.39</td>
</tr>
<tr>
<td>Immunosuppression, N (%)</td>
<td>17 (13.4)</td>
<td>14 (9.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>Surgery within 30 days, N (%)</td>
<td>8 (6.3)</td>
<td>13 (8.8)</td>
<td>0.43</td>
</tr>
<tr>
<td>Charlson Comorbidity Score, Median (IQR)</td>
<td>5 (2 - 7)</td>
<td>4 (2 - 7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Pitt Bacteremia Score, Median (IQR)</td>
<td>2 (0 - 3)</td>
<td>1 (0 - 2)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>MRSA, N (%)</td>
<td>57 (44.9)</td>
<td>68 (46.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Source Of Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocarditis/Intravascular, N (%)</td>
<td>48 (37.8)</td>
<td>47 (32)</td>
<td>0.31</td>
</tr>
<tr>
<td>Bone And Joint, N (%)</td>
<td>33 (26)</td>
<td>36 (24.5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Respiratory, N (%)</td>
<td>19 (15)</td>
<td>19 (12.9)</td>
<td>0.63</td>
</tr>
<tr>
<td>Skin And Soft Tissue, N (%)</td>
<td>20 (15.7)</td>
<td>39 (26.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Other Or Unknown, N (%)</td>
<td>7 (5.5)</td>
<td>6 (4.1)</td>
<td>0.58</td>
</tr>
<tr>
<td>Source Control, N (%)</td>
<td>54 (42.5)</td>
<td>64 (43.5)</td>
<td>0.87</td>
</tr>
</tbody>
</table>
## Results

### Primary Outcome

<table>
<thead>
<tr>
<th></th>
<th>VersaTREK™ N=127</th>
<th>BacT/ALERT® Plus N=147</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time to clearance (days), median (IQR)</strong></td>
<td>2.2 (1.6 - 3.8)</td>
<td>3.9 (2.6 - 6.7)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

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**Diagram:**
- **VersaTREK™** (pre-implementation)
  - 52.8h
- **BacT/Virtuo®** (post-implementation)
  - 94.6h

**Time of Collection**

<table>
<thead>
<tr>
<th>Time of Collection</th>
<th>0</th>
<th>25</th>
<th>50</th>
<th>75</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th>Secondary Outcomes</th>
<th>VersaTREK™ N = 127</th>
<th>BacT/ALERT® Plus N = 147</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Duration of positivity (days), median (IQR)</strong></td>
<td>0 (0 - 0.7)</td>
<td>1.4 (0 - 3.8)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td><strong>Time to positivity (hrs), median (IQR)</strong></td>
<td>16.3 (13.1-21.9)</td>
<td>14.2 (11.5-19.8)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td><strong>Length of stay (days), median (IQR)</strong></td>
<td>10 (7 - 18)</td>
<td>12 (8 - 19)</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>30-day readmission, n (%)</strong></td>
<td>41 (32.3)</td>
<td>40 (27.2)</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>30-day recurrence, n (%)</strong></td>
<td>2 (1.6)</td>
<td>4 (2.7)</td>
<td>0.51</td>
</tr>
<tr>
<td><strong>30-day mortality, n (%)</strong></td>
<td>13 (10.2)</td>
<td>9 (6.1)</td>
<td>0.21</td>
</tr>
</tbody>
</table>
Time Comparison

VersaTrek™
(pre-implementation)

BacT/Virtuo®
(post-implementation)

TTP = time to positivity
TTC = time to clearance
Antibiotic Utilization

Days of Therapy per 100 Patient Days

- **VersaTREK™**
  - Cefazolin: 25
  - Nafcillin: 7
  - Vancomycin: 48
  - Daptomycin: 21
  - Ceftaroline: 5
  - Linezolid: 4
  - Combination: 17
  - Gentamicin: 3
  - Rifampin: 7

- **BacT/ALERT® Plus**
  - Cefazolin: 23
  - Nafcillin: 14
  - Vancomycin: 38
  - Daptomycin: 16
  - Ceftaroline: 3
  - Linezolid: 3
  - Combination: 29
  - Gentamicin: 5
  - Rifampin: 11

P-values:
- P = 0.14
- P < 0.001
- P = 0.06
- P < 0.001
- P < 0.001
- P < 0.001
- P < 0.001
- P < 0.001
Therapy Escalation

- Escalation: 22%
- Inappropriate Escalation: 39.3%

P = 0.02

VersaTREK™: 35.3%
BacT/ALERT® Plus: 47.1%

P = 0.016
Limitations

- **Retrospective Design**
  - Dependent upon accurate notes to clearly identify some baseline characteristics, endpoints, and inclusion/exclusions

- **Clinical Outcomes**
  - Outcomes limited to health system EMR
    - 30-day readmissions, 30-day recurrence, and mortality

- **Statistical Power**
  - Design was not developed with power calculations for secondary endpoints

- **Clinician Differences**
  - Not able to account for differences among prescribers
Effects of the BacT/Virtuo® System

- Increased length of stay
- Increase in overall antibiotic usage
- No difference in mortality
- Changes in prescribing habits

Increased Sensitivity
Future Research

Mortality

• Determine if there is a duration point that impacts mortality using BacT/ALERT® Plus cultures

Cost Effectiveness

• Length of Stay
  • While we found a difference of two days, which could hold clinical significance, a study designed to detect statistical significance is warranted
• Antibiotic Utilization
  • Increase in overall antibiotic utilization, in addition to more costly antibiotics

Organisms

• Expand to look at other organisms responsible for bacteremia to see if there is a similar effect on TTC
Conclusions

The duration of *S. aureus* bacteremia was found to be significantly longer by 1.7 days when comparing the resin-based BacT/ALERT® Virtuo® blood culture system to the charcoal-based VersaTREK™ blood culture system.

The duration of *S. aureus* bacteremia impacts a patient’s clinical course, most notably antibiotic selection, even in scenarios where patients are improving with evidence of clearance:

- Mortality was not significantly different.
- Second and third line therapy options were unnecessarily increased in a number of cases.
Acknowledgements

- Jonathan Grey, Pharm.D., BCPS, BCIDP
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