An Open Label, Three Arm Study of the Safety and Clinical Efficacy of Topical Wound Care vs. Oral Levofloxacin vs. Combined Therapy for Mild Diabetic Foot Infections

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Overview

- Mild DFU’s
- Randomized, 3 arm study
  - Levofloxacin + Saline
  - OIS-1080
  - OIS-1080 + Levofloxacin
- Clinical and Micro Cure
- Observed at 3, 10, and 21 days
Topical Treatment for DFU’s

  – Not randomized, and no control, but showed reduction in cellulitis, odor, edema, and improved granulation tissue.

  – Randomized to saline vs. topical treatment. Demonstrated a statistical improvement with superoxidized saline.
Study Design

Mild DFI (IDSA / UTC 1B)

Screening / Debridement / Culture - Photo

Randomization

OIS-1080  Levo + Saline  OIS-1080 + Levo

<table>
<thead>
<tr>
<th>Visit</th>
<th>Day</th>
<th>∆ Treatment</th>
<th>CE</th>
<th>ME</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>3 ± 1</td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>3 *</td>
<td>10 ± 1</td>
<td>EOT</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>4</td>
<td>21-28</td>
<td>TOC</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

* Primary Objective
Mild Diabetic Foot Infection
### Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>OIS - 1080 (n = 21)</th>
<th>Saline + Levo (n = 21)</th>
<th>OIS-1080+ Levo (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>55.4 ± 12.81</td>
<td>56.5 ± 12.21</td>
<td>59.2 ± 12.94</td>
</tr>
<tr>
<td>Gender (% Male)</td>
<td>76.2%</td>
<td>76.2%</td>
<td>68.0%</td>
</tr>
<tr>
<td>BMI</td>
<td>32.56 ± 5.94</td>
<td>31.68 ± 5.93</td>
<td>30.11 ± 6.39</td>
</tr>
<tr>
<td>Type I Diabetes</td>
<td>23.8%</td>
<td>28.6%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Type II Diabetes</td>
<td>76.2%</td>
<td>71.4%</td>
<td>80.0%</td>
</tr>
</tbody>
</table>
## Baseline Study Ulcer Assessment

|                          | OIS – 1080  
n = 21 | Saline + Levo  
n = 21 | OIS – 1080 + Levo  
n = 25 |
<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length of time of study ulcer present (weeks)</strong></td>
<td>15.80 ± 19.05</td>
<td>13.60 ± 15.55</td>
<td>15.10 ± 23.78</td>
</tr>
<tr>
<td><strong>Wound Area (cm²)</strong></td>
<td>2.26 ± 2.45</td>
<td>1.55 ± 1.25</td>
<td>2.18 ± 1.87</td>
</tr>
<tr>
<td><strong>Min</strong></td>
<td>0.27</td>
<td>0.47</td>
<td>0.31</td>
</tr>
<tr>
<td><strong>Max</strong></td>
<td>8.72</td>
<td>4.63</td>
<td>7.45</td>
</tr>
</tbody>
</table>

Mean ± Standard Deviation
Clinical Success Rate for Visit 3
(ITT Sample)

95% CI for the Clinical Success Rate for Visit 3 (EOT)
(ITT Sample)

Clinical Success Rate (%)

OIS - 1080 (n = 20)    Saline + Levo (n = 21)    OIS - 1080 + Levo (n = 25)
Clinical Success Rate for Visit 4 (ITT Sample)

95% CI for the Clinical Success Rate for Visit 4 (TOC) (ITT Sample)

- OIS - 1080 (n = 20)
- Saline + Levo (n = 21)
- OIS - 1080 + Levo (n = 25)
Clinical Success Rate for Visit 3
(Clinically Evaluable Sample)

95% CI for the Clinical Success Rate for Visit 3
(CE Sample)

Clinical Success Rate

OIS - 1080 (n = 18)  Saline + Levo (n = 18)  OIS - 1080 + Levo (n = 20)
Clinical Success Rate for Visit 4
(Clinically Evaluable Sample)

95% CI for the Clinical Success Rate for Visit 4
(CE Sample)

p < 0.033
Clinical & Micro Response at Visit 3

95% CI for Clinical and Microbiological Success Rate for Visit 3
(ME Sample)

Clinical & Microbiologic Success Rate

Clinical Success          Microbiological Success

OIS -1080 (n = 15)  Saline + Levo (n = 16)  OIS - 1080 + Levo (n = 17)

- Clinical Success  - Microbiological Success
Pathogens Susceptibility at Visit 2

Baseline Pathogens Susceptibility
(ME Sample at Visit 2)

- OIS - 1080 (n=27)
- Levo (n=32)
- OIS - 1080 + Levo (n=31)

All Isolated Pathogens

<table>
<thead>
<tr>
<th>Percent</th>
<th>Susceptible</th>
<th>Resistant</th>
<th>Intermediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>OIS - 1080</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Levo (n=32)</td>
<td>80</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>OIS - 1080 + Levo (n=31)</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
### Treatment Emergent Adverse Events by Relationship to Study Drug

<table>
<thead>
<tr>
<th>Emergent Adverse Event</th>
<th>OIS – 1080 (n = 21)</th>
<th>Saline + Levo (n = 21)</th>
<th>OIS – 1080 + Levo (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely Not</td>
<td>7 (33.3%)</td>
<td>7 (33.3%)</td>
<td>9 (36.0%)</td>
</tr>
<tr>
<td>Probably Not</td>
<td>6 (28.6%)</td>
<td>5 (23.8%)</td>
<td>5 (20.0 %)</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td>2 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>1 (4.0%)</td>
</tr>
</tbody>
</table>
Selected Treatment Emergent Adverse Events by Relationship to Study Drug

• OIS - 1080 + Levo Group
  – Burning sensation: Definite (1)
  – Stomach discomfort: Possible (1)
  – Amnesia: Possible (1)
Conclusions

• The clinical success rate appears to be comparable among the three study arms as shown on the overlapping confidence intervals at Visits 3 and 4.

• The micro response did not correlate with the clinical success:
  – “Head of the snake” theory
  – Other mechanism(s) of action of OIS-1080

• 1 out of 45 patients treated with OIS-1080 had a topical related adverse event but no systemic toxicity.
Oculus Collaborative Group

Blume P & Palladino M
Jordan D
Vayser DJ
Halperin G
Schleicher S
Royall S
Mendicino RW
Jensen JL
Grossman AB
Sharpe JN
Serletic DR
Mulder G
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Gutierrez AA.
Thank you!

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