A Comparison of a Novel Oxysterol Molecule to rhBMP2 in a Rabbit Posterolateral Fusion Model

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My disclosure is in the Final Program and in the AAOS Orthopaedic Disclosure program.

Dr. Parhami discloses that he is a founder of MAX BioPharma Inc., which has licensed the rights to Oxy133 from UCLA, and that he has financial interests in the technology presented here. In addition, as part of the licensing agreement, UCLA holds equity in MAX BioPharma. All other authors state that they have no conflicts of interest.
Background

- Pseudarthrosis is a potential complication of major spinal surgery and fracture surgeries
- Iliac crest autografts, which remain the standard of care, have substantial donor site morbidity and may not provide enough graft volume for large surgeries
- Biologics are an active area of research to find the best possible alternative to iliac crest autograft
Background

- rhBMP2 was approved in 2002 for single level lumbar fusion and its use spread rapidly.
- Recently, concerns about possible complications of rhBMP2 have increased.
Background

- Our lab has previously synthesized a compound, oxysterol 133 (Oxy133), which showed promise as a biological adjunct to fusion
  - Equivalent to rhBMP2 in rat posterolateral fusion model
  - In vitro promotes significant osteogenic marker expression including Runx2, osterix, alkaline phosphatase, bone sialoprotein and osteocalcin
Purpose

- To compare the efficacy of rhBMP2 and oxysterol 133 in a rabbit posterolateral lumbar fusion model
Methods

- In vitro study
- 24 rabbits underwent bilateral posterolateral lumbar fusion at L4-5
  - Groups: control (A), 30 ug rhBMP2 (B), 20 mg oxysterol 133 (C), 60 mg oxysterol 133 (D)
  - Fusion evaluated by fluoroscopy at 4 weeks and by faxitron radiograph, microCT and manual palpation after sacrifice at 8 weeks
Figure 1

- 60 mg Oxy133
- 20 mg Oxy133
- 30 µg BMP2
- Control

* Indicates p < 0.05 compared to group A (Control)

Radiographic Lumbar Spinal Fusion in Rats at 8 weeks
Radiographic Lumbar Spinal Fusion in Rats at 4 weeks
<table>
<thead>
<tr>
<th>Control</th>
<th>30 µg BMP2</th>
<th>20 mg Oxy133</th>
<th>60 mg Oxy133</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
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<td><img src="image7.png" alt="Image" /></td>
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</tbody>
</table>

Figure 2
Fusion by Manual Palpation at 8 weeks

- Group A: 0% fusion
- Group B: 80% fusion
- Group C: 80% fusion
- Group D: 80% fusion

* Indicates p < 0.05 compared to group A
Fusion Assessment by microCT

CT Lumbar Spinal Fusion

* Indicates p < 0.05 compared to group A
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Image 1</th>
<th>Image 2</th>
<th>Image 3</th>
<th>Image 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td><img src="image1" alt="Control Image 1" /></td>
<td><img src="image2" alt="Control Image 2" /></td>
<td><img src="image3" alt="Control Image 3" /></td>
<td><img src="image4" alt="Control Image 4" /></td>
</tr>
<tr>
<td>30 µg BMP2</td>
<td><img src="image1" alt="30 µg BMP2 Image 1" /></td>
<td><img src="image2" alt="30 µg BMP2 Image 2" /></td>
<td><img src="image3" alt="30 µg BMP2 Image 3" /></td>
<td><img src="image4" alt="30 µg BMP2 Image 4" /></td>
</tr>
<tr>
<td>20 mg Oxy133</td>
<td><img src="image1" alt="20 mg Oxy133 Image 1" /></td>
<td><img src="image2" alt="20 mg Oxy133 Image 2" /></td>
<td><img src="image3" alt="20 mg Oxy133 Image 3" /></td>
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<td>60 mg Oxy133</td>
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<td><img src="image4" alt="60 mg Oxy133 Image 4" /></td>
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</tbody>
</table>
# Fusion Rate Summary

<table>
<thead>
<tr>
<th></th>
<th>Manual Palpation</th>
<th>microCT</th>
<th>4 wk radiograph</th>
<th>8 wk radiograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.0%</td>
<td>0.0 %</td>
<td>25.0%</td>
<td>40.0%</td>
</tr>
<tr>
<td>rhBMP2 30 ug</td>
<td>83.3%</td>
<td>67.7%</td>
<td>68%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Oxy133 20 mg</td>
<td>83.3%</td>
<td>91.7%</td>
<td>91.7%</td>
<td>91.7%</td>
</tr>
<tr>
<td>Oxy133 60 mg</td>
<td>80.0%</td>
<td>80.0%</td>
<td>90.0%</td>
<td>100%</td>
</tr>
</tbody>
</table>
Fusion Mass TV on microCT

![Bar chart showing Tissue Volume (mm$^3$) for Oxy 60, Oxy 20, BMP2, and Control.](image)

- **Oxy 60**
- **Oxy 20**
- **BMP2**
- **Control**

* Indicates $p<0.5$ compared to control.
Conclusions

- High dose and low dose oxysterol 133 show equivalent fusion to rhBMP2,
- Given its osteogenic potency, anticipated lack of immunogenicity, and low cost of production, Oxy133 may be an excellent alternative to rhBMP2 for spinal fusion procedures and is worthy of further study.
Thank You

- Dr. Farad Parhami PhD
- Dr. Jeff Wang MD
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- Dr. Scott Montgomery MD
- Dr. Akinobu Suzuki MD
- Dr. Haijun Tian MD
- Dr. Jared Johnson MD
- Kevin Phan BS
- Dr. Elisa Atta PhD
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- Dr. Renata Pereira MD

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- Taylor Hobson BS
Sources Cited