Evaluation of rhPDGF on Allograft Integration in an Ovine Interbody Spinal Fusion Model

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Abstract:
• Lower back pain is a frequent complaint in humans and is commonly caused by degenerative disc disease or spondylolisthesis.
• Lumbar spinal arthrodesis is a common form of treatment, carried out in around 100,000 humans within the U.S. per year.
• Incomplete spinal fusion may result, causing significant morbidity.
• Autograft is often used to increase success rate. However, there is a high level of morbidity and chronic pain associated with autograft collection from the patient’s iliac crest.
• This study is evaluating the use of a buffered bone allograft matrix (mineralised:deminer alal: 1:1 + NaOAc), as an alternative to autograft and INFUSE® (a pre-existing bone graft material containing recombinant human bone morphogenetic protein-2 (rhBMP-2)).
• The combination of the allograft matrix with rhPDGF-BB (recombinant platelet-derived growth factor-biologic) is also being considered, in comparison to autograft, INFUSE® and empty, radiolucent vertebral spacer cages.

Materials and Methods:
• 27 skeletally mature Rambouillet-Columbia ewes were placed under general anaesthetic and prepared for surgery.
• 2cc of autogenous cancellous bone (autograft matrix) was harvested from the iliac crests of sheep numbers 13, 16, 24, 25, 27.
• An anulotomy of L2/L3 and L4/L5 was carried out in all 27 ewes.
• The vertebral endplates were prepared for acceptance of the radiolucent vertebral spacer cage.
• Each disc space was opened and the cage with its contents inserted (see Table 1).

Table 1: Cage contents and endpoint for each sheep.

<table>
<thead>
<tr>
<th>Sheep Number</th>
<th>Implant insertion site: L5-L6</th>
<th>Implant insertion site: L3-L4</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,8</td>
<td>Empty Vertebral Spacer-CR cage</td>
<td>Empty Vertebral Spacer-CR cage</td>
<td>Euthanasia (18wks)</td>
</tr>
<tr>
<td>4,5,9,10,11</td>
<td>Allograft + NaOAc Buffer</td>
<td>Allograft + NaOAc Buffer</td>
<td>Euthanasia (18wks)</td>
</tr>
<tr>
<td>1,3,6,7,12</td>
<td>INFUSE®</td>
<td>INFUSE®</td>
<td>Euthanasia (18wks)</td>
</tr>
<tr>
<td>15,18,22,23,26</td>
<td>Empty Vertebral Spacer-CR cage</td>
<td>Empty Vertebral Spacer-CR cage</td>
<td>Euthanasia (3+mo)</td>
</tr>
<tr>
<td>13,16,24,25,27</td>
<td>Autograft</td>
<td>Autograft</td>
<td>Euthanasia (3+mo)</td>
</tr>
<tr>
<td>14</td>
<td>rhPDGF-BB</td>
<td>rhPDGF-BB</td>
<td>Euthanasia (3+mo)</td>
</tr>
<tr>
<td>17,19,20,21</td>
<td>rhPDGF-BB + allograft</td>
<td>rhPDGF-BB + allograft</td>
<td>Euthanasia (3+mo)</td>
</tr>
</tbody>
</table>

• The site was lavaged with normal saline and routinely closed.
• Appropriate antibiotic treatments were given and postoperative radiographs taken.
• Sheep numbers 1-12 were re-anaesthetised at 9 weeks for radiographs and will be euthanised at 18 weeks.
• Each spine will be explanted, radiographed and returned to necropsy for trimming and formalin fixing in preparation for later sectioning, mounting and staining for histological analysis.
• Sheep numbers 13-27 will be re-anaesthetised at 3 months post-surgery for radiographs and CT scans.
• If fusion is observed, the ewes will be euthanised at 3.5 months. If no fusion is observed, the study will be extended for an additional 1.5 months.
• Each spine will be explanted, radiographed and fixed as for sheep numbers 1-12.

Predicted Results:
• rhPDGF-BB with allograft will provide a competitive alternative to previous treatments, exceeding or equalling the rate and degree of lumbar spinal arthrodesis achieved by INFUSE®, whilst still removing the need for morb id harvesting of autograft.
• On completion of this study and following FDA approval, this product may become the new “gold standard” for lumbar spinal fusion in humans.

Future Development:
• To determine how effective rhPDGF-BB will be alone, without allograft.

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