Viable Disc Tissue Allograft Supplementation in the Treatment of Degenerated Intervertebral Discs:

One Year Results of a Randomized Control Trial

Douglas P. Beall

Radiology and Interventional Spine Services, Summit Medical Center, Edmond, Oklahoma, United States
Disclosures

• VIVEX Biologics consultant
• This trial is registered on www.clinicaltrials.gov (NCT03709901).
• VIVEX Biologics, Inc. sponsored this study and contributed to study design, data monitoring, statistical analysis, and reporting of results and paid for independent data collection, core laboratory services.
• Complete disclosures for all authors reflected in program
Introduction

- Degenerative lumbar disc disease and the development of chronic lower back pain is associated with tissue loss in the nucleus pulposus.

- A viable disc tissue allograft has been developed to augment the tissue loss associated with these degenerative changes.

Cadaver disc injection: the supplemental tissue is dyed green.
Methods

- A prospective, multicentered, blinded randomized, clinical trial for subjects with one or two-level degenerative lumbar disc disease was completed.
  - MRI scans were used to determine the degree of disc degeneration.
  - 218 subjects were randomized (3.5:1:1) to intradiscal injection of viable disc allograft or intradiscal injection of saline or continued non-surgical management (NSM).
  - Efficacy assessments included mean change from baseline and responder analyses in Oswestry Disability Index (ODI) and improvement in Visual Analogue Scale of Pain Intensity (VAS) at 12 months.
  - Adverse events were monitored throughout duration of study.
Primary Outcomes: ODI
Mean clinical outcomes were not significant among the treatment groups

ODI function scores of 179 patients showed reduction of disability for the saline and active allograft groups but increased disability in the conservative care/NSM group up to month three when all patients in this group crossed over to cellular allograft injection.

Subsequently all groups experienced a reduction in disability.

The saline, active allograft and conservative care to crossover groups had reductions in pain of 23.9, 27.4, and 36.5 points respectively on the ODI scale corresponding to reductions in disability of 42%, 53% and 64%.

**Oswestry Functional Outcomes (mean improvements one year)**
- Saline placebo - 20.7 pts 42%
- Active allograft - 27.1 pts 53%
- Crossover - 36.0 pts 64%
Primary Outcomes: VAS

Mean clinical outcomes were not significant among the treatment groups

VAS pain scores of 178 patients showed reduction of pain for the saline and active allograft groups but increased pain in the conservative care/NSM group up to month three when all patients in this group crossed over to cellular allograft injection.

Subsequently all groups experienced a reduction in pain.

The saline, active allograft and conservative care to crossover groups had reductions in pain of 30.5, 34.0, and 46.7 points respectively on the VAS scale corresponding to reductions in pain of 45%, 54% and 65%.

Visual Analog Scale Pain Outcomes (mean improvements one year)

- Saline placebo - 29.6 pts 45%
- Active allograft - 34.8 pts 53.8%
- Crossover - 45.1 pts 65.6%
76.5% of subjects randomized to allograft were responders when as compared to 56.7% in the saline group (p = 0.03)
Minimal Clinical Important Difference in VAS

Exploratory analysis: ≥ 20-point reduction in VAS
Overall p-value = .022

- 91.3% of subjects in the Crossover group and 66.7% in the Treatment group were responders, demonstrating at least a 20-point reduction in VAS at 12 months, compared to 56.7% in the saline group (Overall p-value = 0.022)

<table>
<thead>
<tr>
<th>Group</th>
<th>Responders (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline (n=30)</td>
<td>56.7</td>
<td>.305</td>
</tr>
<tr>
<td>Treatment (n=120)</td>
<td>66.7</td>
<td>.017</td>
</tr>
<tr>
<td>Crossover (n=23)</td>
<td>91.3</td>
<td>.006</td>
</tr>
</tbody>
</table>
Most of the related AEs were musculoskeletal and connective tissue related (19 total events), with back pain being the most prevalent (10 total events). 3 cases of intervertebral disc protrusion were reported in the active allograft group.

In the allograft group, 11 SAEs occurred in 141 subjects (3.5%).

Of the 11 SAEs, 6 were considered possibly related to the treatment and/or procedure.

These 6 SAEs occurred in 2 subjects. Both subjects experienced osteomyelitis with accompanying pain and bacteremia in one case.

No related SAEs were reported in the placebo or crossover groups.

No related AEs were reported in the placebo or NSM (prior to crossover) groups.

### Safety Population

<table>
<thead>
<tr>
<th>Category</th>
<th>Active Allograft N = 141</th>
<th>Crossover N = 39</th>
<th>Saline N = 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects who died</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Number of events (n)</td>
<td>Number of subjects with events % (n/N)</td>
<td>Number of events (n)</td>
</tr>
<tr>
<td>Treatment and/or Procedure Related AEs</td>
<td>23 (11.3%) (16/141)</td>
<td>7 (8.6%) (3/35)</td>
<td>0</td>
</tr>
<tr>
<td>Treatment and/or Procedure Related SAEs</td>
<td>6 (5) (3.5%)</td>
<td>0 (0.0%)</td>
<td>0</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (1.4%) (2/141)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td>3 (1.4%) (2/141)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>General pain</td>
<td>1 (0.7%) (1/141)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Discussion and Conclusions

• This large, multi-centered, prospective, randomized and blinded clinical trial of disc tissue allograft supplementation demonstrated:
  o Clinically significant improvements in pain and functional outcomes.
  o Durable clinical improvements out to 12 months.
  o Viable disc tissue allograft could be a safe and effective non-surgical treatment for subjects who have chronic lower back pain associated with DDD.
• Although primary endpoints did not reach statistical significance, results indicate that viable disc tissue allograft may be a beneficial non-surgical treatment for patients who have chronically painful lumbar degenerative discs.
• Limitations of this study include a comparison to saline, shown to be more representative to an active treatment opposed to a placebo.
• Further research is on-going with 24- and 36-month outcomes.