Selecting End Points for Pivotal Hemodialysis AV Fistula Clinical Trials - Anatomical Surrogates vs. Functional Suitability

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Disclosures

• Major shareholder in Vascular Therapies, Inc.

Background

• Clinical Trials testing interventions to improve Fistula suitability for dialysis
  • Dialysis dependent patients
  • CKD subjects
• Clinical definition of Fistula suitability for dialysis
  • ≥N/Qb 300ml/min for 3 consecutive sessions

• US metrics to define/support Fistula Functionality (Physiological Maturation)
  • Vein diameter of 4 mm
  • AVF blood flow (Qa) >500 mL/min
• These parameters have never been clinically validated in larger trials
• Anatomical metrics have variable co-relation with functional use
• In the DAC study ~45% of the fistulae deemed not suitable for dialysis were anatomically patent

Fistula: Functional vs. Anatomical Failure (DAC)

<table>
<thead>
<tr>
<th></th>
<th>Clonidine (n = 385)</th>
<th>Placebo (n = 373)</th>
<th>Abandoned</th>
<th>Anatomically Patent?</th>
<th>Functionally?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fistula not suitable for dialysis</td>
<td>206/385 (54%)</td>
<td>222/373 (60%)</td>
<td></td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Fistula abandoned with no expectation of future use</td>
<td>103 (48%)</td>
<td>104 (64%)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Fistula not yet in use despite treatment with dialysis</td>
<td>57</td>
<td>47</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Fistula in use during enrollment period but failed to meet suitability criteria</td>
<td>66</td>
<td>41</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>


Fistula: Anatomical Patency vs. Functionality

Functionally Useful: ALL are Anatomically patent
Anatomically patent: ALL are NOT Functionally useful
Methods

- 30 patients undergoing AVF surgery
- 22 Radiocephalic (RCF)
- 8 Brachiocephalic fistulae (BCF)
- All received a Sirolimus-eluting Collagen Implant at and around the anastomosis
- Serial ultrasound exams were performed
- Nephrologist made all cannulation decisions based on clinical exam

Results

- Pre op vein diameter (Mean ± SD)
  - RCF: 2.7±0.5 mm
  - BCF: 3.9±0.6 mm
- 4 RCF thrombosed within 2 weeks and are excluded from the analysis
- All remaining 26 AVF were successfully cannulated for dialysis (Mean 7w; Median 6w)
- At time of cannulation
  - Vein diameter in 22/26 AVF (85%) was ≥6 mm (Range: 5.1-10.1mm)
  - There were no infiltrations
  - At 6 and 12mos ~75% of the AVF maintained functional patency

VT-303 Fistula Maturation (RC AVF)
Change in diameter from pre op to discharge =63%

VT-303 Fistula Maturation (BC AVF)
Change in diameter from pre op to discharge =38%

Vein Diameter ≥4 mm (n=26)

Vein Diameter ≥6 mm (n=26)
Suitability Score

<table>
<thead>
<tr>
<th>Test</th>
<th>Metric</th>
<th>0</th>
<th>1</th>
<th>2</th>
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</thead>
<tbody>
<tr>
<td>Clinical exam</td>
<td>Mature Fistula?</td>
<td>No</td>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Vein Diameter (mm)</td>
<td>&lt;5</td>
<td>5 to 6</td>
<td>6</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Blood flow (Qa) mL/min)</td>
<td>&lt;400</td>
<td>400 to 500</td>
<td>≥500</td>
</tr>
</tbody>
</table>

Mature, Functional Fistula: Suitability Score of ≥4

Summary

- 85% of the cannulated AVF had a vein diameter ≥6 mm
- None of the cannulated fistulae had a vein diameter of <5 mm
- In Clinical Trials
  - Dialysis dependent patients: Demonstration of AVF use (≥2N/300)
  - CKD patients: A suitability score based on clinical and US results may be an option

Thank You