Six month AV Fistulae outcomes Following Local Perianastomotic Delivery of Sirolimus Preliminary Report from a US Phase 3 Clinical Trial (ACCESS Trial)

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Six month AV Fistulae outcomes following Local Perianastomotic delivery of Sirolimus Preliminary Report from a US Phase 3 Clinical Trial (ACCESS Trial)

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Background
AV Fistula (AVF) maturation delay impacts its functional patency and prolongs catheter dependence. USRDS (2015) reports median time to first cannulation of 112 days and only 45% of AVF are suitable for dialysis at 6 months [Range 38% (DAC) to 65% (HFM)]. A prior single arm Phase 2 study (Table) tested the value of perivascular sirolimus delivered intraoperatively at and around the AVF anastomosis from a collagen membrane (drug product; Vascular Therapies, Cresskill, NJ), for improving AVF outcomes.

Methods
Incident ESRD patients undergoing hemodialysis via catheter at time of AVF creation [Radiocephalic (RCF) or Brachiocephalic (BCF)] are eligible for enrollment in this ongoing US Phase 3 multicenter, randomized controlled clinical trial (NCT02513303). The first subject enrolled at each site received the drug product [“Open label” subject, (OL)]. Baseline vascular mapping (cephalic vein ≥2.5 mm; artery ≥2 mm; vein depth ≤5 mm) was performed to ensure suitability.

Results
There were no product related serious adverse events. Table lists key demographic and outcome metrics. Time to First Dialysis (TTFD): Time from AVF creation, to the time when the fistula can support three consecutive 2 needle dialysis sessions with a mean dialysis pump flow of ≥300 mL/min (2N/300). Fistula Suitability for Dialysis at 6 months (FSD6): Ability to use the fistula (2N/300) for two thirds of the dialysis sessions during a 30 day suitability ascertainment period commencing on day 150. Excluding the 2 AVF that thrombosed early, TTFD was <90 days for 11/16 (69%) subjects.

Conclusion
1. Time to maturation and AVF suitability for dialysis at 6 months in the open label Phase 3 subjects are similar to Phase 2 results and signal an improvement in comparison to historical controls.
2. Results are promising and may suggest that prophylactic local treatment with sirolimus at time of AVF creation could predictably reduce catheter dependence to less than 90 days with durable AV fistula functionality.

Enrollment is ongoing in the ACCESS trial.

<table>
<thead>
<tr>
<th>Phase</th>
<th>N</th>
<th>Age (y) Mean (range)</th>
<th>Male</th>
<th>Diabetes</th>
<th>RCF</th>
<th>BCF</th>
<th>Thrombosis*</th>
<th>TTFD (d) Median (range)**</th>
<th>FSD6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 2</td>
<td>30</td>
<td>51 (25-77)</td>
<td>60%</td>
<td>20%</td>
<td>22</td>
<td>8</td>
<td>13% (4/30)</td>
<td>42 (27-150)</td>
<td>76%</td>
</tr>
<tr>
<td>Phase 3 (OL)</td>
<td>18</td>
<td>61 (38-91)</td>
<td>89%</td>
<td>61%</td>
<td>10</td>
<td>8</td>
<td>11% (2/18)</td>
<td>64 (38-157)</td>
<td>89%</td>
</tr>
</tbody>
</table>

* Within 2 weeks of surgery
** Excludes thrombosis prior to first cannulation

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