First-in-Man Evaluation of an Investigational Bioengineered Blood Vessel

Jeffrey Lawson, Marek Iłżecki, Tomasz Jakimowicz, Alison Pilgrim, Stanisław Przywara, Jacek Szmidt, Jakub Turek, Wojciech Witkiewicz, Norbert Zapotoczny, Tomasz Zubilewicz, Laura Niklason

American Heart Association
November 20, 2013
Investigational Bioengineered Vessels

Disclaimer

The Humacyte investigational bioengineered vessel is an investigational biologic currently being studied in Poland and the US to evaluate its potential safety and efficacy when used as a vascular access in patients with End Stage Renal Disease.

This investigational product has not been submitted for regulatory approval by the FDA or any other regulatory authority. Both the clinical significance of the data reviewed in this presentation, and any potential future indication(s), warnings, precautions, and adverse reactions are unknown at this time.

This presentation includes unpublished data as of October 30, 2013.
Limitations of Synthetic Grafts for Dialysis Access

- 2 Recent large dialysis trials with PTFE:

<table>
<thead>
<tr>
<th></th>
<th>Dialysis Access Consortium (DAC) Study(^1)</th>
<th>Acuseal Phase 3 Study(^2)</th>
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<tbody>
<tr>
<td>Number of PTFE grafts</td>
<td>649</td>
<td>138</td>
</tr>
<tr>
<td>Unassisted Patency, 6 Months</td>
<td>&lt; 50%</td>
<td>48%</td>
</tr>
<tr>
<td>Unassisted Patency, 12 Months</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td>Infection</td>
<td>7%</td>
<td>11%</td>
</tr>
</tbody>
</table>

- Huber reported secondary patency rates for PTFE\(^3\):
  - 77% at 6 months
  - 60% at 12 months

- 2/3 PTFE grafts lose primary patency due to stenosis +/- thrombosis\(^1\)

- Miller reported that a mean of 1.22 interventions per PTFE-graft-year is required to maintain patency\(^4\)

Production of Investigational Bioengineered Vessels

Human Vascular Cells Isolated, Screened, Banked

Cells Used to Grow Bioengineered Vessels in Bioreactors

Bioengineered Vessel: 6mm in diameter, 40cm in length

Decellularization
Mechanically Similar to Native Vasculature

<table>
<thead>
<tr>
<th>R&amp;D Data¹</th>
<th>Suture Retention Strength (g)</th>
<th>Burst Pressure (mmHg)</th>
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<tbody>
<tr>
<td>Investigational Bioengineered Vessel</td>
<td>181 ± 18 (N=16)</td>
<td>3337 ± 343 (N=10)</td>
</tr>
<tr>
<td>Human Saphenous Vein</td>
<td>196 ± 29 (N=7)</td>
<td>1599 ± 877 (N=7)</td>
</tr>
<tr>
<td>Human Mammary Artery</td>
<td>138 ± 50 (N=6)</td>
<td>3196 ± 1264 (N=16)</td>
</tr>
</tbody>
</table>

In preclinical studies, investigational bioengineered vessels:
- repopulate with vascular cells\(^1\)
- show little intimal hyperplasia\(^1-3\)

First Experience in Man

Study Design

- Open label, single arm study, 3 sites in Poland, initiated in Dec. 2012
- Upper arm arteriovenous (AV) access for hemodialysis
- End stage renal disease (ESRD) patients who are not candidates for fistula creation
- Use for dialysis from 8 weeks
- Monthly clinical and ultrasound monitoring for first 6 months
- Patients followed for up to 2 years
- 28/30 patients enrolled

Objectives

- Evaluation of safety and tolerability in dialysis patients
- Evaluation of patency and intervention rates
- Assess changes in Panel Reactive Antibody (PRA)
- 6 Month primary endpoint
Surgical Teams

University of Medicine in Lublin
Uniwersytet Medyczny w Lublinie
Prof. Tomasz Zubilewicz
Dr. Stanislaw Przywara
Dr. Marek Ilzecki

Regional Specialist Hospital in Wroclaw
Wojewódzki Szpital Specjalistyczny we Wrocławiu
Prof. Wojciech Witkiewicz
Dr. Jakub Turek
Dr. Norbert Zapotoczny

Medical University of Warsaw
Akademia Medyczna Warszawie
Prof. Jacek Szmidt
Dr. Tomasz Jakimowicz
Dr. Bodhan Solonynko
Study Patient Population and First Human Implant

- 28 Caucasians [17 Male, 11 Female]
- Mean Age: 60 years (Range: 30 – 73)
- Mean BMI 28 (Range: 16 – 38)
- Concomitant diseases
  - Hypertension in 82%
  - Diabetes in 46%
  - Vascular disease in 39%
- 4.1 ± 1.7 prior access procedures/patient

First Human Implant of an Investigational Bioengineered Vessel

Venous Anastomosis

Arterial Anastomosis

Vessel in Upper Arm
Initial Data on Investigational Bioengineered Vessels

100% Overall Patency

- All 28 vessels patent
- 20/28 without intervention
- No infections, no aneurysm

Secondary patency 100%

Primary patency (9 patients at 6 month follow up)
8 of 28 patients lost primary patency since December 2012

- 10 patency interventions in these 8 patients
- 8 thrombectomies (1 with revision of anastomosis, 1 with angioplasty)
- 2 venous anastomosis angioplasties without thrombosis
- 71% Primary unassisted patency

1 steal syndrome: cuff placed
Initial Data on Investigational Bioengineered Vessels

No indication of immune response

- No change in PRA Class I Reactivity [N=6]
- 0% reactivity to PRA Class 2 in pre- & post-implant measurements [N=6]

No dilatation or aneurysms [N=25]

Flow rates suitable for dialysis [N=25]
Investigational Bioengineered Vessel for Dialysis

- Flow rates suitable for dialysis: >500ml/min
- 22 patients using bioengineered vessels for dialysis 3 times per week
- >800 accesses, up to 9 months experience per graft
- Grafts easy to cannulate using standard techniques
- Only one delayed hemostasis requiring intervention
  - Patient had low fibrinogen levels (0.2g/L; Normal range: 2-4g/L)
Summary

Current PTFE grafts have limitations for dialysis access
• Patency rates in PTFE at 6 months: <50% primary, 77% secondary
• Stenoses cause 2/3rds of primary patency losses
• Infection risk of 7-11%

Initial experience with Humacyte investigational bioengineered vessel is encouraging
• 100% patent: All bioengineered vessels are patent
• Intervention to restore or maintain patency in 8/28 patients
• Venous stenosis in only 3/28
  • Consistent with minimal intimal hyperplasia observed in preclinical models
• Used for access
• No infections
• No indications of immune response
• No dilatation or aneurysms

Longer follow up & additional clinical studies required to confirm preliminary observations
Humacyte Investigational Bioengineered Vessel may one day offer the growing ESRD patient population an alternative option for dialysis access

We would like to thank those patients who enrolled for their participation in the ongoing studies.