UPDATE ON BIOENGINEERED GRAFTS FOR VASCULAR ACCESS

Phase 2 Results at 5 Years

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Image Courtesy of Duke University

DISCLOSURES

FINANCIAL DISCLOSURE:

Chief Surgical Officer; Humacyte, Inc.
Dr. Lawson receives salary, and holds stock options, from Humacyte.

DISCLAIMER:

None of the data presented in this lecture is intended to be perceived as “claims” for the potential clinical use of the vascular tissues discussed today.

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.

HUMAN ACELLULAR VESSEL (HAV) IN HEMODIALYSIS ACCESS

Objective: HAV being developed for dialysis access as an alternative to autologous arteriovenous fistula (AVF).

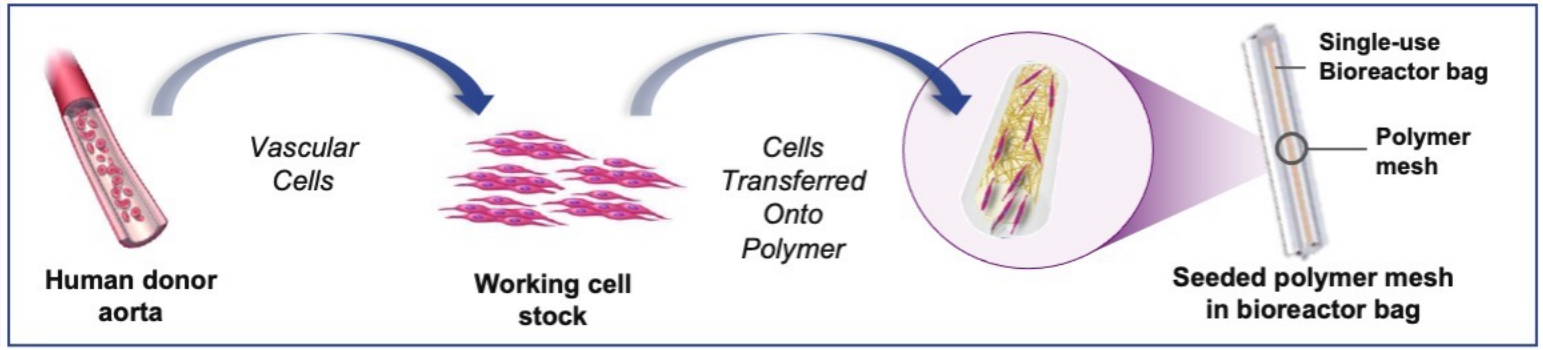
Potential benefits of HAV evaluated in completed and ongoing clinical trials include:

- Off-the-shelf
- Usable within one month after implantation
- Potential for decreased catheter contact time as compared to patients awaiting fistula maturation
- HAV appears to be highly resistant to infection
- HAV has no evidence of immunogenicity
- Host cells repopulate the HAV
- Long-term durability in ongoing studies.

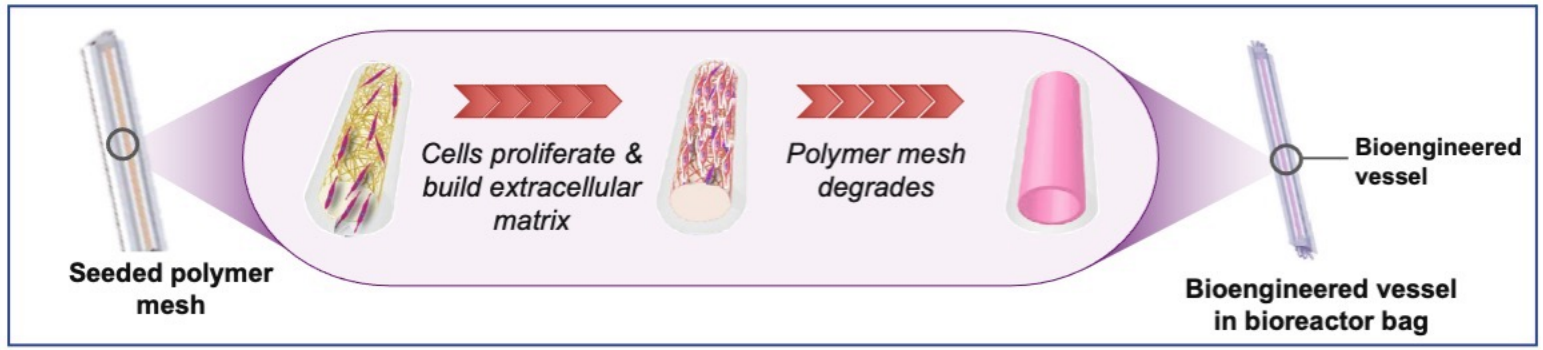
BIOENGINEERED HUMAN ACELLUAR VESSELS (HAVs)

HUMACYTE

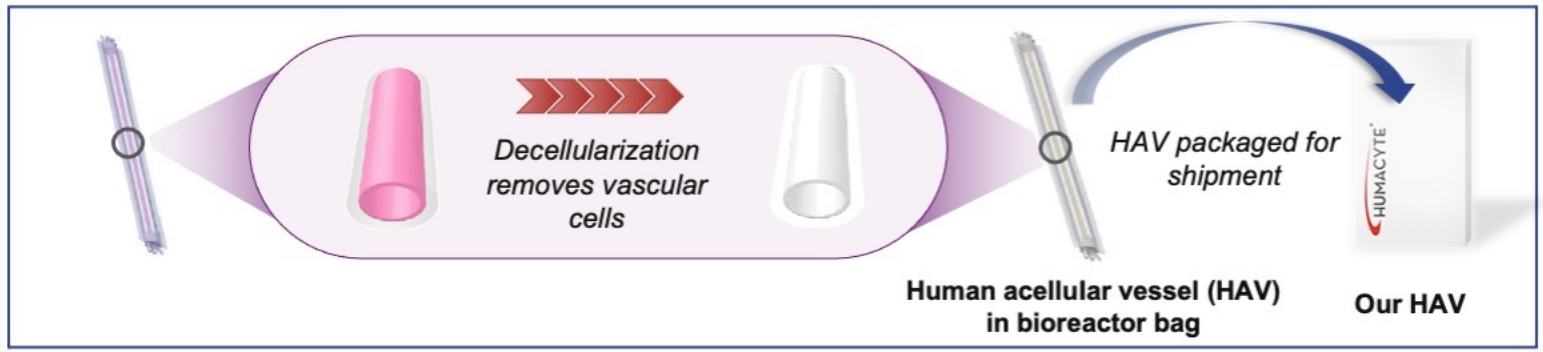
1 Cell Seeding



2 Tissue Formation



3 Cell Removal & Packaging



HAV Clinical Experience

- First implants in 2012
- Over 430 patients
- 800 patient-years
- 8 clinical trials
- 3 investigational indications
- 60 clinical sites
- Over 100 surgeons have implanted the HAV into patients

HAV IN HEMODIALYSIS ACCESS: PHASE 2 STUDY THROUGH 12 MONTHS

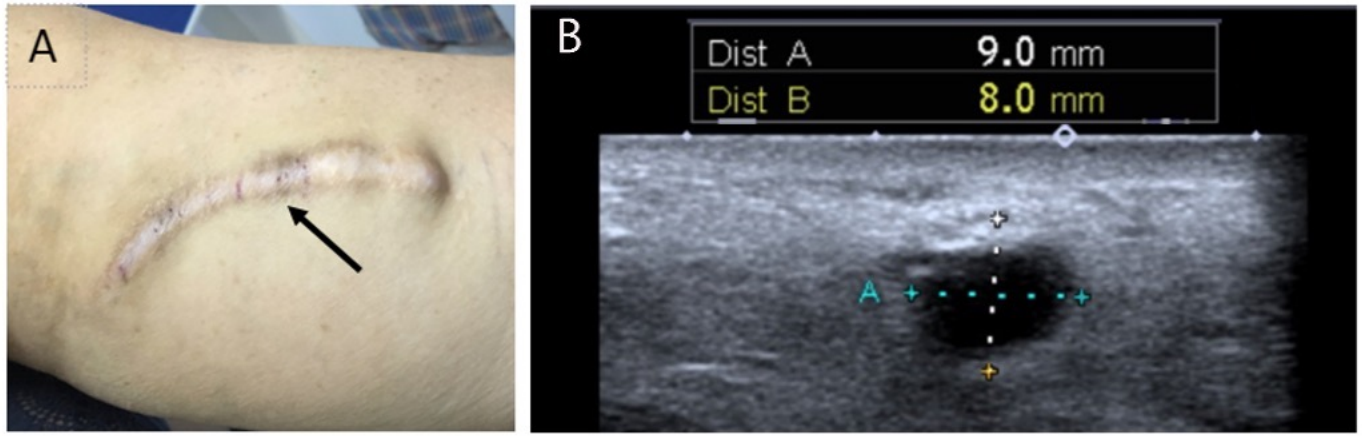
- **Methods:** Six centers in the US and Poland, HAV implanted in patients who were in need of dialysis access and who were suitable for arteriovenous grafting [1].
- **Subjects:** 60 patients, mean follow-up 16 months
  - Age = 59 ± 10y;
  - 77% Caucasian;
  - 90% with hypertension;
  - 43% diabetic;
  - Prior AV accesses: 3.6 ± 2.1.
- **Safety Outcomes:**
  - No aneurysmal degeneration;
  - No clinical rejection;
  - Multiple subjects subsequently received successful kidney transplants.
- **Results:**
  - 12 month HAV outcomes published in *The Lancet* [1]

Phase 2 HAV Results vs. Historical Fistula & ePTFE Data

Conduit	6-month Secondary Patency	12-month Secondary Patency	Infection Rate per patient-year
HAV Phase 2	**97%** (85-98%)	**89%** (74-93%)	**1.3%**
***HISTORICAL publications,* Fistula** [2,3,4]	**61%** [3] (useable for dialysis)	**59.5%** [4]	**4.0%** [5]
***HISTORICAL publications,* ePTFE** [5]	**80%** (75-84%)	**70%**(64-75%)	**9.0%**

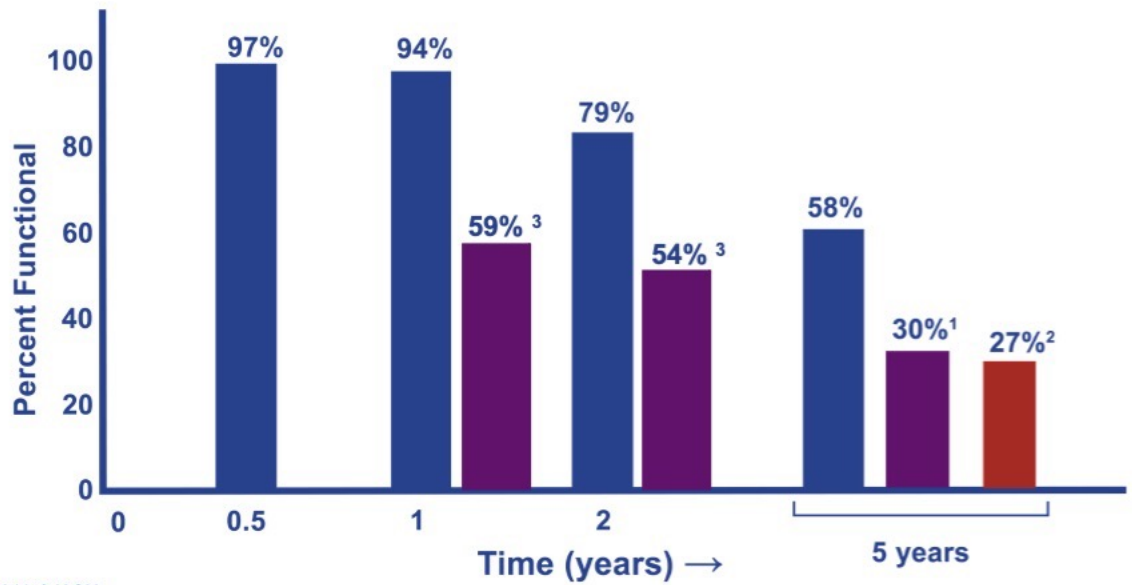
[1] Lawson, J.H. et al. The Lancet 2016; 387: 2026-2034.
[2] Halbert, R.J, et al . Kidney360 December 2020, 1 : 1437-1446
[3] Allon, M., et al. American J Kidney Disease 2018; 71: 677-689.
[4] Arhuidese, I.J., et al. Journal Vascular Surgery 2018; 68: 1166-1174
[5] Al-Jaishi, A.A., et al. JASN 2017; 28: 1839-1850.

HAV IN HEMODIALYSIS ACCESS: PHASE 2 STUDY ≥ 5 YEARS, LONG TERM DURABILITY



A) Patient with access site utilized for 6 years (arrow).

B) Ultrasound of HAV from same patient.



HAV Fistula ePTFE

58% secondary patency at 5 years compares well to ***historical*** ePTFE and arteriovenous fistulas.

[1] Lok, et al; 2013 CJASN
[2] Kakisis et al; 2017, JVS
[3] Arhuidese, et al, 2018; JVS.

HAV REPOPULATES WITH CELLS FROM THE PATIENT OVER TIME [1]

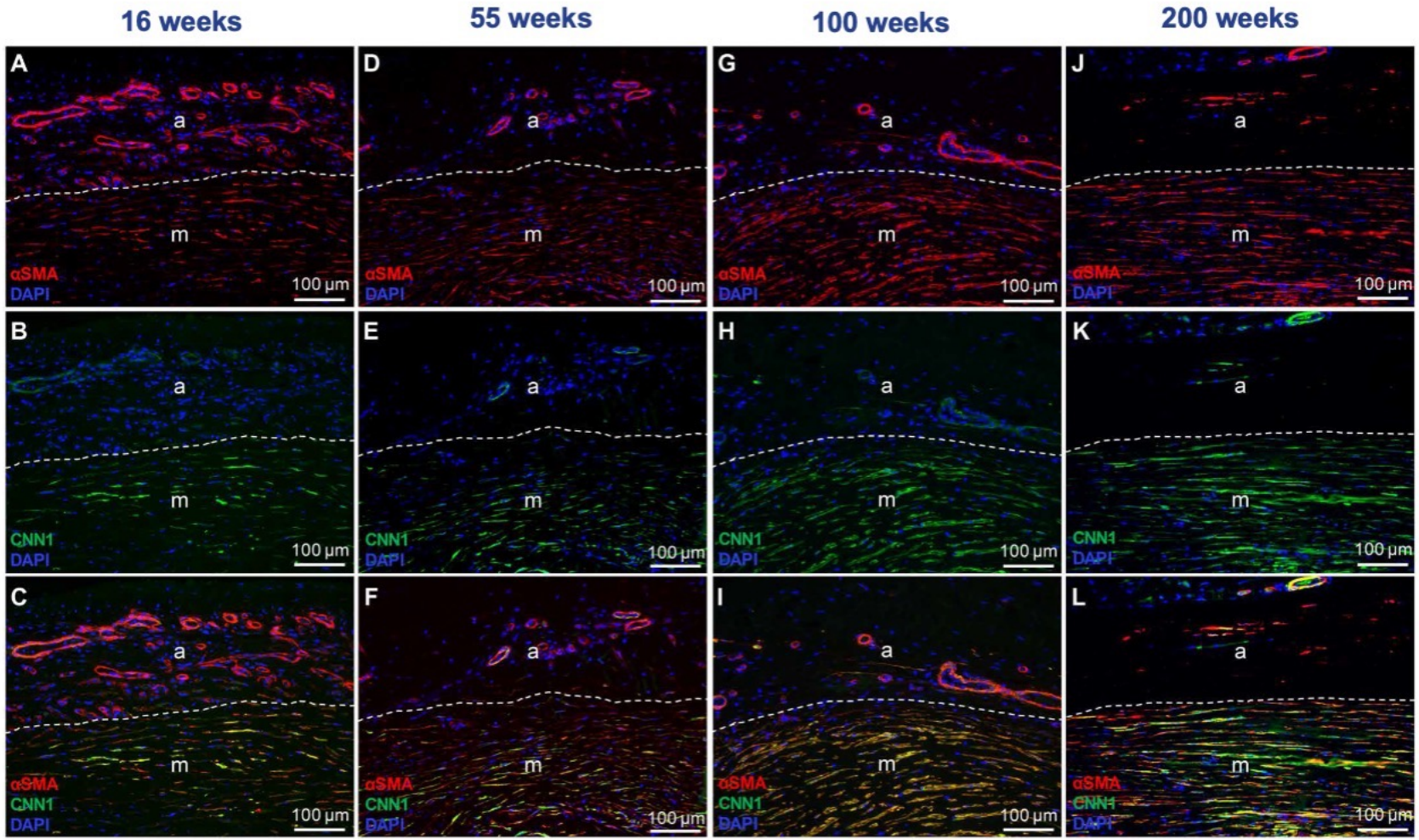


Fig. 4. Infiltration and maturation of aSMA+ host cells within the implanted HAV. Immunofluorescence staining of explanted HAV sections for aSMA (red) and CNN1 (green), a contractile marker of mature SMCs. Developmental maturation indicated by coexpression of CNN1 and aSMA. HAV sections explanted at 16 (**A** to **C**), 55 (**D** to **F**), 100 (**G** to **I**), and 200 (**J** to **L**) weeks after implantation. a, neoadventitia; m, medial layer. The boundary between the neoadventitia and medial layers is delineated by a white dashed line. Nuclei (blue) were counterstained with DAPI.

[1] Kirkton, R.D. et al, Sci Trans Med 2019; 11:eaau6934.

NEXT STEPS FOR CLINICAL EVALUATION OF THE HAV

Phase 2 long-term follow-up results submitted for publication:

Five-year outcomes in patients with end-stage renal disease who received the bioengineered human acellular vessel for Dialysis Access

Tomasz Jakimowicz MD PhD[a]; Stanislaw Przywara MD, PhD[b]; Jakub Turek MD[c]; Malgorzata Guziewicz MD PhD[c]; Marek Ilzecki MD, PhD[b]; Michał Macech MD[a]; Wojciech Witkiewicz MD PhD[c]; Norbert Zapotoczny MD[c]; Tomasz Zubilewicz MD PhD[b]; Robert Kirkton PhD[d]; Alison J Pilgrim MD[e]; Heather L Prichard PhD[d]; William Tente MS[d]; Jeffrey H Lawson MD PhD[d,f]; Laura E Niklason MD PhD[d,g]

Phase 3 studies ongoing:

NCT02644941 (HUMANITY): An Assessment of Humacyte's Human Acellular Vessel in Patients Needing Renal Replacement Therapy: A Comparison with **ePTFE Grafts** as Conduits for Hemodialysis ***(24-month follow-up anticipated soon)***

- 37 centers in the US, German, UK, Poland, Portugal, and Israel; 355 total subjects;
- 1:1 Prospective randomization HAV (6mm x 42cm) vs. ePTFE grafts.

NCT03183245: Compare the Efficacy and Safety of Humacyte's Human Acellular Vessel with that of an **Autologous Arteriovenous Fistula** in Subjects with End-Stage Renal Disease ***(currently enrolling)***

- 30 centers in the US; target 240 total subjects (over 180 subjects enrolled currently).

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