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Implantation of a Bioengineered Vessel Human Acellular Vessel™ (HAV™)

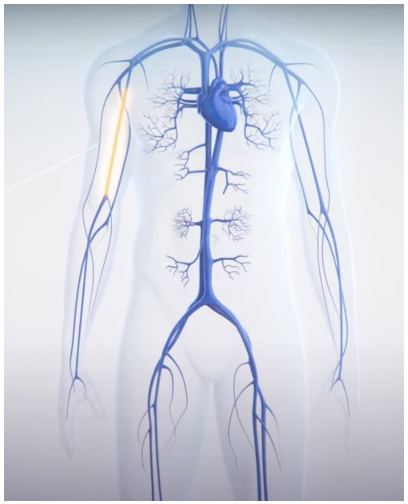
March 2024 ICD-10 Coordination and Maintenance Committee Meeting

The Human Acellular Vessel™ (HAV™) is investigational and has not been approved for sale by the FDA or any other regulatory agency. These slides and the accompanying oral presentation contain forward-looking statements.

HAV Overview

- Human Acellular Vessel™ (HAV™) is a first-of-its-kind, bioengineered, implantable biologic vessel

INDICATION	• HAV is anticipated to be indicated for urgent arterial repair following extremity vascular trauma when synthetic graft is not indicated, and when repair with autologous vein is not feasible
SUPPLIED	• HAV is supplied as a package containing one HAV unit for implantation in a single patient only • HAV is 6 mm in inner diameter and 42 cm in length
PROCEDURE	• HAV is surgically implanted to repair the injured artery • Anatomical location and HAV length decided by surgeon
MECHANISM OF ACTION	• Once implanted, HAV is repopulated by patient's own cells over time, resulting in a remodeled, revascularized, and living blood vessel

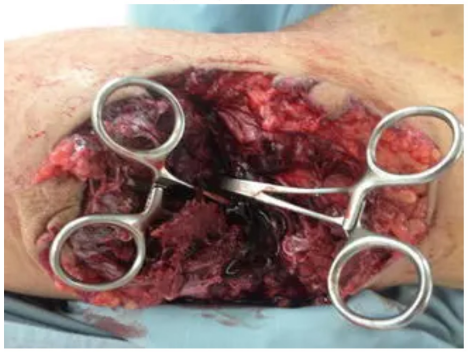


Current Treatment Options for Vascular Trauma

Vascular Trauma, occurring in both civilian and military settings, is categorized by the mechanism of injury (blunt, penetrating, or combination)

- Penetrating trauma can be caused by objects (e.g., bullets), fragments from a blast, or stabs.
- Blunt trauma occurs crush injuries, dislocations and fractures, for example from motor vehicle accidents and falls[1]

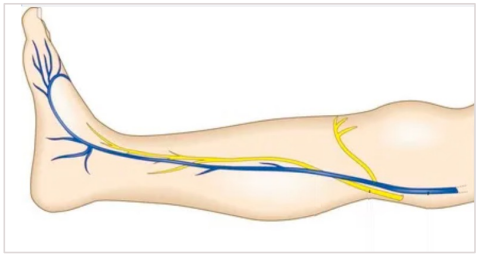
Exit wound of a shotgun injury



Shotgun Wound

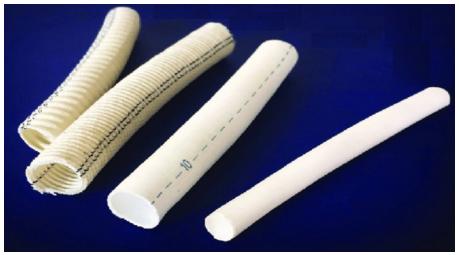
Current Treatment Options[2]

1. Saphenous Vein Grafts



Vein harvest is the current standard of care. Another blood vessel, obtained via surgery, replaces or bypasses the damaged one

2. Synthetic Grafts (ePTFE)

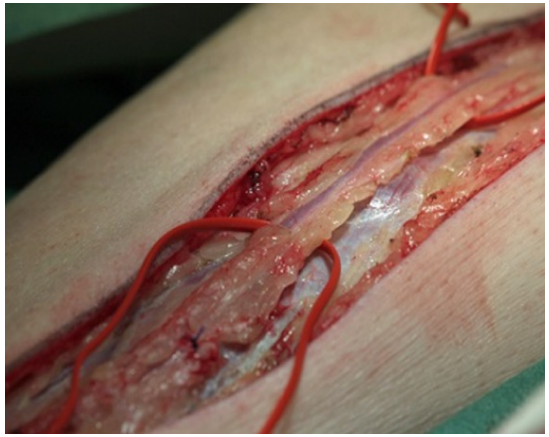


Synthetics are quick and may be used when a suitable vein is not available, but have infection risk and high rates of amputation

Complications from a failed repair, or lack of a suitable vein, can result in amputation

Current Treatment Options Have Significant Limitations

Autologous Vein Grafts



- Harvesting vein adds an hour or more of operative time[3]
- Not all patients have suitable veins for harvesting
- Delayed revascularization significantly increases amputation risk
- Rate of amputation in lower-limb trauma ranges from 5-15%[3,4]

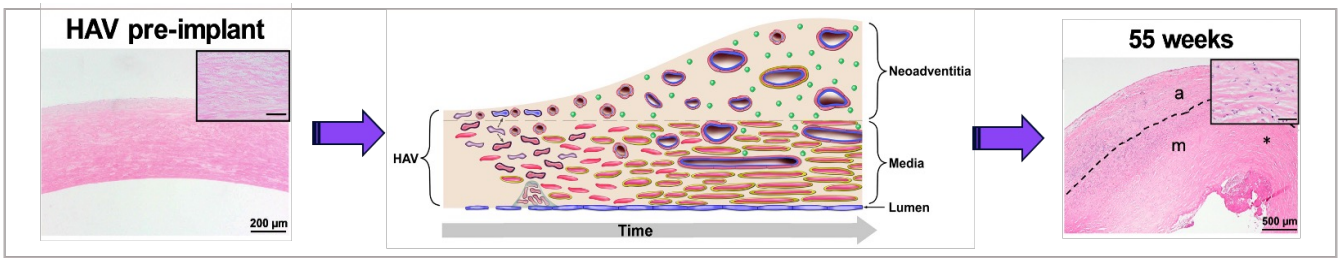
Synthetic (ePTFE) Grafts

- 50% infection rate[5]
- Mortality rate when ePTFE is infected: 8-30%[6]
- Median length of stay 11 days if re-admitted for graft infection
- Amputation rate is 8-15%

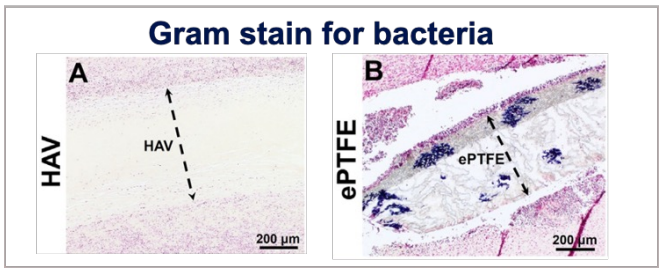
Other non-autologous / non-synthetic grafts (such as cryopreserved), while available, have not been evaluated in arterial trauma and are rarely used

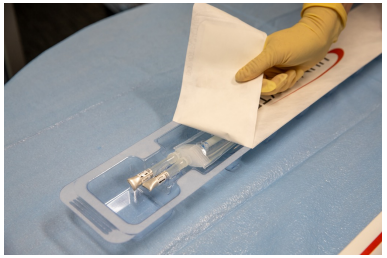
HAV: New Treatment Option for Traumatic Vascular Injury

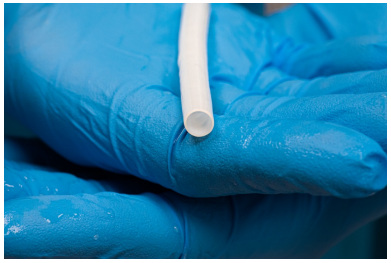
- Potential benefits of the HAV[7]
  - The HAV is a first-of-its-kind, bioengineered, implantable biologic vessel
  - The HAV is quickly accessed from its packaging and is ready for immediate use
    - Harvesting vein from the patient takes an hour or more[7]
  - The HAV repopulates with the patient's own cells, becoming a living tissue[8]



  - The HAV is resistant to infection, compared to synthetic grafts[9]







HAV Manufacturing Process

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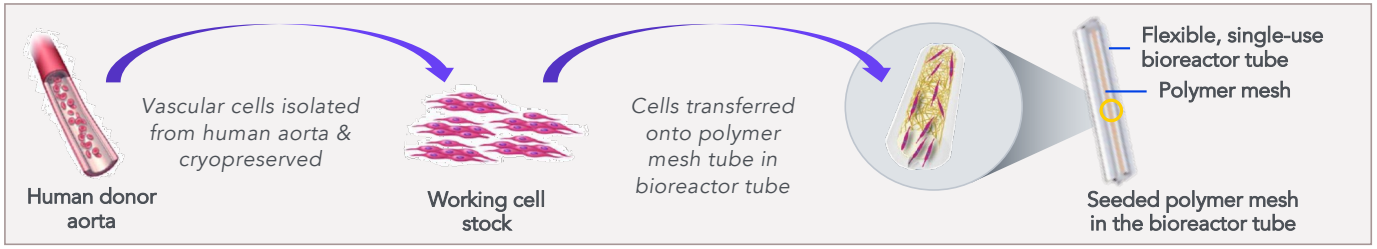
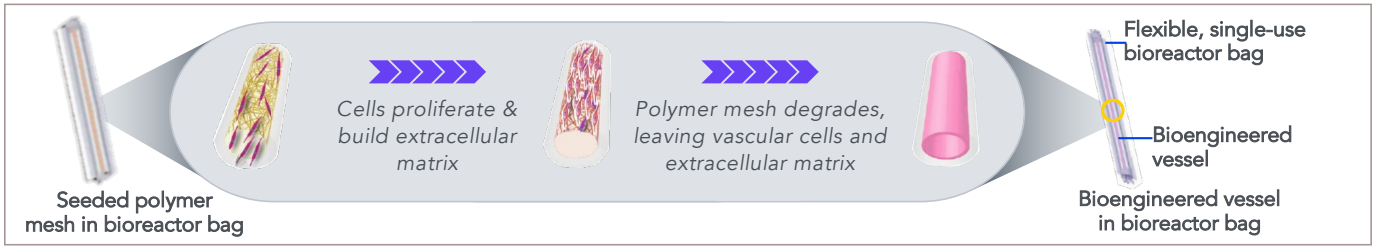
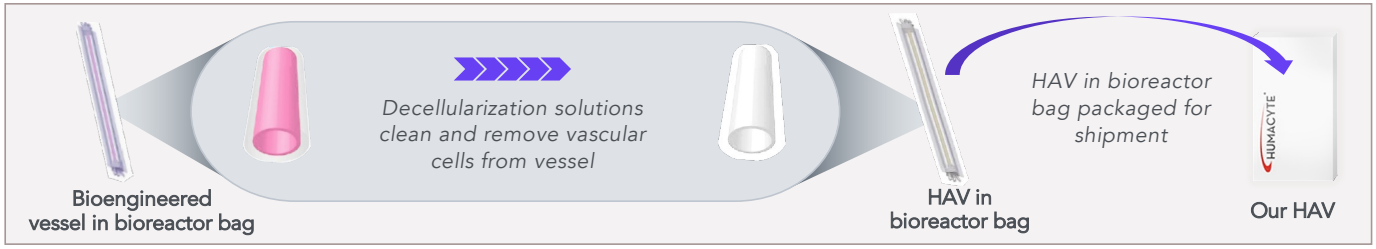
1 Cell seeding



2 Vessel formation



3 Cell removal and packaging



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CLN-PRO-V005 Phase 2/3 Pivotal Trial

Human Acellular Vessel (HAV) in Vascular Trauma
(NCT03005418)

- Single-arm, open label trial
- Level 1 trauma centers in U.S. and Israel
- Arterial injury repair

Primary endpoint 30-day patency in patients with extremity injuries

69 total patients enrolled
51 patients with Extremity Injuries – focus for BLA filing

- ALL patients had no vein available, as assessed by treating surgeons
- Hence, patients would have received synthetic grafts, ligation of the bleeding vessel and/or amputation, had they not received the HAV
- Extremity Injuries at high risk of contamination/infection[10]

- Zero reports of rejection of or allergic reaction to HAV in the clinical studies
- Zero serious adverse reactions; no adverse reactions reported ≥ 5% for the HAV
- Most frequent adverse reactions, with an incidence of ≥3%, include procedural pain (3 patients or 4%) and pyrexia/fever (2 patients or 3%)

- Historical Benchmarks
  - Systematic literature review of synthetics in vascular trauma
- Primary Comparison
  - 30-day endpoint of patency
- Secondary Comparisons
  - Infection rate
  - Amputation rate

Success Criteria
- Comparable Patency
- Infection rate comparable or lower than Synthetic Grafts
- Amputation rate comparable or lower than Synthetic Grafts

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Summary of V005 Pivotal Trial Outcomes

- In V005, patency for HAV was greater than for historical Synthetic Grafts
- Limb salvage with HAV was better than historical Synthetic Grafts
- HAV Infection Rate lower than historical for synthetics, despite V005 patients having higher infection risk
- No unexpected safety signals in this sick and diverse trauma population

MEASURE	TOTAL (n=69)	EXTREMITY (n=51)	SYNTHETIC GRAFT (META-ANALYSIS)[11]
30-day Patency*	89.9%	90.2%	78.9%
Amputation Rate	10.1%	9.8%	24.3%
Limb Salvage Rate	89.9%	90.2%	75.7%
Conduit Infection Rate	2.9%	2.0%	8.4%

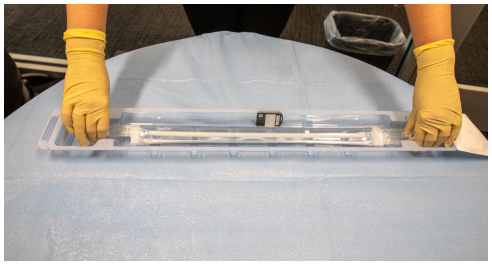
*Patency Rate for V005 is based on Adjudication outcomes from an independent external Adjudication Committee.

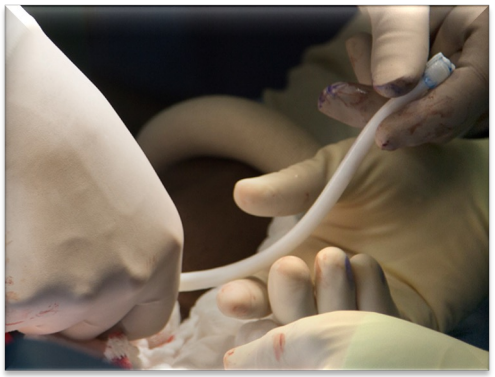
Combined study data from V005+V017 (Ukraine Humanitarian Aid Program (n=17)) further strengthen HAV performance vs. Synthetic Grafts in Patients with Extremity Trauma

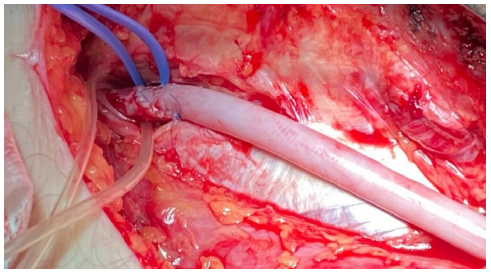
- V017 data: 30-day patency rate was 95% and limb salvage was 100%.
- Zero cases of HAV infections, and zero deaths

HAV Procedure

- Removal from Packaging:
  - HAV is removed from primary packaging per PI instructions
- Preparation:
  - Surgeon determines length to use for HAV, and HAV is cut to length
  - HAV is ready for immediate implantation or can be placed in a basin of sterile saline at room temperature while the patient is being prepped
- Implantation:
  - The injured artery is dissected and isolated proximally and distally to the injury
  - Surgeon makes an anastomosis between HAV and the host vessel, as end-to-end or end-to-side, using non-absorbable, monofilament sutures
  - Prior to anastomosis, silicone mandrel is removed from lumen of HAV
  - If HAV is to be tunneled, a sheath tunneler is used, and the silicone tube remains within the HAV to prevent kinking or twisting in the tunnel
  - Static blood is flushed from lumen of HAV while completing second anastomosis
  - Clamps are released to restore blood flow and check for leaks at anastomosis sites
- Closure:
  - Surgeon inspects operative site carefully prior to closure to ensure that there are no twists, kinks, redundancy, or HAV impingement before and during tissue closure
  - Surgeon inspects the circulation to ensure perfusion to the distal vascular bed







Medical Record Documentation / Regulatory Status

- FDA assigned a Prescription Drug User Fee Act (PDUFA) target action date of August 10, 2024
  - Biologics License Application (BLA) was submitted on December 11, 2023
  - FDA accepted and granted Priority Review to Humacyte's BLA on February 8, 2024

RMAT designation granted by FDA [May 2, 2023]

Priority designation granted by Department of Defense [November 2018]

- Documentation of HAV will be included in the operative report and may be referred to as:
  - Human Acellular Vessel
  - Brand Name TBD

Summary

- Human Acellular Vessel (HAV) is a first-of-its-kind, bioengineered, implantable biologic vessel that is anticipated to be indicated for urgent arterial repair following extremity vascular trauma when synthetic graft is not indicated, and when repair with autologous vein is not feasible
  - FDA: RMAT Designation
  - DoD: Priority Designation
- HAV is surgically implanted to repair the injured artery through a multi-step process
- Once implanted, HAV is repopulated by patient's own cells over time, resulting in a remodeled, revascularized, and living blood vessel
- Current treatment options (saphenous vein grafts, synthetic grafts, non-synthetic/non-autologous grafts) have significant limitations
- **Current ICD-10-PCS coding does not uniquely capture the HAV preparation and implantation process, and does not allow for accurate reporting and outcomes tracking**

References

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Thank You