Disclosures

2015–2019	Scientific Adv. Board & Consultant, Proteon Therapeutics, Inc.
2016	Advisory Board, Humacyte, Inc.
2017, 2018	Consultant, Merck Sharp & Dohme Corporation
2017, 2018	Consultant, Medtronic Corporation
2018	Consultant, Semma Therapeutics
2019, 2021-2024	Consultant, Laminate Medical Technologies
2019 – 2025	Consultant (including joint research venture), Mitobridge, Inc.
2020 – 2024	Consultant, Humacyte, Inc.

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Study Rationale

- Arteriovenous fistulas (AVFs) are a preferred method for initial vascular access in patients requiring hemodialysis (HD)
- However, failure of AVF maturation can drive increased catheter use and associated increased morbidity/mortality
- **ATEV™ (Acellular Tissue Engineered Vessel)** is a potential alternative vascular access option to AVFs, with preliminary data demonstrating low infection rates, and without the associated maturation failure

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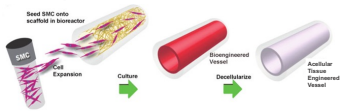
Humacyte's Acellular Tissue Engineered Vessel (ATEV)



- **Off-the-shelf, immediately available with 18-month shelf life**
- **ATEV has a low risk of infection as it mimics native vascular tissue**
- **Universally implantable with no immuno-suppression**

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Study Design: CLN-PRO-V007

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A prospective, multicenter, open-label, randomized, two-arm, comparative study

- 242 ESKD patients on HD eligible for AVF or AVG creation
- 30 centers in the US

1:1 R

- **Acellular Tissue Engineered Vessel (ATEV)** — Surgically implanted in the upper extremity (n = 123)
- **Autogenous AV Fistula (AVF)** — Surgically created in the upper extremity (n = 119)

Follow-Up

- All patients with study access will be followed for 24 months

12-month outcomes results from this study are as of cut-off date of 22 April 2024

CLN-PRO-V007; ClinicalTrials.gov, NCT03183245

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Key Eligibility Criteria

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INCLUSION CRITERIA	Adults with ESKD receiving HD eligible for AVF or AVG creation
	Estimated life expectancy >2 years
EXCLUSION CRITERIA	Planned AVF creation that requires more than one stage to complete
	Candidates who are able to get the optimal fistula: Radiocephalic AVF in the forearm
	Uncontrolled diabetes [HbA1c >10%]

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Key Outcomes

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Primary Efficacy	**Co-Primary Endpoints** • Functional patency* at 6 months • Secondary patency** at 12 months
Key Secondary Efficacy	• Duration of usability*** at 12 months
Safety	• Infections related to any HD access at 12 months • Adverse events of special interest (AESI) • HD access related interventions at 12 months

*Functional Patency is dialysis with 2 needles for ≥75% of dialysis sessions over a continuous 4-week period
**Secondary Patency at Month 12 is maintained if a patient achieved functional patency at Month 6 and SA was not abandoned by Day 365
***Duration of Usability is defined as time from successful 2-needle cannulation to abandonment

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Baseline Characteristics

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Characteristic	ATEV (N=123)	AVF (N=119)
Age, Mean (SD), Y	57.1 (13.61)	60.1 (13.06)
Age > 65 years, N (%)	39 (31.7%)	42 (35.3%)
HIGH RISK GROUPS FOR AVF NON-MATURATION		
Female, N (%)	37 (30.1%)	33 (27.7%)
Obese (BMI ≥ 30), N (%)	51 (41.5%)	42 (35.3%)
Diabetes, N (%)	82 (66.7%)	83 (69.7%)
≥ 2 Factors (Female, Diabetes, BMI ≥ 30)	48 (39.0%)	45 (37.8%)

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Key Endpoint Analysis

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Co-Primary Endpoints	Analysis by Time Point				Joint Analysis	
	ATEV (N=123)	AVF (N=119)	Relative Patency*	Exploratory P-Value	Relative Patency**	P-Value
Functional Patency at Month 6	81.3%	66.4%	1.22	0.0082	1.17	0.0071
Secondary Patency at Month 12	68.3%	62.2%	1.10	0.3184		

*Relative Patency is ATEV patency / AVF patency (eg, Relative Patency at Month 6 is 81.6/66.4 = 1.22, 22% improvement over AVF).
** Joint relative patency is a model-based average of patency at Month 6 and Month 12 (1.17 implies 17% average improvement over AVF)
P-value is based on jointly modeling of 2 co-primary endpoints, exploratory p-values for individual time point are from Pearson's Chi-square test

Key Secondary Endpoint	ATEV	AVF	Difference	P-value
Duration of Usability (months)	7.5	6.1	1.4	0.0164

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Benefits in Patency for High-Risk Sub-Groups

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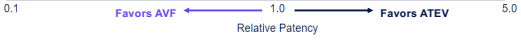
	AVF N	ATEV N	Relative Patency (95% CI)	P-value
Diabetic	83	82	1.26 (1.08, 1.46)	0.0024
Obese (BMI ≥ 30)	42	51	1.53 (1.21, 1.94)	0.0001
Females	33	37	1.65 (1.28, 2.12)	<0.0001
>=2 Factors	45	48	1.74 (1.36, 2.23)	<0.0001
All Patients	119	123	1.17 (1.04, 1.32)	0.0071



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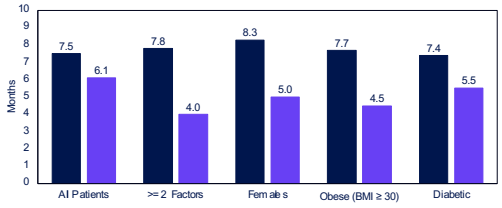
Duration of Use for ATEV vs AVF Over 12 Months



	All Patients	>= 2 Factors	Females	Obese (BMI ≥ 30)	Diabetic
Difference	1.4	3.8	3.3	3.2	1.9
P-value	0.0164	0.0003	0.0011	0.0015	0.0155

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Low Incidence of Infection in ATEV and AVF

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	ATEV		AVF	
	Subjects n (%)	Events	Subjects n (%)	Events
HD access-related Infections	**11 (9.1)**	**12**	**12 (9.9)**	**14**
Blood stream	6 (5.0)	7	7 (5.8)	8
Local	5 (4.1)	5	5 (4.1)	6
SA-related Infections	**4 (3.3)**	**4**	**1 (0.8)**	**1**
Blood stream	2 (1.7)	2	0	0
Local	2 (1.7)	2	1 (0.8)	1

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Safety Outcomes: Overall

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Overview of Treatment-Emergent Adverse Events

	ATEV		AVF	
	Subjects n (%) (N=121)	Events	Subjects n (%) (N=121)	Events
Treatment-Emergent Adverse Events (TEAEs)	119 (98.3)	1211	117 (96.7)	828
Serious Adverse Events (SAEs)	99 (81.8)	391	74 (61.2)	215
Adverse Events of Special Interest				
Thrombosis	63 (52.1)	126	11 (9.1)	12
Stenosis	79 (65.3)	228	57 (47.1)	115
Pseudoaneurysm	18 (14.9)	22	4 (3.3)	4
Aneurysm	2 (1.7)	2	2 (1.7)	3
Rupture	0	0	2 (1.7)	2
Steal Syndrome	1 (0.8)	1	7 (5.8)	7

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Thrombosis and Stenosis Events Resolved

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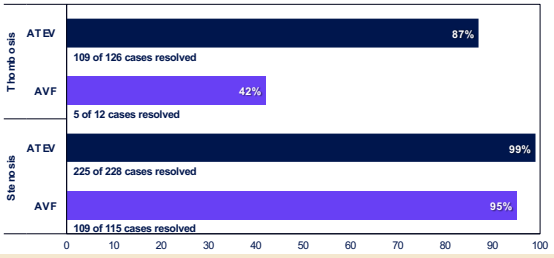

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Interventions on the Study Access

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	ATEV		AVF	
	Subjects n (%)	Events N	Subjects n (%)	Events N
SA access related intervention	**84 (69.4)**	**326**	**71 (58.7)**	**161**
Angioplasty	73 (60.3)	169	50 (41.3)	82
Stent	33 (27.3)	46	10 (8.3)	11
Thrombectomy	56 (46.3)	96	2 (1.7)	2
Balloon Assisted Maturation	0	0	8 (6.6)	27
DRIL	0	0	1 (0.8)	1
Partial Removal/Excision	1 (0.8)	1	1 (0.8)	1
Surgical Revision	13 (10.7)	14	28 (23.1)	32

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Conclusions

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- **ATEV (Acellular Tissue Engineered Vessel) demonstrated improved outcomes vs AVFs in ESKD patients requiring HD access with respect to:**
  - ATEV superior to AVF in terms of overall patency
  - ATEV superior to AVF in terms of duration of use
- **Greater benefits in patients with higher risk of AVF non-maturation**
  - Female, Obese, and Diabetic patients
  - Benefit is even greater in patients with more than one AVF non-maturation risk factor
- **ATEV's safety profile vs AVF demonstrated:**
  - Similar low incidence of infection
  - Lower rates of ruptures or surgical revision procedures
  - No need for interventions to support maturation
  - More thrombosis and stenosis events requiring maintenance interventions; majority of cases were successfully resolved

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V007 Surgical Teams

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Dr. Villa	Lubbock Surgery Center
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