

Tessuti ingegnerizzati per Graft: i risultati preliminari e nuove prospettive

Matteo Tozzi

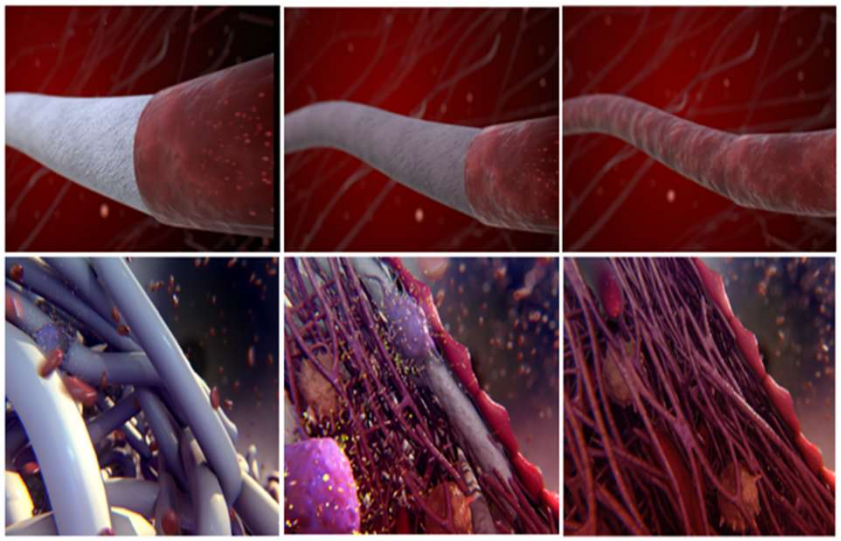
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UNIVERSITÀ DEGLI STUDI
DELL'INSUBRIA

RestoreX - Endogenous Tissue Restoration (ETR) Technology: TRANSFORMATIVE implants to evolve into new living, long-lasting tissue

The most significant breakthrough in vascular replacement technology in over **60 years**

- Long-term patency
- Endogenous Tissue With Host Collagen And Endothelium Compliant With Flowing Blood (ETR)
- Highly resistant to infection



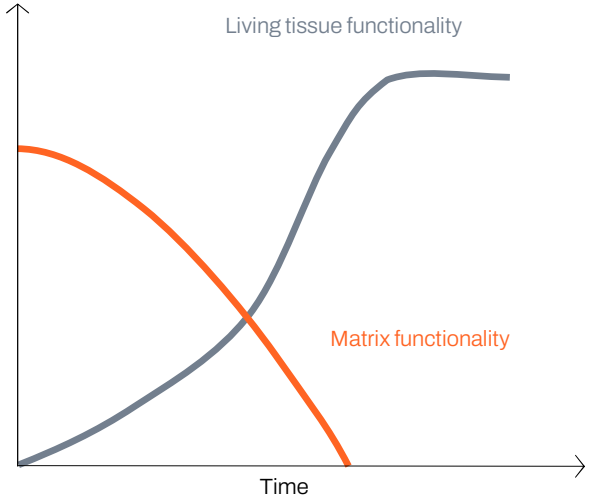
>170 patients globally have received this implant

4 clinical trials globally

2 pivotal trials

Xeltis' vascular conduits driven by a revolutionary advancement in novel polymer technology

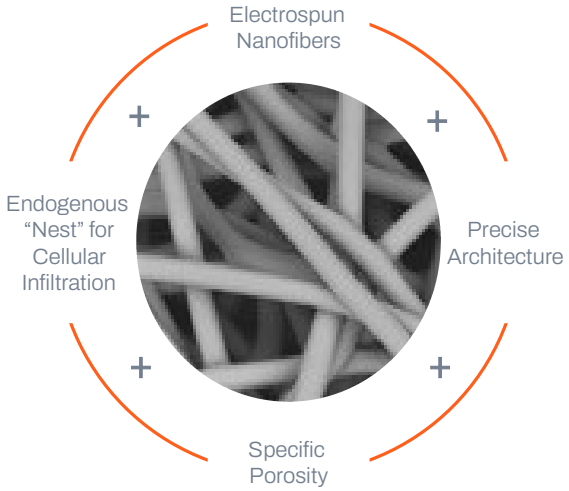
Supramolecular chemistry creating novel class of Polymers - Nobel Prize winning science



Polymer degradation and new tissue creation go hand in hand

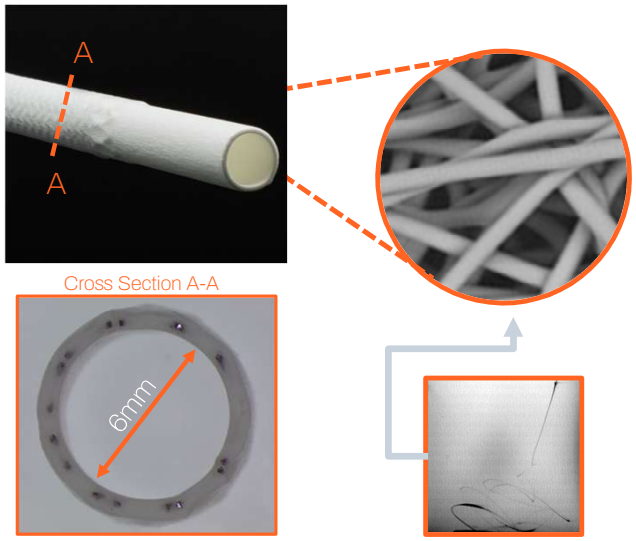
Exclusively to Xeltis

Precise electrospinning



Porous conduit design allows for patient's immune system to infiltrate and generate healthy response

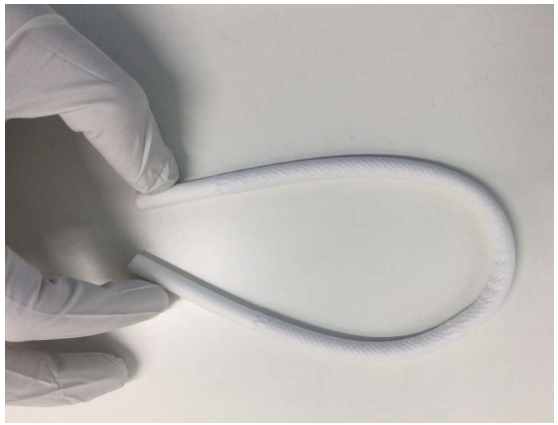
Combined with laser cut strain release system that avoids kink and provide support



The aXess AV dialysis access conduit

Enabling the body to create its own vessel

From an arteriovenous implant...

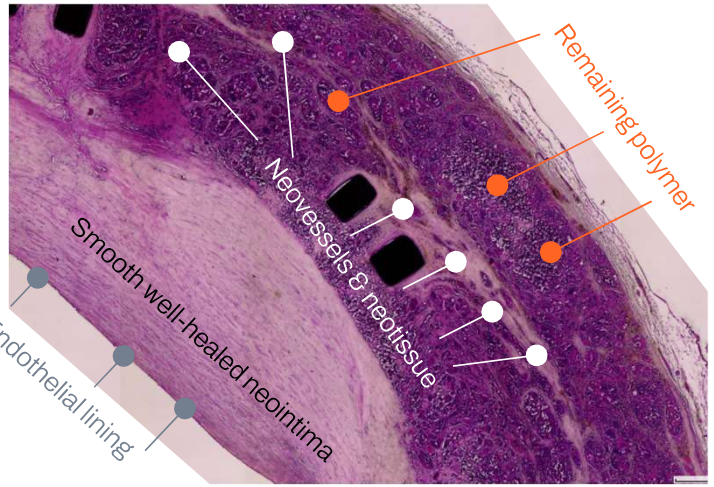


Endogenous Tissue Restoration (ETR)

... to a living natural conduit

14 months follow-up in human

Implant polymer interspersed with neotissue and neovessels



Cross-section of supramolecular vessel transforming into natural tissue (ETR)

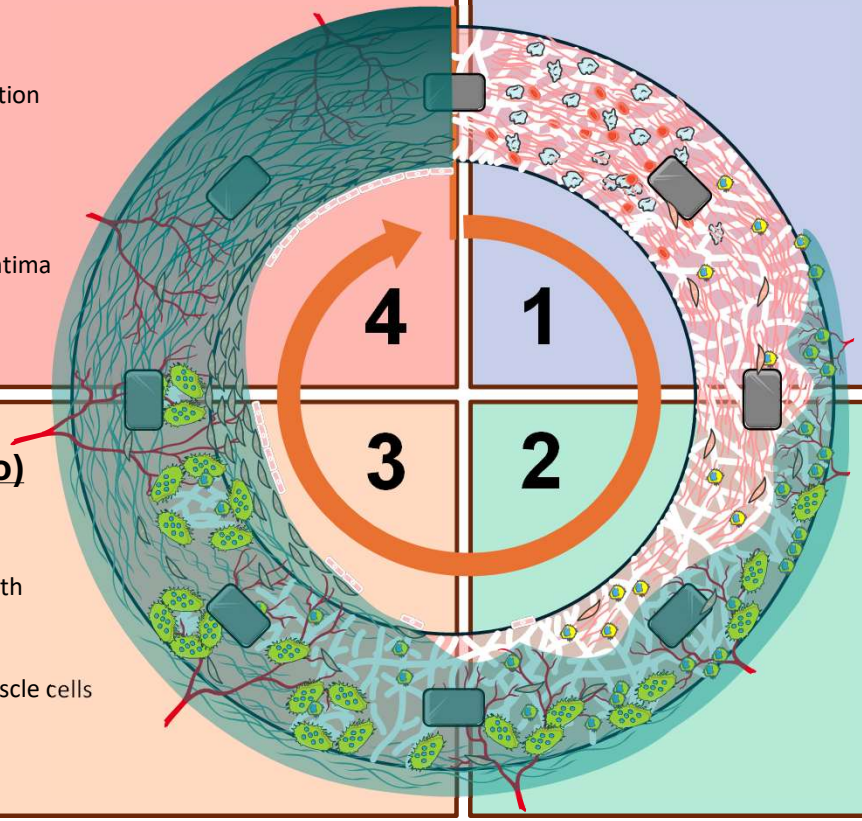
Proposed paradigm based on currently available preclinical and clinical data

4. Final phase (>24 mo)

- Uniform & complete polymer absorption
- Collagenized wall with inflammation resolution (neomedia)
- Reduction in transmural vascularity (quiescence)
- Mature, endothelialized, stable neointima

1. Early Phase (0-3 mo)

- Hemostasis within minutes after implant by fibrin and other blood components
- Diffuse macrophage infiltration with onset of polymer absorption at ablumen
- Abluminal early physiological healing and tissue growth



3. Advanced phase (6-24 mo)

- Formation of giant cell-rimmed, actively absorbing, polymer islands
- Locally complete polymer absorption with resolution of inflammation
- Transmural capillary formation
- Neointima formation rich in smooth muscle cells with focal endothelial cells

2. Intermediary phase (3-12 mo)

- Continued polymer absorption with abluminal giant cell formation
- Early formation of capillaries originating from abluminal tissue
- Onset of new connective tissue formation (via myofibroblasts)

Supramolecular polymer implant

Microskeleton nitinol strut (SRS)

Fibrin, platelets & red blood cells

Macrophage

Foreign Body Giant cell

Smooth muscle cell /myofibroblast

Endothelial cell

(transmural) blood vessels

Collagen

Comparison between remodeled aXess Hemodialysis conduit and alternative solutions

aXess – after remodeling

- Endothelial lining of the lumen
- Collagen-rich generally thin neointima containing circumferentially-arranged SMC/myofibroblasts
- aXess graft replaced by vascularized collagen-rich tissue and interspersed SMC/myofibroblasts
- Collagen-rich vascularized tissue capsule surrounding graft

Normal Artery

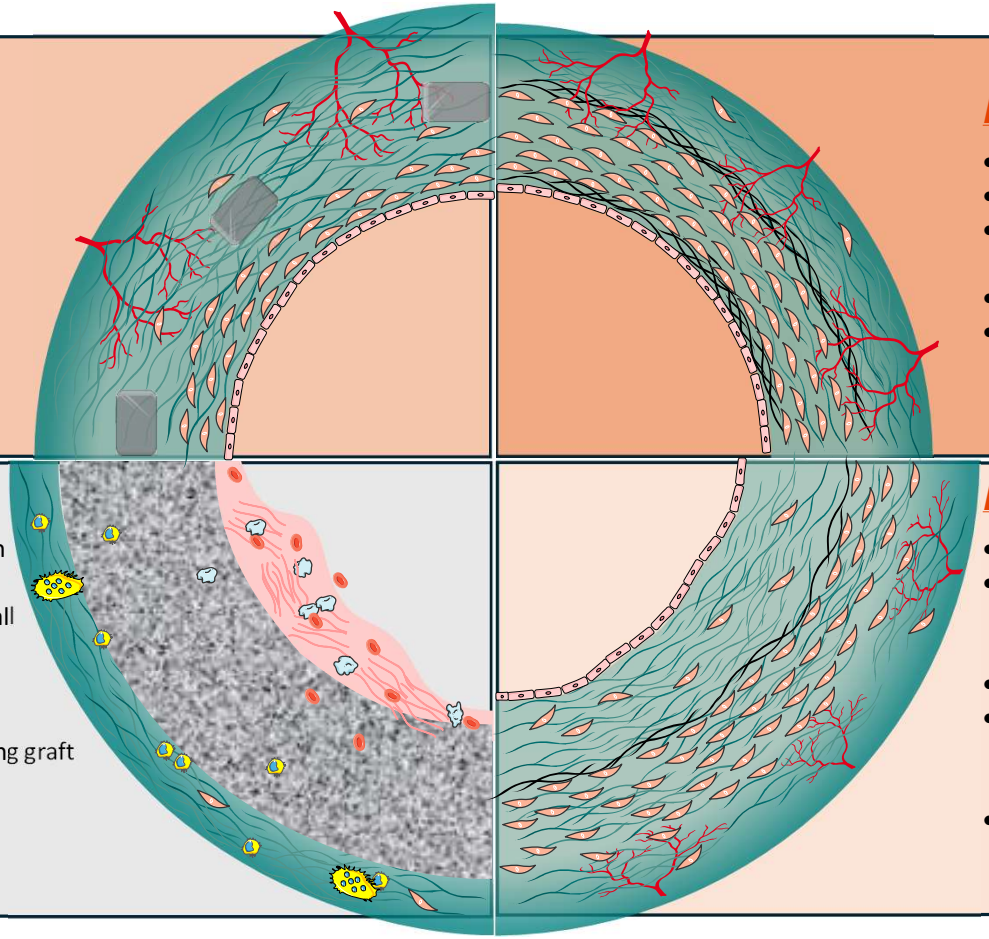
- Monolayer endothelialized intima
- Internal elastic lamina
- Media with densely packed circumferentially-arranged SMC interspersed with collagen
- External elastic lamina
- Vascularized collagen-rich external adventitia

ePTFE graft

- Variable thrombus/fibrin deposition on graft lumen – no endothelial lining
- Minimal cell infiltration within graft wall
- Minimal to mild inflammation at graft external surface
- No graft vascularization
- Collagen-rich tissue capsule surrounding graft

Remodeled Vein (Fistula)

- Endothelial lining of the lumen
- Collagen-rich thick neointima formed during fistula maturation – with interspersed SMC/myofibroblasts
- Internal elastic lamina
- Dilated/enlarged media with moderately packed circumferentially-arranged SMC interspersed with collagen
- Vascularized collagen-rich external adventitia



ePTFE implant

Microskeleton nitinol strut (SRS)

Fibrin, platelets & red blood cells

(transmural) blood vessels

Macrophage

Foreign Body Giant cell

Smooth muscle cell /myofibroblast

Endothelial cell

Elastin

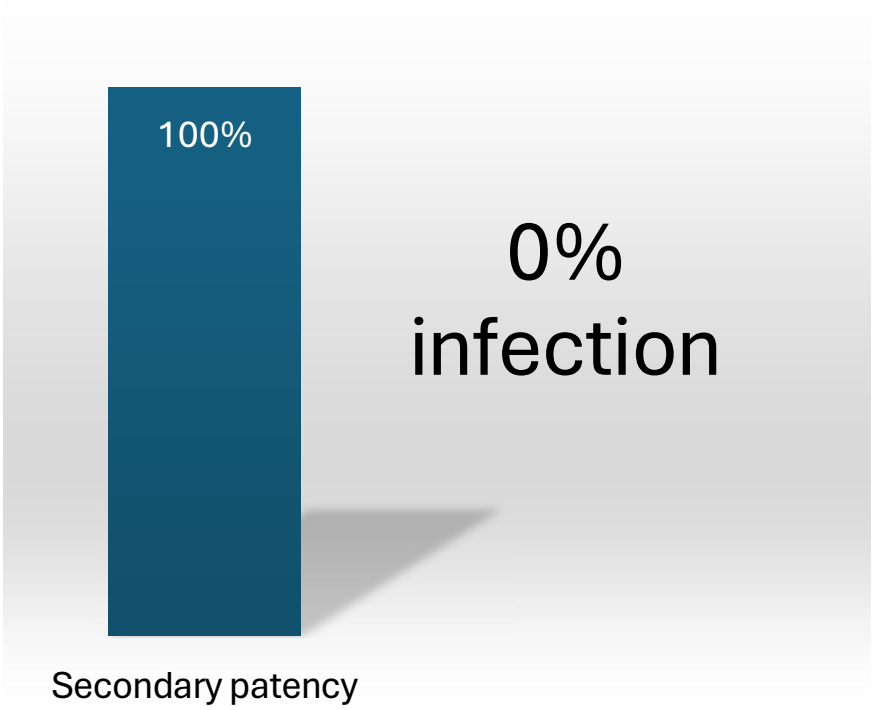
Collagen

aXess EU FIH trial

12-month results – high patency rates & no infection to date

- FIH single arm prospective trial
- 20 patients enrolled from Jun 2021 to Sep 2022 in Belgium, Italy, Latvia and Lithuania
- 2 censored patients (deaths non device related)
- Primary endpoints met @ 6 months
- Full study follow-up - 5 years

Baseline patient characteristics	
Men (N; %)	13; 65%
Mean age (years ± SD)	59 ± 14
Failed fistula (N; %)	12; 60%
Comorbidities (N; %)	
Hypertension	20; 100%
Diabetes	5; 25%
Cardiovascular disease	13; 65%
Aspirin use (N; %)	14; 70%
Operative date	
Mean operative time (minutes ± SD)	121 ± 43
Intraprocedural success (%)	100
Intraprocedural complications (N)	0
Implant configuration • Straight • Loop	 4; 20% 16; 80%
12-month reintervention rate	1.19

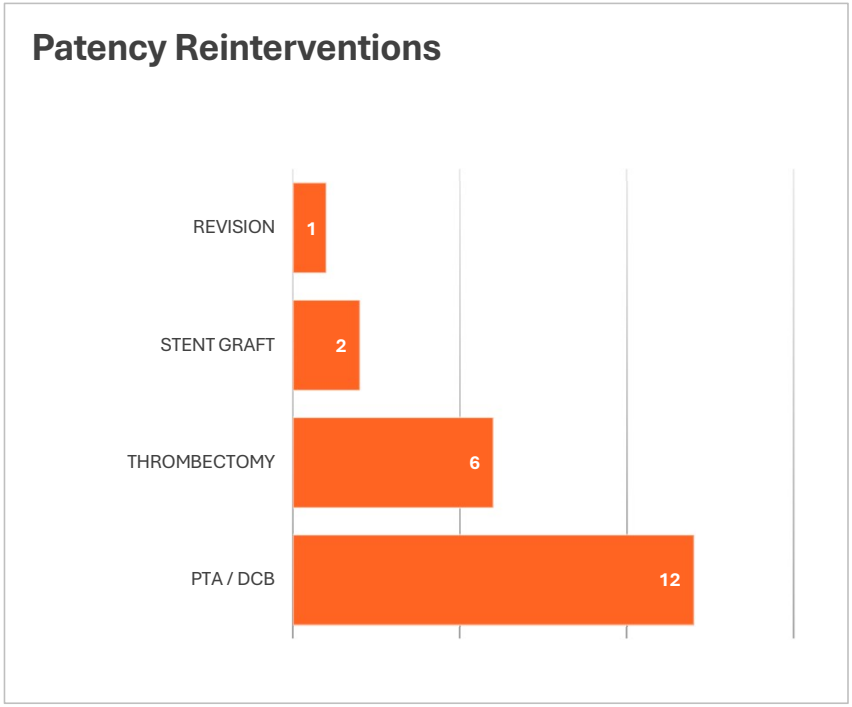


aXess EU FIH trial

12-month results

Dialysis	
Hemodialysis sessions completed	~ 942
Days to first cannulation (median; range)	32; 15 – 194
Standard of care cannulation techniques (%)	100

Reintervention rates	
aXess FIH study	**1,19**
Other AVG devices [1]	3,3
AVF [1]	1,8
Humacyte [2]	1,9



[1] Voorzaat BM, Janmaat CJ, van der Bogt KEA, Dekker FW, Rotmans JI. Patency Outcomes of Arteriovenous Fistulas and Grafts for Hemodialysis Access: A Trade-Off between Nonmaturation and Long-Term Complications. Kidney360. 2020 Jul 23;1(9):916-924.

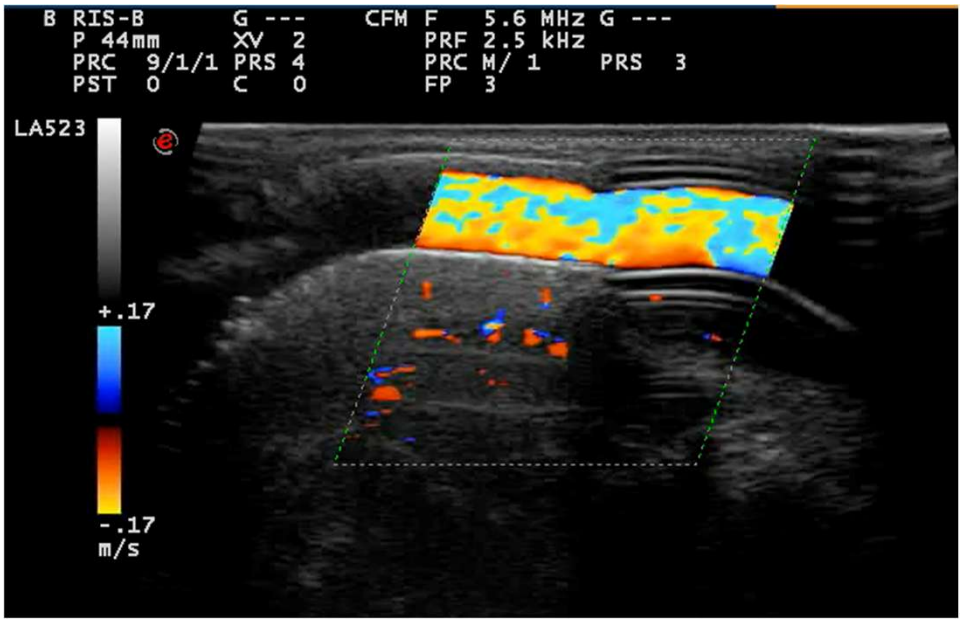
[2] J.H. Lawson et al, "Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials" Lancet, 2016; 387: 2026-34

aXess EU FIH trial

12-month results

Reinterventions

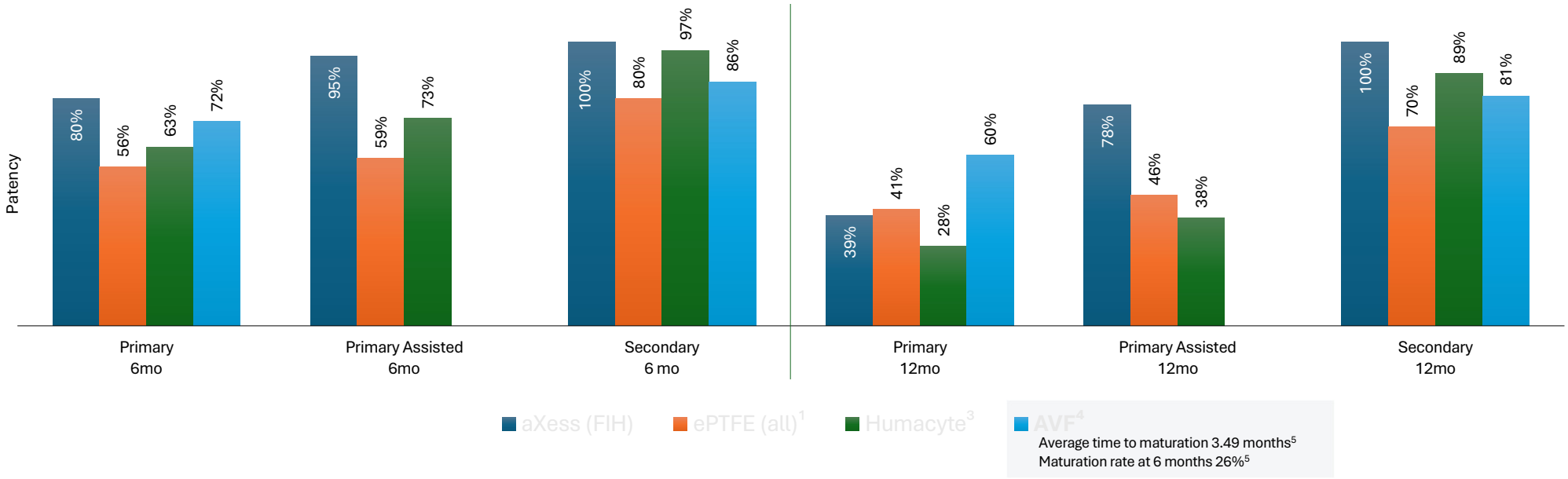




aXess EU FIH trial

12-month results

aXess *vs* ePTFE, Humacyte, Fistula



[1] R.J. Halbert et al, "Patency of ePTFE Arteriovenous Graft Placements in Hemodialysis Patients" 2020
[3] J.H. Lawson et al, "Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials" Lancet, 2016; 387: 2026-34
[4] T.S. Huber et al, "Patency of autogenous and polytetrafluoroethylene upper extremity arteriovenous hemodialysis accesses: A systematic review" 2003
[5] L.C. Bylsma et al. "Arteriovenous Fistulae for Hemodialysis: A Systematic Review and Meta-analysis of Efficacy and Safety Outcomes" Eur J Vasc Endovasc Surg (2017) 54, 513-522

aXess EU Pivotal trial
Study Design

1. European Pivotal Study
2. Multi-center, prospective single-arm
3. 120 subjects
4. 5 years follow-up

Primary endpoints

- Freedom from device related serious adverse events at 6 months
- Primary patency at 6 months

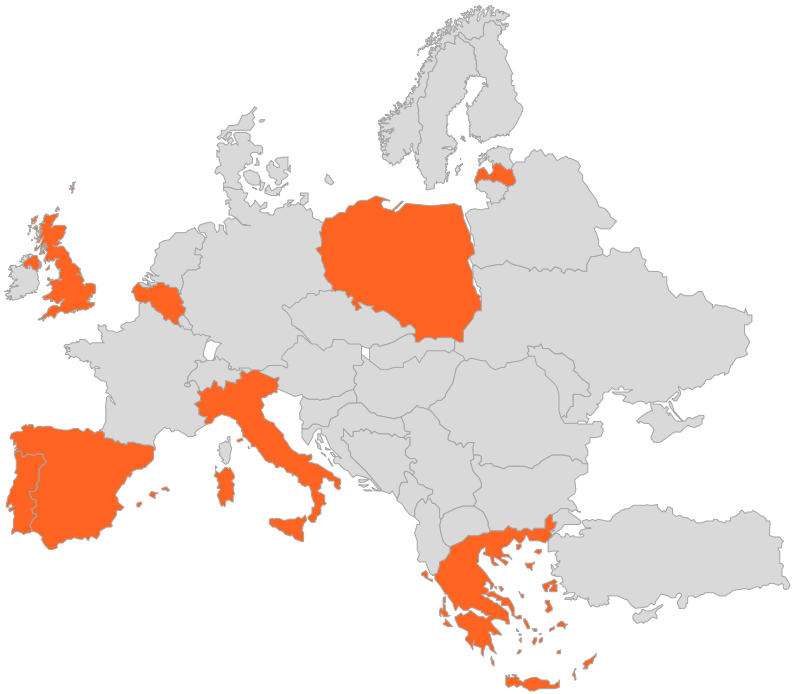
Secondary endpoints

- **Implantation success rate**
- **Patency** (primary, primary assisted, secondary, and functional) rates at 6, 12, 18, 24 and 60 months
- Time (expressed in months) to **first intervention** and to access abandonment
- Rate of access-related **interventions** required to achieve/maintain patency at 6, 12, 18, 24, and 60 months
- Freedom from **device-related SAE** at 12, 18, 24, and 60 months
- Rate of access site **infections** at 6, 12, 18, 24, and 60 months
- Proportion of hemodialysis sessions completed via central venous catheter (**CVC**) during the first 12 months of access creation and access cannulation, irrespective of access abandonment
- Time to **first cannulation**
- Following first cannulation, number of days with **CVC** in situ (catheter contact time) during the first 12 months, irrespective of access abandonment

aXess EU Pivotal trial

Enrollment completed December 2024

120 Patients enrolled at **18 EU sites** in **8 countries**



Countries	Sites
Belgium (N=13)	AZ Sint Jan Brugge ZOL Genk
Greece (N=2)	University General Hospital of Patras LAIKO General Hospital of Athens
Italy (N=35)	Università degli studi dell'Insubria Policlinico di Sant'Orsola Bologna Università degli studi di Padova Azienda Ospedaliero Universitaria di Bari
Latvia (N=1)	Pauls Stradins Clinical University Hospital
Poland (N=11)	MEDINET Wroclaw
Portugal (N=37)	Grupo de Estudos Vasculares Porto Hospital de Santa Maria Lisbon DaVita Sacavém
Spain (N=15)	Hospital Clínic de Barcelona Hospital Universitario de la Ribera Bellvitge University Hospital
United Kingdom (N=6)	Queen Elizabeth University Hospital Glasgow University Hospital Birmingham

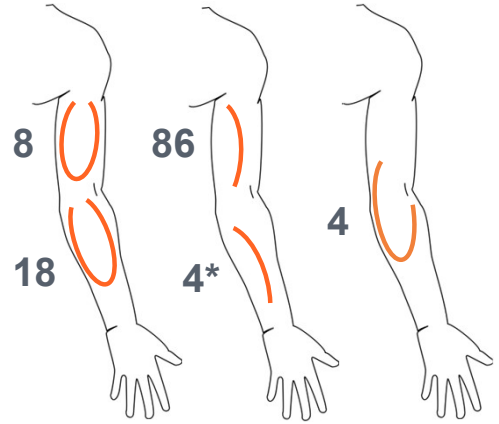
aXess EU Pivotal trial

Baseline characteristics

Baseline patient characteristics	
Number of patients enrolled	120
Men (N; %)	63 ; 53%
Mean age (years ± SD)	64 ± 15
Previous CVC (N; %)	80; 67%
Failed fistula (N; %)	40; 33%
Multiple previous fistulas (N; %)	20; 17%
Failed AVG (N; %)	8; 7%
Comorbidities (N; %)	
Diabetes (all)	47; 39%
Cardiovascular disease	25; 21%
Nicotine Usage (n/N; %)	
Current	16/120; 13%
Previous	29/120; 24%

Operative data	
Mean operative time (minutes ± SD)	98 ± 37
Implantation Success rate (N, %)	118, 98%
Implant configuration • Straight • Loop	 90 ; 75% 30 ; 25%
Post operative Aspirin use (N; %)	57; 48%

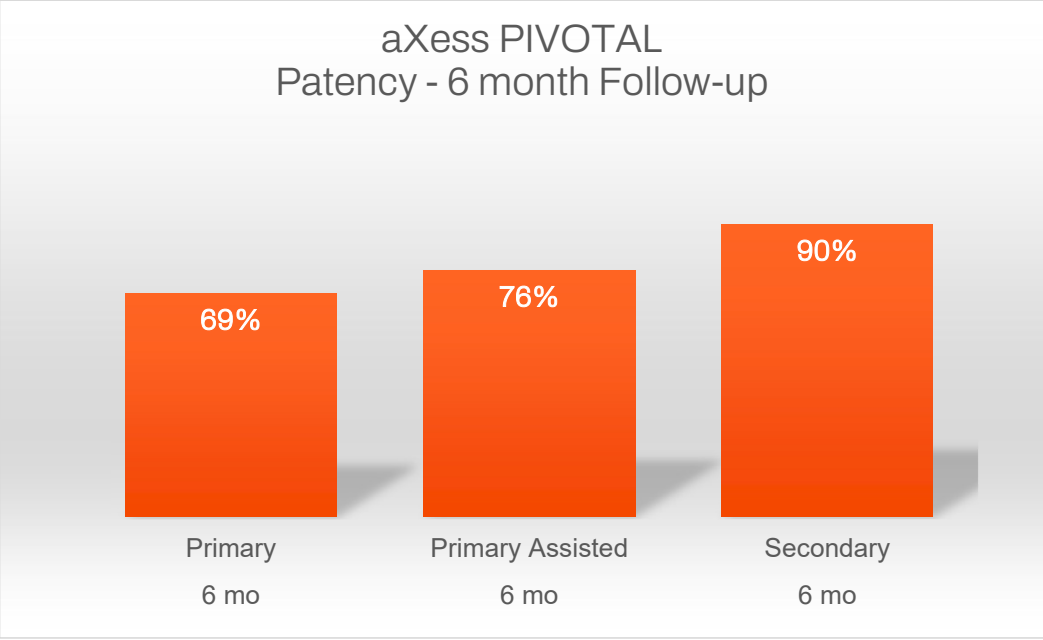
Implant Configuration:

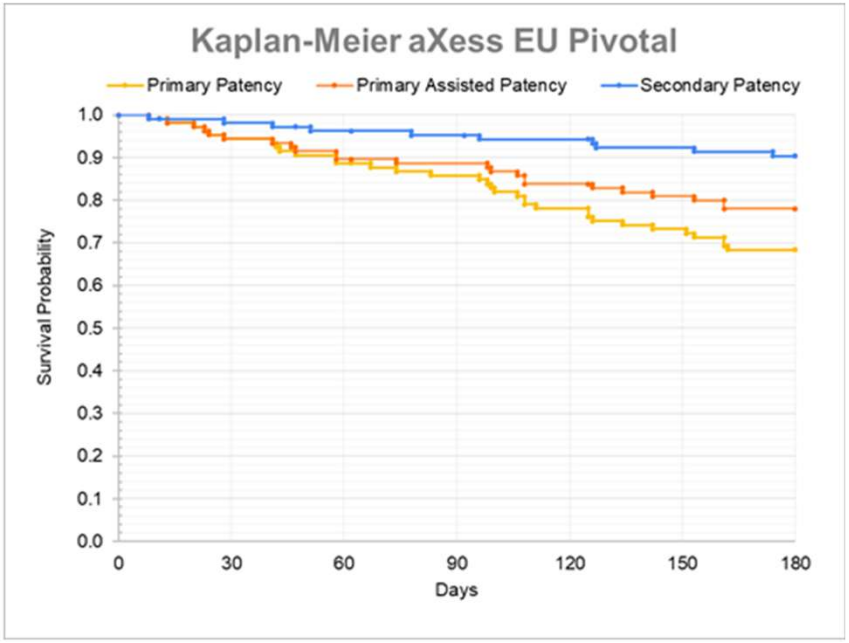


** 1 patient with lower arm straight crossing the elbow*

aXess EU Pivotal trial

6-month Results

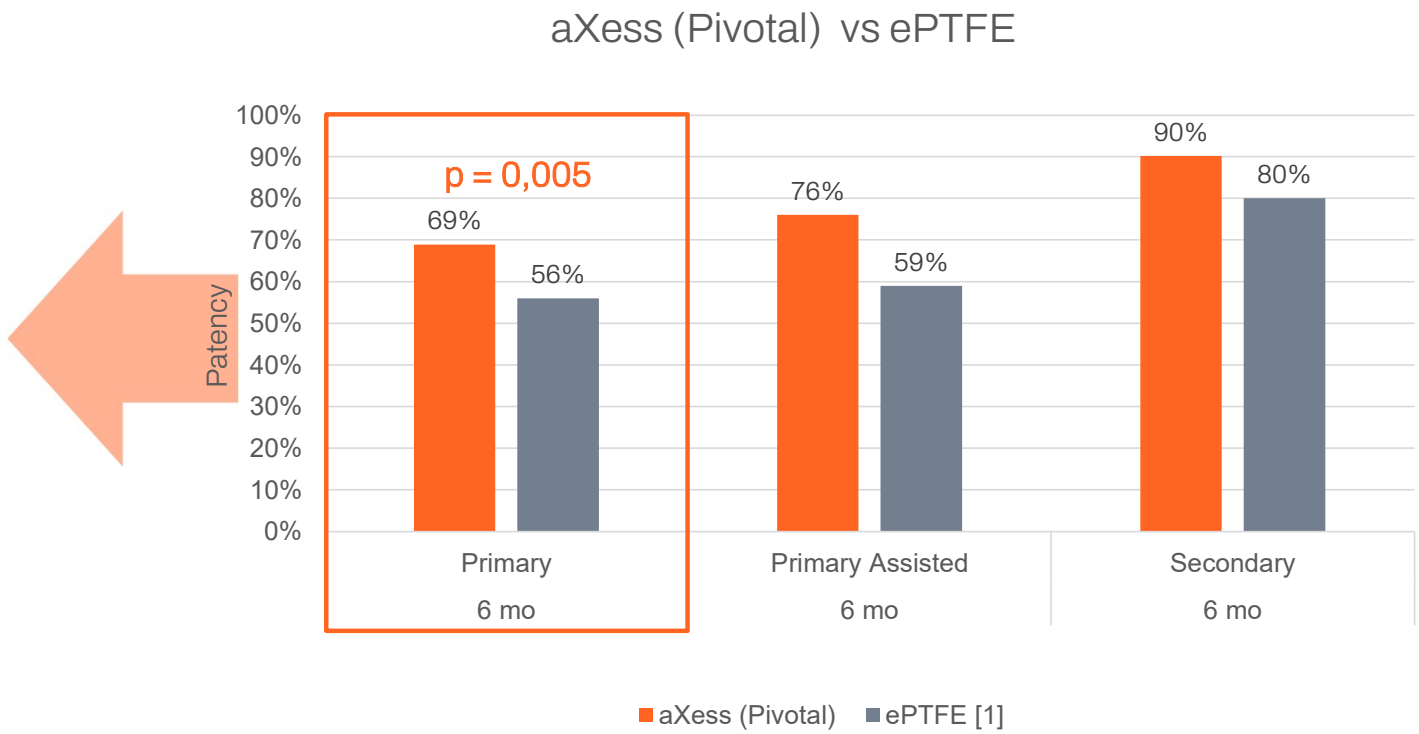




aXess EU Pivotal trial

6-month Results vs ePFTE Performance Goal

aXess showed favorable outcomes compared to ePTFE (OPC)



[1] R.J. Halbert et al, "Patency of ePTFE Arteriovenous Graft Placements in Hemodialysis Patients" 2020

aXess EU Pivotal trial

Infections at 6-month follow-up



Dialysis data of 120 pts	
Number of patients cannulated (N)	101
Days to first cannulation (median; range)	39; 14 – 391
Total number of dialysis sessions at 6mo follow up	4662

Cannulation related infections (3%)

1 Partial explantation (interposition)
2 Resolved with antibiotics

Very low infection rates compared with ePTFE

Antibiotics seem to be effective
- no biofilm creation, strong wall penetration

aXess Pivotal EU trial

Re-intervention rates

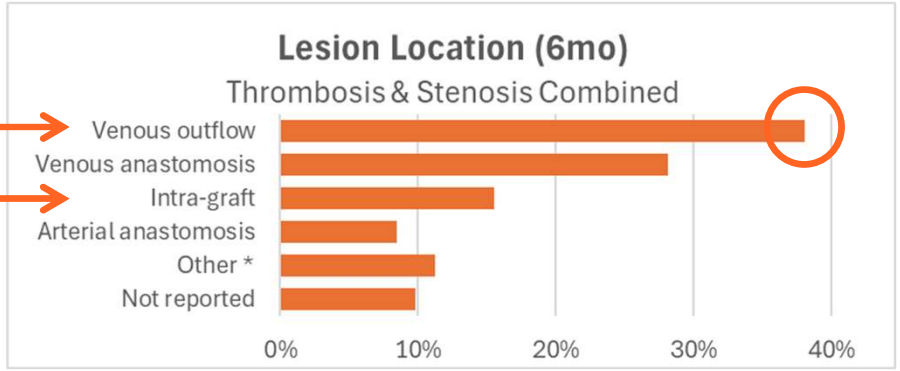
Patency-Related Reintervention Rate	6 mo per patient year	12 mo per patient year	Cumulative per patient year
aXess EU Pivotal study	1,1	1,4	1,3
Other AVG devices [1]	-	-	3,3
PTFE [2]	-	-	2.6
AVF (matured) [1]	-	-	1,8

[1] Voorzaat BM, Janmaat CJ, van der Bogt KEA, Dekker FW, Rotmans JI. Patency Outcomes of Arteriovenous Fistulas and Grafts for Hemodialysis Access: A Trade-Off between Nonmaturation and Long-Term Complications. Kidney360. 2020 Jul 23;1(9):916-924.
[2] P. Marcus, A. Echeverria, M. Cheung, E. Kfoury, K. Shim, and P. H. Lin, "Early Cannulation of Bovine Carotid Artery Graft Reduces Tunneled Dialysis Catheter-Related Complications: A Comparison of Bovine Carotid Artery Graft Versus Expanded Polytetrafluoroethylene Grafts in Hemodialysis Access," Vasc Endovascular Surg, vol. 53, no. 2, pp. 104–111, Feb. 2019

- *Patency related intervention rate is 2.5X less than other AVG devices*
- *Patency related intervention rate is ~30% lower than fistulas*

Common to all AVF & AVG patients

Only 15% intra-graft related



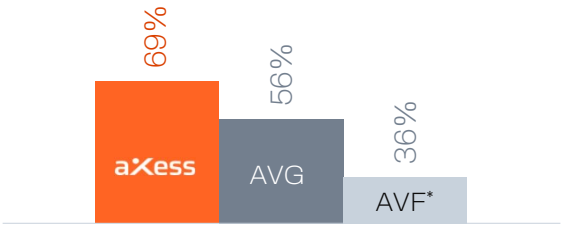
* Listed reasons: limb spasticity, dehydration, hypotension, hyper coagulability, mis-puncture, thrombin injection, intra graft thrombosis, high levels of hematocrit and Hb

aXess Pivotal EU trial

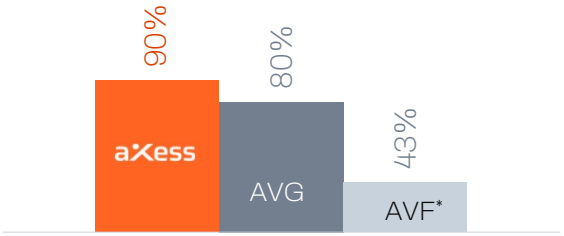
Current clinical outcomes

HIGHER PATENCY

P value = 0,005

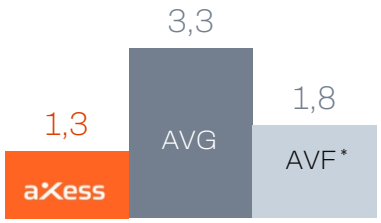


Primary patency @6mo



Secondary patency @6mo

FEWER REINTERVENTIONS

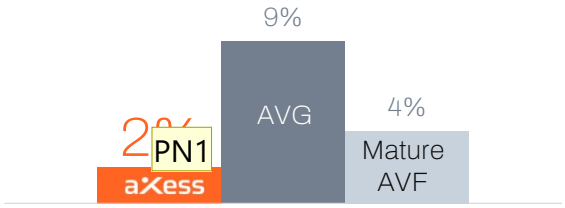


Cummulative reintervention rate

3X FEWER INTERVENTIONS vs. AVG

>30% FEWER INTERVENTIONS VS. AVF

INFECTION RESISTANCE



Cannulation-related infections @12mo

ANNUAL HEALTHCARE COST OF $28K PER US PATIENT

NOTE* Includes impact of maturation failures and maturation-related interventions

Diapositiva 18

PN1 We say 3% above

Paulo Neves | Xeltis; 2025-11-24T22:25:38.910

aXess EU Pivotal trial

Cannulation and Dialysis parameters

Cannulation

Number of patients cannulated (N)	101
Total number of dialysis sessions at 6mo follow up	4662
Bevel down: Bevel up:	167 → 88.83% 21 → 11.17%
Stainless steel: Plastic cannula:	187 → 93.0 % 14 → 7.0 %
16G: 17G: 15G: 14G:	169 → 82.44% 21 → 10.24% 13 → 6.34% 2 → 0.98%

Dialysis

Rope ladder usage:	Yes: 173 → 92.02% No: 15 → 7.98%
Average (spKt/V): Range (min–max):	1.508 0.51 – 2.26
Median URR: Range (min–max):	71.30 % 36.63 % – 85.00 %
Average HD time:	3h 56min
Stainless steel: Plastic cannula:	187 → 93.0 % 14 → 7.0 %
Average Qb: Average Venous pressure: Average Arterial pressure:	316 180 144

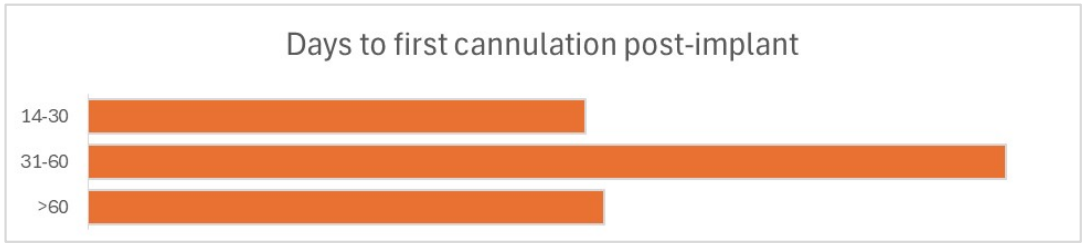
PN1

aXess Pivotal EU trial

Shown benefits

Proven success in the dialysis clinics

- First cannulation as early as 14 days
  - 27% of patients cannulated within 14-30 days
- Extremely low bleeding complications due to cannulation < 0.02%
- Post-cannulation Time To Hemostasis (TTH) was between 5 - 10 min. (mean 7.4 min.) in >95% of patients
- Low cannulation related infection rates





Diapositiva 20

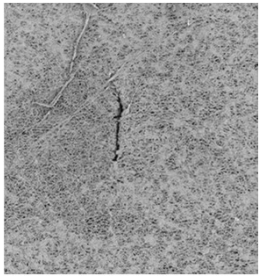
PN1 Would not use pooled data, does it add much?

Paulo Neves | Xeltis; 2025-11-24T22:25:18.007

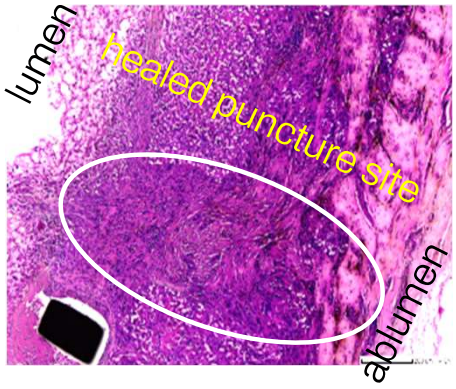
aXess allows true remodeling & healing after graft puncture

aXess

Bench: recoil after puncture



In vivo: healing & integration with neotissue

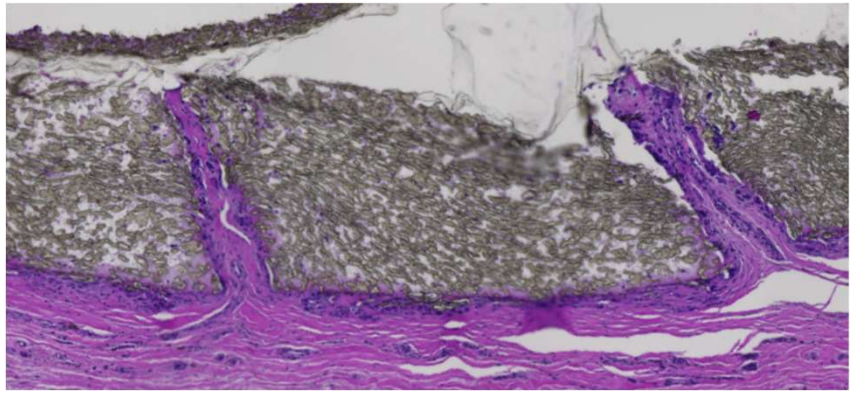


ePTFE

Bench: puncture hole



In vivo: no graft healing & integration



aXess FIH & Pivotal EU pooled data

Baseline characteristics

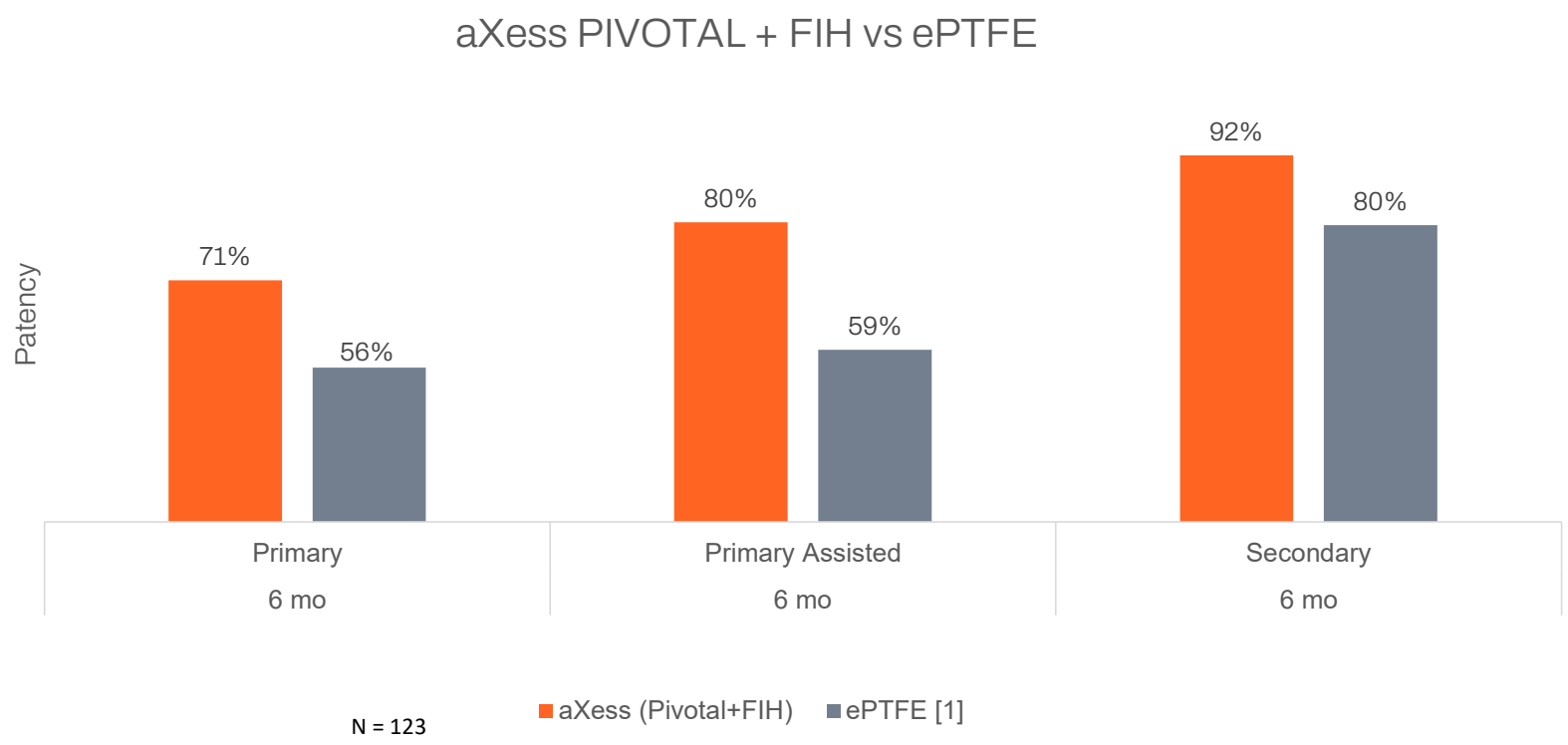
Baseline patient characteristics	
Number of patients enrolled	140
Men (N; %)	76 ; 54%
Mean age (years ± SD)	64 ± 15
Previous CVC (N; %)	91; 65%
Failed fistula (N; %)	52; 37%
Multiple previous fistulas (N; %)	21; 15%
Comorbidities (N; %)	
Diabetes (all)	52; 37%
Cardiovascular disease	43; 31%
Nicotine Usage (n/N; %)	
Current	17/139; 12%
Previous	36/139; 26%

Operative data	
Mean operative time (minutes ± SD)	103 ± 38
Implantation Success rate (N, %)	138, 99%
Intraprocedural complications (N)	8
Implant configuration • Straight • Loop	 94 ; 67% 46 ; 23%
Post operative Aspirin use (N; %)	71; 51%

PN1

aXess FIH & Pivotal EU pooled data

6-months results aXess (N=140) vs ePTFE



[1] R.J. Halbert et al, "Patency of ePTFE Arteriovenous Graft Placements in Hemodialysis Patients" 2020

Pooling of the aXess studies justified based on the same CEC, DSMB, and inclusion/exclusion criteria

Note(*) Exploratory analysis — single-arm study evaluated against FDA Objective Performance Criteria; the study was not designed or powered to demonstrate statistical superiority

Diapositiva 23

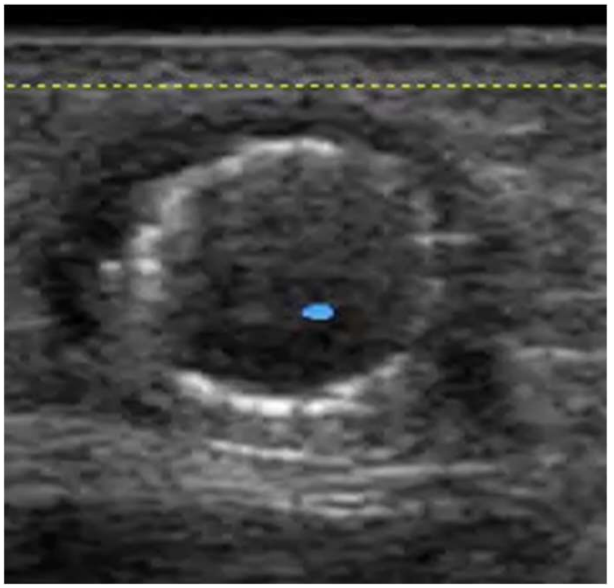
PN1 Would not use pooled data, does it add much?

Paulo Neves | Xeltis; 2025-11-24T22:23:59.782

aXess EU Pivotal trial
Closing remarks

1. Proven safe and easy implantation
2. Better patency than ePTFE benchmarks
3. Low infection rates, antibiotics are effective at treating infections
4. aXess becomes a tissue-like pulsating conduit
5. Highly effective cannulation and dialysis sessions with 16 & 17 G needles

Proof of compliancy in remodelled tissue



ePTFE grafts vs

The Xeltis technology could it replace Goretex one day ?

ePTFE grafts



- Small pores
- Limited cell ingrowth
- No remodeling
- Biofilm formation
- No neointima / endothelization

aXess conduit



- Large pores
- Significant cell ingrowth
- Positive remodeling with neotissue and neovessels development
- No biofilm formation
- Neointima formation and evidence of endothelization

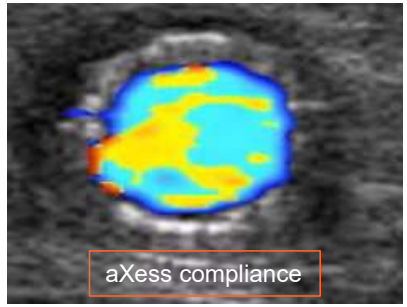
PN1

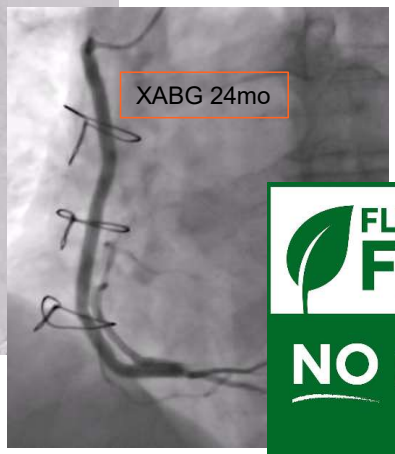
Xeltis Technology and The Potential Benefits

Polymer Biodegradable Grafts to Create Autogenous Living Conduits?

- Creation of autogenous conduits
- Better compliance to match flow-dynamics
- Better infection resistance
- Off the shelf, ready for implantation
- PFAS free









Diapositiva 26

PN1 This one is excellent, would move up after #19

Paulo Neves | Xeltis; 2025-11-24T22:25:01.921

MC1 0 I toke the liberty of changing flourine to fluorine in the image - apparently chatgpt can also correct spelling in images….

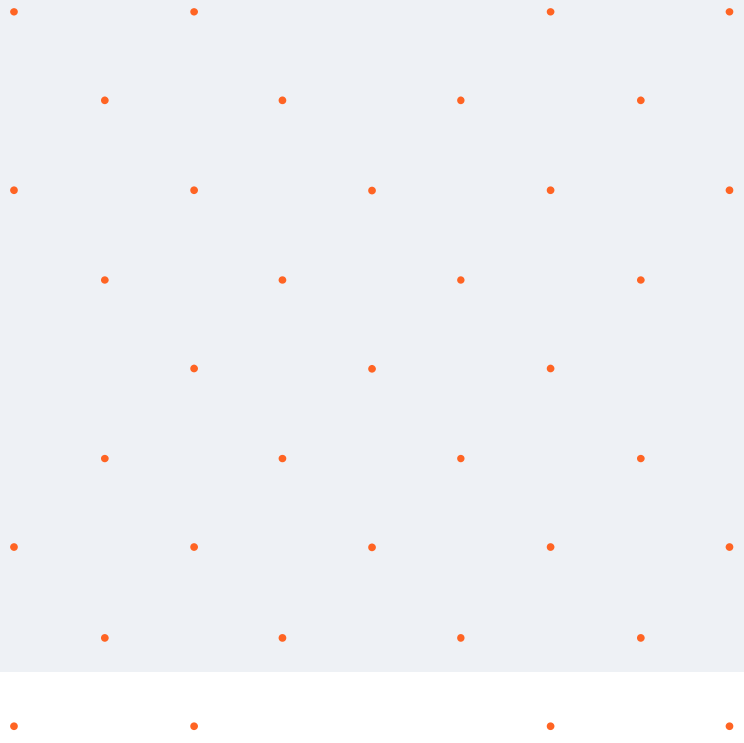
Martijn Cox | Xeltis; 2025-12-02T09:16:58.301

aXess Pivotal US trial
Status

Currently 30+ Patients enrolled at 8 active sites in 6 states



State	Sites	PIs
Mississippi	Greenwood Leflore Hospital - Greenwood	Dr. Lucas III
North Carolina	Surgical Specialists of Charlotte	Dr. Burgess
Texas	Flow Vascular Medical Center – Houston Houston Methodist Hospital	Dr. Illig Dr. Peden
Arizona	Arizona Kidney Disease & Hypertension Centers (Phoenix) Arizona Kidney Disease & Hypertension Centers (Tuscon)	Dr. Wang Dr. Yang
Massachusetts	Brigham & Womens	Dr. Selim
Florida	Sarasota Memorial Hospital	Dr. Wagner



Thank you