CONTROVERSES ET ACTUALITÉS EN CHIRURGIE VASCULAIRE

CONTROVERSIES & UPDATES IN VASCULAR SURGERY

JANUARY 25-27 2018

MARRIOTT RIVE GAUCHE & CONFERENCE CENTER

PARIS, FRANCE WWW.CACVS.ORG

Does heparin impregnated graft improve patency and reduce the cost of lower limb bypass? The REPLACE trial

Y. Gouëffic, MD, PhD

Department of vascular surgery, University hospital of Nantes, France

Disclosure

Speaker name: Yann Gouëffic

☒ have the following potential conflicts of interest to report:

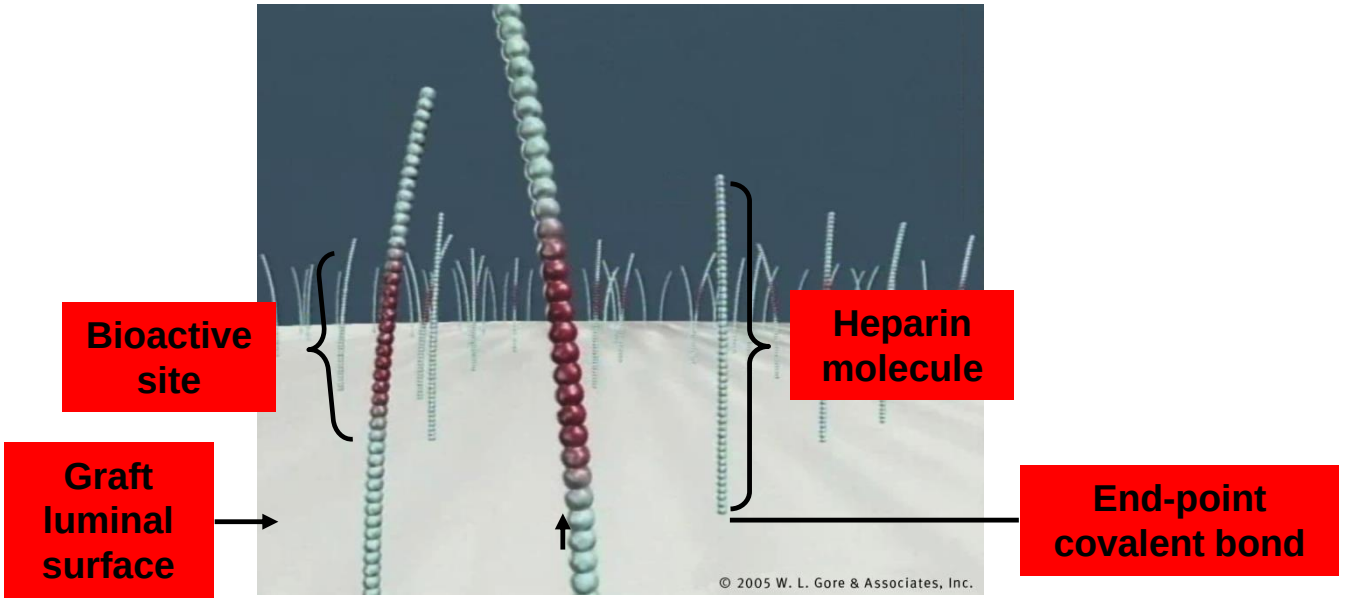
☒ Receipt of grants/research support
Details: Abbott; Bard; Medtronic; Terumo; WL Gore

☒ Receipt of honoraria and travel support
Details: Abbott; Bard; Boston Sc; Cook; WL Gore; Medtronic; Perouse; Spectranetics

☐ do not have any potential conflicts of interest to report

Propaten® technology

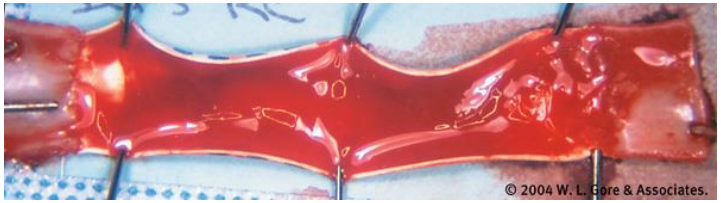
- **Heparin molecules are bound directly to the luminal surface of the graft.**
- **CARMEDA® BioActive Surface (CBAS® Surface)**



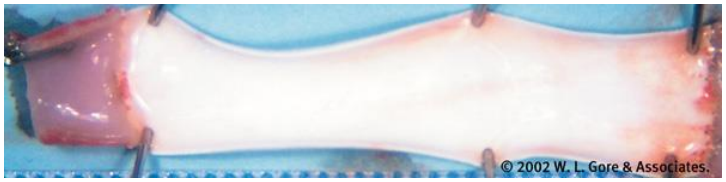
Propaten® expected benefits in humans

Thromboresistance

Crude PTFE



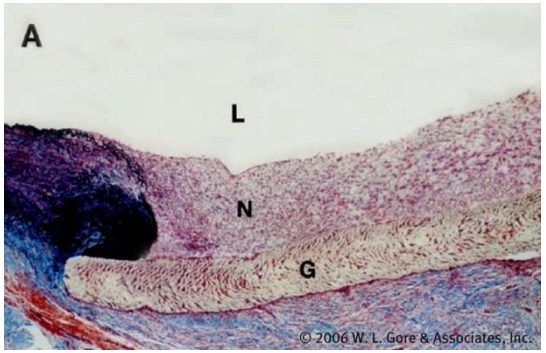
PROPATEN®



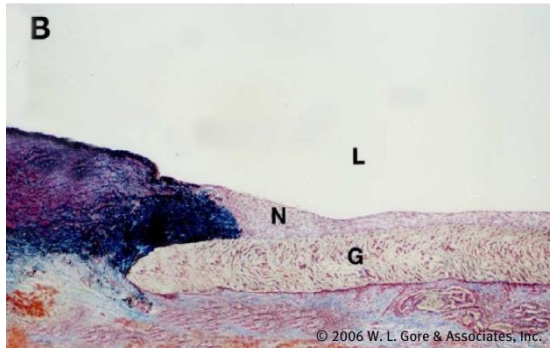
In-vivo canine carotid artery interposition model

Neointimal Hyperplasia Reduction

Crude PTFE



PROPATEN®



Canine femoro-femoral artery bypass grafting model.

Registries for BTK 2-years primary patency for Propaten® grafts

BTK 2-year primary patency for Propaten®: 75.6%

Studies	Date	Authors	Patients	2-year Primary Patency	Bypass localization
Lower limb revascularization with a new bioactive Prosthetic graft: Early and late results	2008	Dorigo et al. (1)	34	80,6%	BTK
Results with heparin-bonded polytetrafluoroethylene grafts for femorodistal bypasses	2006	Peeters et al.(3)	41	72,6%	FP3 + FC
Infrainguinal ePTFE vascular graft with bioactive surface heparin bonding	2005	Walluscheck et al. (4)	17	81,0%	BTK
Heparin-bonded expanded polytetrafluoroethylene grafts for infragenicular bypass in patients with critical limb ischemia: 2-year results	2008	Dorrucci et al. (5)	20	85,0%	BTK
Heparin-bonded ePTFE grafts compared with vein grafts in femoropopliteal and femorocrural bypasses: 1- and 2-year results	2009	Daenens et al.(6)	57	83,0%	FP3 + FC

Dorigo W. Lower limb revascularization with a new bioactive prosthetic graft: early and late results. Ann Vasc Surg. 2008 Peeters P. Results with heparin bonded polytetrafluoroethylene grafts for femorodistal bypasses. J Cardiovasc Surg (Torino). 2006.Walluscheck KP. Infrainguinal ePTFE vascular graft with bioactive surface heparin bonding. First clinical results. J Cardiovasc Surg (Torino). 2005. Dorrucci V. Heparin-bonded expanded polytetrafluoroethylene grafts for infragenicular bypass in patients with critical limb ischemia: 2-year results. J Cardiovasc Surg (Torino). 2008. Daenens K. Heparin-bonded ePTFE grafts compared with vein grafts in femoropopliteal and femorocrural bypasses: 1- and 2-year results. J Vasc Surg. 2009.

The Scandinavian Propaten® Trial

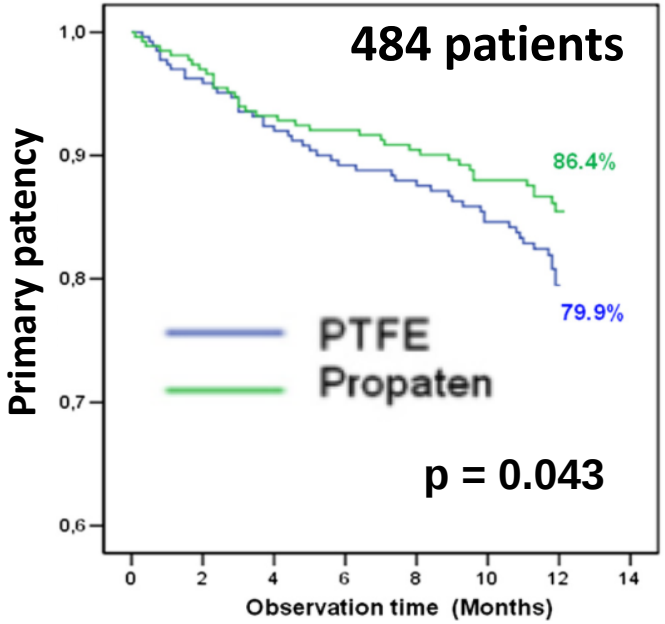
The aim of this study was to compare the primary patency at 1 year of heparin-bound PTFE (Propaten) versus pure PTFE grafts

Prospective	✔
Multicenter	✔
Randomized 1:1	✔
Data monitoring committee	✔
Published	✔

Primary endpoint:
Primary patency @ 1-year
(duplex scan)

Inclusion criteria

- IC or CLI
- Indication for femfem cross-over or fempop bypass above or below the knee with an artificial graft.



Lindholt, Eur J Vasc endovasc surg, 2011

Subgroup analyses

Table 2 Subgroup analyses concerning the type of bypass in general and further subgrouped according to present chronic critical lower limb ischaemia or intermittent claudication.

		Primary patent	N	Primary patency	Odds ratio	*P*-value
Fem–fem cross over bypasses						
All	Crude PTFE	131	147	89 (84–93)%		
	Propaten	144	160	90 (84–94)%	0.910 (0.437; 1.896)	0.800
Claudicants	Crude PTFE	85	88	97 (91–99)%		
	Propaten	98	106	92 (86–96)%	2.312 (0.595; 8.997)	0.215
Critical ischaemia	Crude PTFE	46	59	78 (66–87)%		
	Propaten	46	54	85 (73–93)%	0.615 (0.233; 1.625)	0.327
Fem–pop bypasses						
All	Crude PTFE	87	126	69 (61–77)%		
	Propaten	91	112	81 (73–88)%	0.515 (0.281; 0.944)	0.030
Claudicants	Crude PTFE	64	86	74 (64–83)%		
	Propaten	56	68	82 (72–90)%	0.623 (0.283; 1.373)	0.238
Critical ischaemia	Crude PTFE	23	40	58 (42–72)%		
	Propaten	35	44	80 (66–90)%	0.348 (0.133; 0.912)	0.032

Lindholt, Eur J Vasc endovasc surg, 2011

Original article

Five-year outcomes following a randomized trial of femorofemoral and femoropopliteal bypass grafting with heparin-bonded or standard polytetrafluoroethylene grafts

J. S. Lindholt[1,2,7], K. Houlind[1,3], B. Gottschalksen[4], C. N. Pedersen[5], H. Ravn[1,3], B. Viddal[8], G. Pedersen[9], M. Rasmussen[6], C. Wedel[4] and M. B. Bramsen[7]

[1]Cardiovascular Centre of Excellence in the Region of Southern Denmark (CAVAC), [2]Elitary Research Centre CIMA, Department of Cardiovascular and Thoracic Surgery, Odense University Hospital, Odense, Departments of Vascular Surgery, [3]Kolding Hospital, Kolding, [4]Slagelse Hospital, Slagelse, [5]Aalborg University Hospital, Aalborg, and [6]Rigshospitalet, Copenhagen, and [7]Cardiovascular Research Unit, Viborg Hospital, Viborg, Denmark, and Departments of Vascular Surgery, [8]Stavanger University Hospital, Stavanger, and [9]Haukeland University Hospital, Bergen, Norway

Correspondence to: Professor J. S. Lindholt, Department of Cardiothoracic and Vascular Surgery T, Odense University Hospital, Søndre Boulevard 29, DK-5000 Odense C, Denmark (e-mail: jes.sanddal.lindholt@rsyd.dk)

Conclusion: In this study there was no difference in primary graft patency between Hb-PTFE and standard PTFE grafts. Patients receiving Hb-PTFE grafts for critical limb ischaemia were more likely to have a patent graft at 5 years than those with standard PTFE grafts.

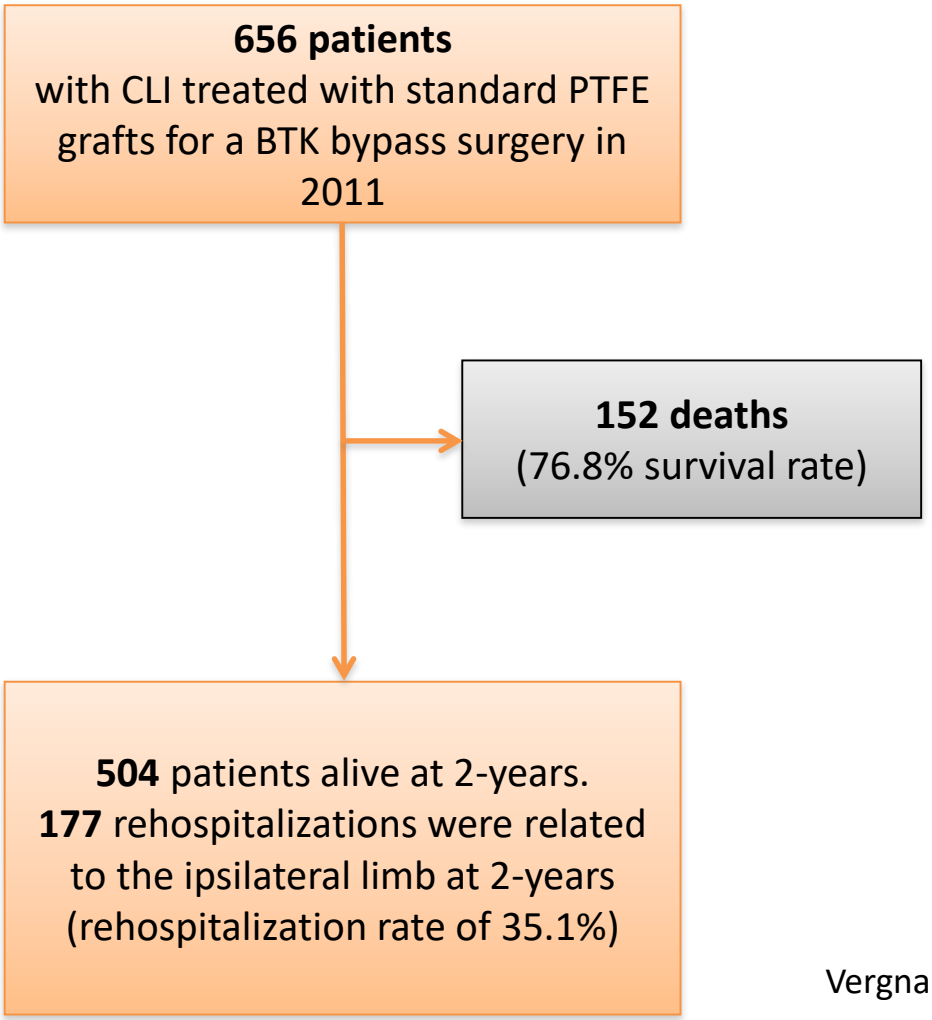
Lindholt, Br J Surg, 2016

Cost effectiveness of BTK bypasses in CLI patients

- To establish a medico-economic model to assess the budget impact of a progressive penetration of **Propaten®** grafts over a 5-years in France.
- French expenditure database (2011):
  - *cases of **crude PTFE** graft for below the knee bypasses*
  - *reintervention (2 years FU period)*

Vergnaud, BMJ Open, in Press

Retrospective data from the national expenditure database



Vergnaud, BMJ Open, in Press

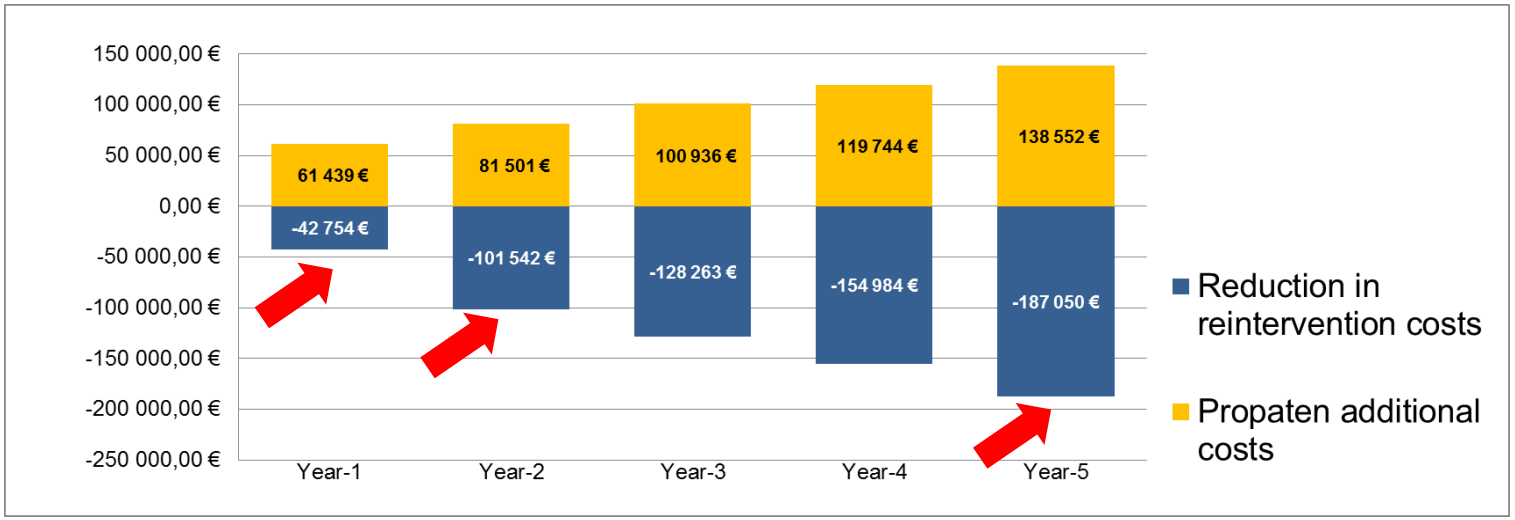
Values fed to the model and their sources

Clinical Data	Values	Sources
First rehospitalization rate due to graft of interest	35.1% (177/504)	French rehospitalization data, adjusted for mortality and contralateral reintervention
Pooled primary patency for Propaten grafts:	75.6%	Own calculations
Cost Estimates	**Values**	**Sources**
Mean initial intervention cost	12,290€	Own calculations (PMSI-based)
Rehospitalization mean cost (one rehospitalization)	10,689€	Own calculations (PMSI-based)
Propaten initial additional cost	627€	GORE®
ePTFE reimbursement tariff	639€	FNHI online data
Market Data	**Values**	**Sources**
Initial Market Penetration	15%	NA
Annual Market Penetration Increase	5%	NA
Population growth	-1.0%	ATIH

Vergnaud, BMJ Open, in Press

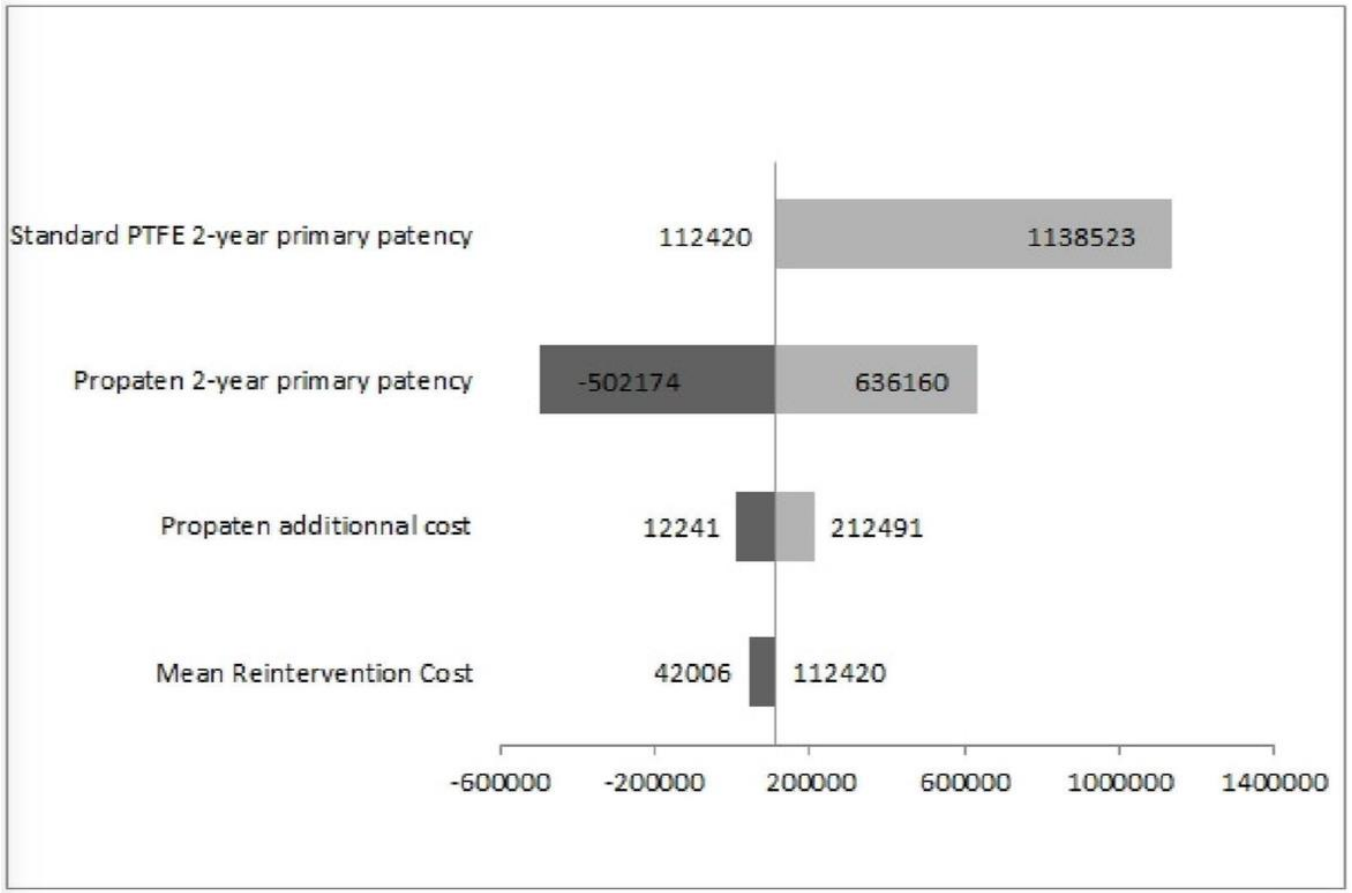
Budget impact comparison after 5 years

After 5 years, the total difference between the observed crude PTFE and the simulated Propaten + crude PTFE groups was estimated at 112,420 €, in favor of Propaten grafts



Year	ePTFE alone (3215)	Propaten + ePTFE (2414 + 801)						Cost difference
	Total costs (€)	ePTFE grafts	Propaten grafts	Initial additional cost (€)	Rehospitalizations	Rehospitalizations avoided	Total cost (€)	
Total	47,871,515 €	2414	801	502,174 €	726	57	47,759,095 €	-112,420 €

Sensitivy analysis



Vergnaud, BMJ Open, in Press

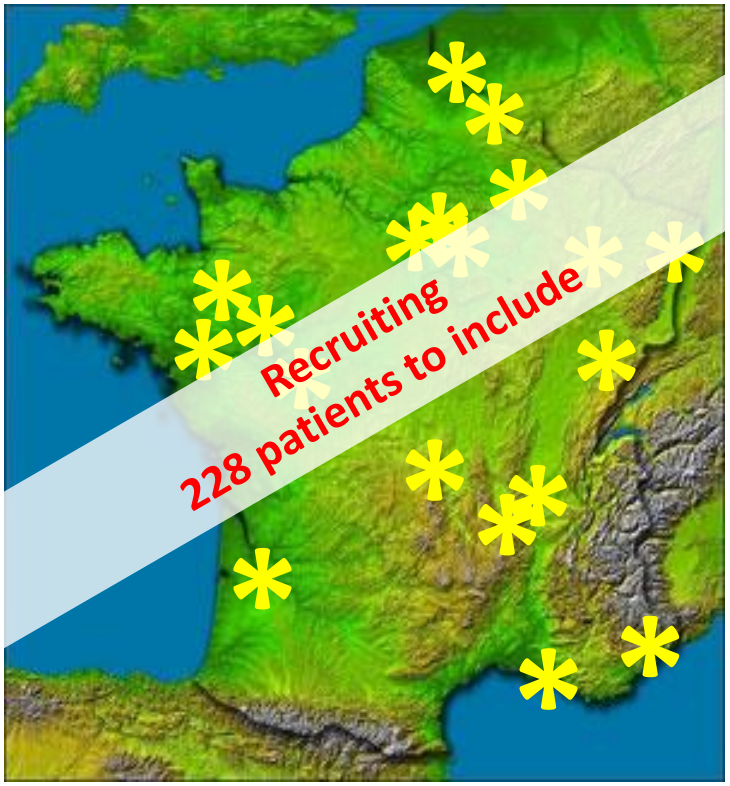
Take home messages

- **Registries for BTK 2-year primary patency for Propaten® grafts showed a high patency rate.**
- **Our model-based analysis showed a strong economic incentive in favor of the widespread use and reimbursement for Propaten®.**
- **However, type I level clinical evidence is still lacking for BTK Propaten® bypasses in CLI patients.**

REPLACE

ClinicalTrials.gov Identifier: submitted

Polytetrafluoroethylen (PTFE) vascular prostheses with heparin bonded luminal surfaces vs crude ePTFE in the treatment of critical limb ischemia lesions in the absence of a suitable autologous vein



PIs: Y. Gouëffic, E. Rosset, E. Steinmetz, J.P. Favre (on behalf of AURC)

Sponsor: Nantes university hospital

20 centers: CHU de Nantes, CHU de Dijon ; CHU Ambroise Paré ; CHU de Rennes, CHRU Lille ; Hôpital de la Timone ; CH Valenciennes ; CHU Angers ; CHU Besançon ; CHU de Bordeaux ; CHU Lyon ; Hôpital Européen Georges Pompidou ; Chu de Nice ; Hôpital Bichat ; CHU Poitiers, CHU Saint Etienne ; CHU de Nancy ; CHU Reims ; CHU de Strasbourg, CHU de Clermont Ferrand

REPLACE trial

Sponsor Nantes University Hospital - *TECCO trial, NCT01353651*

- **Investigator initiated study**
- **RCT multicenter and controlled**
- **Rigorous data collection process, independent**
- **Adjudication by:**
  - *Duplex ultrasound core laboratory*
  - *Data safety monitoring board*
- **Follow-up includes**
  - 1, 6, 12, and 24-month clinical assessment
  - 1, 12 and 24-month stent x-ray
- **Phone calls** (3, 9, 15 et 18 mo)

- **Monitoring with 100% source data verification**
- **Modified intent to treat analysis / Per protocol analysis**
- **Sample size calculation: 228 patients**
- **Randomly assigned in a 1:1 ratio**
- **80% power** *to detect a between-group difference of 20% percentage points in the morbid-mortality rate at a two-sided alpha level of 0.05 (25% in the surgery group and 5% in the stenting group).*

Endpoints

Primary endpoint: Primary patency at 1 year

It was defined as a patent graft without any intervention to open up or prevent a graft occlusion. Demonstrably patent graft should be by duplex ultrasound color-flow scan (independent core lab assessment)

Secondary endpoints

Technical success/Perioperative complications/Primary and secondary sustained clinical improvement/Secondary patency/MACE/MALE/Limb salvage/TVR/Secondary and assisted patency/Death (all cause)/Ankle brachial index/Quality of life

Patients selection

Main in. criteria

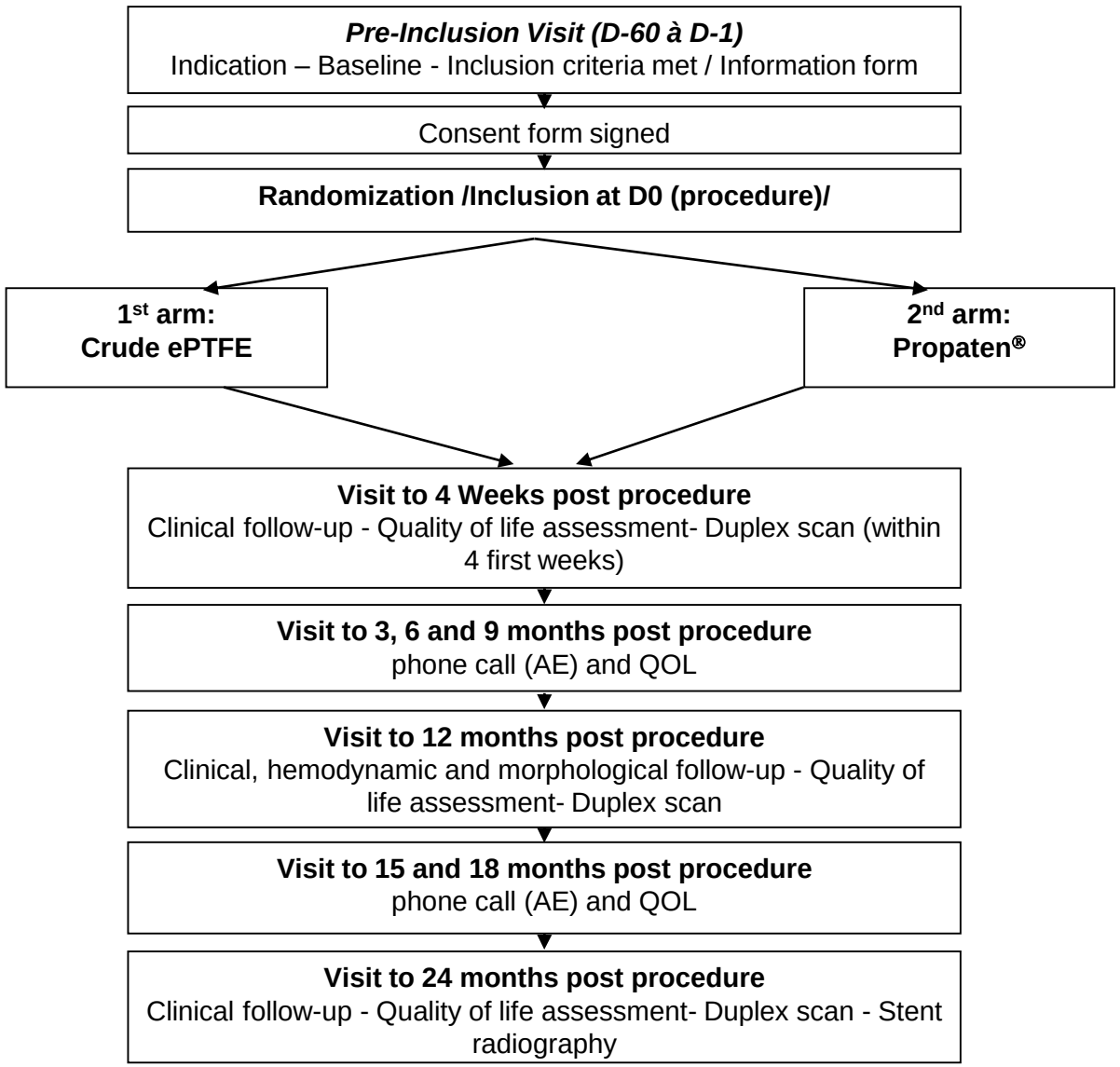
- Rutherford classification: 4-6
- Indication of below the knee bypass with an artificial graft
- Absence of an available autologous vein
- Adequate popliteal or tibial revascularization target,

Main ex. criteria

- Prior below-knee ipsilateral surgical bypass
- Revascularisation planned at the foot level
- Planned above ankle amputation on ipsilateral limb within 4 weeks of index procedure

REPLACE trial flow chart

ClinicalTrials.gov Identifier: submitted



Study duration

- Overall duration of the study: 48 months
- Enrollment period: 24 months
- Patient follow-up period: 24 months

CU in 2022 !!