Can Legflow improve treatment of long femoropopliteal lesions: The REFLOW outcomes

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LINC 2020– Leipzig

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My disclosures

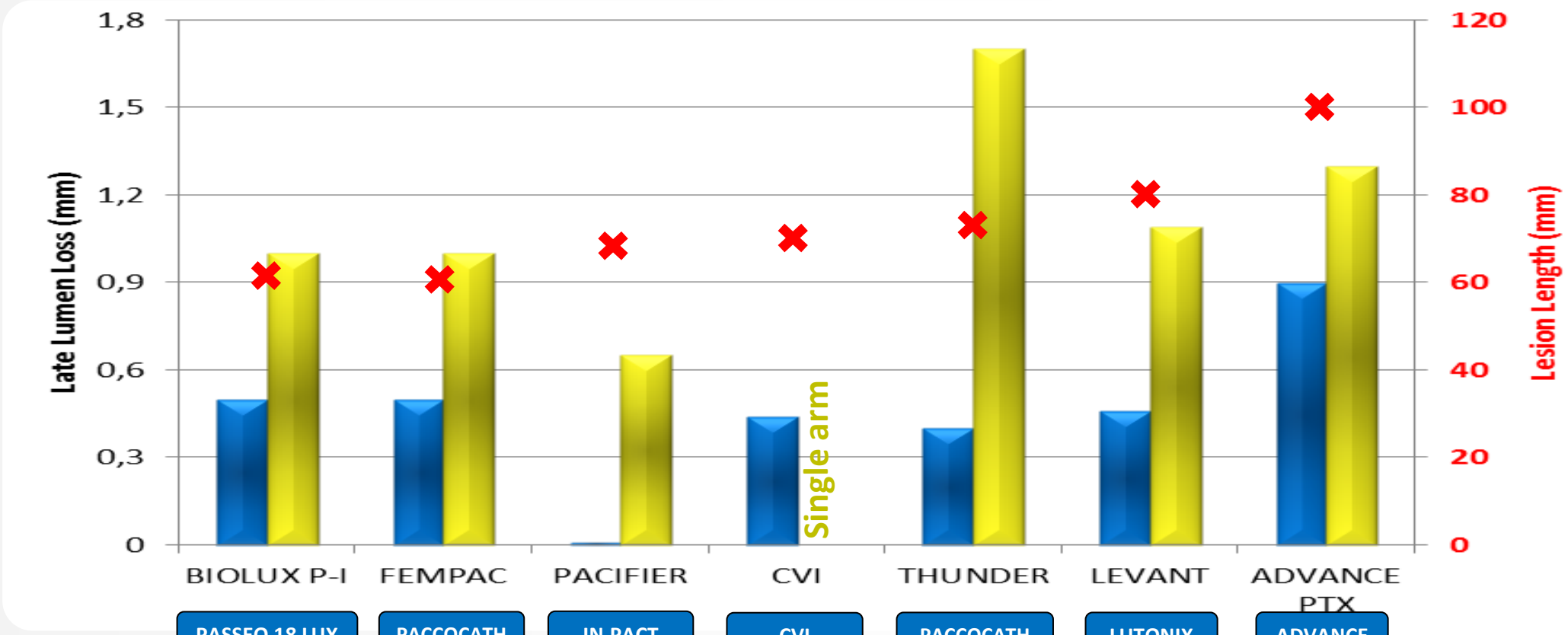
☒ I do not have any potential conflicts of interest to report

o I have the following potential conflicts of interest to report:

- ❑ Consulting
- ❑ Employment in industry
- ❑ Stockholder of a healthcare company
- ❑ Owner of a healthcare company
- ❑ Other(s)

DCB-treatment works… Proof of concepts

DCB POBA



PASSEO 18 LUX	PACCOCATH	IN.PACT	CVI	PACCOCATH	LUTONIX	ADVANCE
PTX 3µgr/mm² + BTHC	PTX 3µgr/mm² + Ultravist	PTX 3,5µgr/mm² + Urea	PTX Excipient?	PTX 3µgr/mm² + Ultravist	PTX 2µgr/mm² + polysorbate & sorbitol	PTX 3µgr/mm² No excipient
P=0.033	P=0.031	P=0.001		P<0.001	P=0.016	P=0.12

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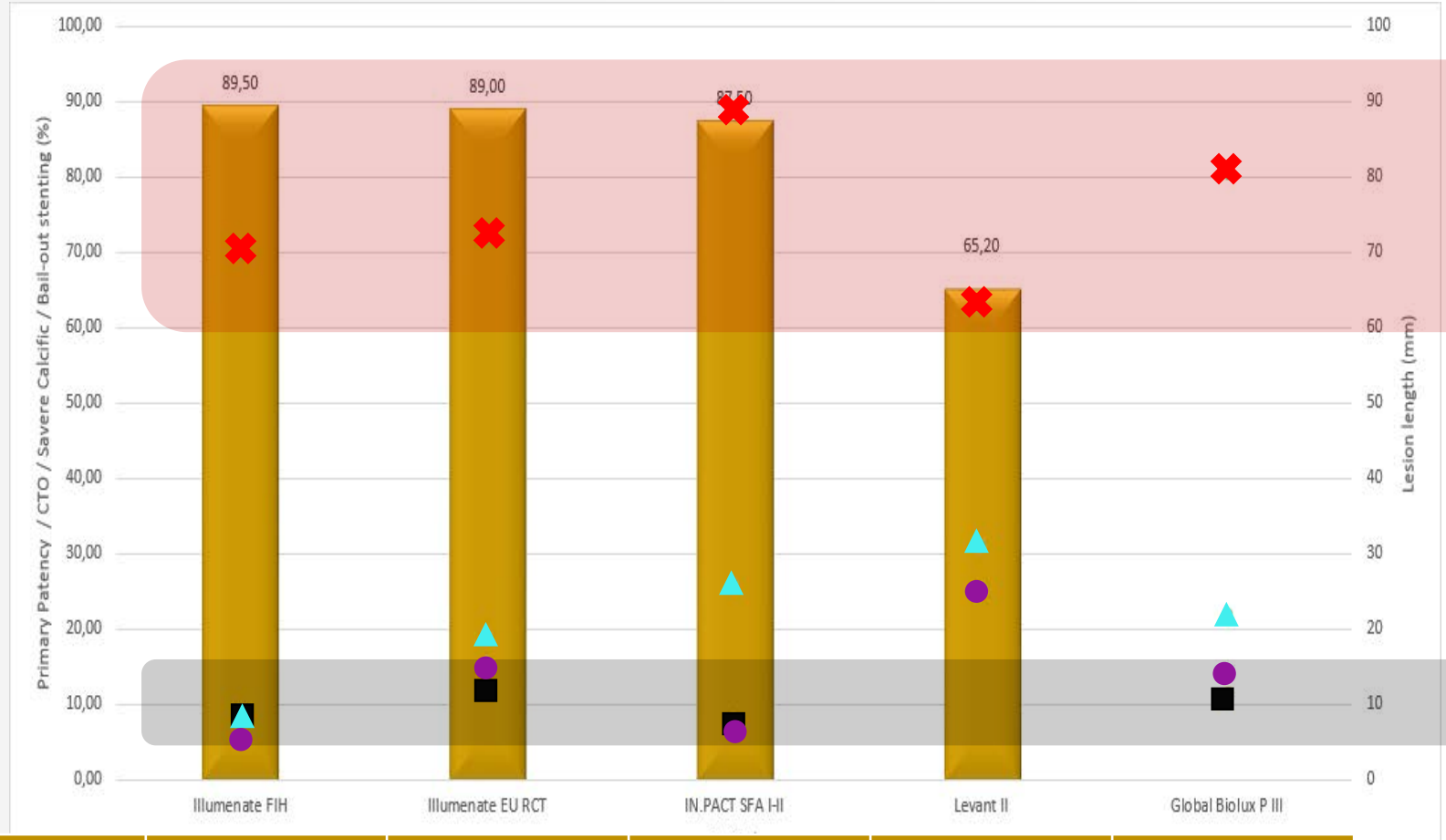
1-Year Patency Rates of DCB (in ideal circumstances)



Short lesions

Limited calcification

Primary Patency (%)	89.50	89.00	87.50	65.20	N.A.
Lesion Length (mm)	70	72	89.4	62.9	80.4
% Bail-out stenting	6	15.4	7.3	2.5	14.5
% CTO	9.4	19.2	25.8	31.2	22.1
% Severe Ca++	9.4	12.7	8.1	N.A.	11.7

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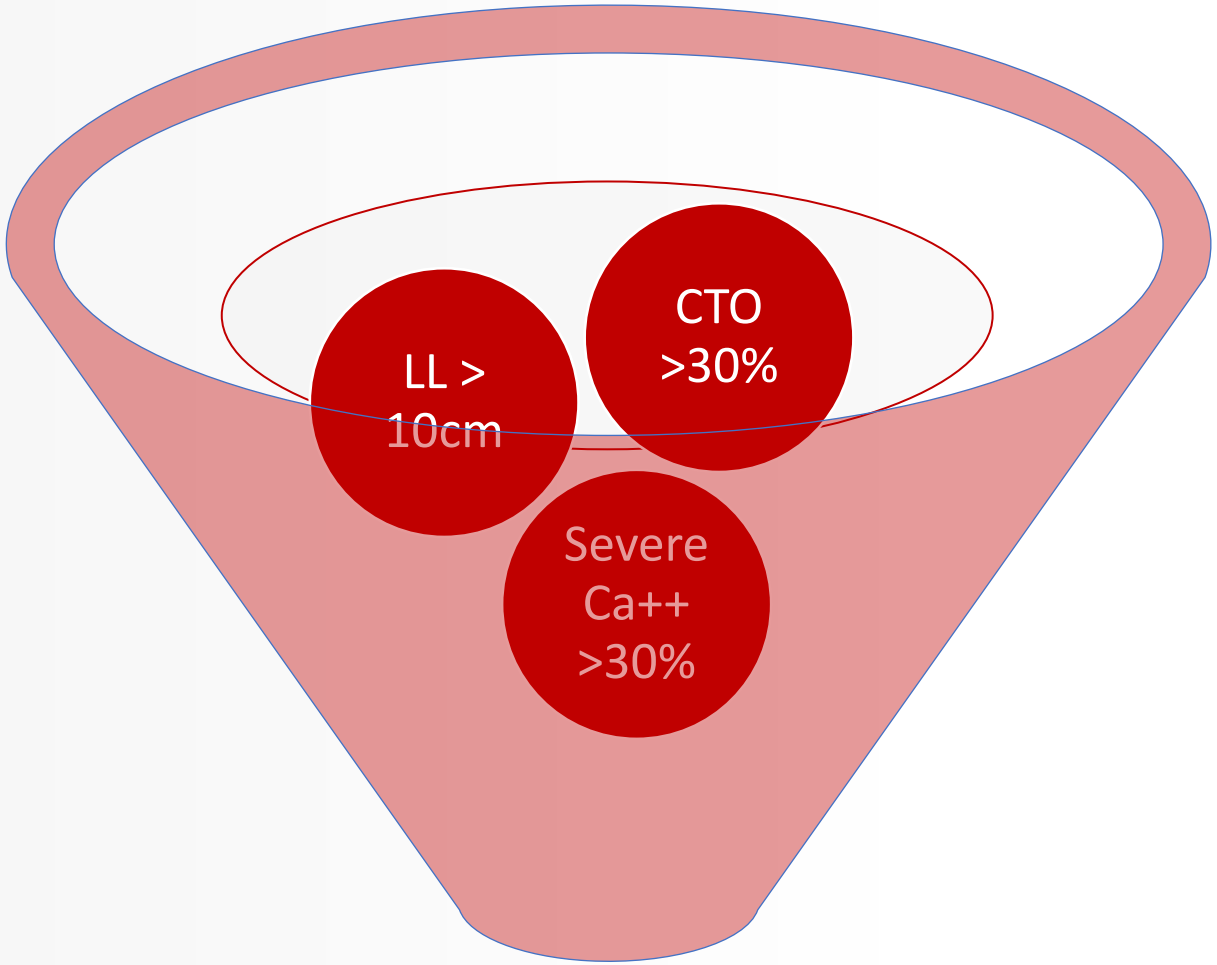
However in “Real Life”…



REFLOW study

A study investigating the Efficacy of the LEGFLOW Paclitaxel-Eluting for the treatment of long femoropopliteal lesions(TASC C&D)

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Legflow Drug Coated Balloon

CARDIONOVUM
Life deserves the best

SAFEPAX® **3rd generation, unique paclitaxel non-crystalline matrix system**

SAFEPAX® matrix system, proprietary formulation of **Lipophilic** and **Polymeric** Ammonium Salt based excipient for PTX DCBs

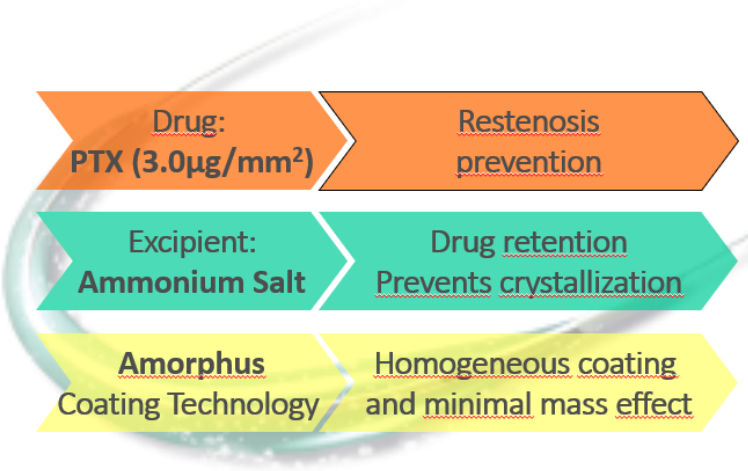
- **Minimum wash off rate**
- **Prevents PTX crystallization on the balloons surface**

CARDIONOVUM portfolio

LEGFLOW® RX/OTW
Peripheral Balloons Dilatation Range.
Platforms: 0.014" 0.018" 0.035"

APERTO® OTW
Hemodialysis Shunt Balloon, up to 20 bar
Platform: 0.0.035"

RESTORE® DEB
Paclitaxel Releasing PTCA Balloon Catheter
Platform: 0.014"



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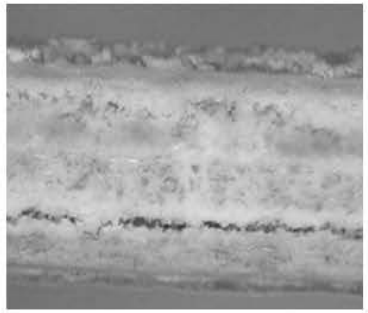
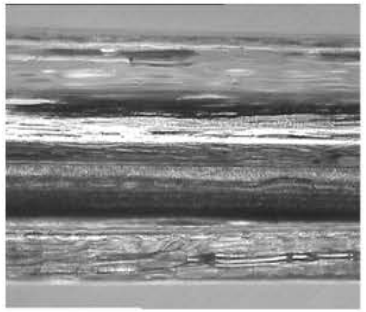
Legflow Drug Coated Balloon

	COATING CLASSES	
	OLD: CRYSTALLINE	NEW: AMORPHOUS
Device	 The surface is white-dusty	 Transparent surface, no brittle powder
Optical Image Measuring (100x)	 Crystalline Hydrophilic Coating DCB	 **CARDIONOVUM** DCBs

Legflow Drug Coated Balloon

	COATING CLASSES	
	OLD: CRYSTALLINE	NEW: AMORPHOUS
Coating look	 Sugar cube (crystalline sugar).	 Honey (non-crystalline sugar)
Matrix	 Crystalline	Crystalline excipients (ex: Hurea, Sorbitol, etc.) and crystalline PTX: they built a rigid crystals shape (white crust formed by crystals of PTX +excipient)
	 Amorphous	Polymeric excipients (ex: Ammonium salt) and non-crystalline PTX: "melt" PTX in an elastic matrix. A Polymeric excipient is made by very long molecules chain without a specific and rigid shape

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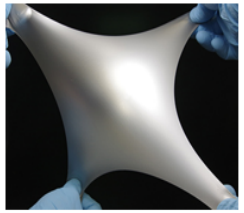
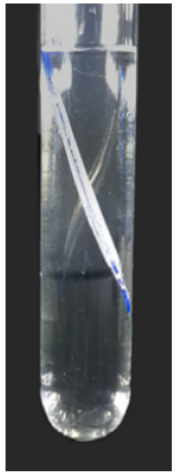
Legflow Drug Coated Balloon

	COATING CLASSES	
	OLD: CRYSTALLINE	NEW: AMORPHOUS
Mechanical stress response	 Crystalline coating is affected by mechanical stress due to the rigid structure of crystralline excipients.	 Amorphous coating is not affected by mechanical stress due to the elastic, polymeric excipients

During inflation, early DCBs generations coating is affected by flaking.

COMPETITORS



During inflation, Safepax (Amorphous coating) is not affected by flaking. Ammonium Salt prevents any crystallization on the balloon surface.

Cardionovum ® has the highest coating stability (paclitaxel loss during handling & wash-off) of DCBs without compromising performance[1]

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Study design

- **Study Objective:**
  To evaluate the performance of the **LEGFLOW Paclitaxel-Eluting** Peripheral balloon catheter for the treatment of **long femoropopliteal lesions (TASC C&D)**.

- **Primary Endpoint:**
  Primary Patency at 12 months, defined as absence of a hemodynamically significant stenosis on duplex ultrasound (systolic velocity ratio ≤2.4) at the target lesion and without reintervention.

Participating centers

- **BELGIUM**
  - M. Bosiers, K. Deloose, J. Callaert - AZ Sint-Blasius, Dendermonde
  - P. Peeters, J. Verbist, W. Van den Eynde - Imelda Hospital, Bonheiden
  - L. Maene, R. Beelen - OLV, Aalst
  - K. Keirse - RZ Heilig Hart, Tienen
  - J. Hendriks, P. Lauwers – University Hospital Antwerp, Edegem

- **GERMANY**
  - G. Torsello – St. Franziskus-Hospital Münster
  - D. Scheinert – Universitätsklinikum Leipzig

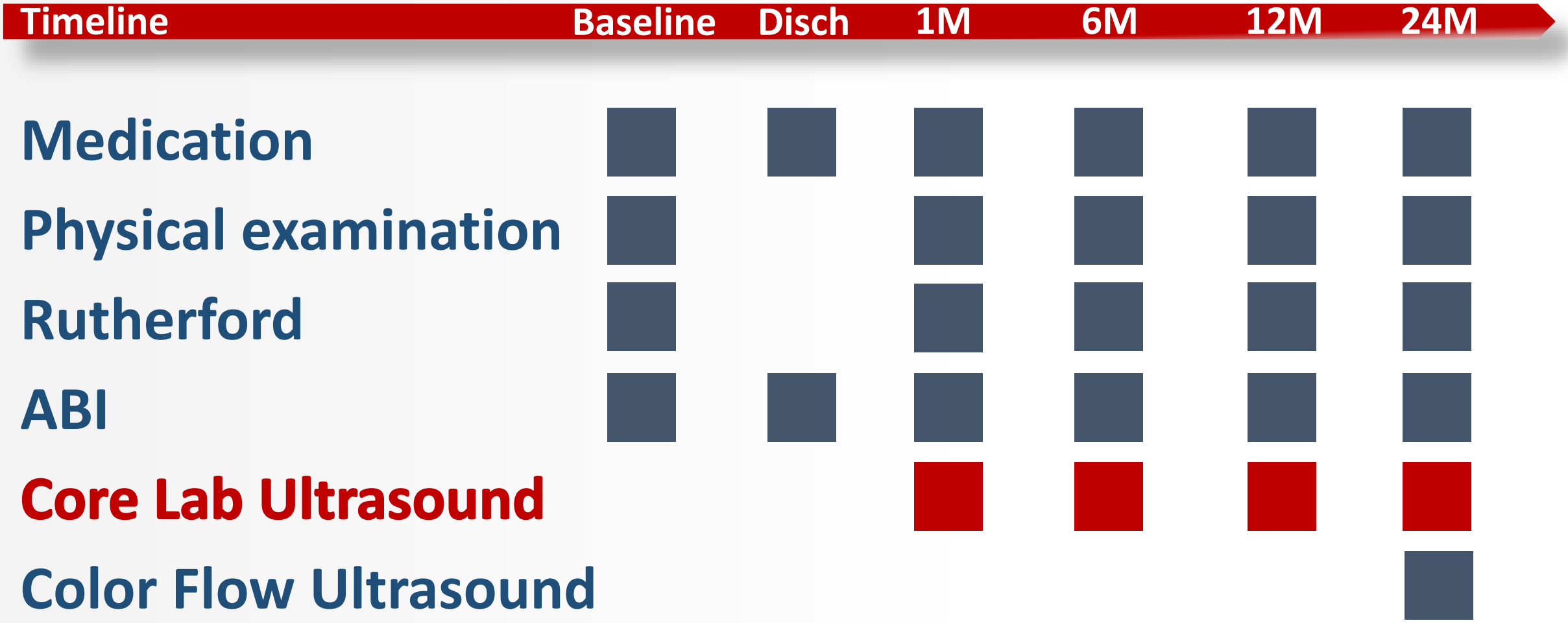
Inclusion criteria

120 out of 120 patients enrolled (100%)

Main inclusion criteria

- **Rutherford classification from 2 to 5**
- **De novo lesion** in the femoropopliteal arteries, suitable for endovascular therapy
- Total target lesion length **> 150mm**

Study overview



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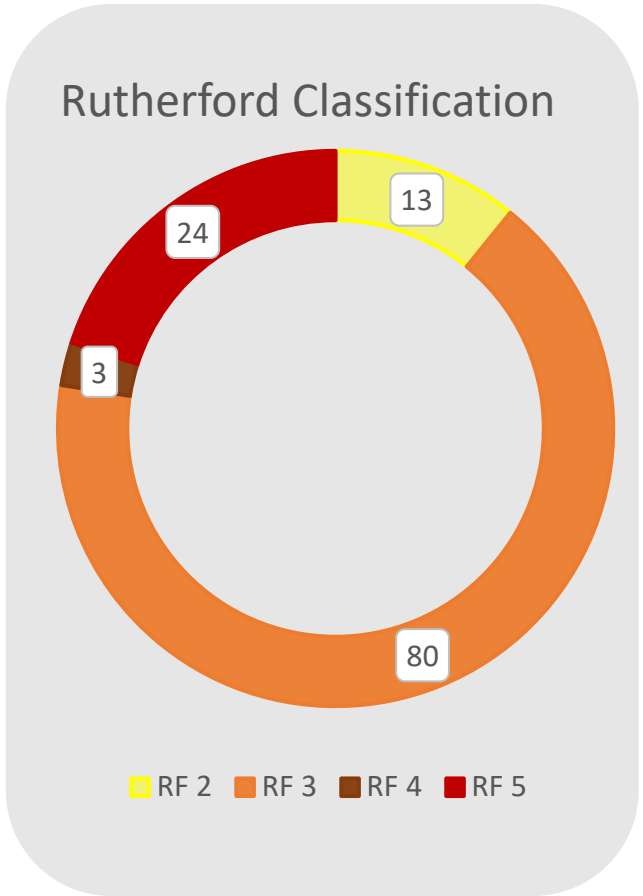
Patient Demographics

	N = 120
Male *(%)*	65.80% *(79/120)*
Age *(min – max)*	71.06 *(35.05 – 93.16) years*
Nicotine abuse *(%)*	56.67% *(68/120)*
Hypertension (%)	***77.50% (93/120)***
Diabetes mellitus *(%)*	30.00% *(36/120)*
Renal insufficiency *(%)*	15.00% *(18/120)*
Hypercholesterolemia *(%)*	53.30% *(64/120)*
Obesity *(%)*	19.20% *(23/120)*



Procedural characteristics

	N = 120
Procedure time ***(min-max)***	***52.17*** ***(19-165) minutes***
Scopy time *(min – max)*	7.32 *(1.7 – 39.24) minutes* **missing information for 2 patients*
Contrast *(min – max)*	88.09 *(9 – 195) mL*
Cross-over performed *(%)*	*83.33% (100/120)*
Inflow Lesion *(%)*	*10.83% (13/120)*
Outflow lesion *(%)*	*21.67% (26/120)*

Lesion Characteristics

	N = 120
Lesion length ***(min – max)***	**216.08** ***(150 – 390) mm***
Ref Vessel Diameter *(min – max)*	5.40 (4.05 – *6.00) mm*
Pre-dilatation	64.20% (77/120)
1 DCB (%) 2 DCB's (%) 3 DCB's (%)	25.83% (31/120) 57.50% (69/120) 16.67% (20/120)
Post-dilatation (%)	22.50% (27/120)
Bail-out stenting ***(%)***	35.00% ***(42/120)***
Occlusion *(%)*	45.00% *(54/120)*
Calcified lesion (%)	**67.50%** ***(81/120)***

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Paclitaxel --> mortality?

Risk of Death Following Application of Paclitaxel Stents in the Femoropopliteal Artery of the Leg: A Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, Stavros Spiliopoulos, Panagiotis Kitrou, Miltiadis Krokidis, an

Originally published 6 Dec 2018 | https://doi.org/10.1161/JAHA.118.011245 | Journal of the American He

Study	Ev	Weight (random)
ZILVER-PTX [19]		20.6%
FINN-PTX [18]		1.5%
IN.PACT SFA [82]		3.7%
FEMPAC [29]		8.9%
LEVANT I [27]		9.4%
LEVANT II [26]		21.4%
CONSEQUENT [30]		2.6%
ILLUMENATE EU [32]		9.9%
ISAR-STATH [51]		2.9%
ISAR-PEBIS [55]		1.7%
ACOART I [40]		14.2%
IN.PACT SFA JAPAN [41]		3.2%
Fixed effect model		--
Random effects model		00.0%

Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80

0.01 0.1 1 10 100

Recommendations

Based on the FDA's review of available data and the advisory panel conclusions, the FDA recommends that health care providers consider the following:

- Continue diligent monitoring of patients who have been treated with paclitaxel-coated balloons and paclitaxel-eluting stents.
- When making treatment recommendations, and as part of the informed consent process, consider that there may be an increased rate of long-term mortality in patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents.
- Discuss the risks and benefits of all available PAD treatment options with patients. For many patients, alternative treatment options to paclitaxel-coated balloons and paclitaxel-eluting stents provide a more favorable benefit-risk profile based on currently available information.
- For individual patients judged to be at particularly high risk for restenosis and repeat femoropopliteal interventions, clinicians may determine that the benefits of using a paclitaxel-coated device outweigh the risk of late mortality.
- In discussing treatment options, physicians should explore their patients' expectations, concerns, and treatment preferences.
- Ensure patients receive optimal medical therapy for PAD and other cardiovascular risk factors as well as guidance on healthy lifestyles including weight control, smoking cessation, and exercise.
- Report any adverse events or suspected adverse events experienced with the use of paclitaxel-coated balloons and paclitaxel-eluting stents.

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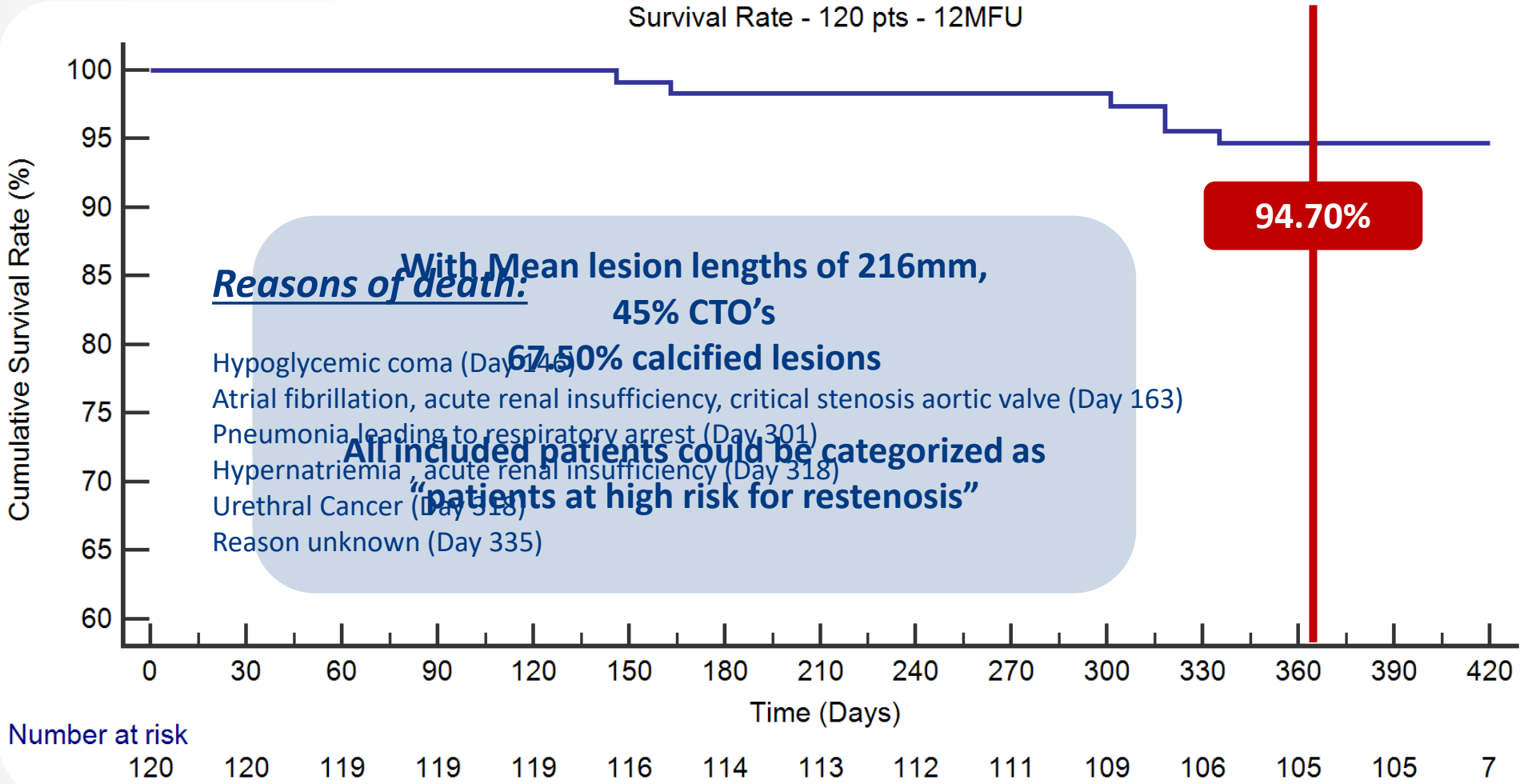
12-month Survival Rate in 120pts



With Mean lesion lengths of 216mm,
45% CTO's
67.50% calcified lesions

Reasons of death:

Hypoglycemic coma (Day 145)
Atrial fibrillation, acute renal insufficiency, critical stenosis aortic valve (Day 163)
Pneumonia leading to respiratory arrest (Day 301)
Hypernatriemia , acute renal insufficiency (Day 318)
Urethral Cancer (Day 318)
Reason unknown (Day 335)

All included patients could be categorized as "patients at high risk for restenosis"

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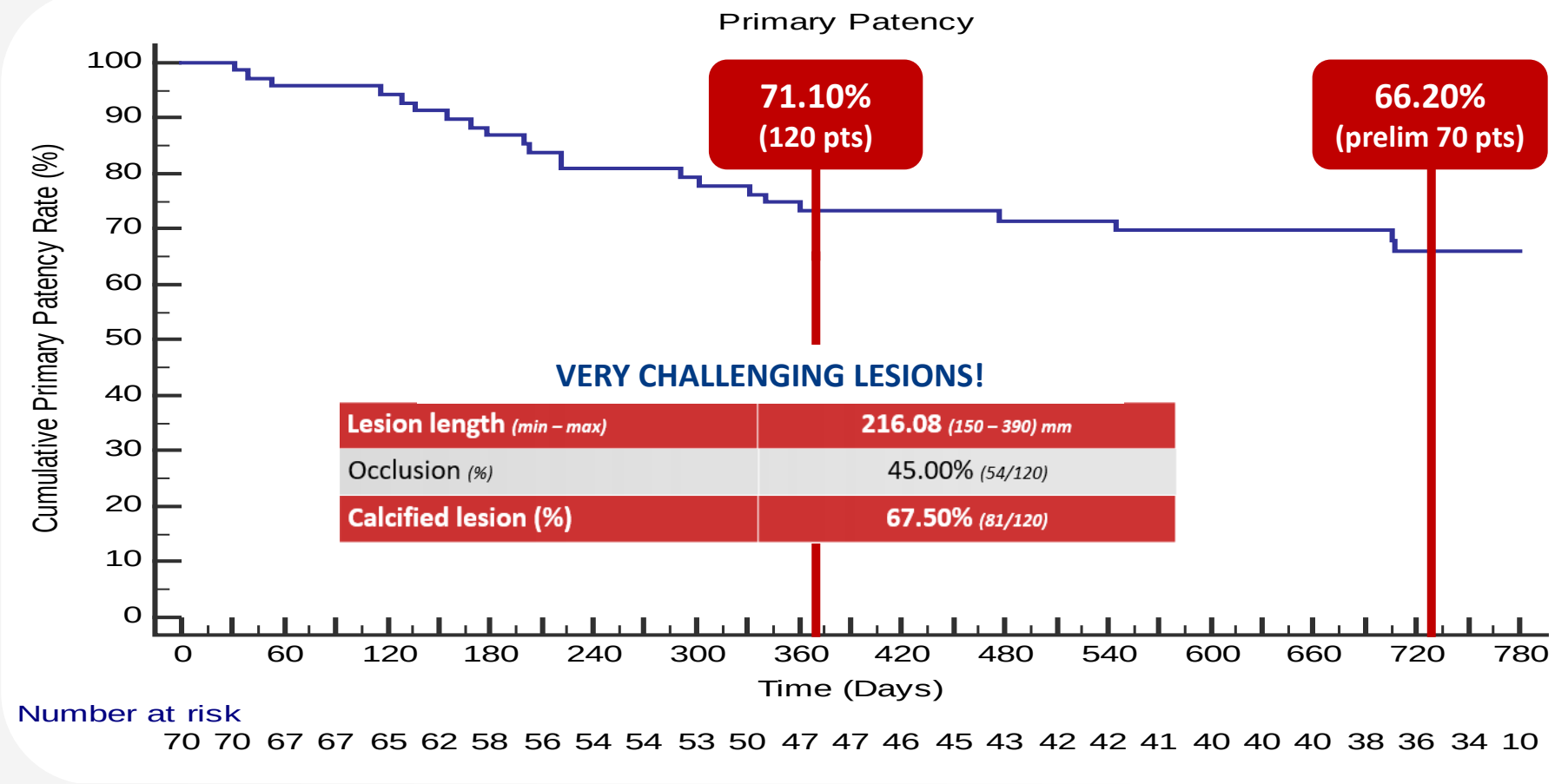
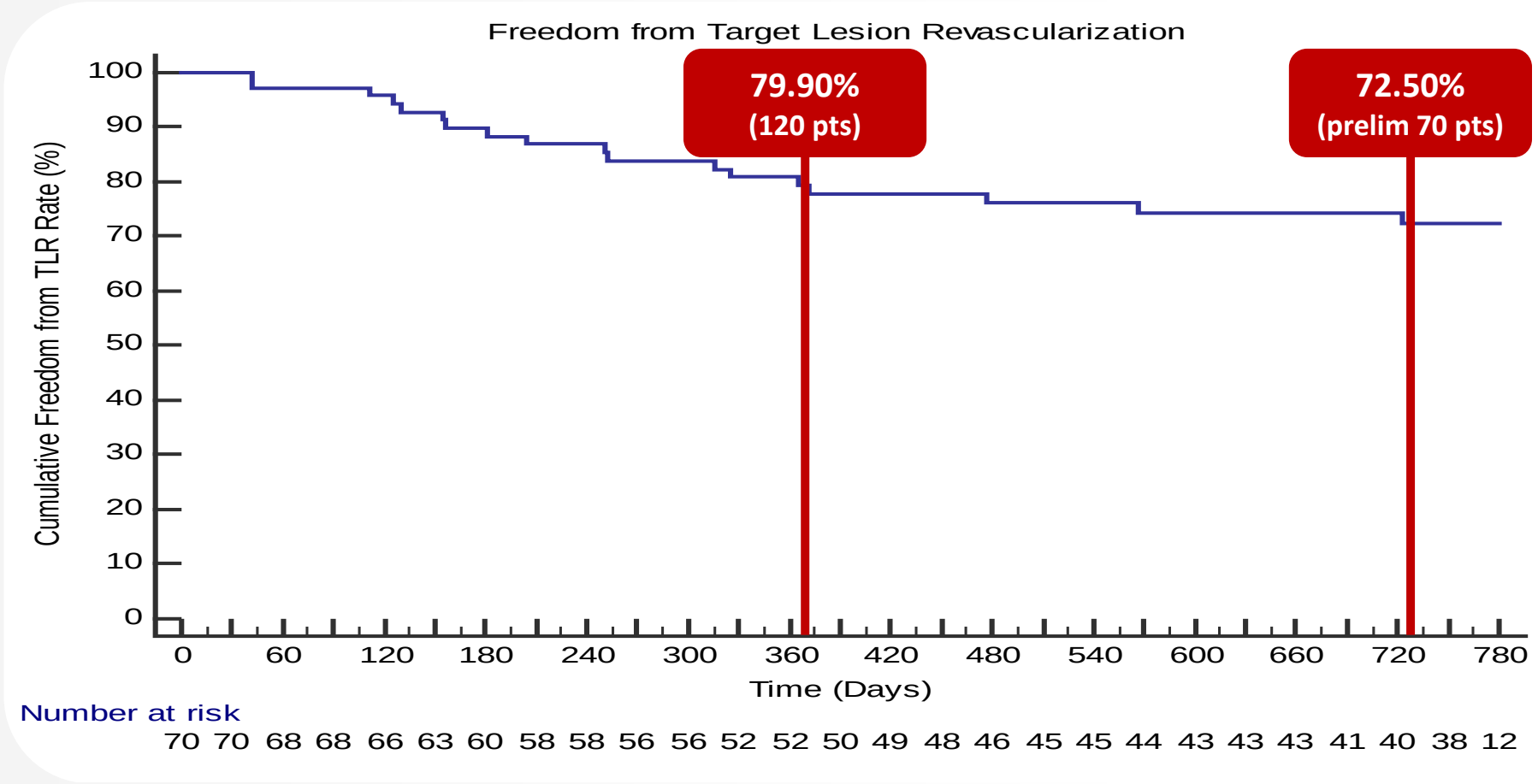
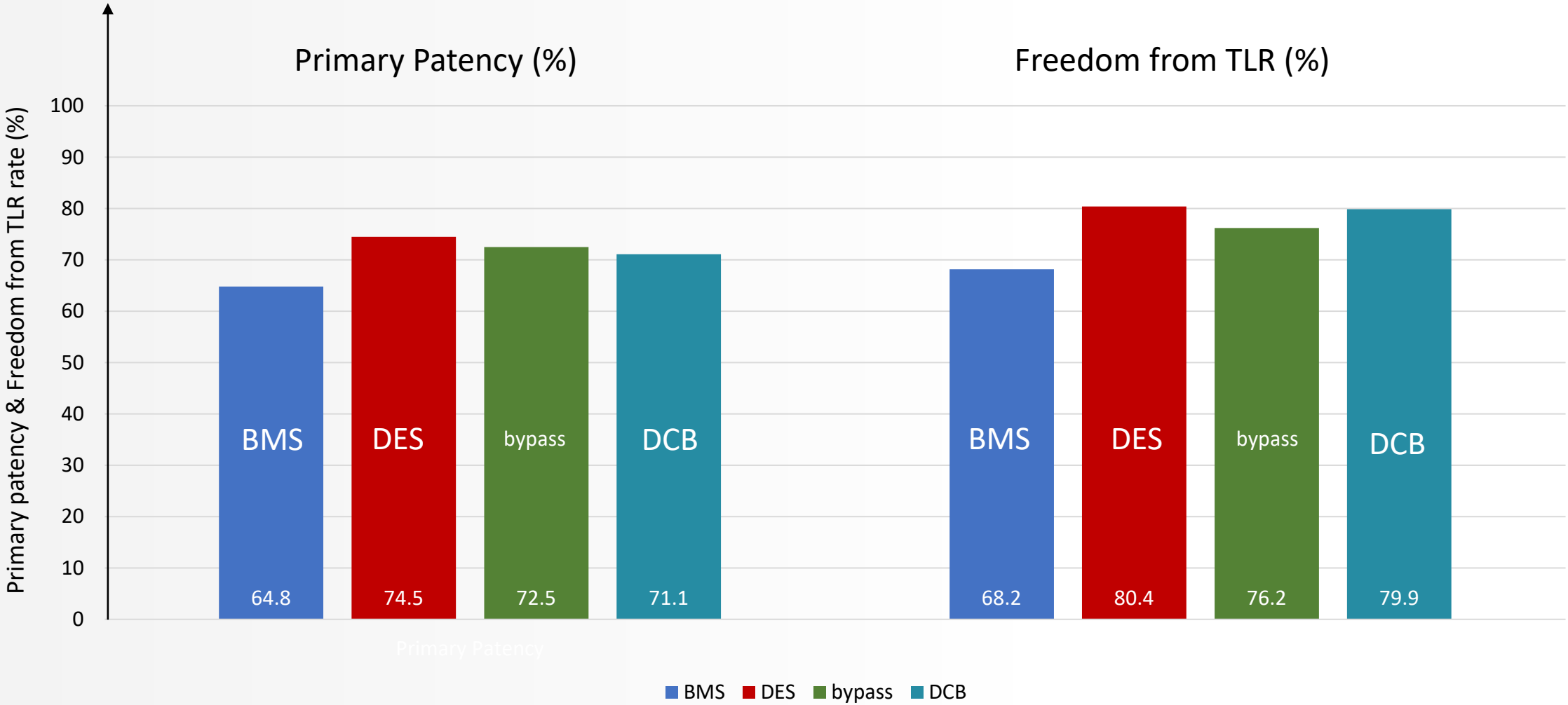
Primary Patency at 12M (120pts) & 24M (70pts)



Freedom from TLR at 12M (120 pts) & 24M (70pts)



12-Month REFLOW results in perspective (lesions >20cm)



BMS : Durability 200 study

DES : ZILVERPASS Zilver PTX results

Bypass ZILVERPASS results

DCB : REFLOW results

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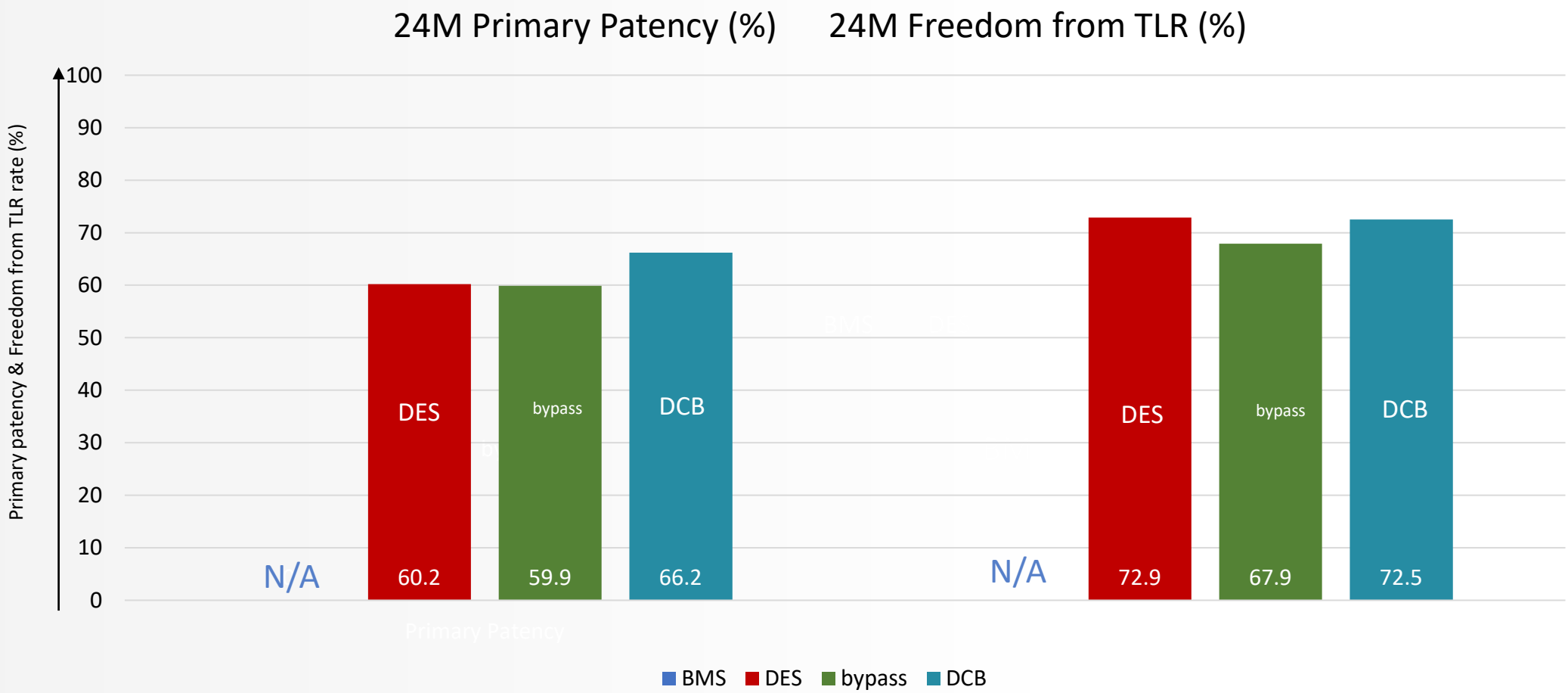
24-Month REFLOW results in perspective (lesions >20cm)



BMS : Durability 200 study

DES : ZILVERPASS Zilver PTX results

Bypass ZILVERPASS results

DCB : REFLOW results

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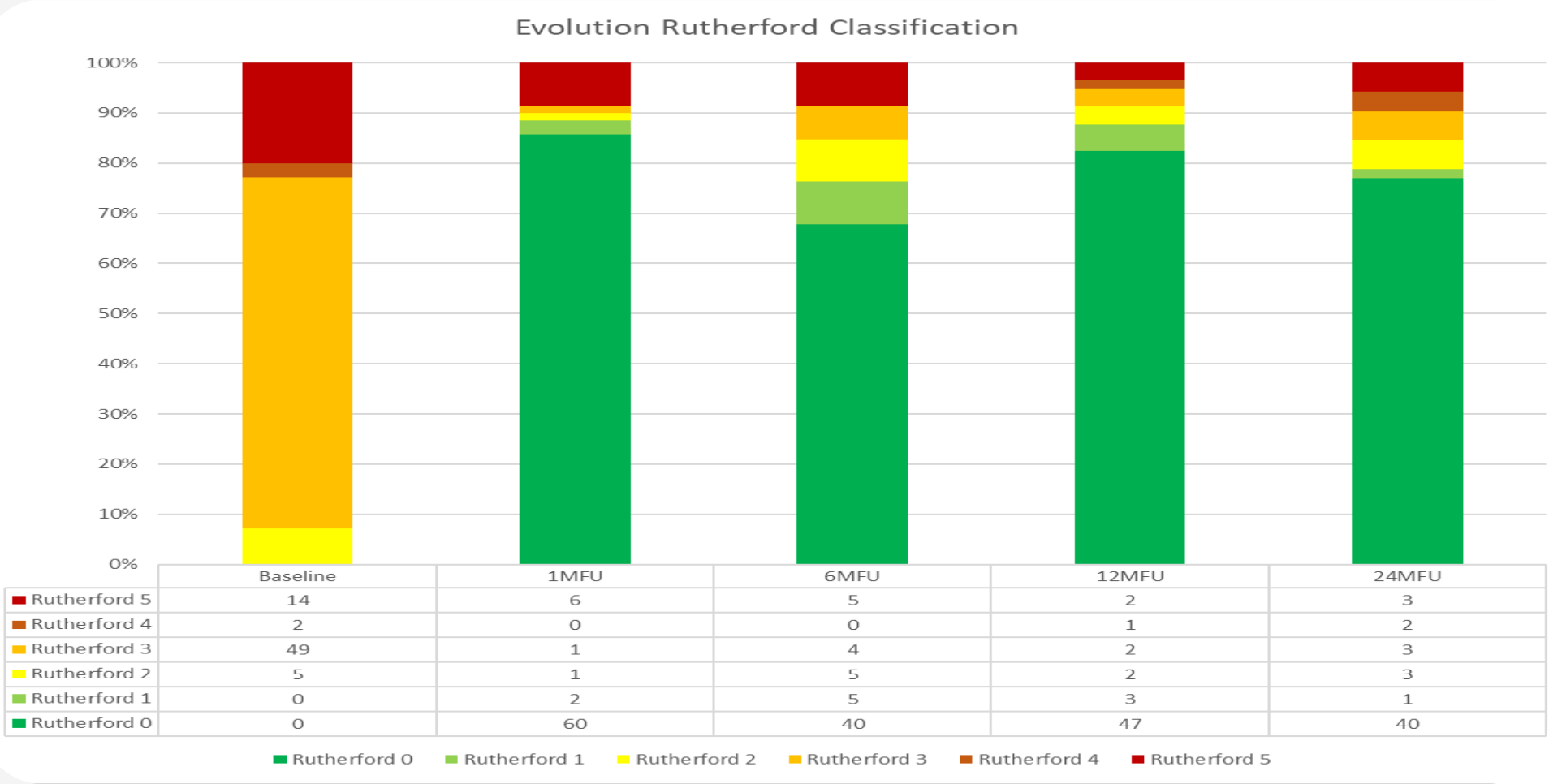
Clinical Benefit - Rutherford evolution in 70pts



	Baseline	1MFU	6MFU	12MFU	24MFU
Rutherford 5	14	6	5	2	3
Rutherford 4	2	0	0	1	2
Rutherford 3	49	1	4	2	3
Rutherford 2	5	1	5	2	3
Rutherford 1	0	2	5	3	1
Rutherford 0	0	60	40	47	40

Conclusion

- Final 12-month and preliminary 24-month results suggest that the LEGFLOW DCB is a valid and **effective** alternative to treat **“real-life”** long, complex and calcified femoropopliteal lesions

- With a 94.70% survival rate at 12-month, the LEGFLOW DCB proves it’s **safety**

- Awaiting for final longer-term results (24-month data)