

# High risk of restenosis patients' treatment: Update in the REFLOW trial

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# Disclosure slide

Speaker name: Koen Deloose, MD

I have the following potential conflicts of interest to report:

Consulting: Abbott, BD, Biotronik, Boston Scientific, Cook, CTI vascular, iVascular, Medtronic, Philips, Terumo, CyndRX, Profusa

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

I do not have any potential conflict of interest

## Recommendations for paclitaxel-coated balloons and paclitaxel-eluting stents in the treatment of peripheral arterial disease

date: 03/07/2019

### Recommendations

While further investigation is in progress, the FAMHP takes this safety signal very seriously and makes the following recommendations (FR - NL) to healthcare professionals:

- Do not use paclitaxel DCBs or DESs as a preferred treatment for intermittent claudication until further notice. Carefully estimate the risks and benefits for each patient.
- Discuss the risks and benefits of all available treatment options for PAV with patients. Inform patients about the uncertainty of increased mortality.
- Ensure proper follow-up for patients who have already been treated with a paclitaxel DCB or DES.
- Report any adverse event involving a paclitaxel DCB or DES to FAMHP using our online [adverse event form](#).

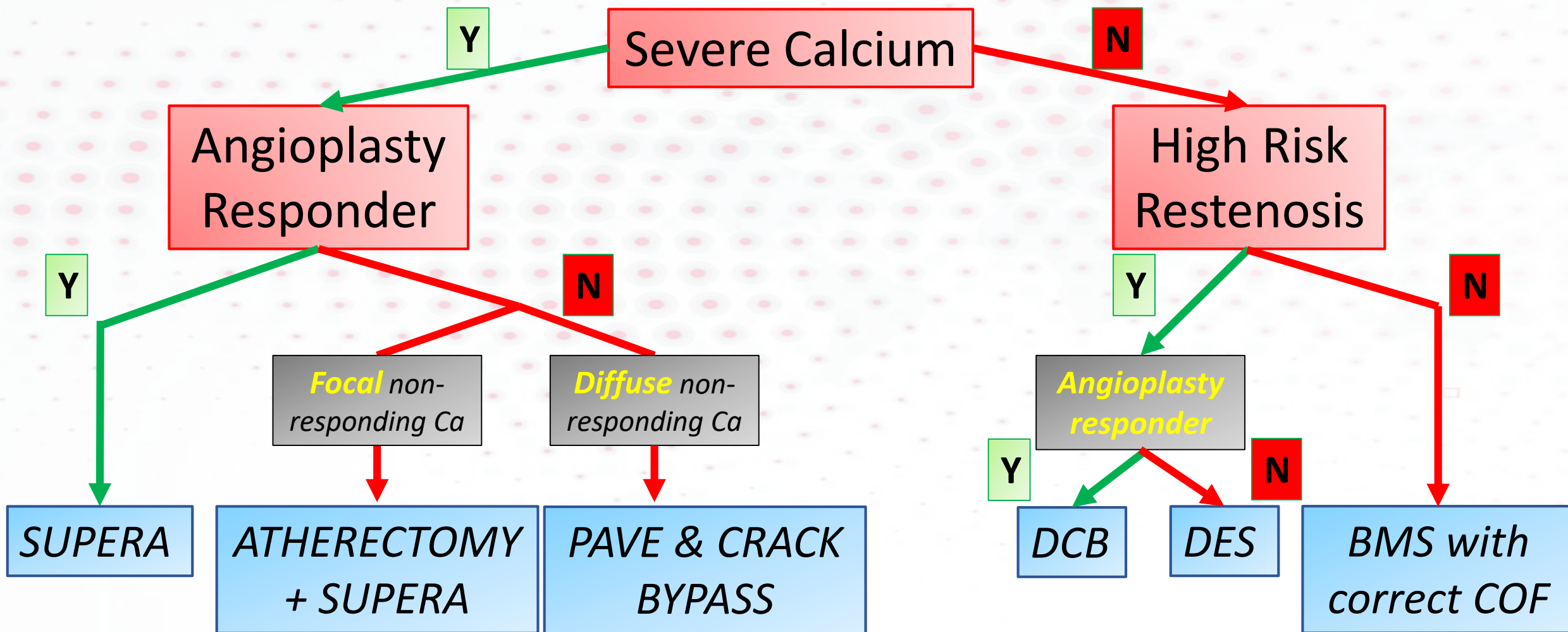
Patients who are worried or have any questions about these aids should talk to their attending physician.

**Federal Agency for Medicines and Health Product,  
July 3<sup>rd</sup> 2019**

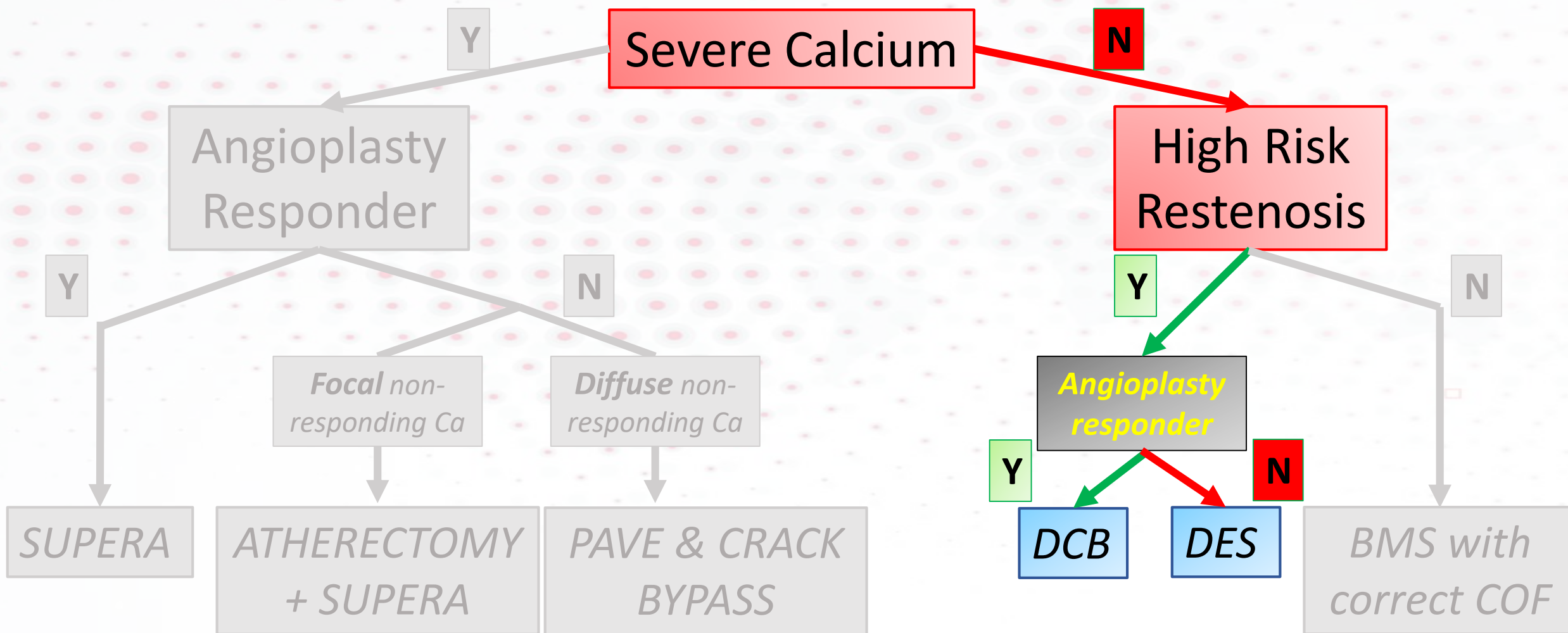
How to  
continue...?



# “3 questions/answers”- based treatment algorithm



# “3 questions/answers”- based treatment algorithm



# High Risk of Restenosis?

## Patient Specific Factors

- *Critical Limb Ischemia*
- *Diabetes Mellitus*
- *End Stage Renal Disease*
- *Poor Run-off*

## Lesion Specific Factors

- *Length*
- *Small vessel diameter*
- *Occlusion*

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- Shammass NW. Restenosis after lower extremity interventions: Current status and future directions. *J EVT* 2009; 16(Suppl I):I170-I182.
- Schillinger M et al. Restenosis after percutaneous angioplasty: The role of vascular inflammation. *Vasc Health Risk Manag* 2005; 1(1):73-78.
- Dieter RS et al. Overview of restenosis in peripheral arterial interventions. *Endovascular Today* 2004; 36-38.

# Reflow study



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

- **Study Objective:**

To evaluate the performance of

**LEGFLOW Paclitaxel-Eluting Peripheral balloon**

catheter for treatment of long femoro-

popliteal lesions (TASC C&D) in **120 patients**.

- **Primary Endpoint:**

**Primary Patency @12 months**, defined as

absence of hemodynamically significant stenosis

on DUS (peak systolic velocity ratio  $\leq 2.4$ ) @target




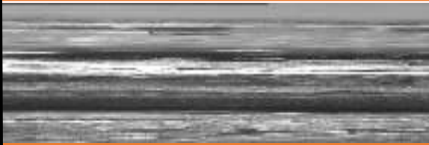






lesion & without reintervention.





# We need a stable coating matrix...



	OLDER GENERATION CRYSTALLINE COATINGS		NEWER GENERATION AMORPHOUS COATINGS	
Device		Surface covered with white powder		Smooth, transparent surface
Optical image measuring (100x)		Crystalline, hydrophilic coating		Amorphous, lipophilic coating
Look		Crystalline sugar		Honey
matrix		Rigid crystal shape of crystalline excipient/PTX		Non crystalline PTX melted with polymeric excipient in an elastic matrix
Mechanical stress response		Rigid crystalline coating affected by mechanical stress factors		Elastic, polymeric amorphous coating not affected by mechanical stress

# Reflow study : participating centers/timeline

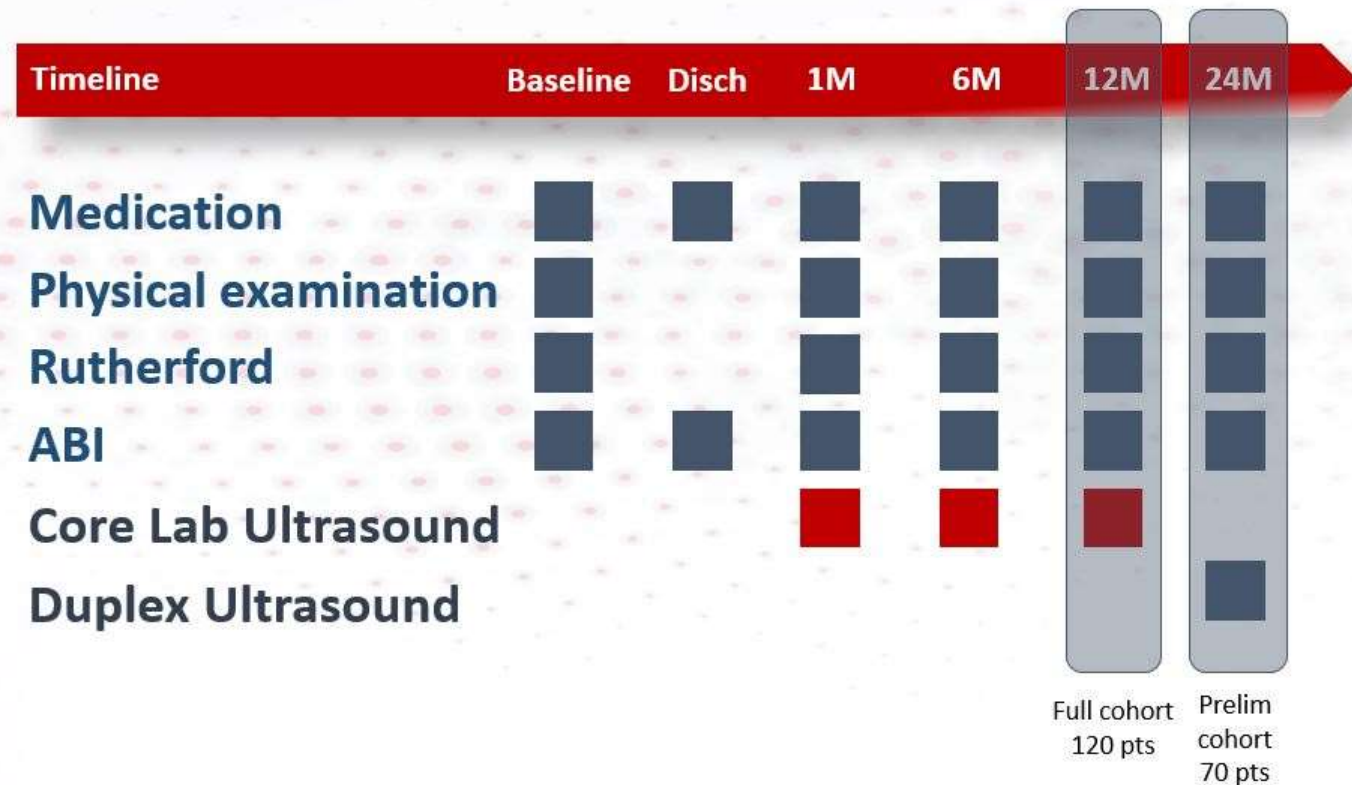


## • BELGIUM

- 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*

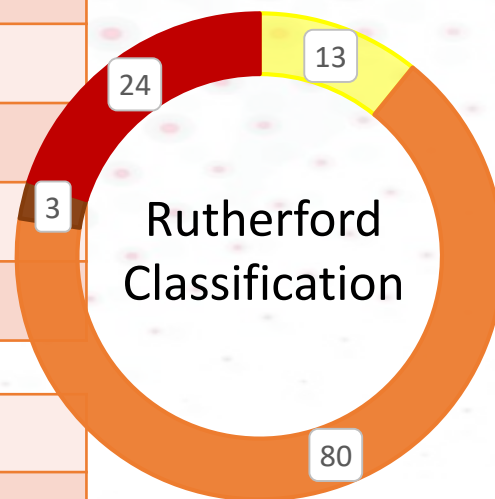
## • GERMANY

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



# Reflow study : patient demographics procedural characteristics

	<b>N = 120</b>
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)
Claudicants	77.5% (95/120)
CLI	22.5% (27/120)



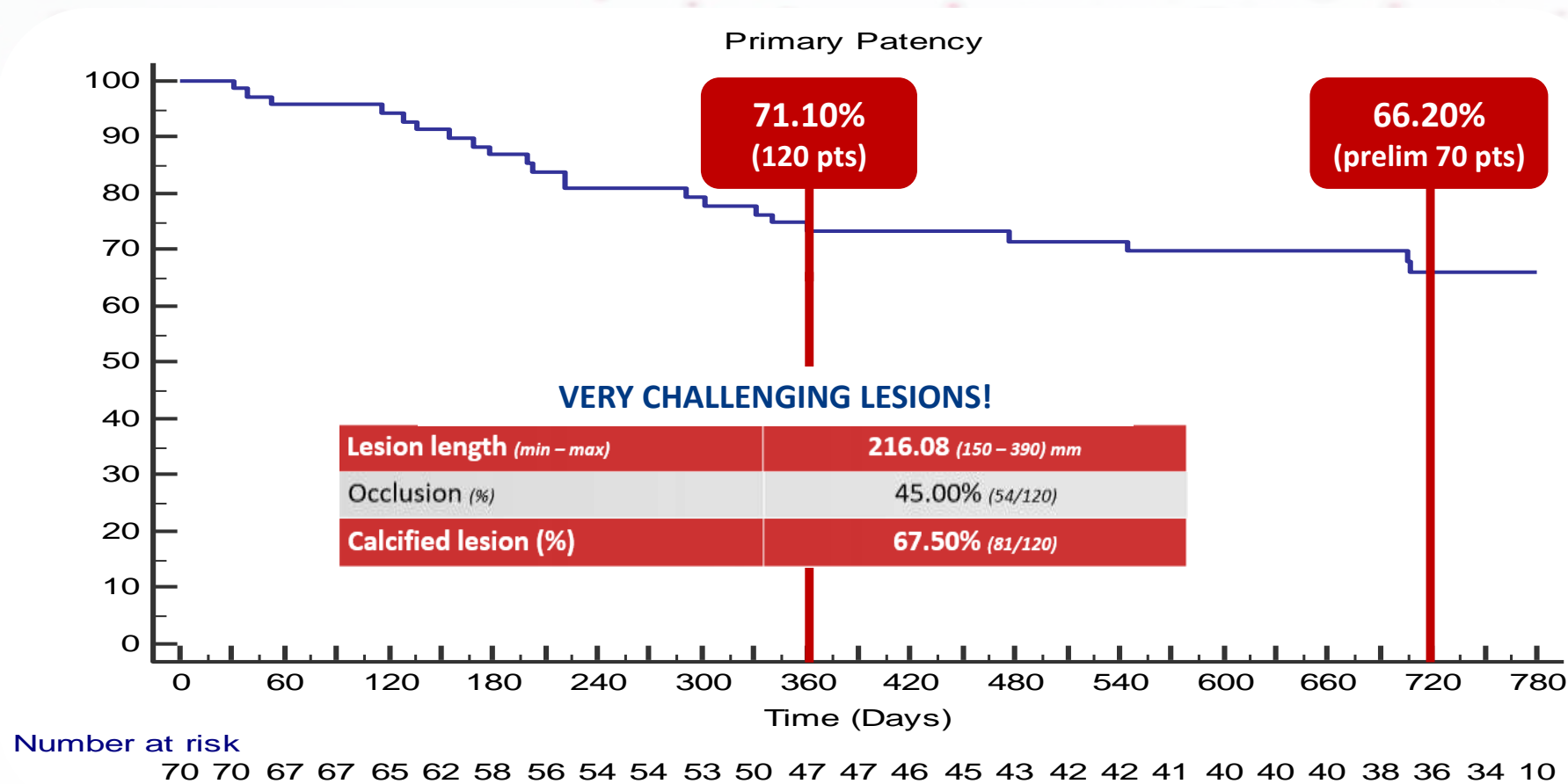
■ RF 2 ■ RF 3 ■ RF 4 ■ RF 5

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

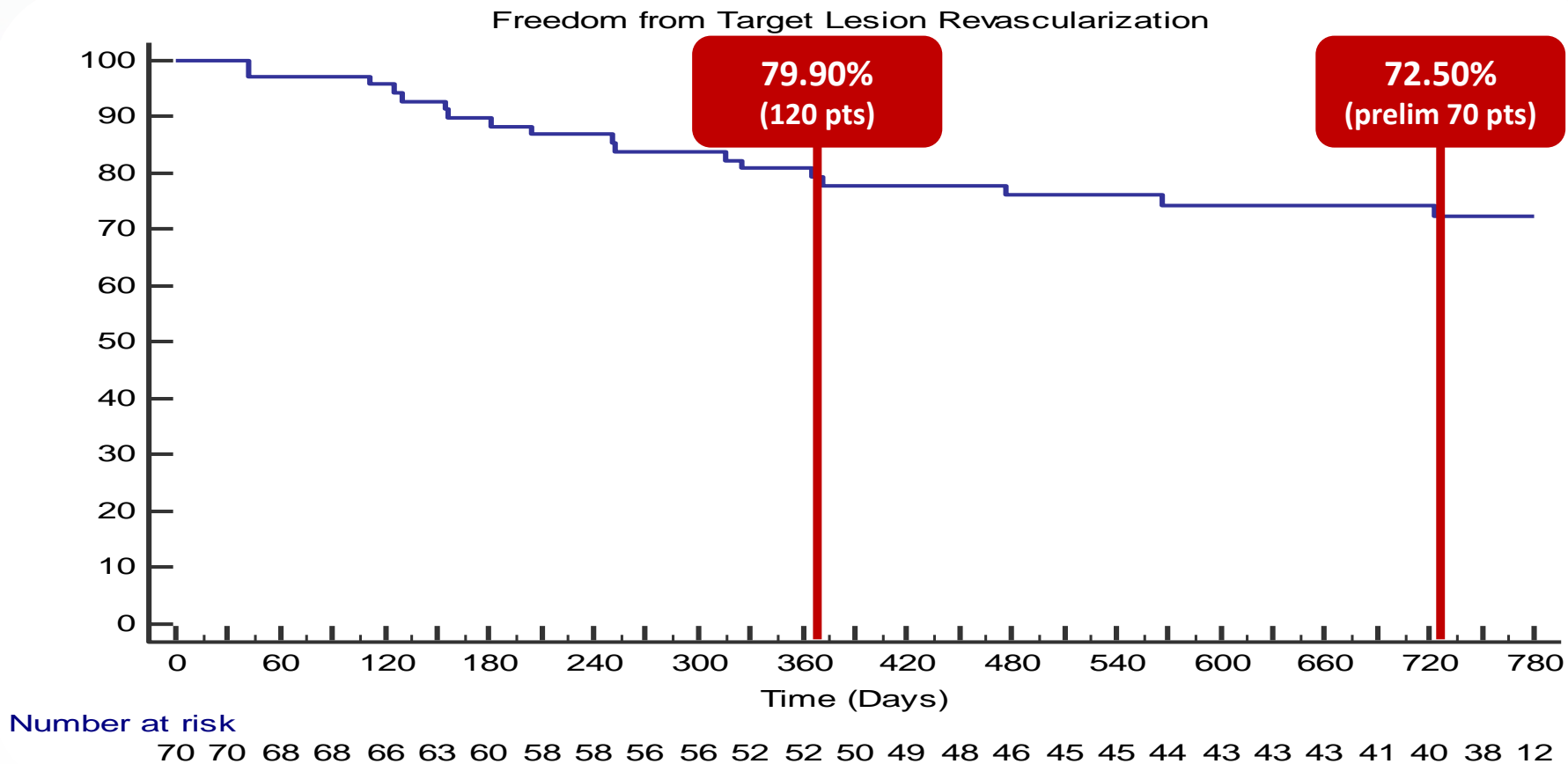
# Reflow study : Lesion characteristics

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

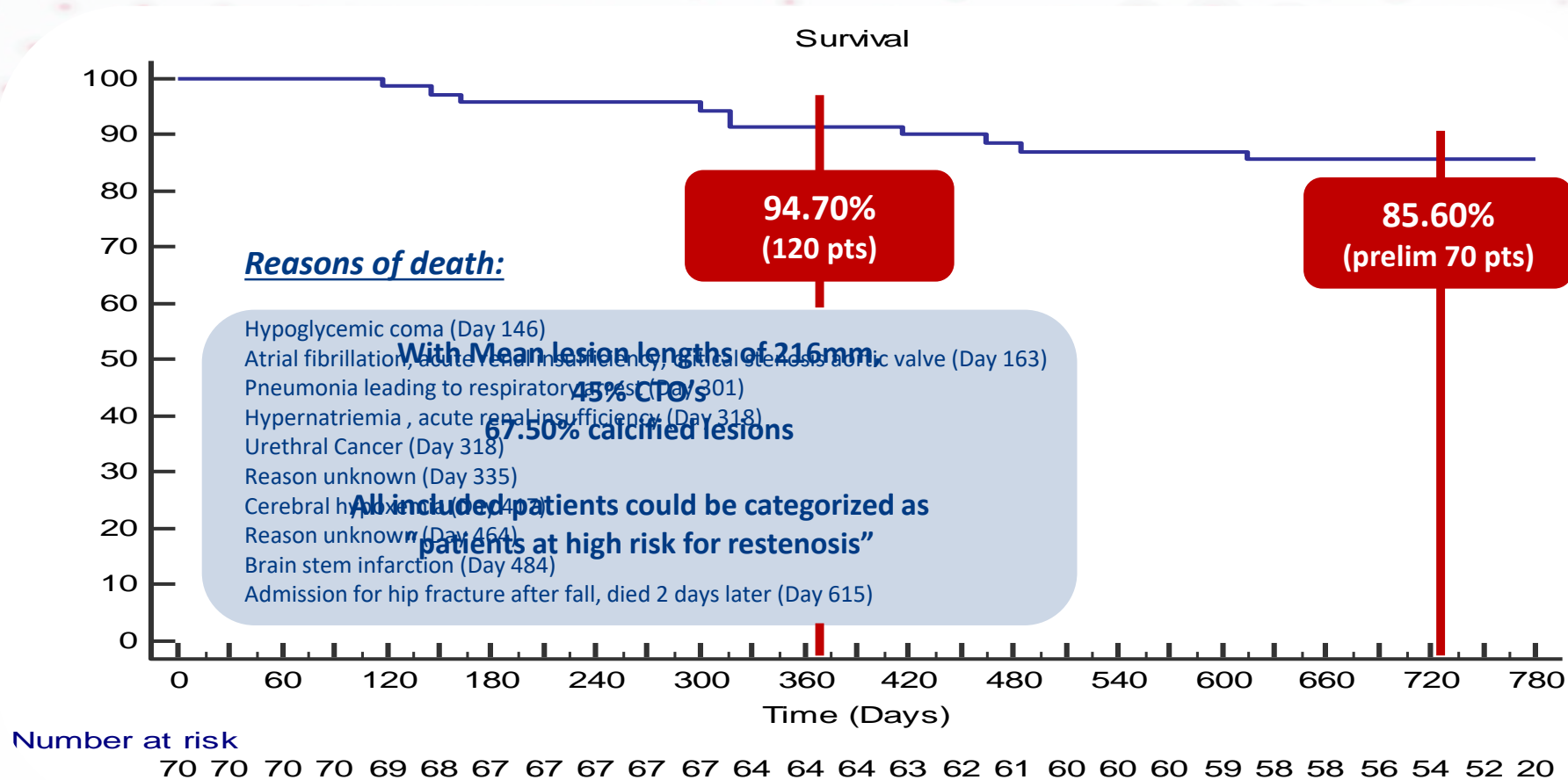
# Reflow study : Primary Patency @12/24 m



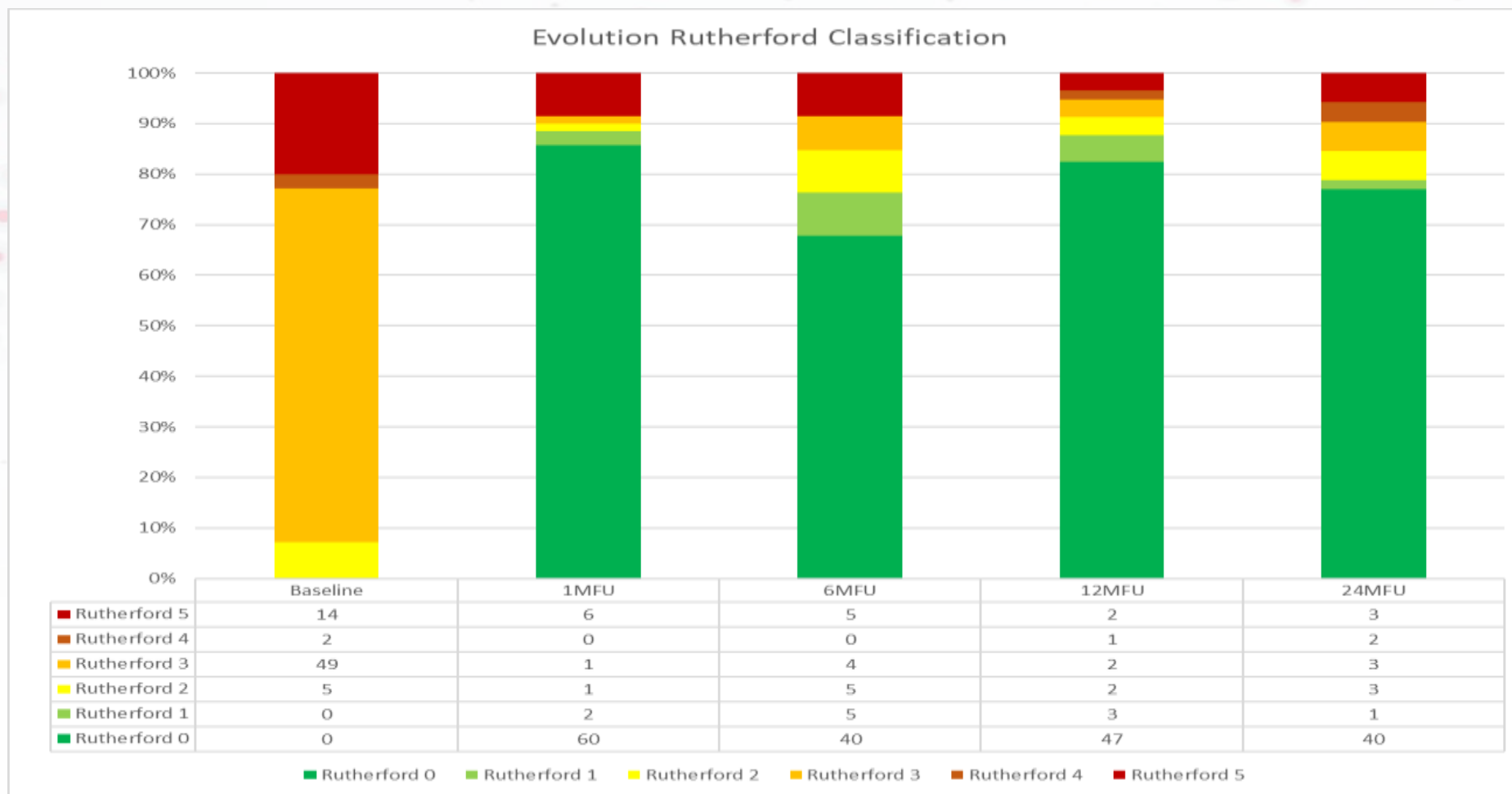
# Reflow study : Freedom TLR @12/24 m



# Reflow study : Survival @12/24 m



# Reflow study : clinical outcome



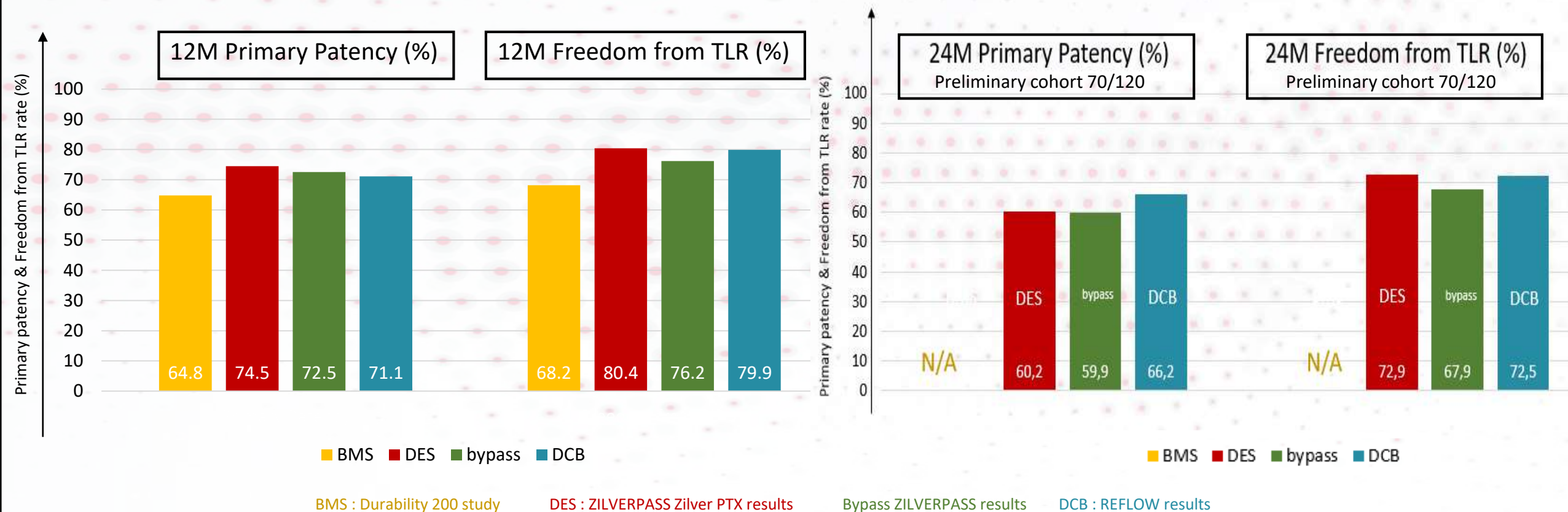


# Reflow study : safety profile (full cohort)

<b>Primary Safety Endpoint (120 pts)</b>	<b>30 days</b>
Device or procedure related death (N)	0
CD-TLR (N)	1
Target Limb Amputation (N)	0

<b>MAEs (N=120 pts)</b>	<b>180d</b>	<b>210d</b>	<b>365d</b>	<b>395d</b>
Death (N)	2	2	6	6
CD-TLR (N)	11	12	22	26
Target Limb Major Amputation (N)	0	0	0	0

# Reflow study in perspective...lesions >20cm



# Reflow study in summary

- Safety issues with some DCB's created official authority statements, saying that all PTX-based technology needs to be reserved for patients **at high risk for restenosis & reintervention**
- Newer generation DCB's, like the Legflow, with stable amorphous SAFEPAX coating, are developed **to optimize drug uptake in "hostile environments"**
- **The Reflow study** demonstrates in a complex lesion population (mean lesion length 22cm) good outcomes : **full cohort 1 year patency of 71% and freedom from TLR of 80%**.
- In a preliminary cohort of 70 patients **24 month data are available : patency of 66% and freedom from TLR of 72%**
- If we benchmark with other treatment strategies like BMS, DES and (prosthetic) bypass surgery in these complex lesions @high risk, we can conclude **these data are remarkable**

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