Instent restenosis: DCB all or selective use

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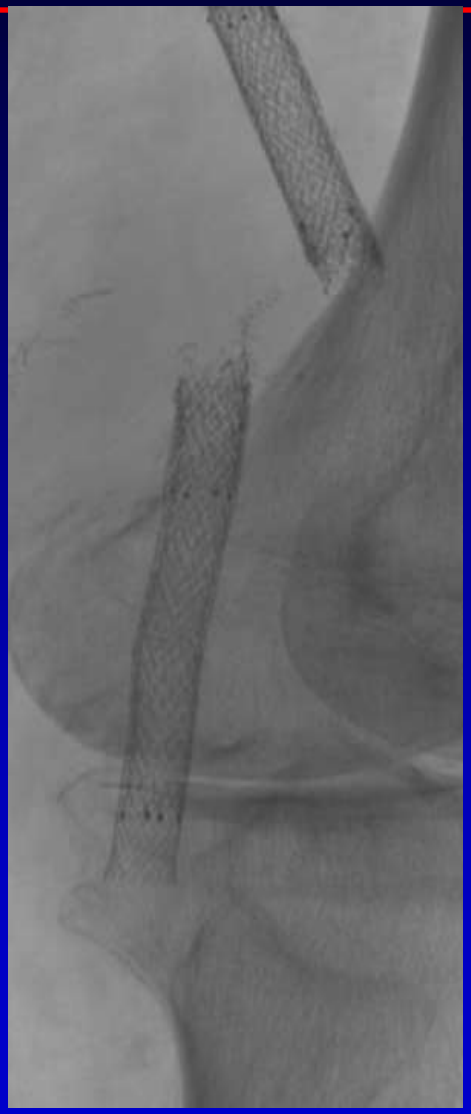
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott, Covidien/Medtronic
• Consulting (non-compensated)	• Covidien/Medtronic, Boston Scientific, Abbott
• Major Stock Shareholder/Equity	• Arsenal, Primacea, TissueGen, CV Ingenuity, Spirox, Scion Cardiovascular, Syntervention, Essential Medical
• Royalty Income	• None
• Ownership/Founder	• Innovation Vascular Partners, Consulting
• Intellectual Property Rights	• None
• Other Financial Benefit	• None

Shortcoming of SFA-Stents

- Stent Fracture
- Insufficient Radial Strength



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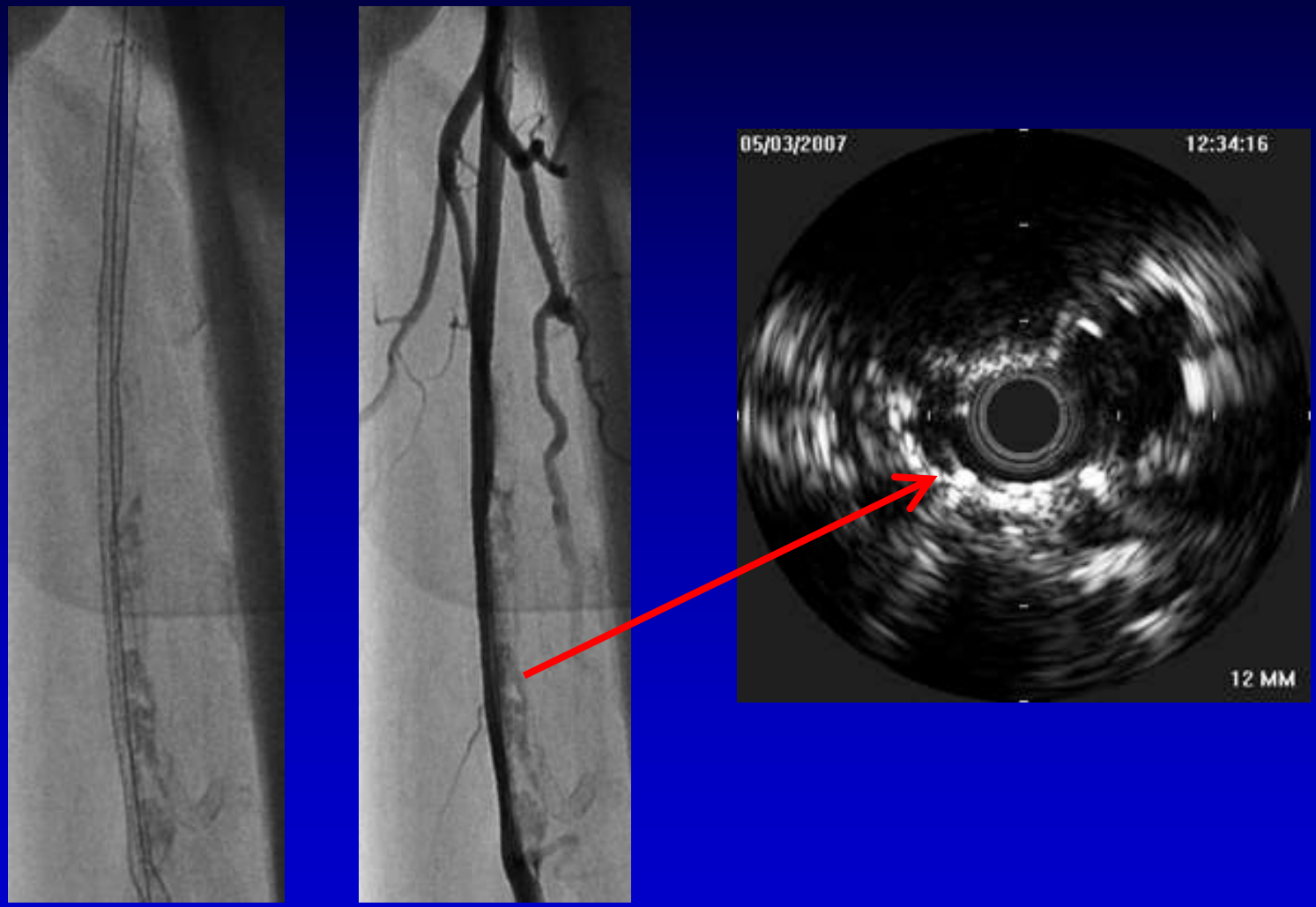
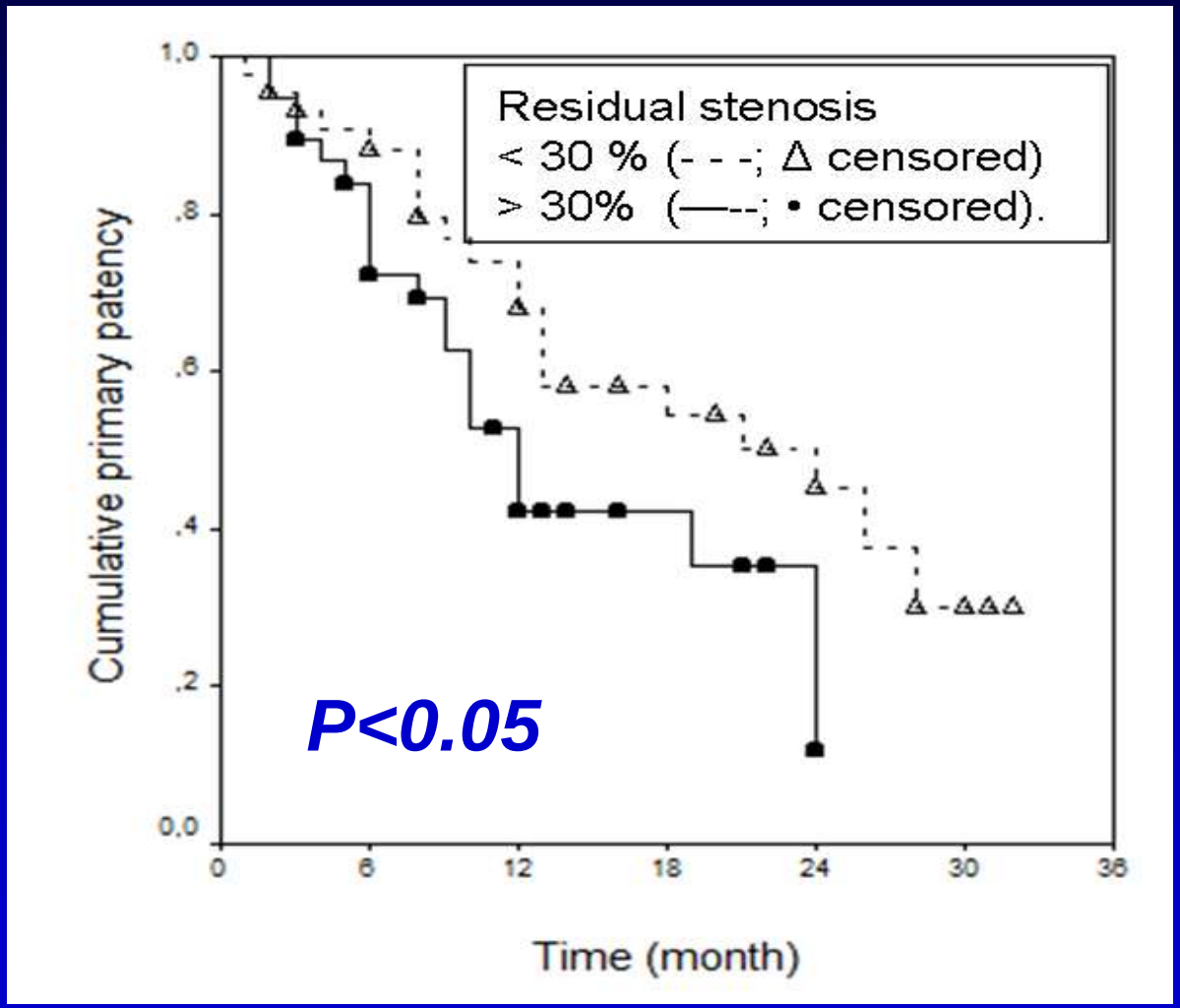
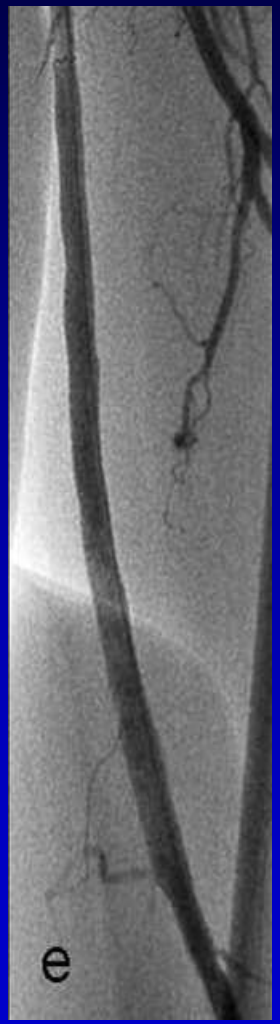
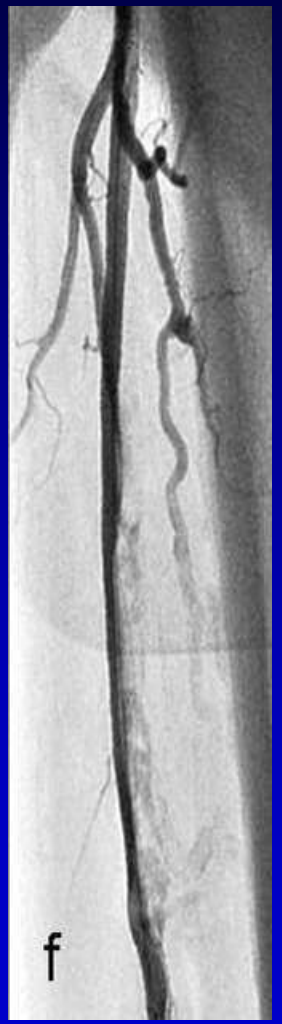


Insufficient radial strength in calcified lesions

Impaired primary patency due to residual stenosis







Y Bausback et al, J Endovasc Ther 2011

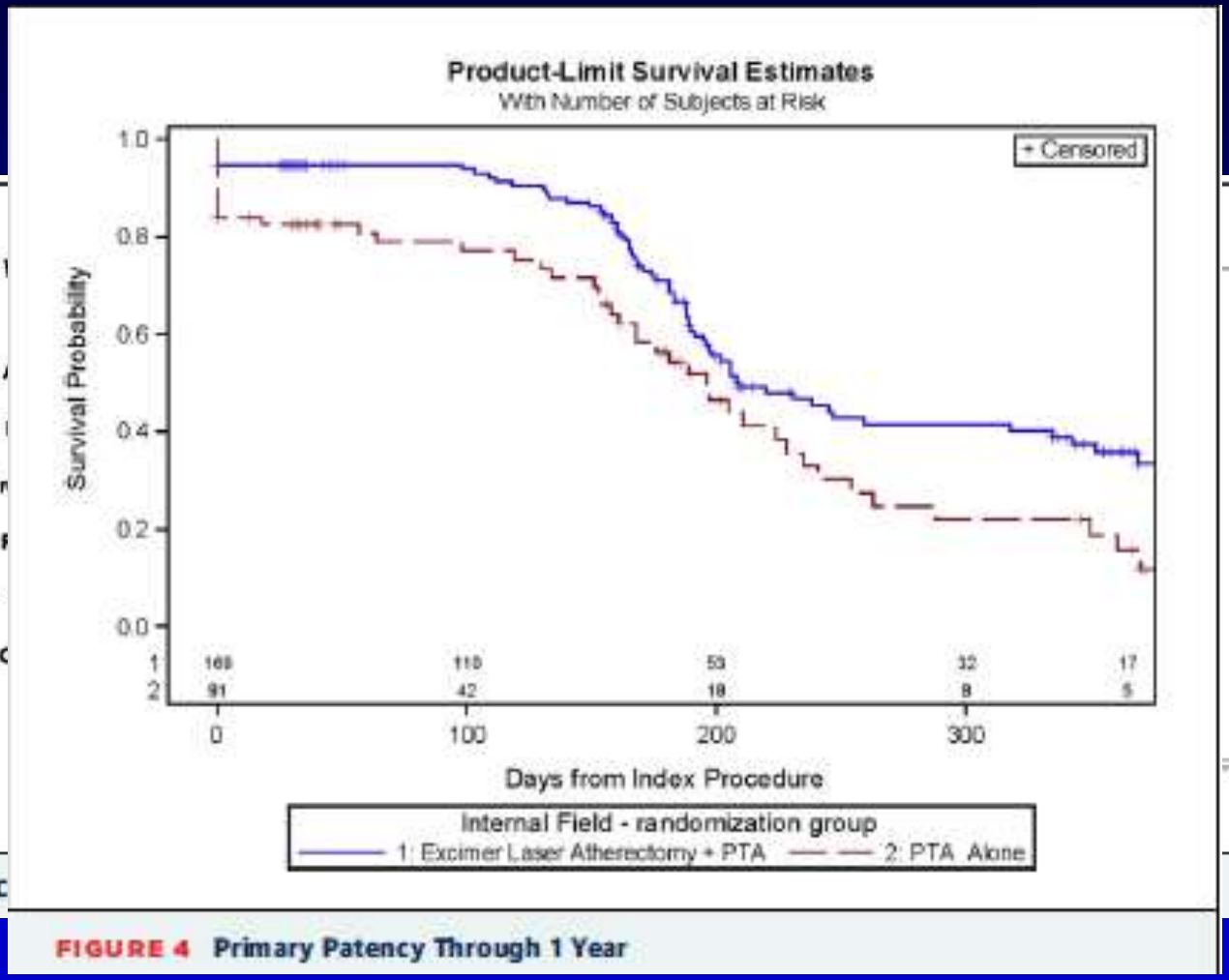


FIGURE 4 Primary Patency Through 1 Year

Dipple et al JACC Cardiov Interv 2015 (8) 92-101

IN.PACT Global Study In-Stent Restenosis Imaging Cohort

DCB Components	*IN.PACT Admiral*
Platform	**PTA Balloon** — Admiral® PTA balloon ***4-7 mm diameters*** ***40, 60, 80, 120 mm lengths***
Drug	**Paclitaxel** — Proven anti-proliferative drug **3.5 *µg*/mm²**
Excipient	**Urea** — Facilitates drug transfer **Naturally occurring, non-toxic**
Coating Process	**Medtronic** — ***Reliable, scalable, uniform drug coating process***

Brodmann, VIVA presentation 2015

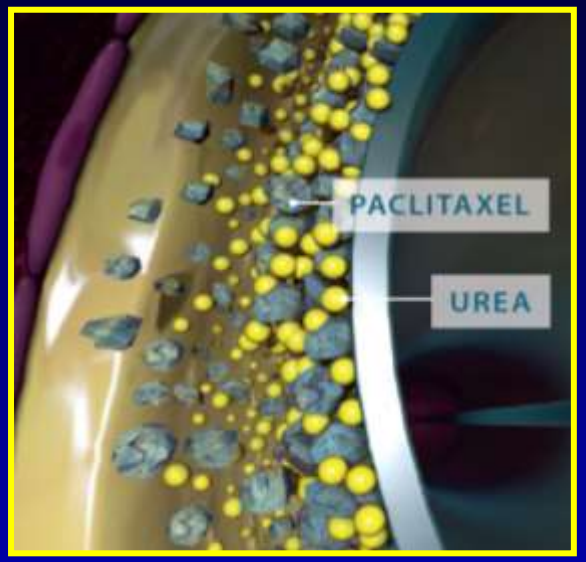
IN.PACT DCB Mechanism of Action

Manufacturing:

- Balloon coated with matrix in semi-inflated state, then wrapped

During Transit to Lesion:

- Majority of matrix protected within folds of the balloon



DCB Matrix Coating:

- *Paclitaxel+ Urea*

DCB Inflation:

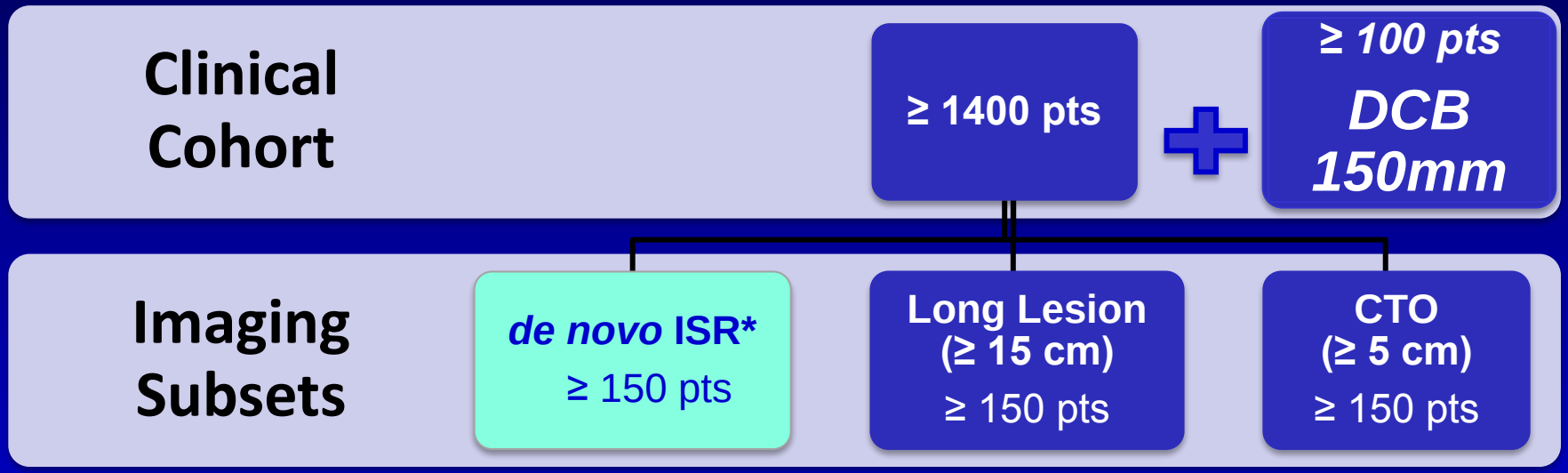
- *Matrix contacts blood*
- *Blood hydrates urea*
- *Urea releases paclitaxel*

Paclitaxel Hydrophobic and Lipophilic Properties:

- *Facilitates transfer from balloon and stickiness to vessel wall*
- *Migrates through vessel wall deep into the media and adventitia*
- *Remains in vessel wall fro over 180 days at therapeutic levels*[1]

1.Data on file at Medtronic (GLP Study FS208; GLP Study PS516)

IN.PACT Global Study Patient Cohorts



1538 patients enrolled

**ISR is not an approved indication in the US*

M Brodman VIVA presentation 2015

IN.PACT Global Study
*Primary Endpoints**

Safety

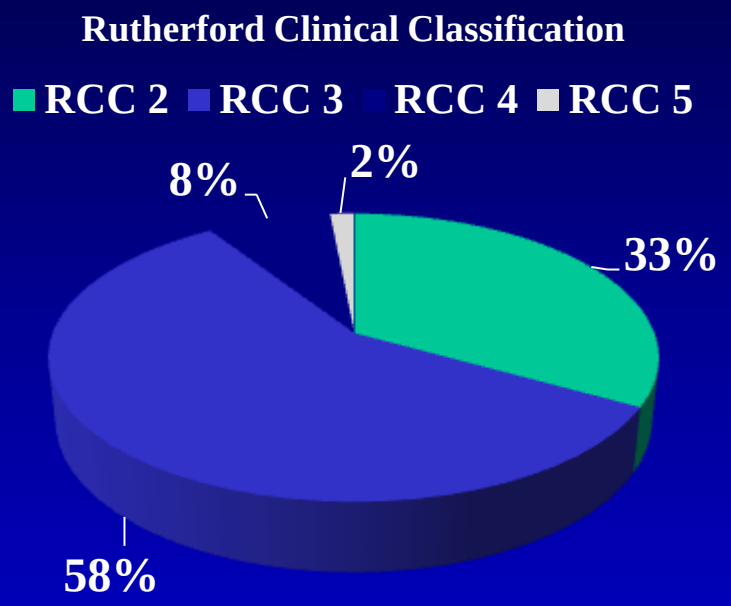
- ***Composite***
  - *30-day freedom from device- and procedure-related mortality*
  - *12-month freedom from major target limb amputation and clinically-driven TVR*

Efficacy

- ***Imaging Cohort: 12-Month Primary Patency***
  - *Freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤ 2.4.*

IN.PACT Global ISR Imaging Cohort: Baseline Clinical Characteristics

Characteristics	N=131 Subjects
Age (Y)	67.8 ± 10.1
Male Gender (%)	69.5% (91/131)
Diabetes (%)	35.1% (46/131)
Insulin Dependent Diabetes (%)	15.3% (20/131)
Hypertension (%)	81.5% (106/130)
Hyperlipidemia (%)	72.1% (93/129)
Current Smoker (%)	35.9% (47/131)
Obesity (BMI ≥ 30 kg/m²) (%)	17.6% (23/131)
Coronary Heart Disease (%)	36.5% (46/126)
Carotid Artery Disease (%)	19.8% (23/116)
Renal Insufficiency[1] (%)	9.9% (11/111)
Previous Peripheral Revasc. (%)	100.0% (131/131)
Concomitant BTK Disease (%)	43.3% (55/127)
ABI	0.667 ± 0.187 (124)



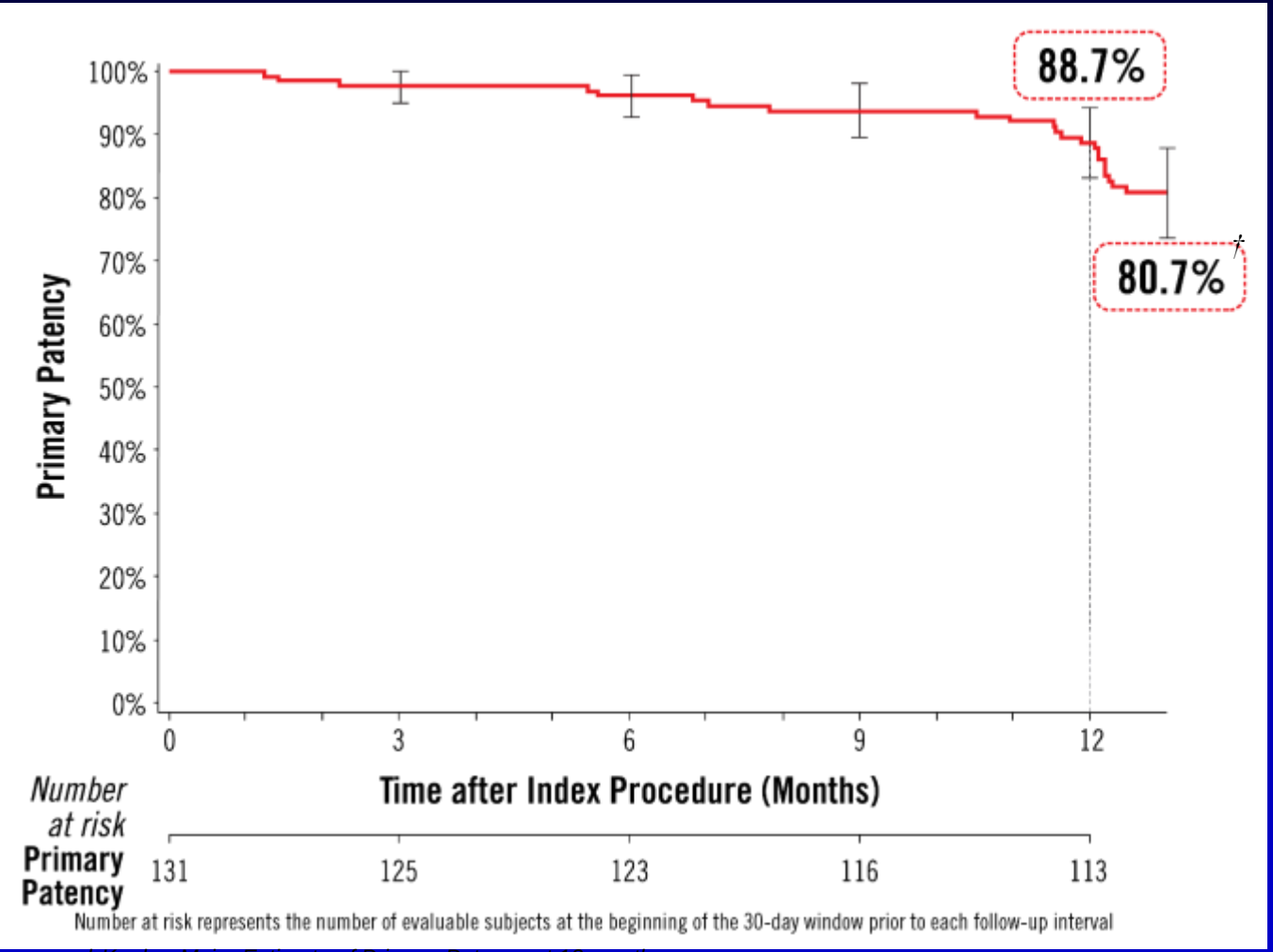
1. Baseline serum creatinine ≥1.5 mg/dL

IN.PACT Global ISR Imaging Cohort: Lesion/Procedural Characteristics

Lesion	N=149
Lesion type:	
De Novo	0.0% (0/149)
Non-stented Restenotic	0.0% (0/149)
In-Stent Restenosis	100.0% (149/149)
Lesion Length (cm)	17.17 ± 10.47
Total Occlusions (%)	34.0% (48/141)
Calcification (%)	59.1% (78/132)
Severe Calcification (%)	8.3% (11/132)
RVD (mm)	5.222 ± 0.601
Diameter Stenosis (pre-treatment) (%)	84.8 ± 14.9
Dissections (%): 0	69.1% (103/149)
A-C	26.2% (39/149)
D-F	4.7% (7/149)

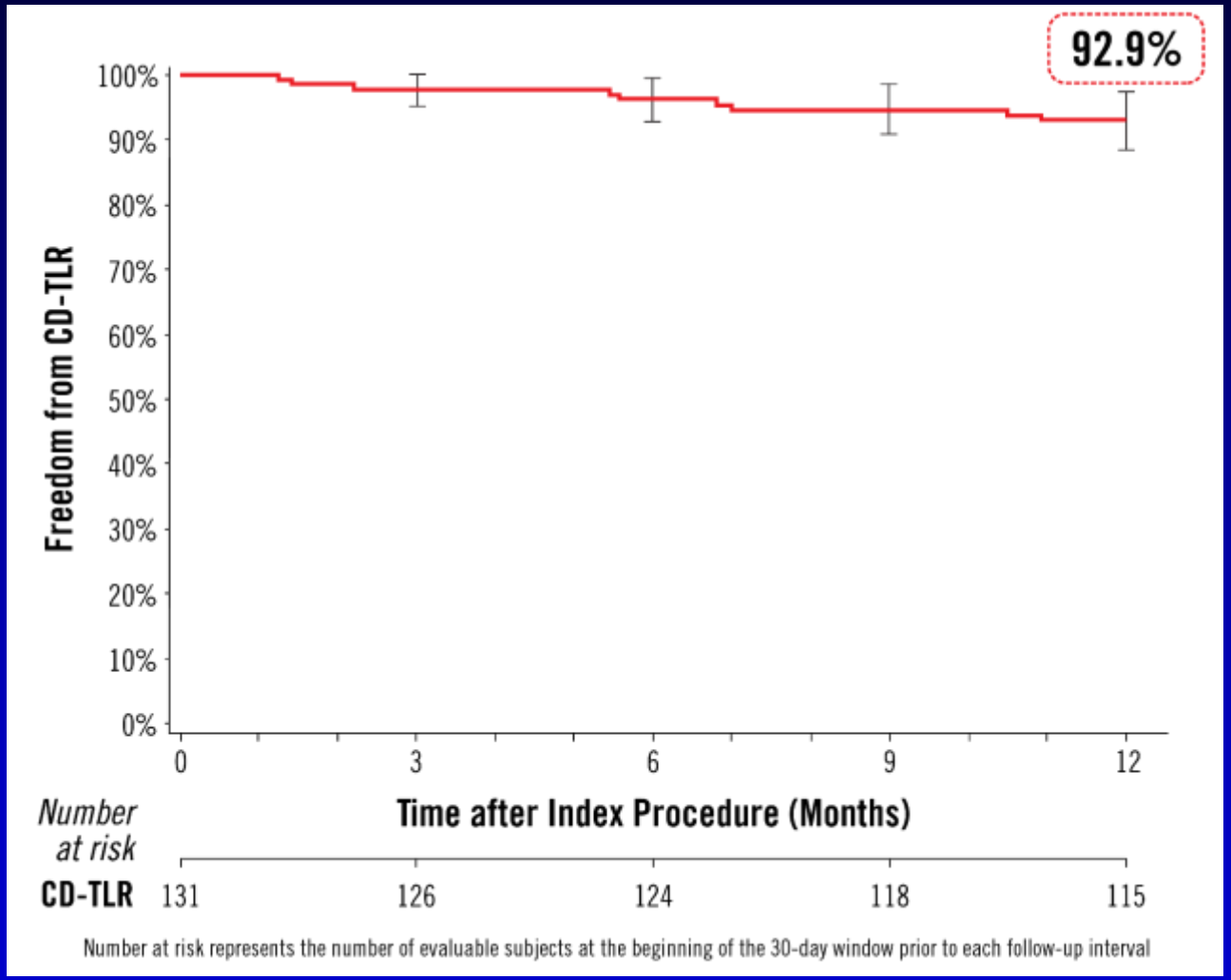
Procedural Characteristics	
Device Success [1]	99.6% (282/283)
Procedure Success [2]	99.2% (130/131)
Clinical Success [3]	98.5% (129/131)
Pre-dilatation	64.1% (84/131)
Post-dilatation	26.0% (34/131)
Provisional Stent	14.5% (19/131)

IN.PACT Global ISR Imaging Cohort: Kaplan-Meier Estimate of Primary Patency



† Kaplan-Meier Estimate of Primary Patency at 13 months

IN.PACT Global ISR Imaging Cohort: Freedom from Clinically-driven TLR



IN.PACT Global ISR Imaging Cohort: Additional Outcomes

Clinically-Driven TLR [1]	**7.3% (9/124)**
Primary Safety Endpoint [2]	**91.1% (113/124)**
Major Adverse Events [3]	**8.9% (11/124)**
Death (all-cause)	**0.0% (0/124)**
Major Target Limb Amputation	**0.0% (0/124)**
Thrombosis	**0.8% (1/124)**
Any TLR	**8.1% (10/124)**
Any TVR	**9.7% (12/124)**

1. Any re-intervention within the target lesion(s) due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI.

2. Composite of 30-day freedom from device- and procedure-related mortality and 12-month freedom from major target limb amputation and clinically-driven TVR.

3. Major Adverse Events: Composite of death, major target limb amputation, clinically-driven TVR, and thrombosis.

Lutonix Global SFA Real-World Registry ISR Sub group Analysis

	All Subjects	ISR
Total Lesion Length (mm)	101.2 ± 84.2 (685)	154.4 ± 97.1 (89)
2 or More Lesions Treated, % (n/N)	15.6% (108/691)	16.9% (15/89)
Treated Length (mm)	136.6 ± 89.7(685)	182.1 ± 90.5 (89)
Calcification, % (n/N)	50.2% (238/474)	37.7% (26/69)
Total Occlusion, % (n/N)	31.2% (214/686)	28.1% (25/89)
Most Distal Lesion location %, (n/N)		
Proximal SFA	8.0% (55/690)	4.5% (4/89)
Mid SFA	24.8% (171/690)	24.7% (22/89)
Distal SFA	37.2% (257/690)	41.6% (37/89)
Proximal Popliteal	16.8% (116/690)	18.0% (16/89)
Mid Popliteal	10.1% (70/690)	5.6% (5/89)
Distal Popliteal	3.0% (21/690)	5.6% (5/89)

12 Month Results All Subjects vs ISR

	All Subjects % (n/N)	ISR % (n/N)
Freedom from TLR	**94.2% (599/636)**	**91.5% (75/82)**
30 Day Safety	**99.7% (678/680)**	**100.0% (88/88)**

12 Month Secondary Endpoints All Subjects vs ISR

	All Subjects % (n/N)	ISR % (n/N)
Major Index Limb Amputation	0.5% (3/632)	0.0% (0/82)
Minor Index Limb Amputation	0.5% (3/630)	0.0% (0/82)
Reintervention for Treatment of Embolization to the Distal Vasculature	0.5% (3/631)	0.0% (0/82)
Reintervention for Treatment of Thrombosis of the Target Vessel	1.1% (7/631)	1.2% (1/82)

Conclusions

- Instent restenosis remains an ongoing challenging subset of stented patients
  - Recurrent stenosis
  - Diffuse failure
- Simple measures, PTA have a high failure mode
- InPact real world registry is reported and adjudicated via core lab measures
- Results confirm both safe and effective for long lesions of 17 cm, 88.7% PP
- Lutonix confirms patency and outcomes via TLR that are very high
- Critically, a direct comparator trial is necessary to evaluate DCB therapies and their effectiveness