Class effect of DCB ?

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Drug coated balloon devices (*Peripheral artery*)

Device	Company	Coating	Drug dose (µg/mm²)	CE mark*
Advance 18 PTX™	Cook Medical, Bloomington, IN, USA	Paclitaxel	3.0	Yes
Cotavance®	Bayer Schering Pharma AG, Berlin, Germany	Paclitaxel–iopromide	3.0	Yes
Freeway™	Eurocor, Bonn, Germany	Paclitaxel–shellac	3.0	Yes
IN.PACT™ Admiral, Amphirion, Pacific	Medtronic Vascular, Santa Clara, CA, USA	Paclitaxel–urea	3.0	Yes
Lutonix DCB® (Moxy)	BARD, Murray Hill, NJ, USA	Paclitaxel–polysorbate/sorbitol	2.0	Yes
Legflow®	Cardionovum, Warsaw, Poland	Paclitaxel–shellac	3.0	Yes
Passeo-18 Lux®	Biotronik, Bülach, Switzerland	Paclitaxel–butyryl-tri-hexyl citrate	3.0	No → Yes
Stellarex®	Covidien, Mansfield, MA, USA	Paclitaxel	2.0	No → Yes

* ***Lutonix DCB® and IN.PACT™ are currently approved by the FDA for clinical use in USA.***

Byrne RA, Joner M. et al. Nat Rev Cardiol. 2014;11:13-23

In.Pact

Sequent Please

SurModics

ELUTAX

Pantera Lux

Moxy

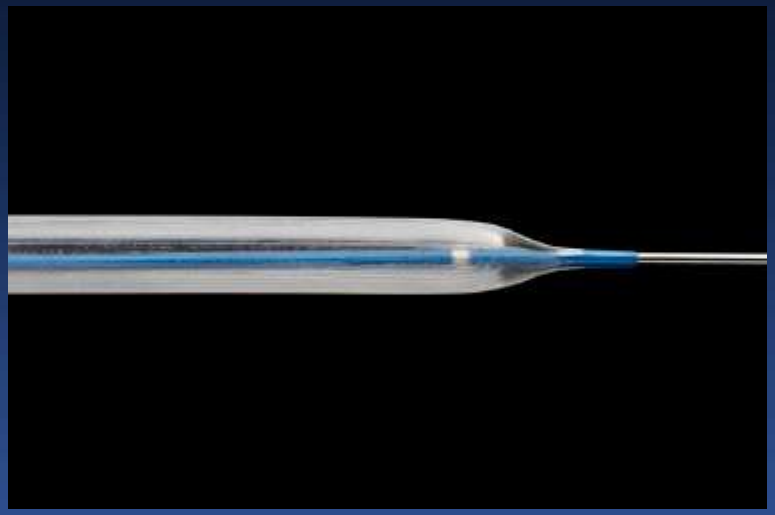
Comparison of Drug-Coated Balloon Arms of LEVANT II and IN.PACT SFA Trials

	LEVANT II DCB (N=316)	IN.PACT SFA DCB (N=220)
Balloon characteristics		
Balloon	Moxy (Lutonix)	Admiral (Medtronic)
Drug	Paclitaxel	Paclitaxel
Dose	2 μg/mm^2	3.0 μg/mm^2
Excipient	Polysorbate, sorbitol	Urea
Clinical characteristics		
Age, yrs	67.8 ± 10	67.5 ± 10
Diabetes	43.4	40.5
Current smoking	35.1	38.6
Rutherford class 2	29.4	37.7
Rutherford class 3	62.7	57.3
Angiographic characteristics		
Lesion length, cm	6.27 ± 41.40	8.94 ± 4.89
Severe calcification	10.4	8.1
Total occlusion	20.6	25.8
12-month outcomes*		
Primary patency	65.2	82.2
24-month outcomes		
Primary patency	58.6	72.4

Different dose, different coating, different carrier: Does these matter ?

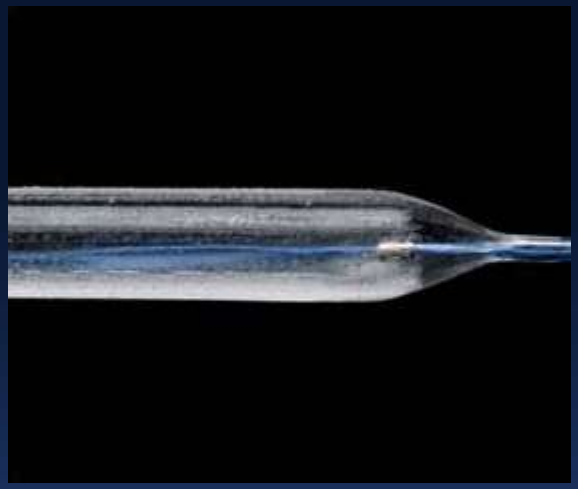
Coating technology

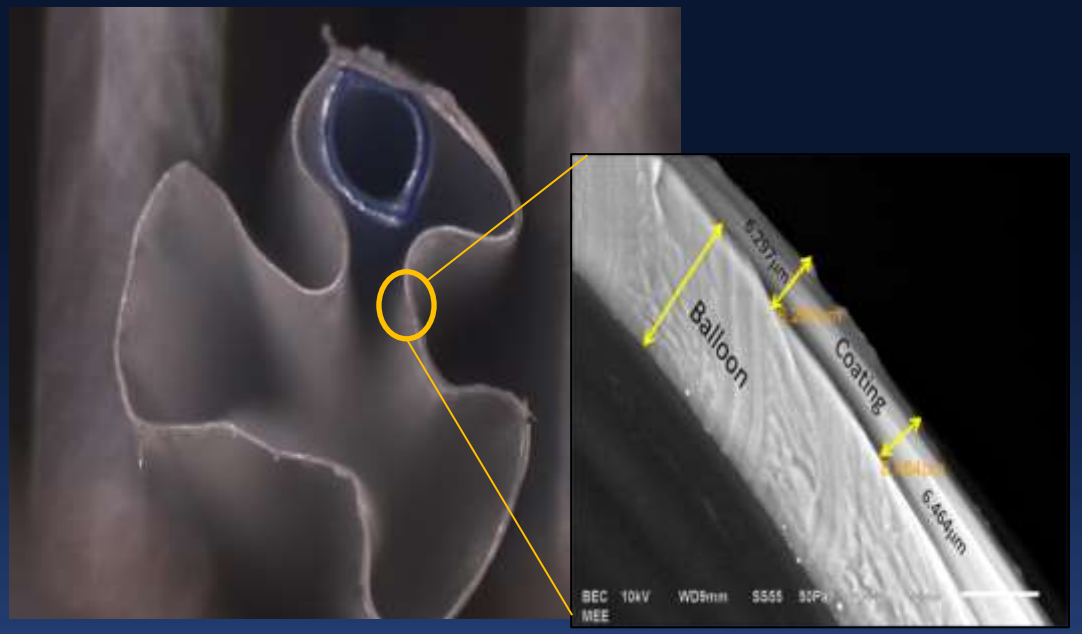
Lutonix 035

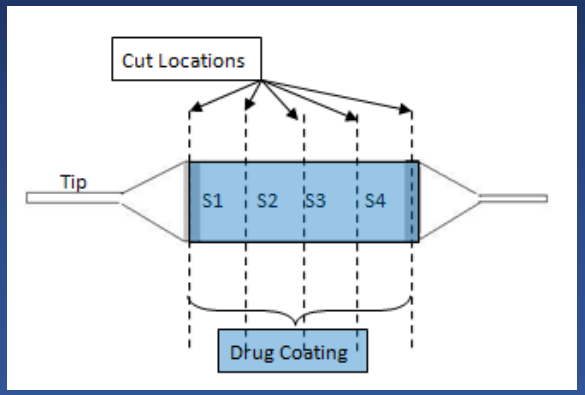


IN.PACT

Lutonix coating: drug uniformity



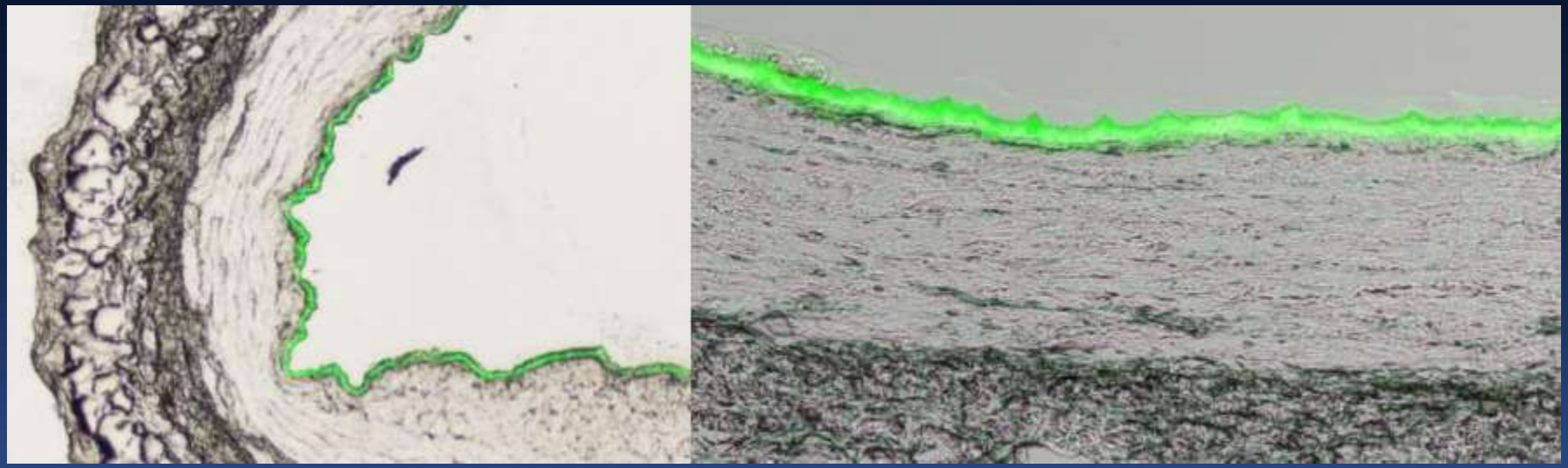




Coating uniformity analysis	
Segment to segment variability	± 4.0%
Longitudinal segment variability	± 2.7%

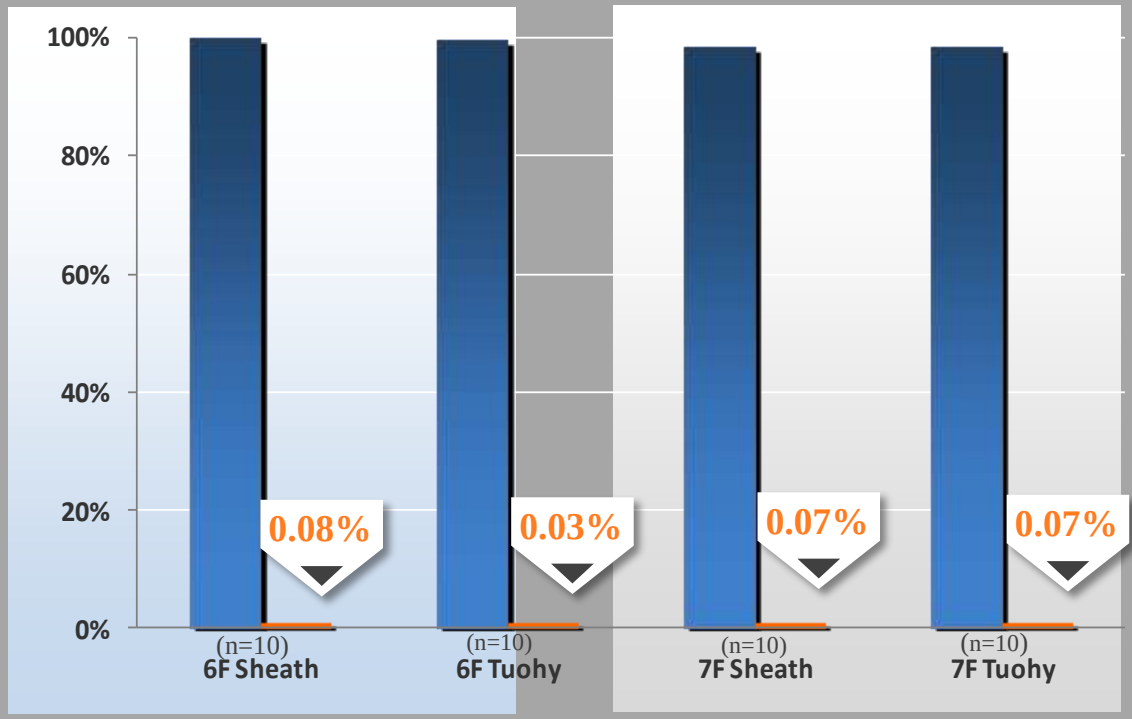
Lutonix coating: drug delivery

In vivo Fluorescent-labeled PTX to Excised Porcine artery



Lutonix coating uniformity allows uniform drug delivery

Lutonix coating: drug retention



*Terumo Pinnacle Destination

Drug load preserved on balloon post-insertion through sheath valve or tuohy

Durability of coating preserved through insertion

IN.PACT coating: drug durability and uniformity

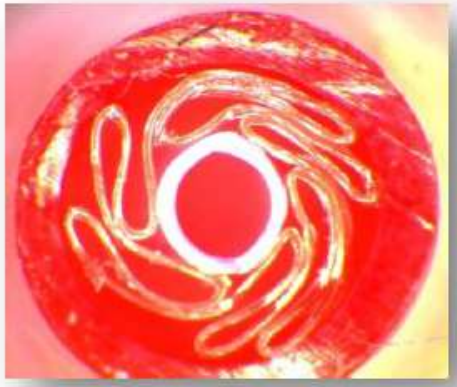
DURABLE

Balloon coating

in semi-inflated shape:

~ 60-70% of dose protected

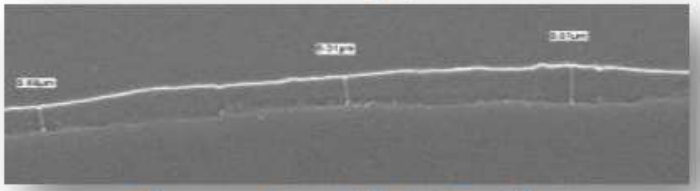
within balloon folds[1]



UNIFORM

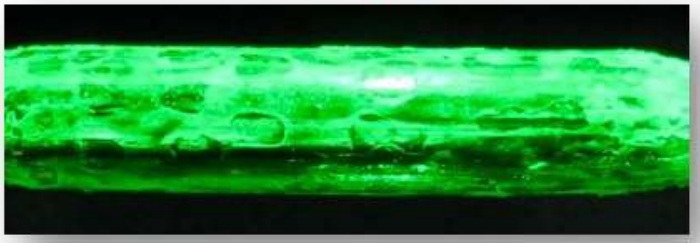
Longitudinal Coating Thickness

Uniformity+/- 6%

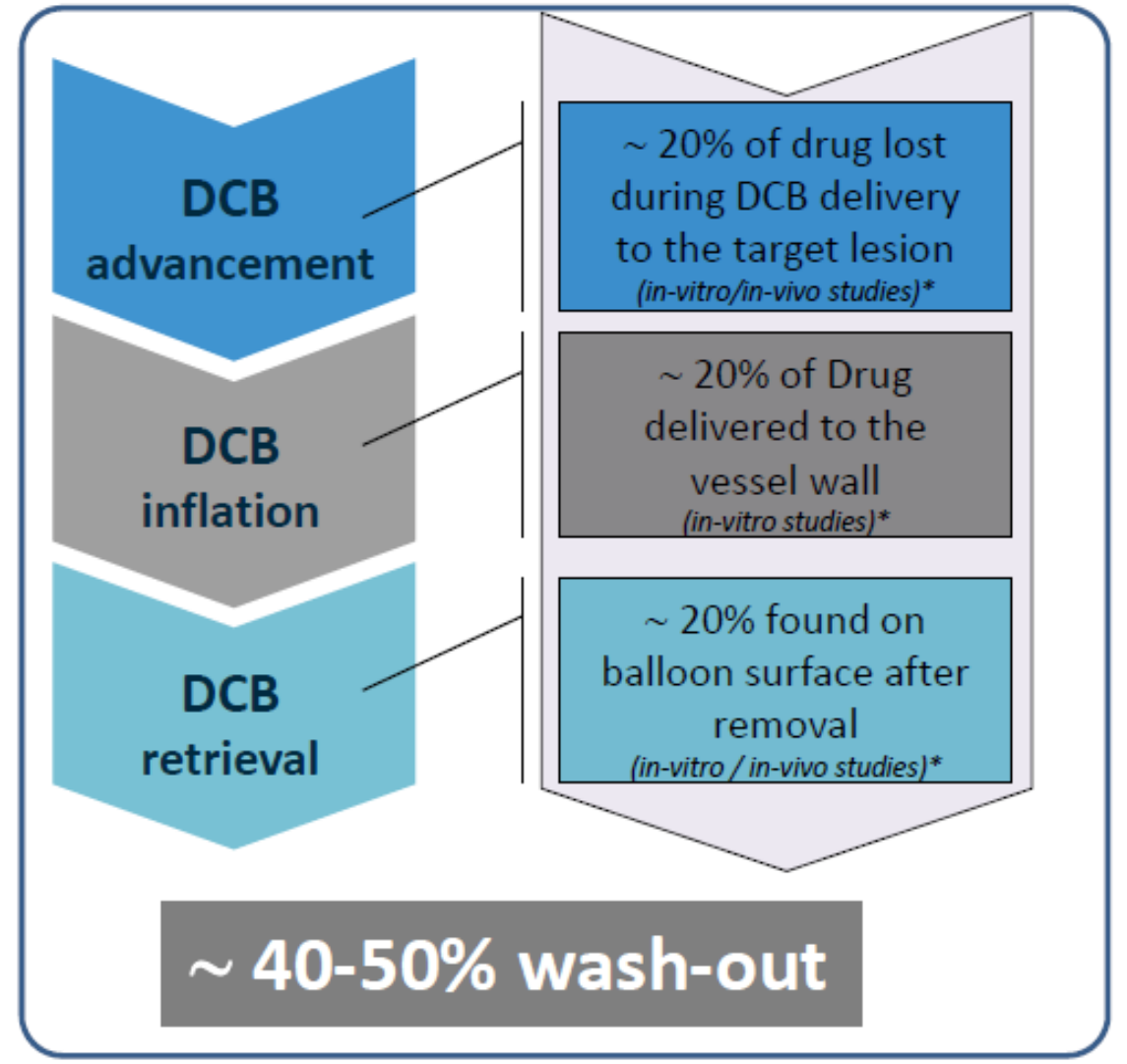


Circumferential Coating

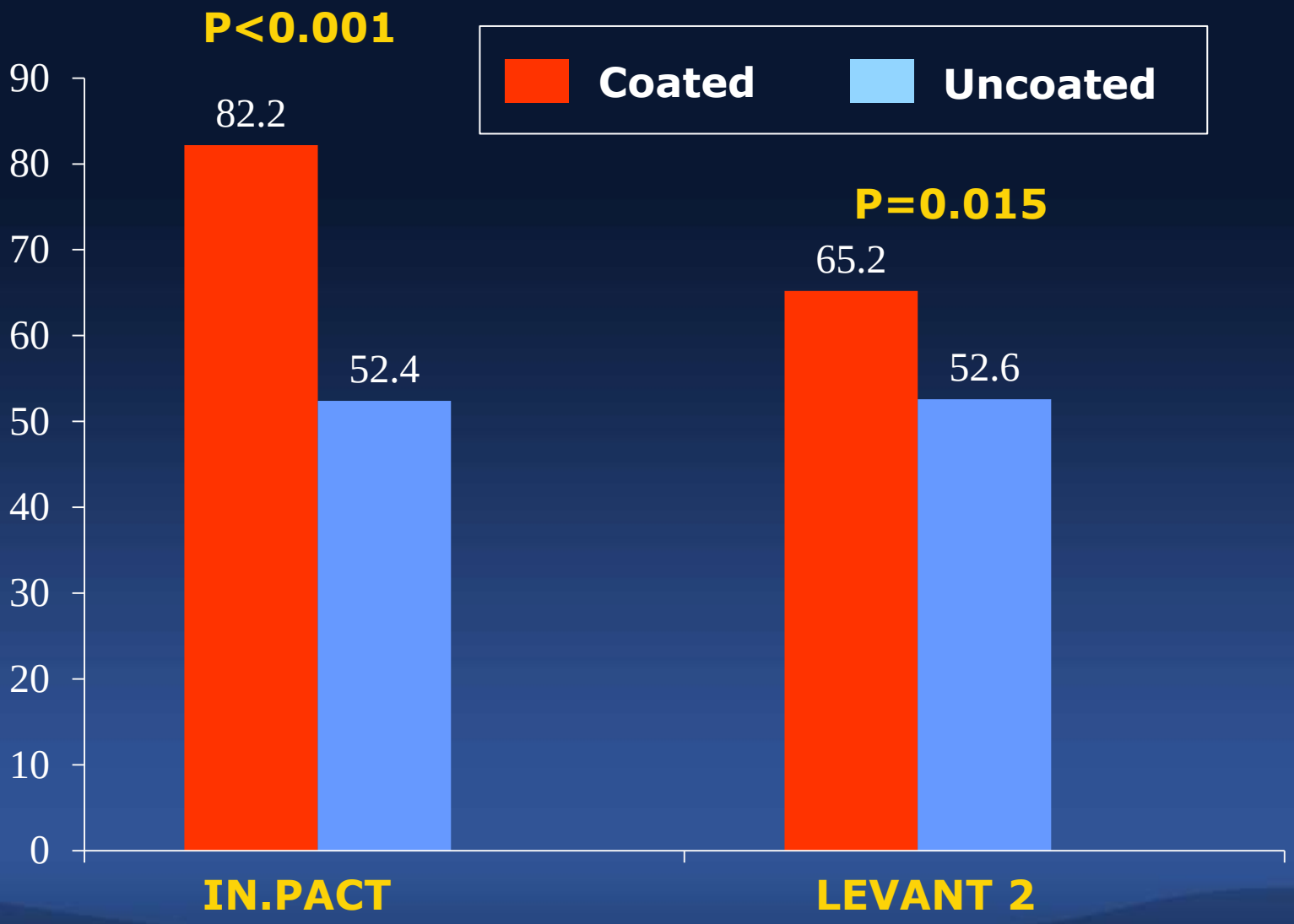
Uniformity +/- 2%



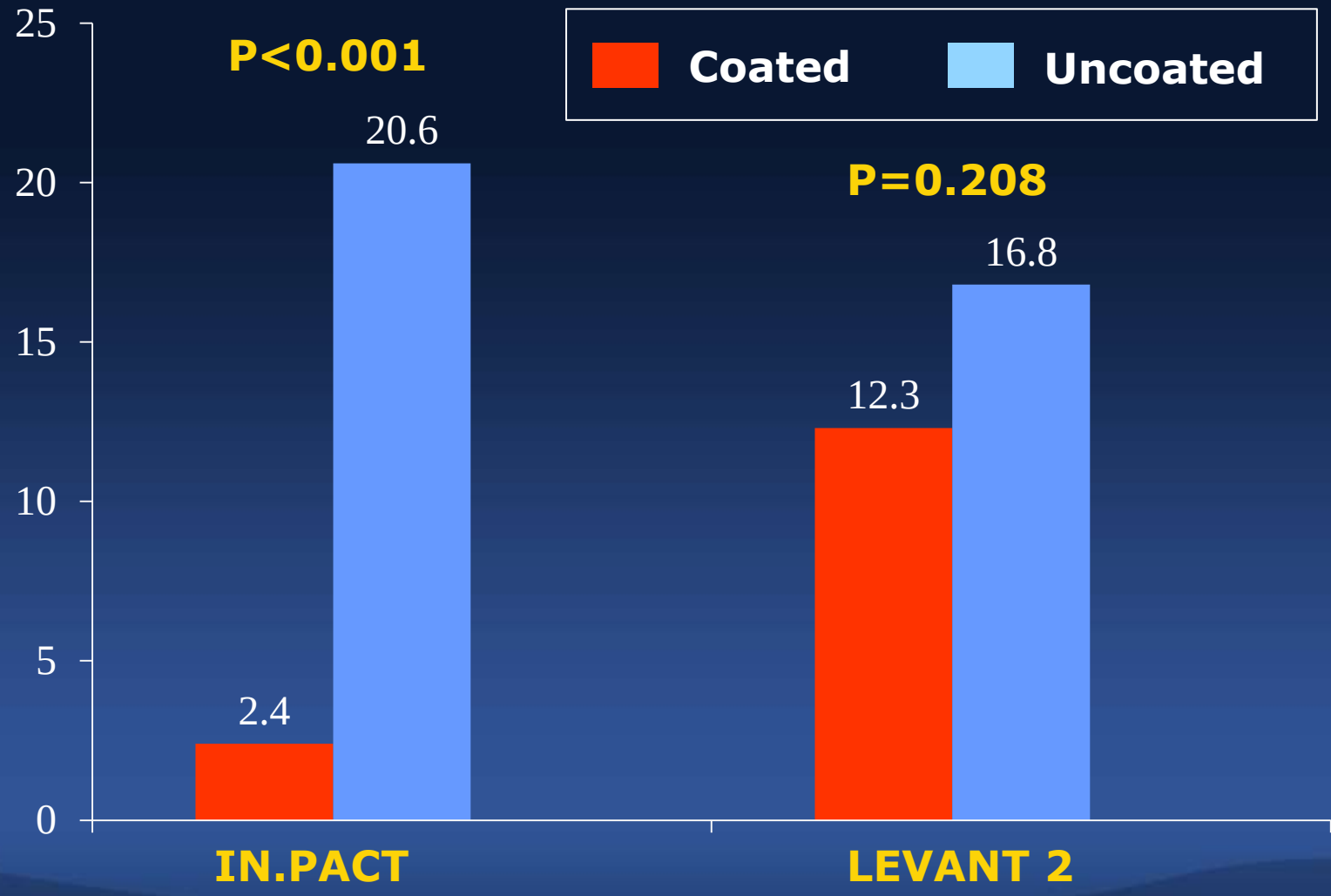
IN.PACT coating: drug delivery



12-month Primary patency



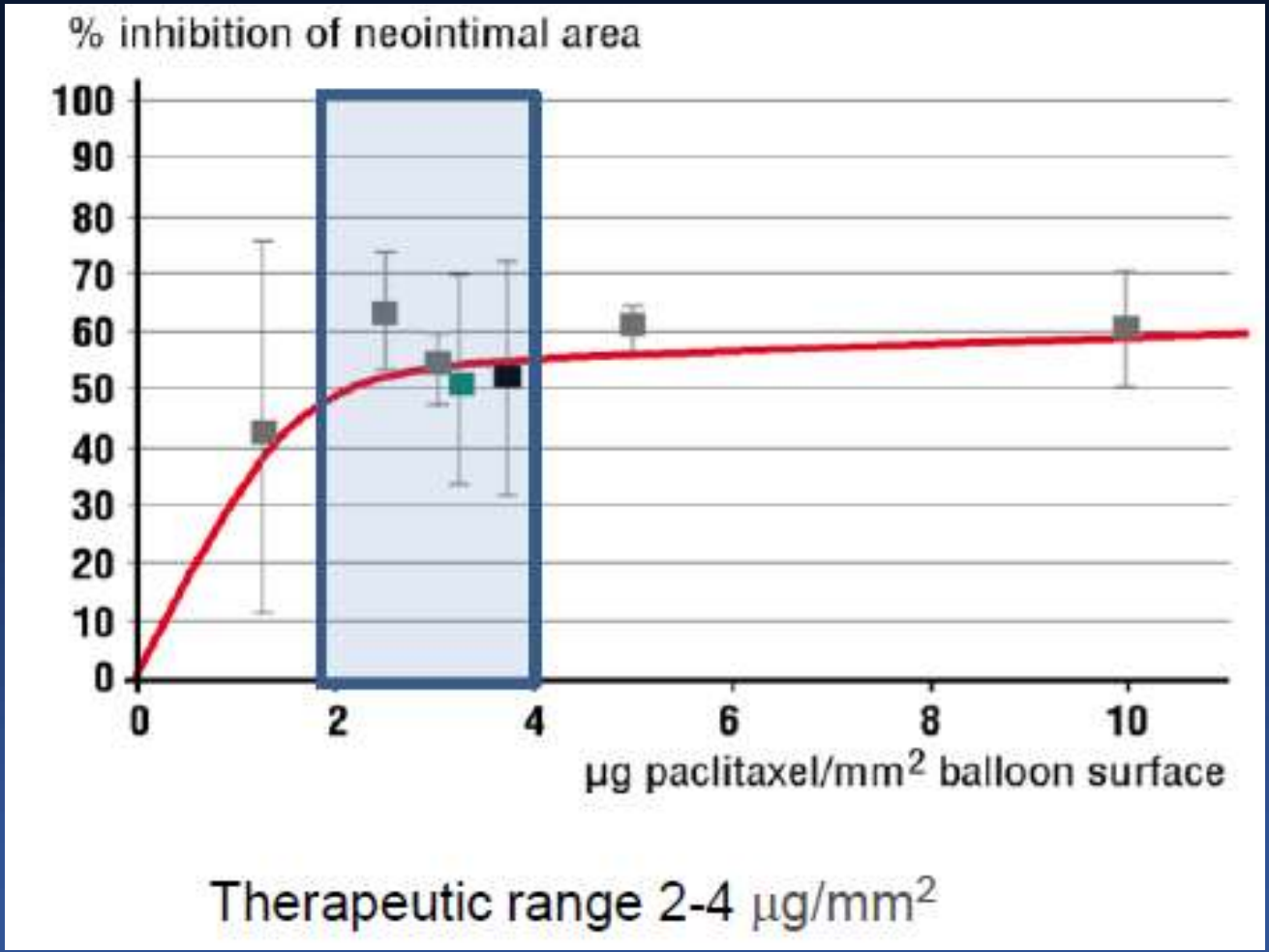
12-month clinical driven TLR



Different dose, different coating, different carrier:
Does these matter ?

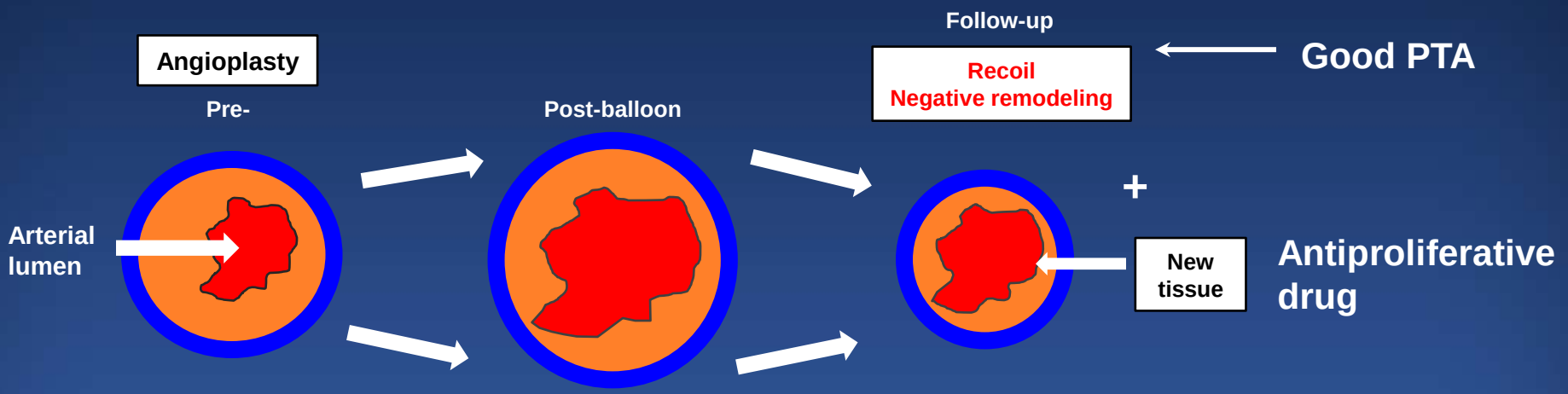
IN.PACT looks better, but
…. Not absolute because …

Paclitaxel: wide therapeutic range



DCB Mechanism of Action

Mechanical (vessel recoil and negative remodeling) and bilological response (smooth muscle cell proliferation) due to injury during PTA leads to restenosis

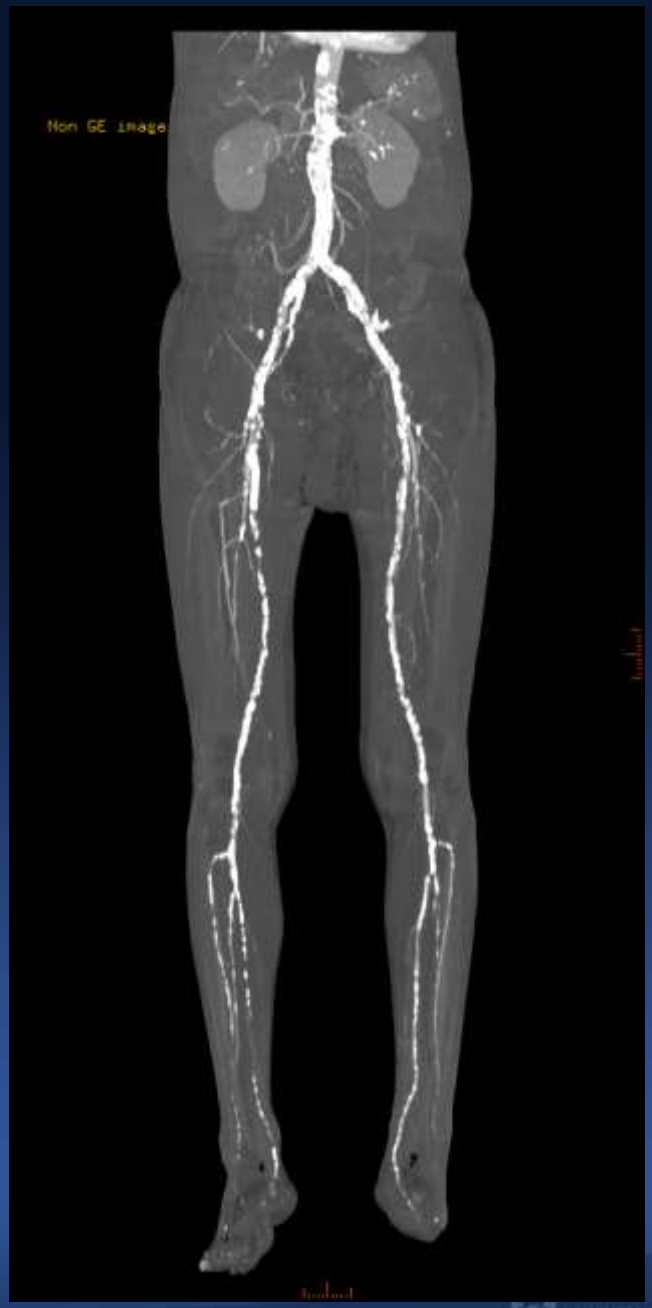


Paclitaxel inhibits cell proliferation

Good Mechanical PTA + Good drug delivery = optimal outcomes

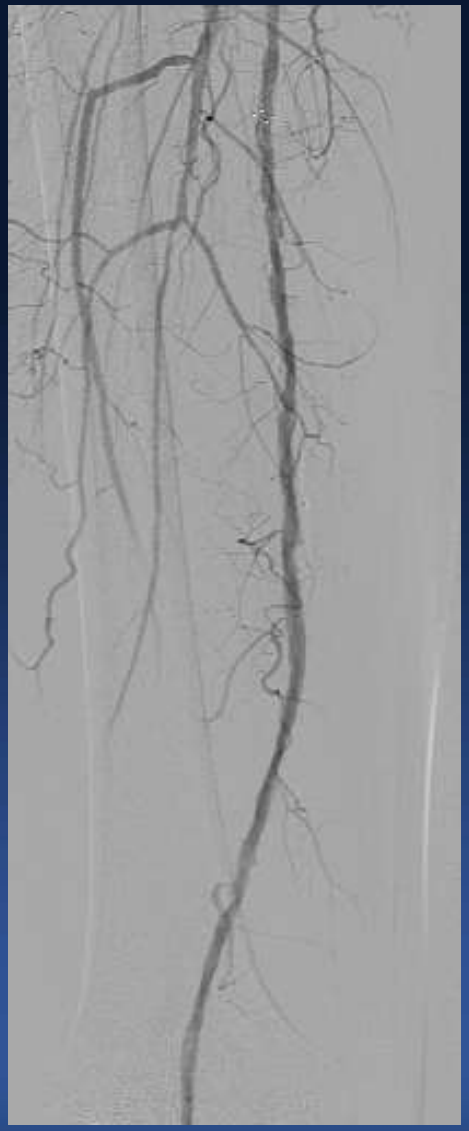
M/71

RT CLI
DM
HTN

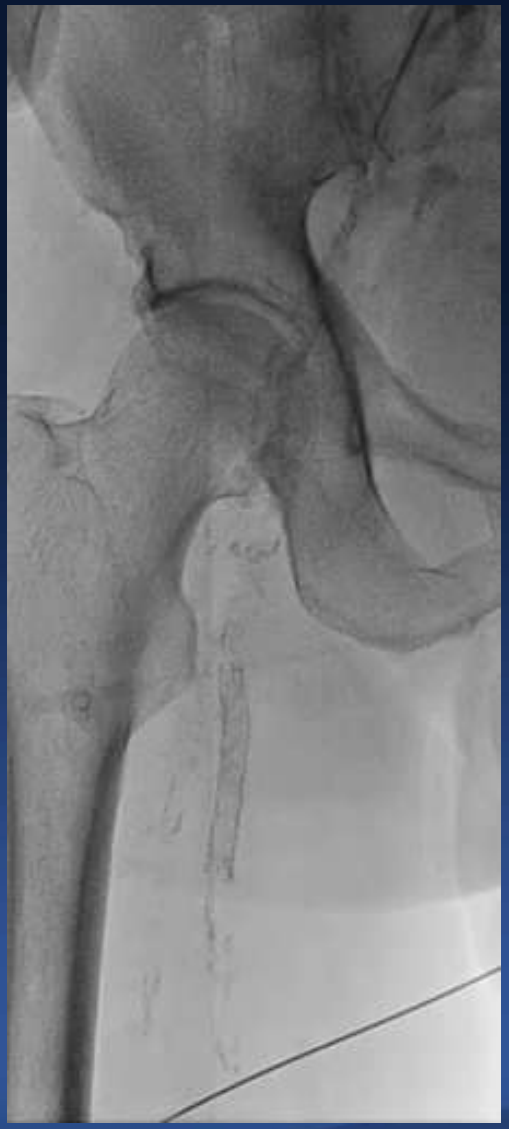


Pre-intervention

Post-DCB



10 days later



Mechanical stretching is more important to maximize the DCB effect

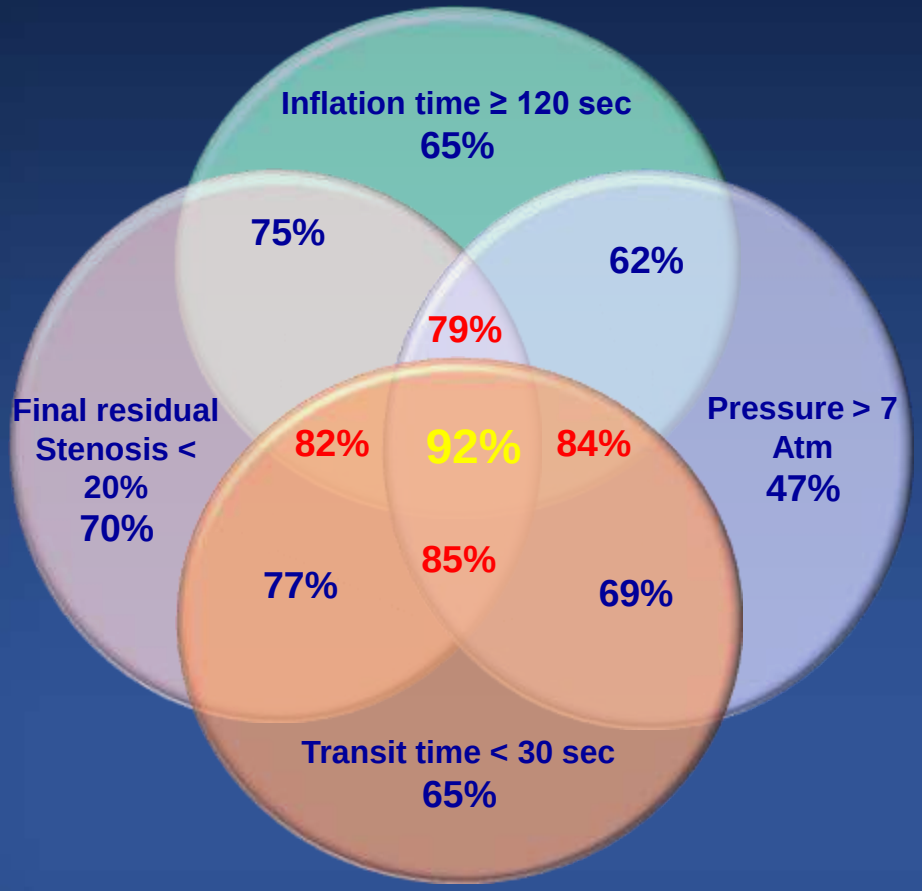
Optimal Drug Delivery and DCB Outcomes

DCB Outcomes Influenced by:

- Balloon Transit Time
- Balloon Inflation Pressure
- Balloon Inflation Time
- Final % Diameter Stenosis

Indicators from Levant 2 Data Analysis

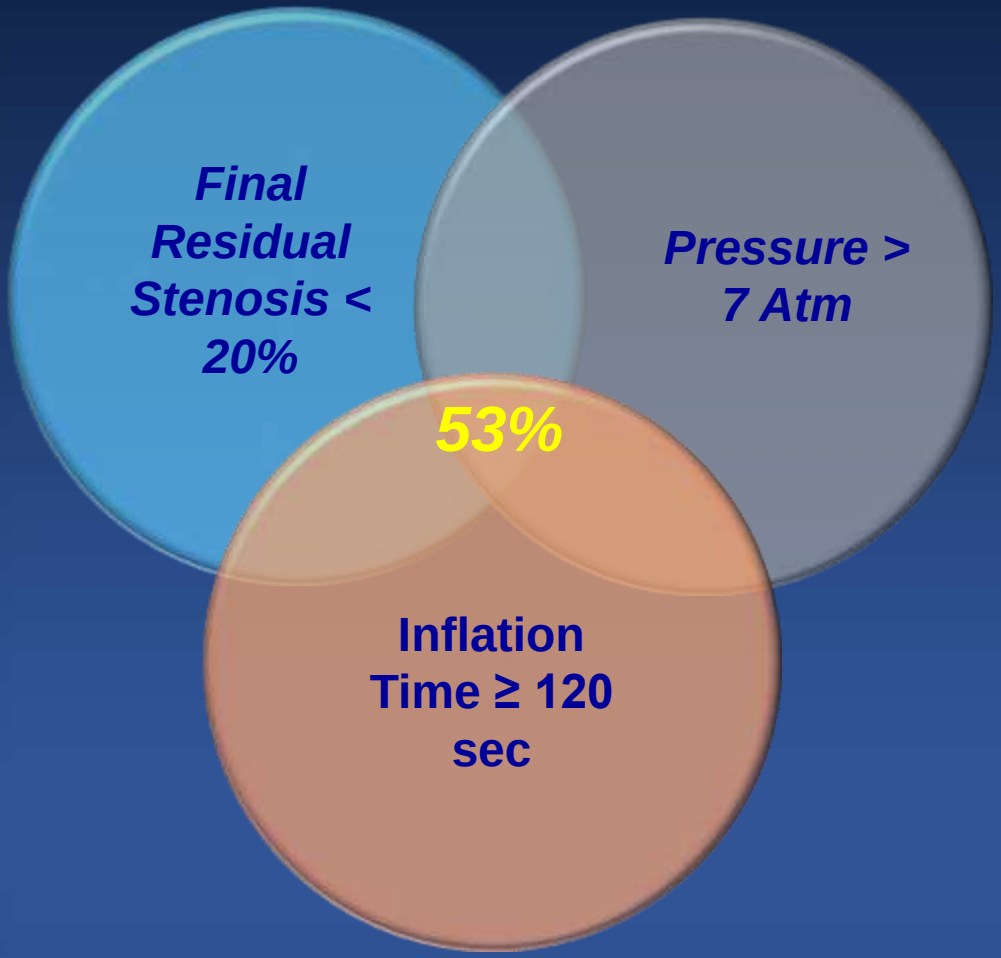
Levant 2 DCB Procedural Variable Analysis



DCB Primary Patency:

- ✓ Improved with 3 variables
- ✓ Optimal with 4 variables

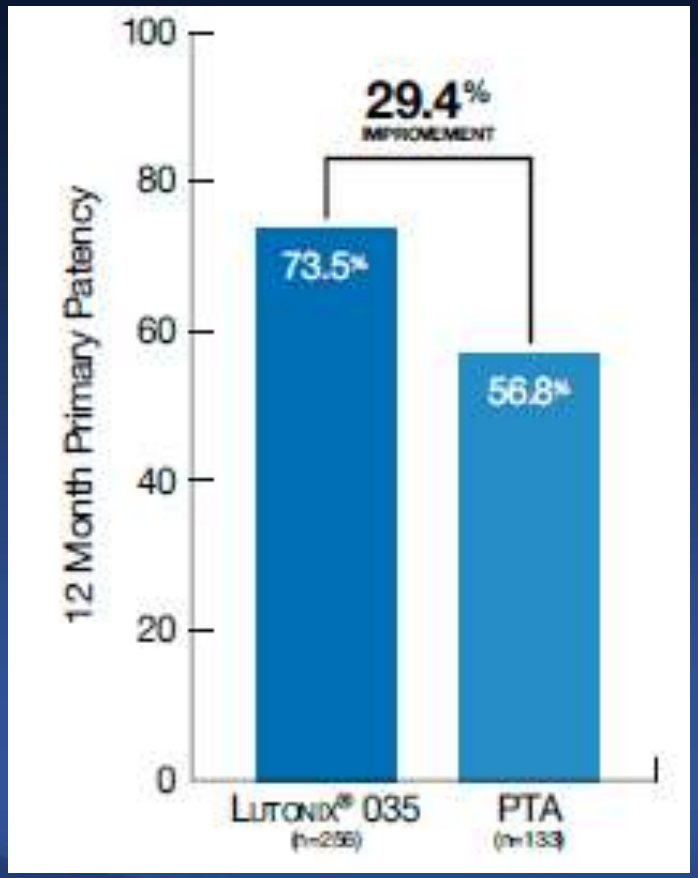
Levant 2 PTA Procedural Variable Analysis



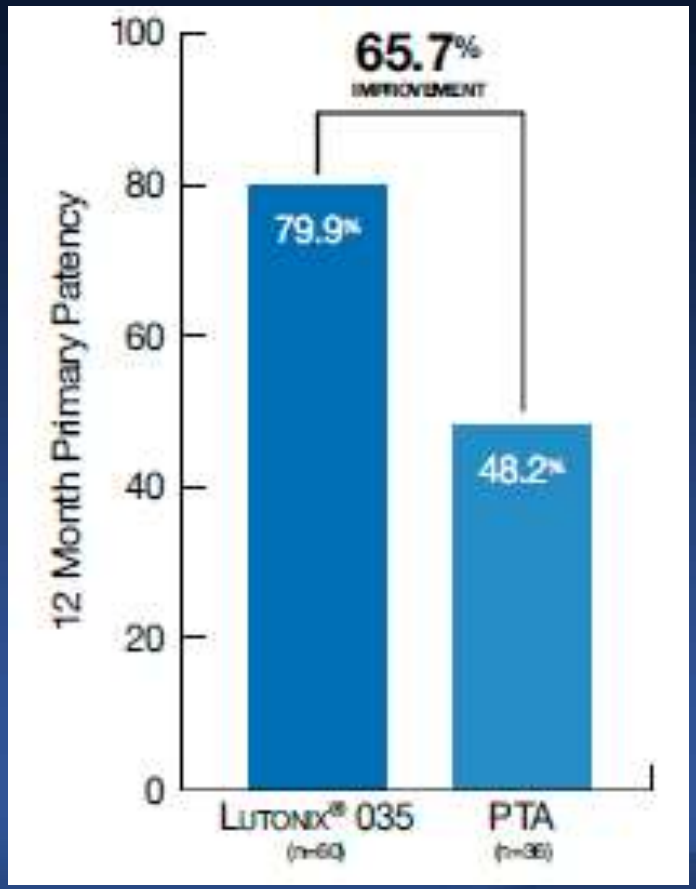
Optimal Angioplasty alone results in 53% Primary Patency

Full Wall Apposition Facilitated Drug Delivery and Showed Increased Primary Patency*

LEVANT 2 Clinical Trial
0.9:1 Balloon to Artery Ratio



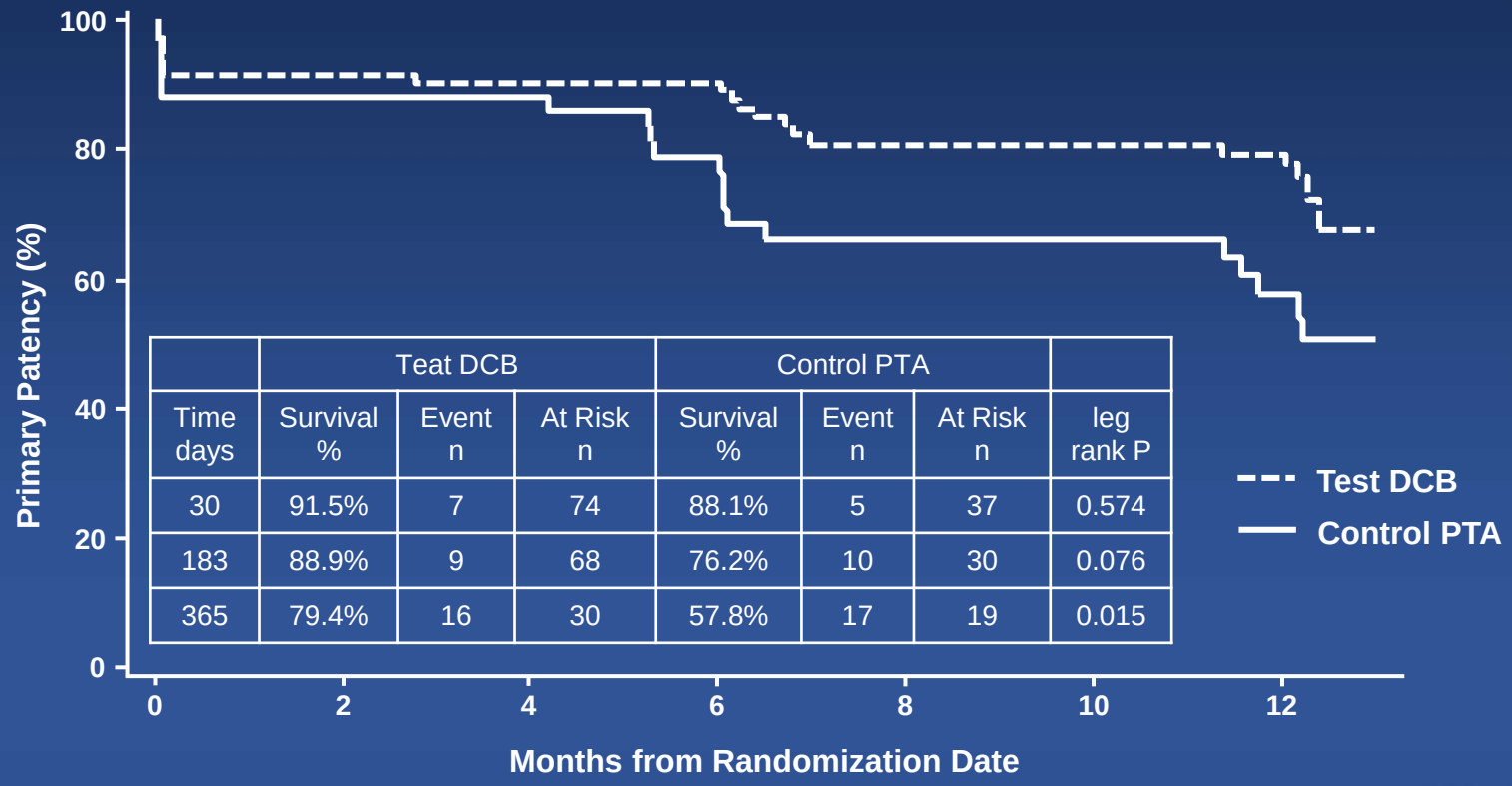
LEVANT 2 Full Wall Apposition
≥1.04: 1 Balloon to Artery Ratio



LEVANT II trial
German subgroup analysis

Primary Patency Kaplan Meier

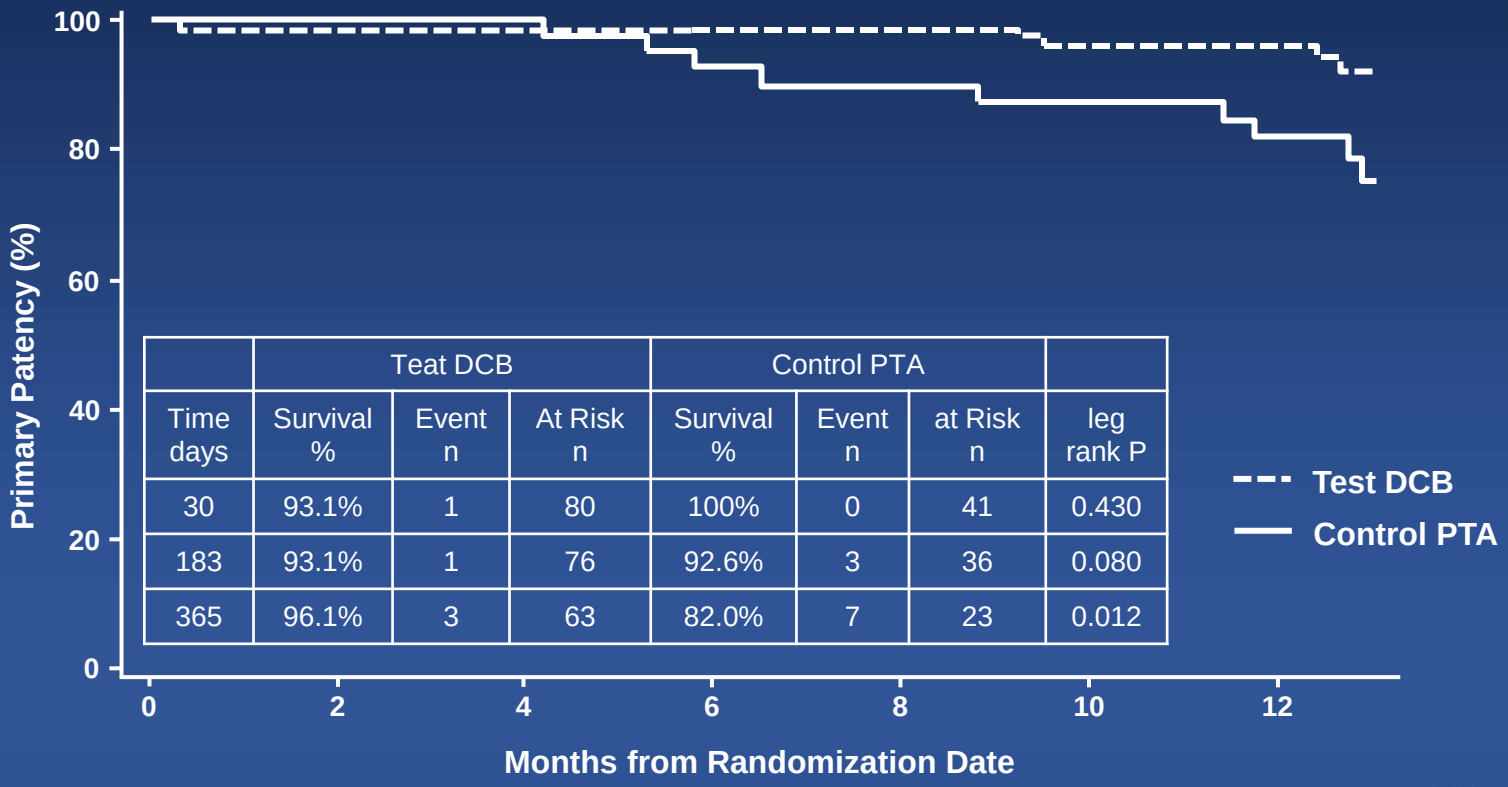
Efficacy, Primary Patency	Lutonix DCB (N=83)	Standard PTA (N=43)	Difference	P-value
@365 days	79.4%	57.8%	21.6%	0.015



	Teat DCB			Control PTA			
Time days	Survival %	Event n	At Risk n	Survival %	Event n	At Risk n	leg rank P
30	91.5%	7	74	88.1%	5	37	0.574
183	88.9%	9	68	76.2%	10	30	0.076
365	79.4%	16	30	57.8%	17	19	0.015

Freedom from TLR Kaplan Meier

Efficacy, Primary Patency	Lutonix DCB (N=83)	Standard PTA (N=43)	P-value
@365 days	96.1%	82.0%	0.012

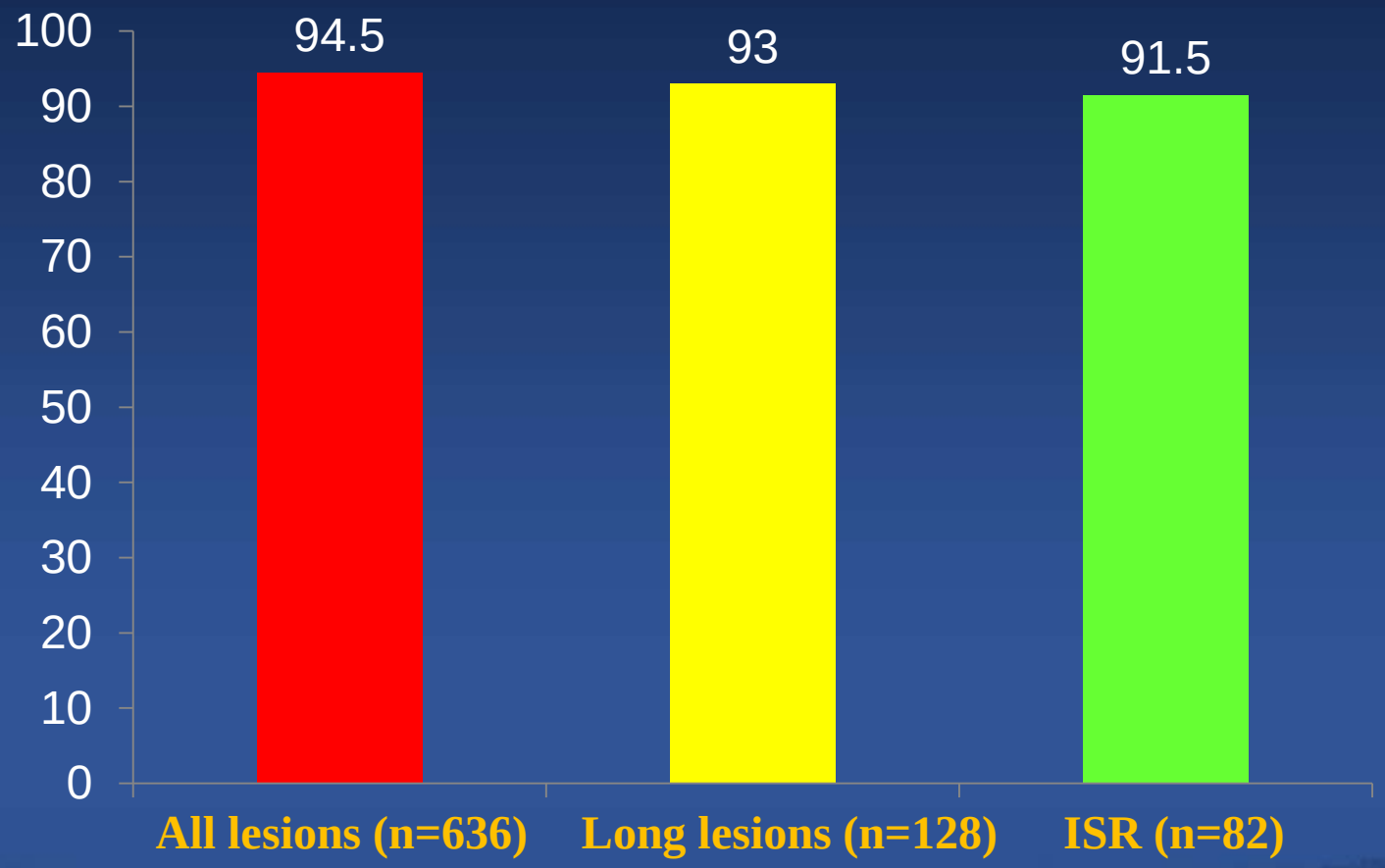


	Teat DCB			Control PTA			
Time days	Survival %	Event n	At Risk n	Survival %	Event n	at Risk n	leg rank P
30	93.1%	1	80	100%	0	41	0.430
183	93.1%	1	76	92.6%	3	36	0.080
365	96.1%	3	63	82.0%	7	23	0.012

Complex lesion subset

- Long lesions
- CTO
- Calcification
- In-stent restenosis

Lutonix Global SFA Real-World Registry
Sub group Analysis (1 year TLR free rate)



Results Across IN.PACT Clinical Studies at 1 Year

Consistent clinical outcomes with the IN.PACT Admiral DCB across studies and complex femoropopliteal lesions.

	IN.PACT SFA (DCB Arm) (N= 220)	IN.PACT GLOBAL Long Lesion Imaging Cohort (N= 157)	IN.PACT GLOBAL ISR Imaging Cohort (N= 131)	IN.PACT GLOBAL CTO Imaging Cohort (N= 126)
Lesion Length (Mean ± SD, cm)	8.94 ± 4.89	26.40 ± 8.61	17.17 ± 10.47	22.90 ± 9.75 (occluded length of 11.97 ± 8.11)
Primary Patency[1]	87.5%	91.1%	88.7%	84.4%
CD-TLR	2.4%	6.0%	7.3%	12.2%
Primary Safety Endpoint[2]	95.7%	94.0%	91.1%	87.8%
Major Target Limb Amputation	0.0%	0.0%	0.0%	0.0%

1. *Kaplan-Meier survival estimate at 12 months*
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.*

Conclusions

- LEVANT 2 and IN.PACT trial showed that DCB for TASC II A & B femoropopliteal lesions achieves good clinical one-year outcomes regarding primary patency and TLR.

- Base on previous randomized trials, *Not all drug-coated balloon* is alike because of different drug dose and coating technology. However, the important things in DCB strategy is mechanical stretching and well apposition of DCB in vessel wall

- Both global registry have equal event rate in-terms of TLR-free survival in patients with complex lesion subsets

- Before head to head comparison comes out, each single device deserves its own clinical efficacy and safety studies

Thank you for your attention