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DES in leg arteries

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Disclosure slide

- ☐ 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)
- ☑ I do not have any potential conflict of interest

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en's (COV) Stellarex DCB Gets CE Mark Approval

uity Research Published on January 09, 2015 | No Comments

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alyst Report) Stellarex drug-coated balloon (DCB) has
roval in Europe. Designed to treat patients with
PAD), Stellarex DCB is part of Covidien's vascular

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Article by:

Drug-coated balloon keeps leg arteries open

BY GENE EMERY

BOSTON | Wed Feb 13, 2008 5:02pm EST

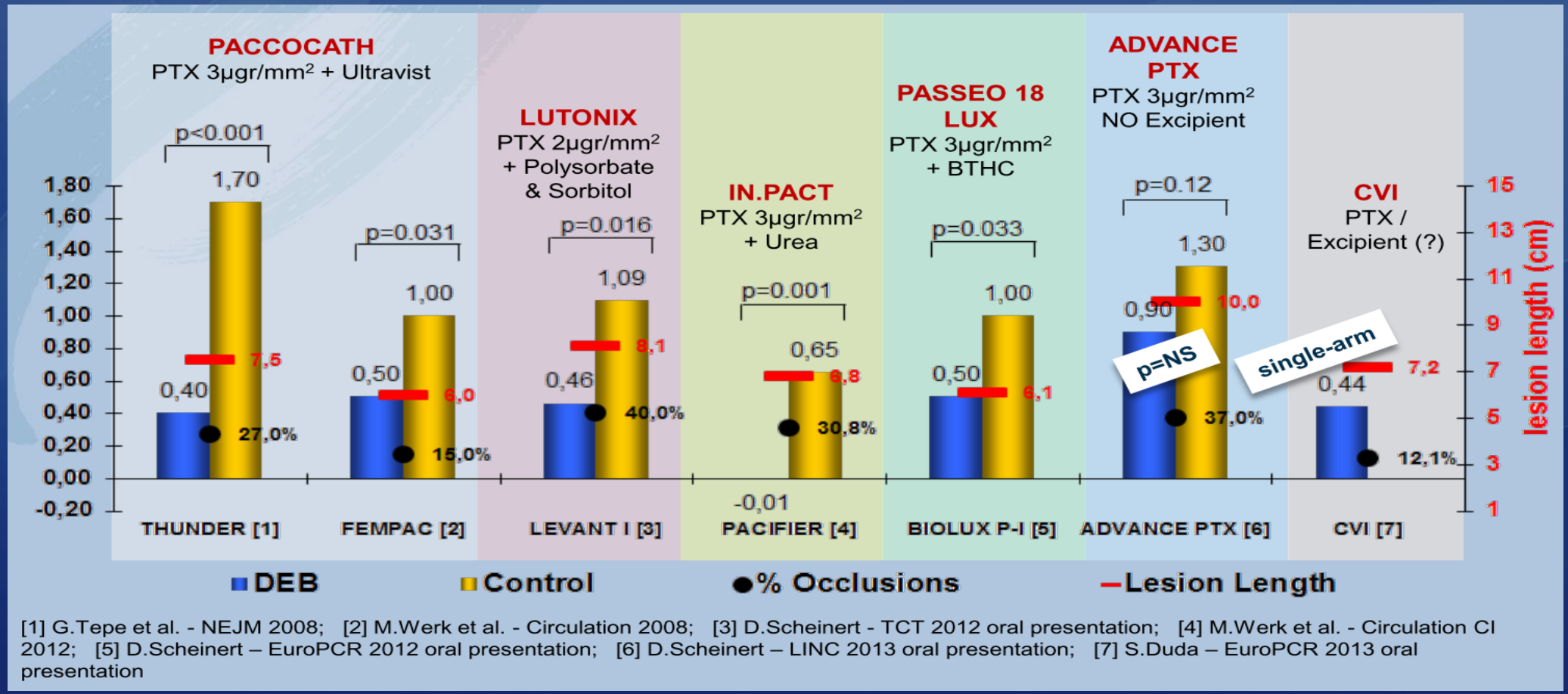
Star Tribune

Receives CE Mark For Drug-Coated Balloon

Innovative Technology Strengthens Company's Leading Portfolio of Solutions for Peripheral Vascular Disease

MISSION: IMPOSSIBLE

And the results seem fantastic…. **PROOF OF CONCEPTS**



[1] G.Tepe et al. - NEJM 2008; [2] M.Werk et al. - Circulation 2008; [3] D.Scheinert - TCT 2012 oral presentation; [4] M.Werk et al. - Circulation CI 2012; [5] D.Scheinert – EuroPCR 2012 oral presentation; [6] D.Scheinert – LINC 2013 oral presentation; [7] S.Duda – EuroPCR 2013 oral presentation

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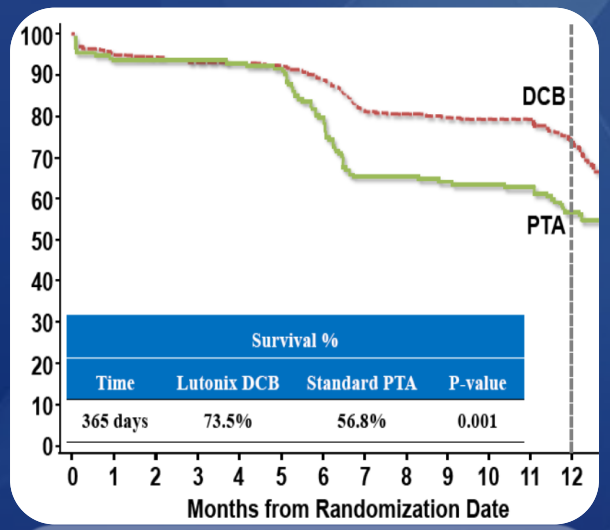
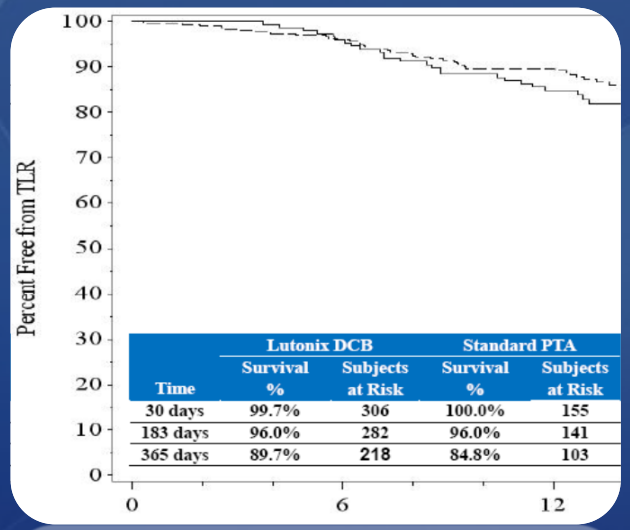
And the results seem fantastic…. **PIVOTAL RCT'S**

LEVANT 2 Clinical Trial



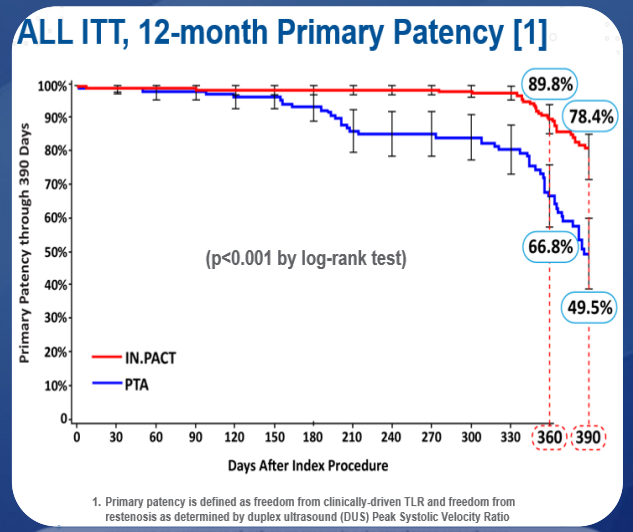


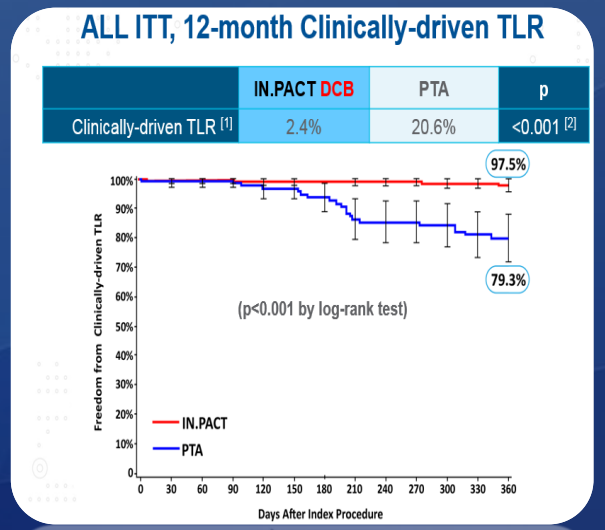
Primary patency 1 yr 73,5%

Freedom TLR 1 yr 89,7%

Rosenfield K et al, presented @ VIVA2014, Las Vegas, US

IN.PACT SFA I-II Trial





Primary patency 1 yr 89,9%

Freedom TLR 1 yr 97,5%

Tepe et al, presented @ CX2014, London,GB

MISSION: IMPOSSIBLE

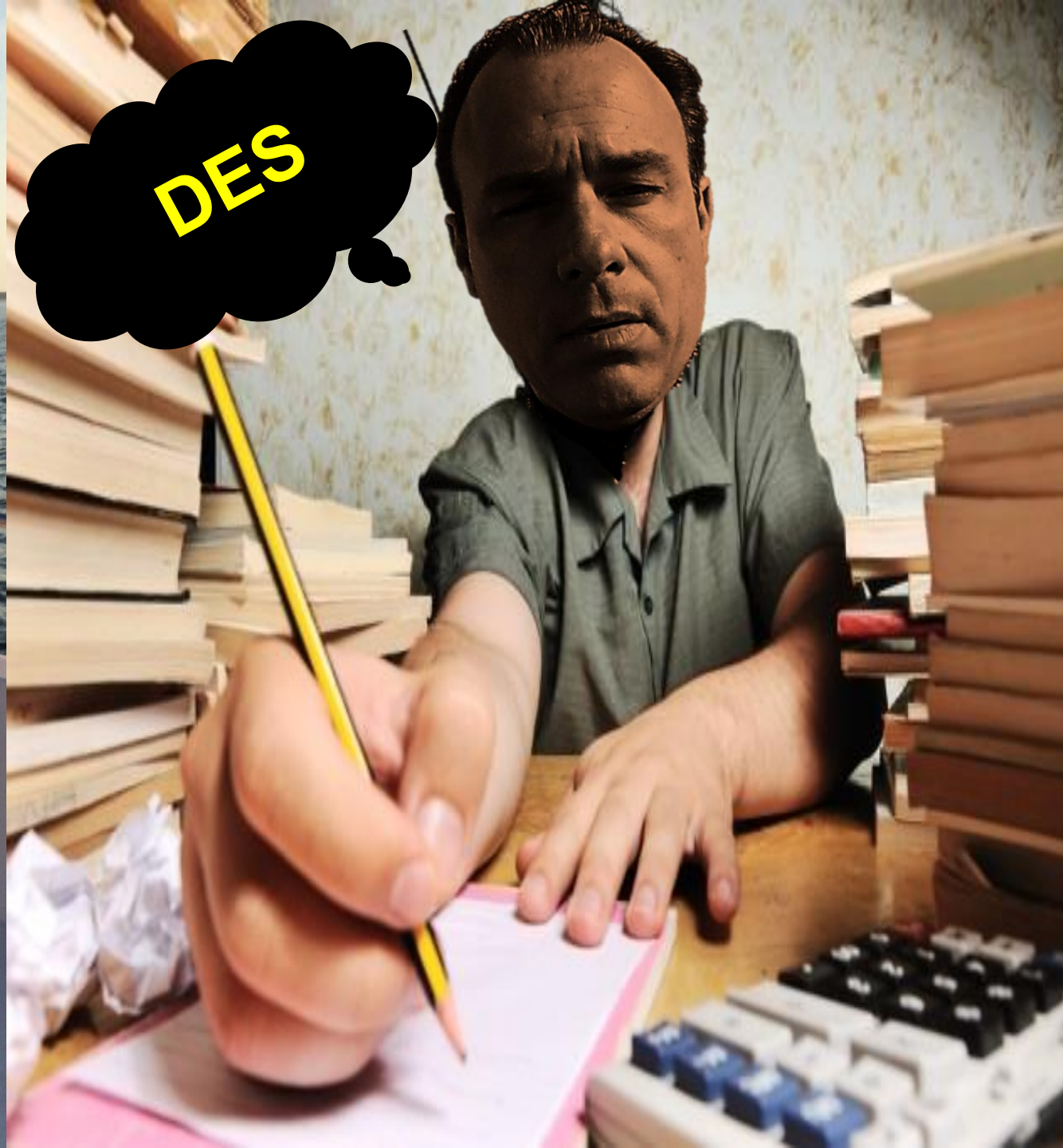
*And the results seem fantastic…***REAL WORLD, ALL COMERS STUDY**

IN.PACT Global Study

12-month Efficacy	
Freedom from Clinically-driven TLR	91.3% (527/577)
12-month Safety	
Primary Safety Endpoint [1]	89.6% (517/577)
Major Adverse Events [2]	13.5% (78/577)
Death (all-cause)	3.3% (19/577)
Major Target Limb Amputation	0.3% (2/577)
Any TLR	9.0% (52/577)
Any TVR	9.9% (57/577)

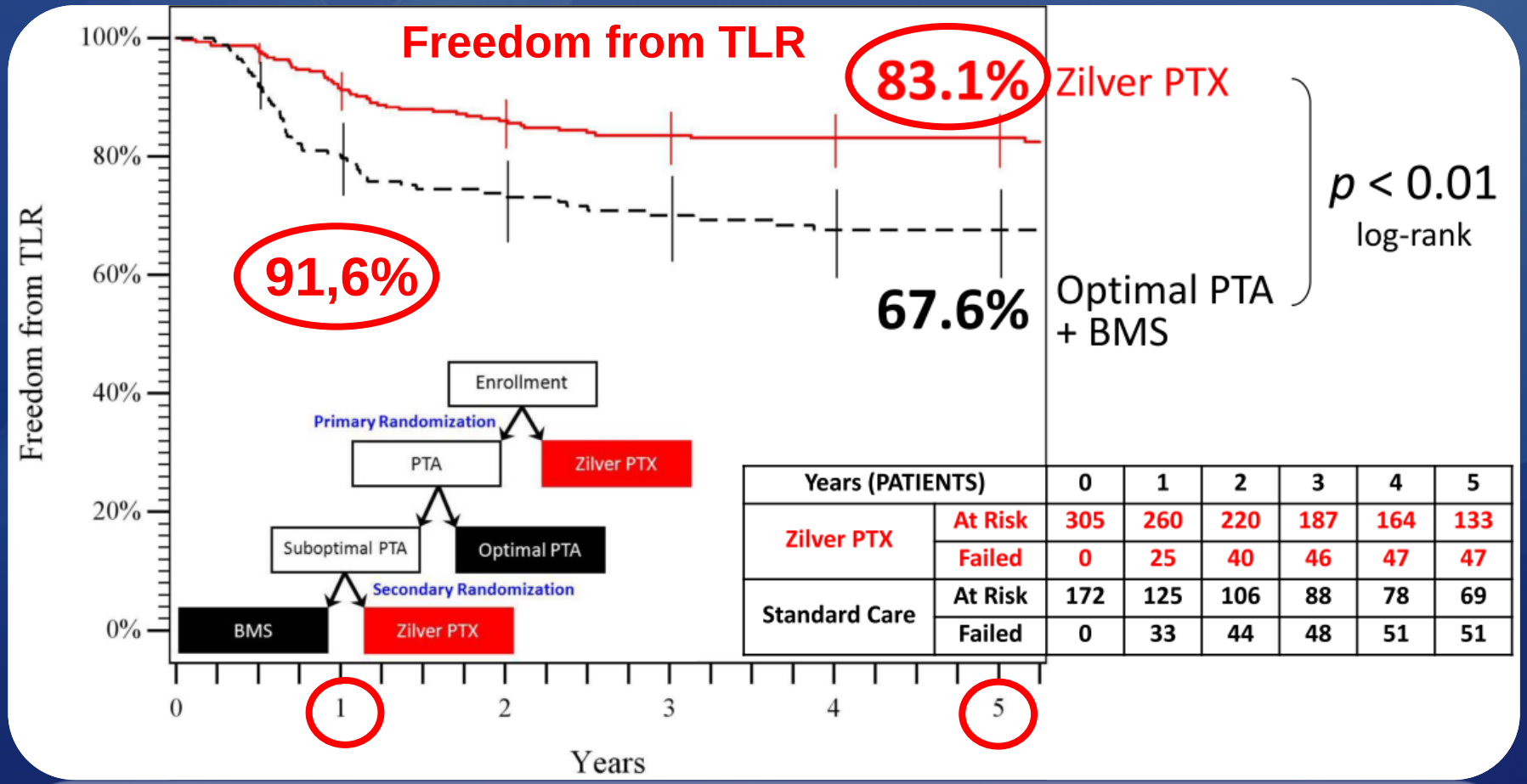
Tepe G. JVIR 2015 ; 26(1):150


DCB'ssss

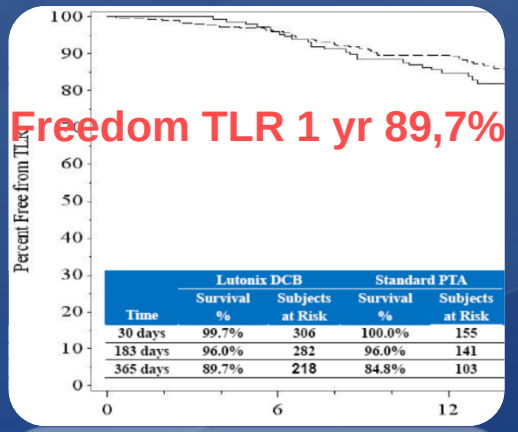

DES

However…

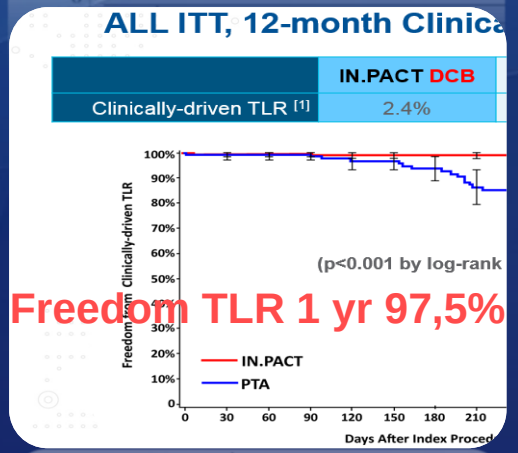
ZILVER PTX Clinical Trial



Years (PATIENTS)		0	1	2	3	4	5
Zilver PTX	At Risk	305	260	220	187	164	133
	Failed	0	25	40	46	47	47
Standard Care	At Risk	172	125	106	88	78	69
	Failed	0	33	44	48	51	51



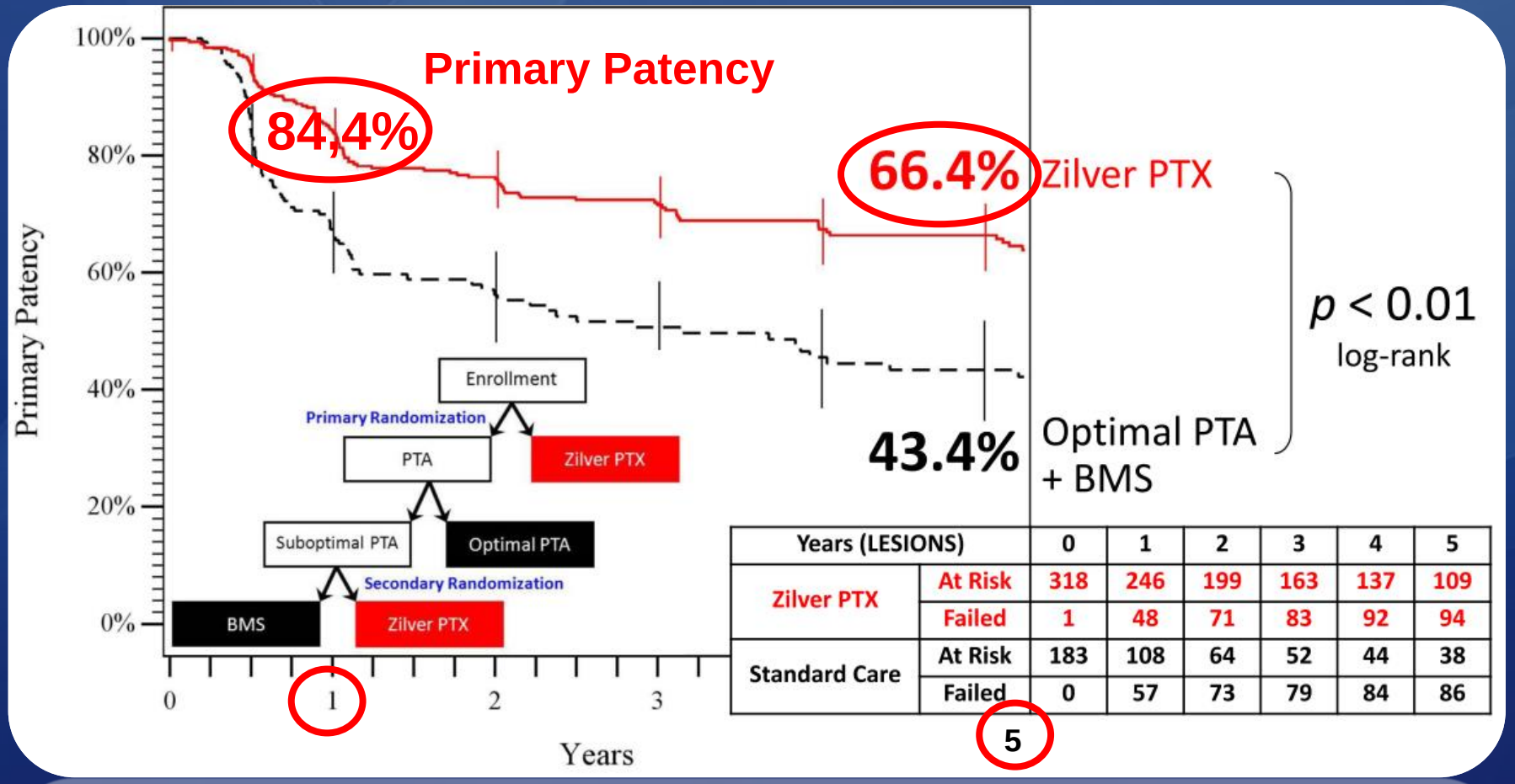
Time	Lutonix DCB Survival %	Lutonix DCB Subjects at Risk	Standard PTA Survival %	Standard PTA Subjects at Risk
30 days	99.7%	306	100.0%	155
183 days	96.0%	282	96.0%	141
365 days	89.7%	218	84.8%	103



Dake et al. Presented @ VIVA 2014, Las Vegas, US

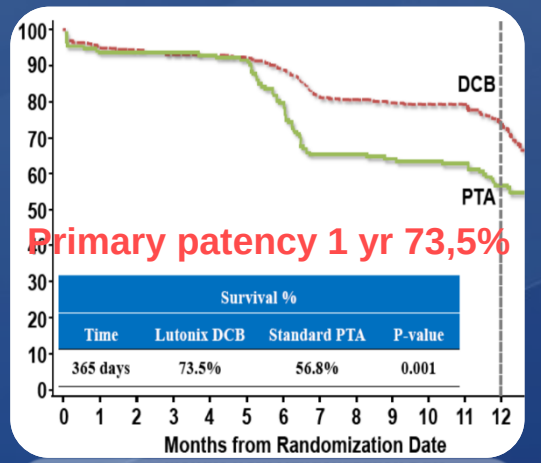
However…

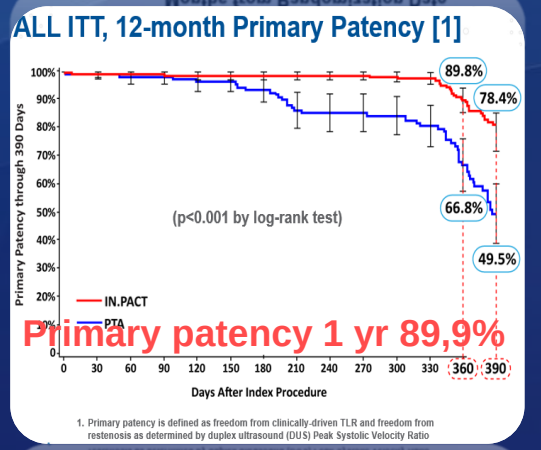
ZILVER PTX Clinical Trial



Years (LESIONS)		0	1	2	3	4	5
Zilver PTX	At Risk	318	246	199	163	137	109
	Failed	1	48	71	83	92	94
Standard Care	At Risk	183	108	64	52	44	38
	Failed	0	57	73	79	84	86

5

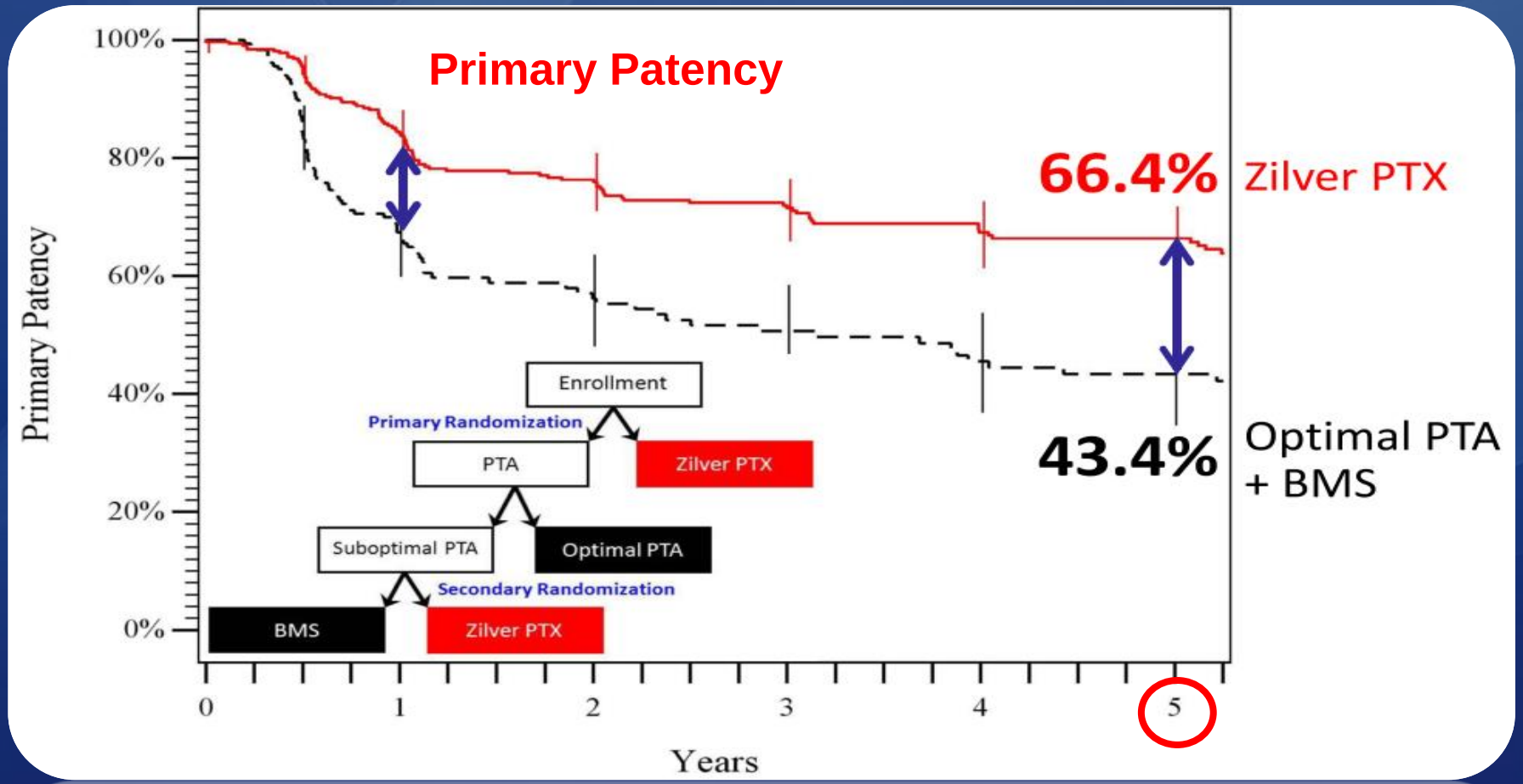




Dake et al. Presented @ VIVA 2014, Las Vegas, US

However…

ZILVER PTX Clinical Trial



Zilver PTX continues to show benefit through 5 years

Dake et al. Presented @ VIVA 2014, Las Vegas, US

Remark 1

1. Durable, long-term, peer reviewed data have to be demonstrated…

THUNDER TRIAL

	PTX balloon	POBA	P value
LLL 6 months	0.4 ± 1.2	1.7 ± 1.8	<0.001
LLL 5 years	0.7 ± 1.9	1.5 ± 1.3	0.54

Remark 2

2. Primary patency based on core lab DUS with the same PSVR….

LEVANT 2 Clinical Trial PSVR < 2.5 -> using PSVR < 2.0 (cfr Zilver PTX) :

no difference anymore between the Lutonix balloon and POBA

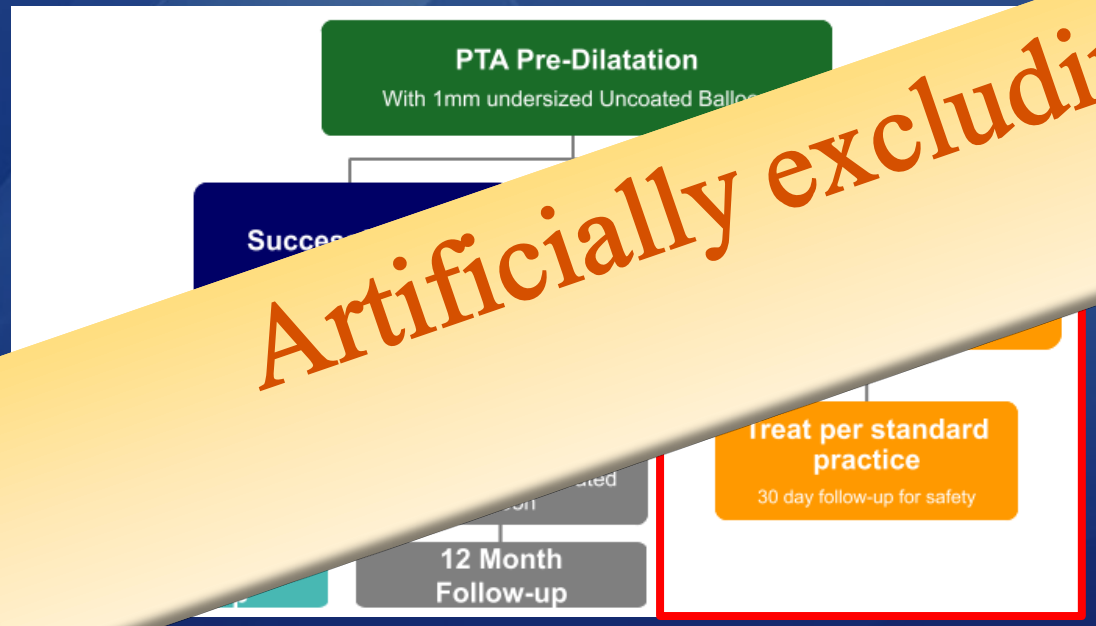
	Lutonix	Control PTA	*P* Value
Primary composite safety endpoint (freedom from perioperative death and 12-month index limb amputation [above and below the ankle], index limb reintervention and index limb-related death)	83.9%	79%	0.005
12-month primary patency (Kaplan-Meier, PSVR = 2.5)	73.5%	56.8%	< 0.001
12-month primary patency (PSVR = 2.0)	53.2%	45%	0.13*
Total TLR at 12 months	12.3%	16.8%	0.208*

*No statistically significant difference.

Remark 3

3. Predilatation “screening” and exclusion criterium if “non re

LEVANT 2 Clinical Trial



xclusions

- P2-P3 lesions
- In-stent restenosis, post-DCB restenosis, or previous bypass
- Unsuccessful pre-dilatation

Artificially excluding severe calcified lesions

Remark 4

4. Artificially low provisional stent rates

	LEVANT 2 Clinical Trial	IN.PACT SFA I-II Trial	ZILVER PTX Clinical Trial
Provisional stenting%	1.8	7,3	na

	Thunder	FemPac	Levant I	Italian Registry	Pacifier	Debellum	Leipzig Registry	Zeller Registry
Length (cm)	7.5	6.1	8.1	7.6	7	7.6	24	19
Stent-Rate %	4	9	24	12	21	57	23.3	18.3

IN.PACT GLOBAL Trial

Inclusion criteria

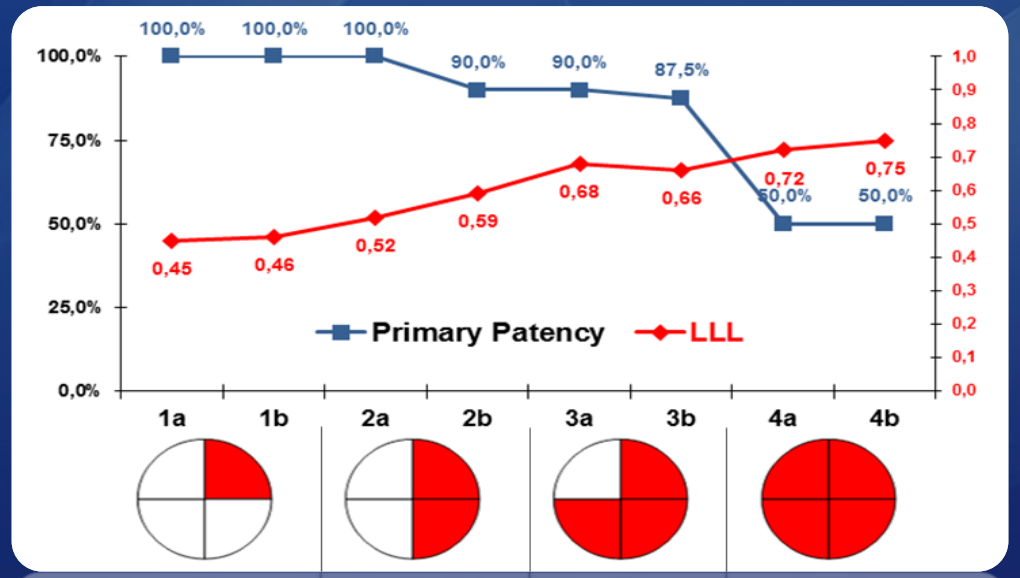
- Single or multiple Lesions in full femoropopliteal tract
- *de novo + restenotic (ISR or non-ISR)* lesions
- Stenosis & Occlusions of all lengths
- Predilatation is @physicians' discretion

Lesion length (cm)	12.23 + 9.59
Total occlusions (%)	35.8
Severe calcification (%)	10.4
Predilatation (%)	75.4
Provisional stenting (%)	**24.7**

Remark 5

5. Avoiding Ca++ circumstances…

	LEVANT 2 Clinical Trial	IN.PACT SFA I-II Trial	ZILVER PTX Clinical Trial
Severe calcification %	10,4	8,1	37,3



Ca distribution/ severity

affect

LLL/primary patency

Ca++ represents

a barrier to optimal drug

absorption

Data adapted from Cook Medical, Dpt of Health & human services - Tepe G, presented @ CX2014, London ,UK - Fanelli et al. Cardiovasc Intervent Radiol 2014;37:898-907

Remark 6

6. Lack of data in “real world” long lesions…

1 retrospective, dual center study with propensity score stratification

1 single center registry

	Mean lesion length (mm)	Number	1yr PPR (%) (duplex US)	2yr PPR (%) (duplex US)
Leipzig Registry	*240*	*260*	*82,4**	*na*
Zeller Study	*190*	*228*	*76,1**	*na*

*Provisional stent rates of 23,3% & 18,3%

Schmidt A et al, presented @ LINC 2013 - Zeller et al. J Endovasc Ther 2014;21:359-368

Remark 6

6. Lack of data in “real world” long lesions…

	Mean lesion length (mm)	Number	1yr PPR (%) (duplex US)	2yr PPR (%) (duplex US)
Zilver PTX SAS TASC C & D	***226***	***135***	***77,6***	***Na***
Zilver PTX PMS LL	***189***	***45***	***86,1***	***Na***
Japanese PMS LL	***186***	***703***	***81***	***na***

Bosiers et al. J CardioVasc Surg 2013 ;54(1) : 115-22
Zeller et al. Presented @ LINC 2014, Leipzig, Germany
Hiroyoshi Yokoi et al. Presented @ VIVA 2014, Las Vegas, US

Remark 7

7. DCB effectiveness may not be a CLASS EFFECT…

Each DCB stands on the merits of its data, need to be evaluated & compared (different excipients, different pharmacokinetics, different coatings…)

Elutax SV™	Aachen Resonance, Luxembourg, Luxembourg	Paclitaxel
Advance 18 PTX™	Cook Medical, Bloomington, IN, USA	Paclitaxel
Cotavance®	Bayer Schering Pharma AG, Berlin, Germany	Paclitaxel–iopromide
Freeway™	Eurocor, Bonn, Germany	Paclitaxel–shellac
IN.PACT™ Admiral, Amphirion, Pacific	Medtronic Vascular, Santa Clara, CA, USA	Paclitaxel–urea
Lutonix DCB® (Moxy)	BARD, Murray Hill, NJ, USA	Paclitaxel –polysorbate/sorbitol
Legflow®	Cardionovum, Warsaw, Poland	Paclitaxel–shellac
Passeo-18 Lux®	Biotronik, Bülach, Switzerland	Paclitaxel–BTHC
Stellarex®	Covidien, Mansfield, MA, USA	Paclitaxel

Remark 8

- Please Yann, don’t come with economical considerations….

Conclusion

Ideal dream world

Short TASC A & B lesions

Not calcified

Perfect predil result

1 year follow-up

Using liberal PSVR criteria

With some DCB’s

Conclusion