ILLUMENATE European Randomized Trial: 2-Year Results

Marianne Brodmann, MD
Division of Angiology, Medical University of Graz
Graz, Austria

Disclosure

Speaker name:

Marianne Brodmann

I have the following potential conflicts of interest to report:

- [x] 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

Background

- Drug-coated balloons are becoming a front-line therapy for SFA treatment
- 12-month primary patency rates were significantly higher than PTA across several DCBs and trials[1-4]
- However, longer-term data on DCBs are limited and variable[5,6]

DCB	Drug & Dose	Treatment Effect*	
		1 year	2 year
IN.PACT Admiral	3.5 µg/mm^2	✓	✓
Lutonix	2µg/mm^2	✓	⊘
Stellarex	2µg/mm^2	✓	-

*Defined as a significantly higher primary patency rate as compared to PTA

- Can a low-dose DCB deliver enough drug to provide a durable treatment effect at 2 years?

1. G. Tepe et al. Circulation. 2015 Feb 3;131(5):495-502
2. K.Rosenfield et al.. N Engl J Med 2015
3. H. Schroeder et al. *Circulation.* 2017;135(23):2227-2236.
4. P. Krishnan et al. Circulation. 2017;CIRCULATIONAHA.117.028893
5. C Laurich, Oral presentation, SVS 2015
6. J. Laird et al. J Am Coll Cardiol 2015;66:2329-38

ILLUMENATE EU RCT Overview

- Study Device: Stellarex DCB
  - Low-dose DCB, hybrid formulation consisting of both amorphous and crystalline PTX
- Objective: Demonstrate safety and efficacy of the Stellarex DCB vs. standard PTA for treatment of arterial disease in the SFA and/or popliteal arteries
- Prospective, randomized (Stellarex DCB vs. PTA), multi-center
- Patients will be followed for 5 years
- Rigorous trial methodology with independent adjudication by:
  - *Angiographic Core Laboratory*[1]
  - *Duplex Ultrasound Core Laboratory*[2]
  - *Clinical Events Committee*
  - *Data Safety Monitoring Board*
- Monitoring with 100% source data verification

1. SynvaCore, Springfiedld, IL
2. VasCore, Boston, MA

ILLUMENATE EU RCT Investigators

Dr. Henrik Schroeder : Jewish Hospital, Berlin National Principal Investigator	**Prof. Marianne Brodmann:** LKH University Hospital Graz
Dr. Beata Lux: St Joseph Hospital, Berlin	**Prof. Peter Reimer:**Clinical Center, Karlsruhe
Dr. Dirk-Roelfs Meyer: Lutheran Hospital Hubertus, Berlin	**Prof. Markus Duex:** Hospital Nordwest GmbH, Frankfurt a. Main
Dr. Karsten Krueger: Vivantes Humboldt Hospital, Berlin	**Dr. Goetz Voshage:** Robert Koch Clinical Center, Gehrden
Dr. Karsten Krueger: Vivantes Clinic Spandau, Berlin	**Prof. Giovanni Torsello:** Saint Francis Hospital GmbH, Münster
Dr. Volker Sesselmann: SHR Central Clinic, Suhl	**Prof. Gunnar Tepe:** RoMed Hospital, Rosenheim
Prof. Martin Zwaan: Ammerland-Clinic GmbH, Westerstede	**Prof. Claus Nolte-Ernsting:** Lutheran Hospital, Mülheim
Prof. Thomas Albrecht: Vivantes Clinic Neukölln, Berlin	**Prof. Christian Loewe**: University Hospital, Vienna
Prof. Roman Fischbach: Altona-Asklepios Clinic, Hamburg	**Dr. Martin Werner:** Hanusch Hospital of WGKK Group, Vienna

Baseline Patient Characteristics

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	Stellarex	PTA	p
Age (years)	66.8 ± 9.2 (222)	69.0 ± 8.6 (72)	0.079
Male	72.1% (160/222)	68.1% (49/72)	0.514
Rutherford Clinical Category			0.525
2	15.4% (34/221)	21.1% (15/71)	
3	82.8% (183/221)	77.5% (55/71)	
4	1.8% (4/221)	1.4% (1/71)	
Diabetes	37.4% (83/222)	36.1% (26/72)	0.846
Hypertension	77.9% (173/222)	83.3% (60/72)	0.326
Hyperlipidemia	61.7% (137/222)	68.1% (49/72)	0.332
Smoking Status			0.188
Never Smoked	10.8% (24/222)	16.7% (12/72)	
Previous or Current	89.2% (198/222)	83.3% (60/72)	
ABI	0.72 ± 0.21 (212)	0.69 ± 0.26 (68)	0.250

Baseline Angiographic Data

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	Stellarex	PTA	p
Lesion Length (cm)	7.2± 5.2 (250)	7.1 ± 5.3 (79)	0.878
Lesion Type			
De Novo	92.1% (234/254)	89.9% (71/79)	0.529
Restenotic	7.9% (20/254)	10.1% (8/79)	
Total Occlusion	19.2% (48/250)	19.0% (15/79)	0.967
Calcification			
None/Mild	55.8% (140/251)	59.5% (47/79)	0.775
Moderate	31.5% (79/251)	30.4% (24/79)	
Severe*	12.7% (32/251)	10.1% (8/79)	
Diameter Stenosis (%)	78.7 ± 16.0 (250)	80.8 ± 15.7 (79)	0.297
Reference Vessel Diameter (mm)	5.02 ± 0.79 (250)	4.77 ± 0.69 (79)	0.012
# of Patent Run-off Vessels			
0	8.5% (18/211)	5.9% (4/68)	0.229
1	19.0% (40/211)	13.2% (9/68)	
2	32.2% (68/211)	45.6% (31/68)	
3	40.3% (85/211)	35.3% (24/68)	

Per core lab adjudication

*Calcification that extends ≥ 2 cm and is circumferential **or** ≥60% of total lesion length

2-year Primary Patency

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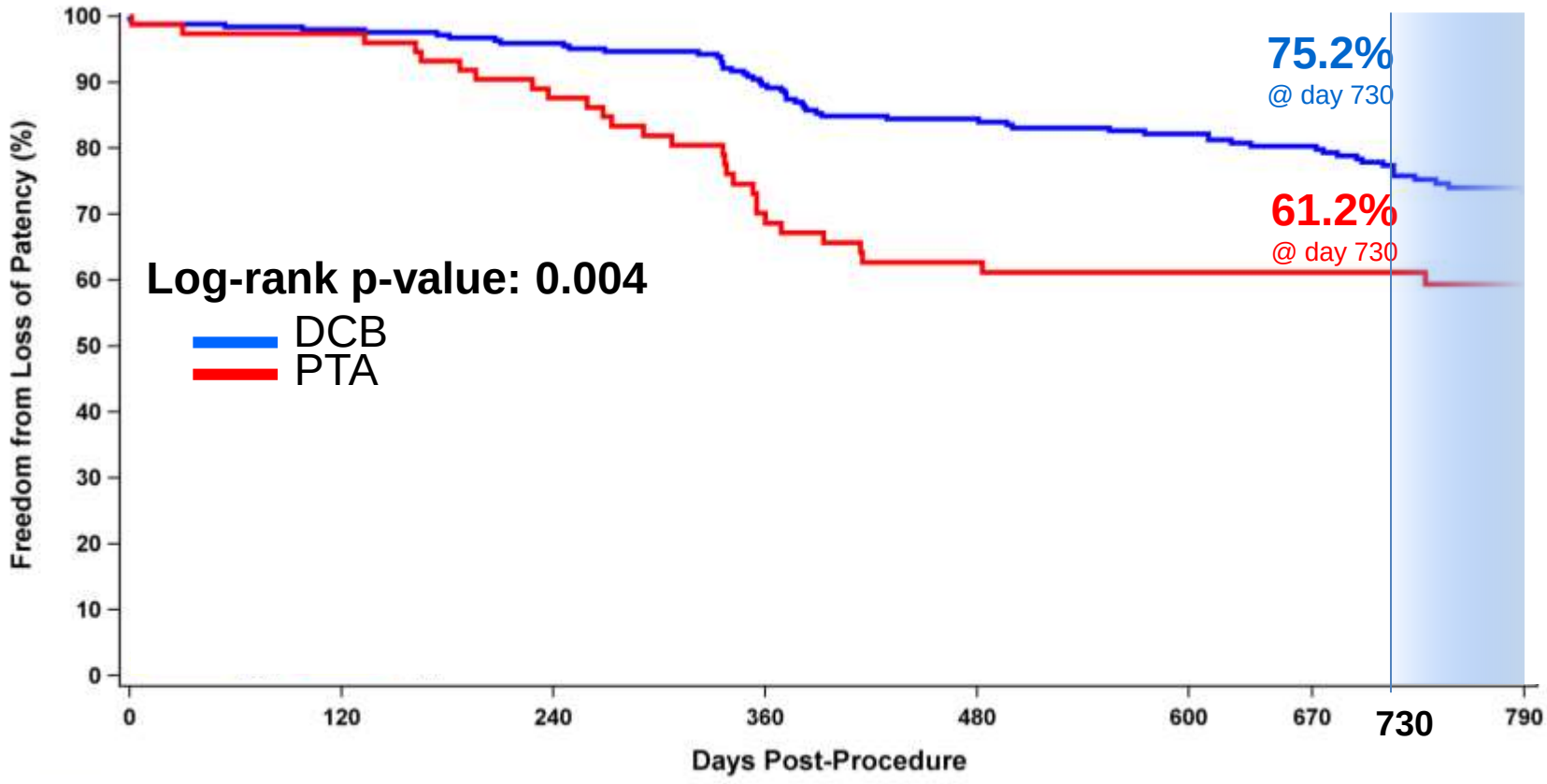

Days	365	730	790
DCB Event Free	89.2%	75.2%	73.3%
PTA Event Free	68.7%	61.2%	59.3%

Patency is defined as absence of target lesion restenosis (as assessed by the duplex ultrasound core laboratory based on PSVR ≤ 2.5) and freedom from clinically-driven target lesion revascularization (CD-TLR).

2-year Primary Patency

(exact rate through 790 days)

Primary Efficacy Endpoint[1]	DCB	PTA	Difference [95% CI][3]	p-value[3]
Patency at 24 Months	75.9% (145/191)	61.0% (36/59)[2]	14.9% [1.1%, 28.7%]	0.025

1.Patency is defined as absence of target lesion restenosis (as assessed by the duplex ultrasound core laboratory based on PSVR ≤ 2.5) and freedom from clinically-driven target lesion revascularization (CD-TLR) through 790 days.

2. The original 12 month patency rate for the PTA arm was 60.6% (40/66). When 3 additional subjects are included as success carried backwards due to newly available 2 year data, the post-hoc 12 month rate is 64.2% (43/67).

3. Confidence interval of the difference is asymptotic. p-value was based on the chi-square test.

2-year Freedom from CD-TLR

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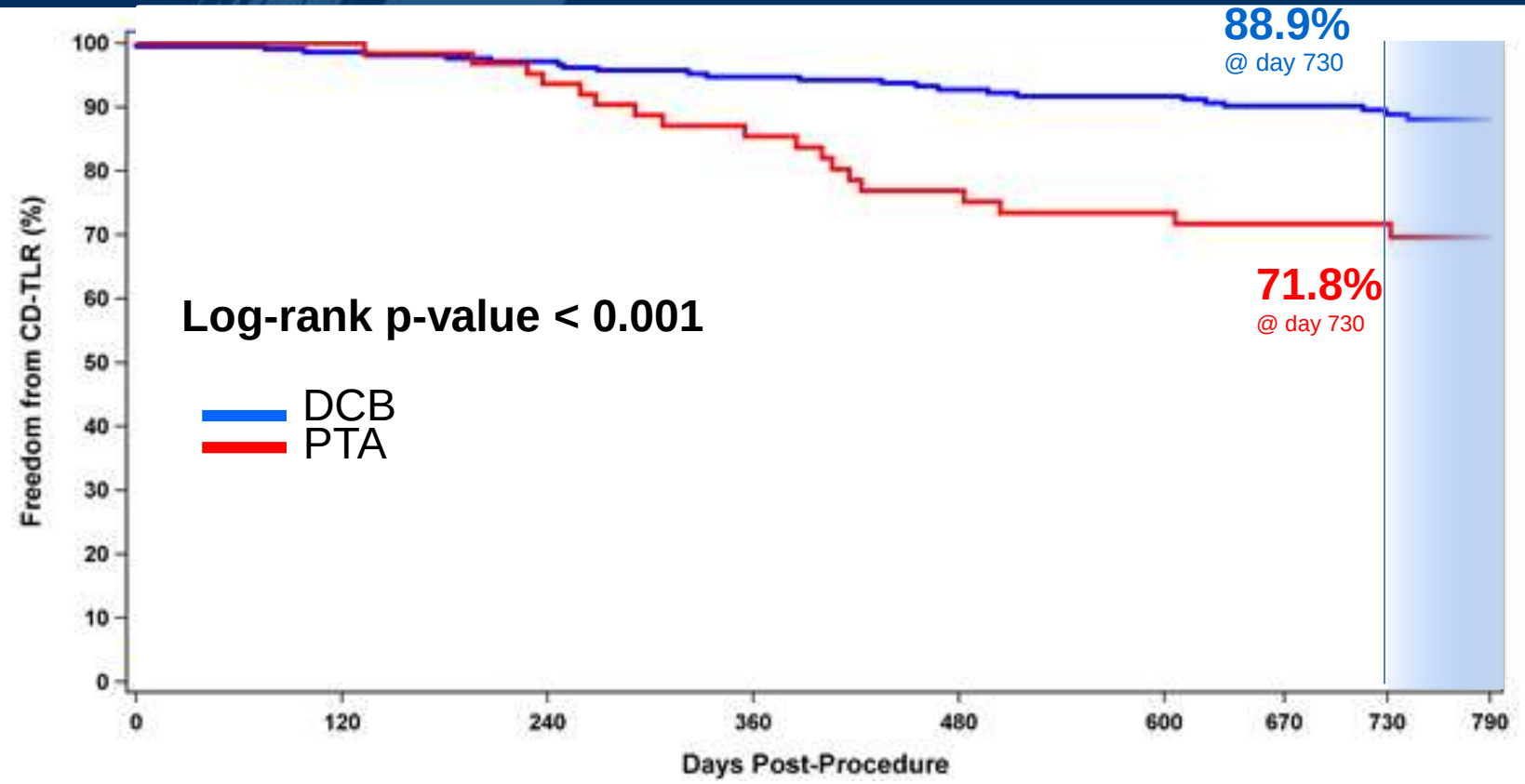

Days	365	730	790
DCB Event Free	94.8%	88.9%	88.1%
PTA Event Free	85.4%	71.8%	69.7%

Key Safety Endpoints at 2 Years*

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	DCB	PTA	P-value
All-Cause Death	**6.5% (13/199)**	**5.1% (3/59)**	**1.000**
Major Adverse Events[1]	**14.0% (27/193)**	**31.7% (19/60)**	**0.002**
Cardiovascular Death	1.6% (3/191)	1.7% (1/59)	1.000
Target Limb Amputation	1.1% (2/188)	0.0% (0/58)	1.000
Clinically-driven TLR	12.1% (23/190)	30.5% (18/59)	<0.001

*Includes all MAEs reported through 790 days post-procedure
Sum of the components may not add up to the overall rate as some subjects may experience more than one event type.
Numbers are % (n/N) The numerator is the number of subjects with an event prior to the close of the visit window. The denominator includes subjects with an event or those without an event having follow-up on or past the opening of the visit window.

Clinically-driven TLR

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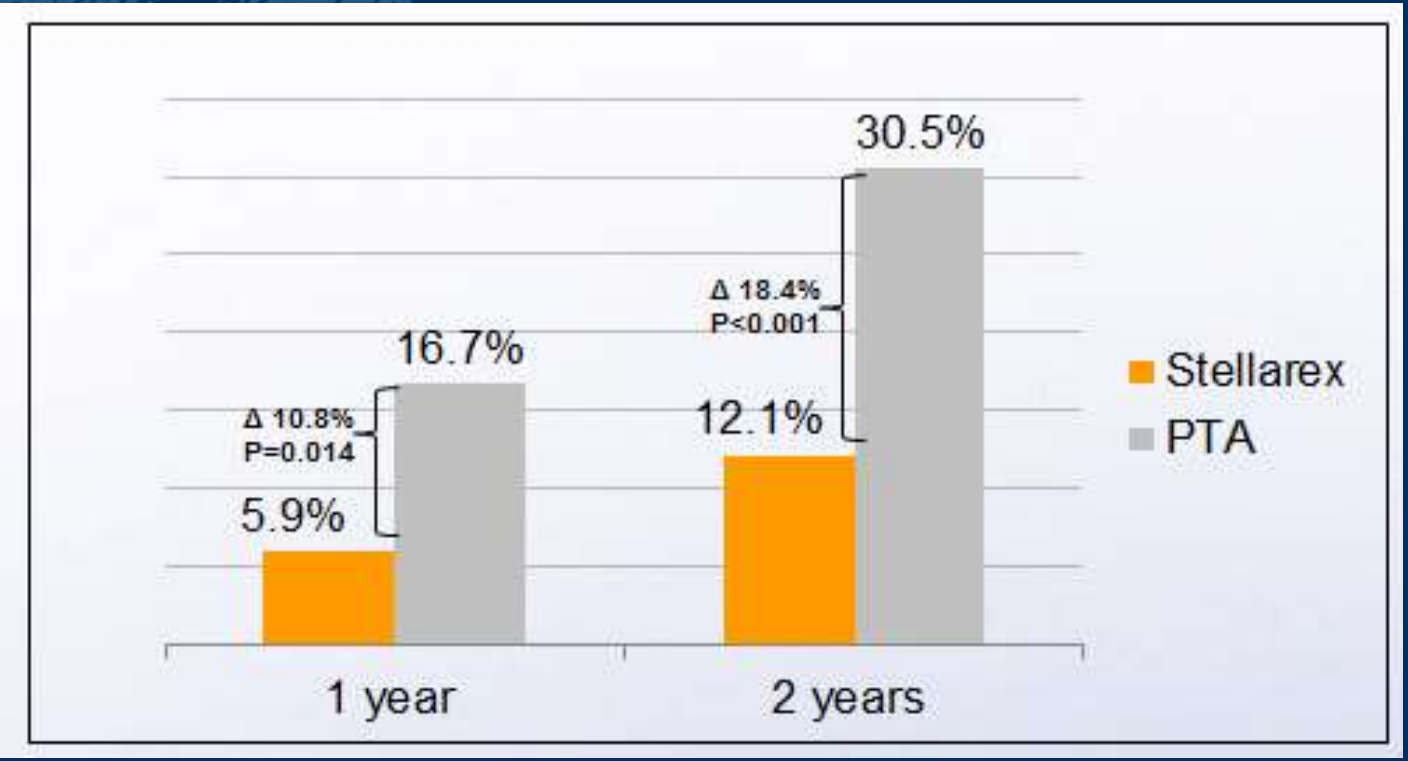
- Significant treatment effect observed out to 2 years
- Treatment effect increased from 1 to 2 years



Clinical & Functional Improvements

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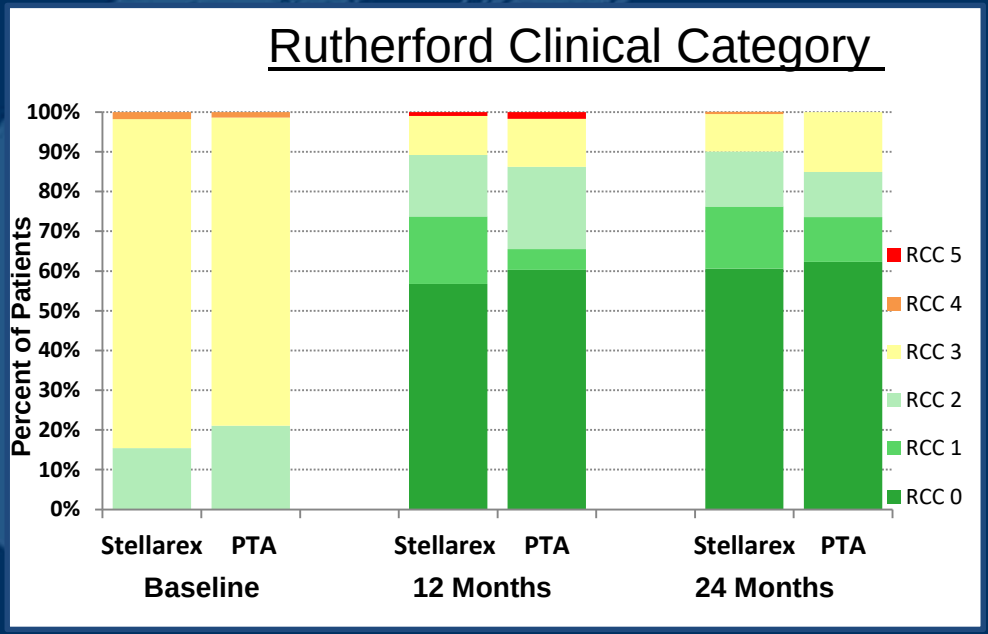
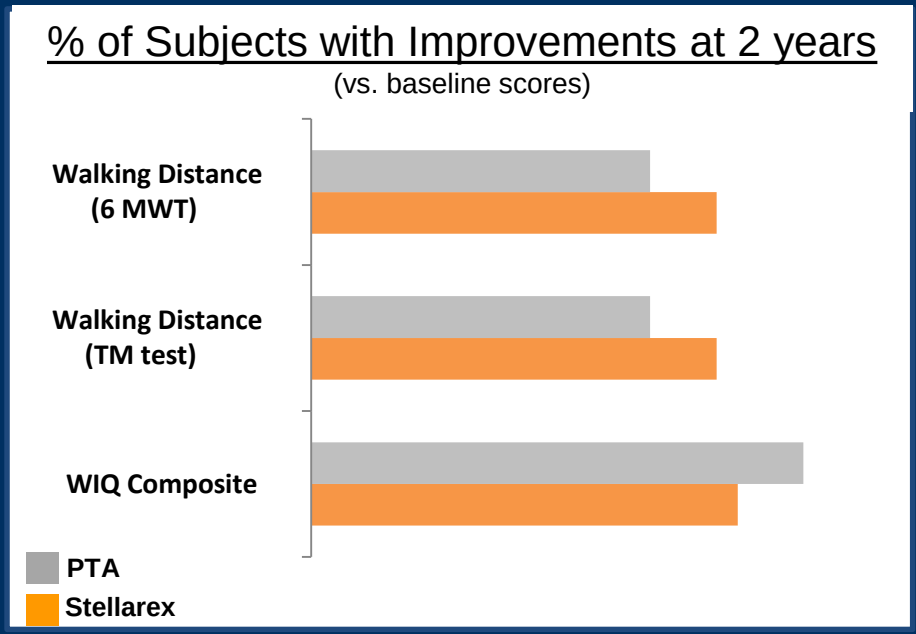
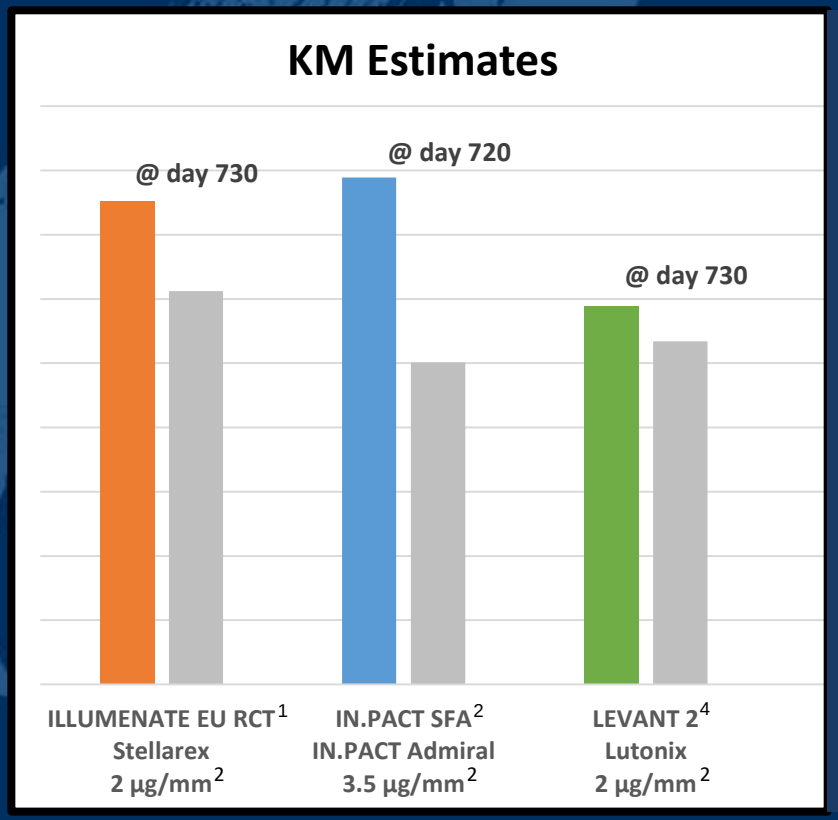
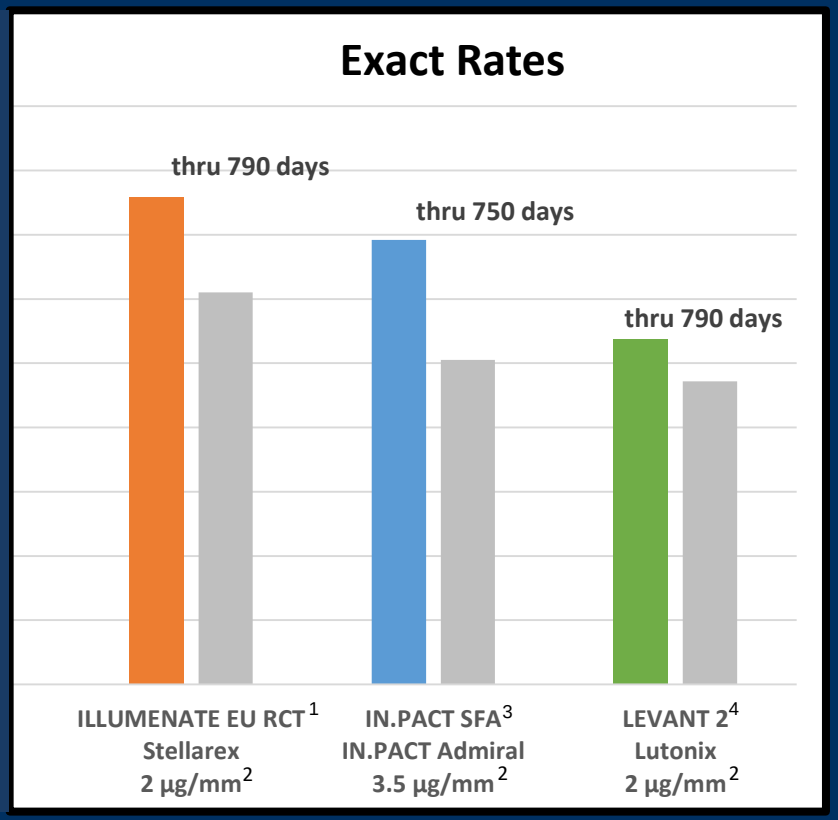
➢The DCB cohort maintained similar outcomes with 60% fewer reinterventions





Data in Context
DCB Primary Patency Rates at 2 Years





1. M. Brodmann VIVA 2017, Las Vegas, NV. September 11-14, 2017.
2. Laird et al. J Am Coll Cardio 2015;66:2329-38
3. Medtronic IN.PACT Admiral Instructions for Use, Rev. 1F
4. Bard Lutonix Instructions for Use http://www.bardpv.com/wp-content/uploads/2017/02/BAW1387400r3-Lutonix-DCB-IFU-with-GeoAlign-5F.pdf

Conclusions

- Durable treatment effect demonstrated, with no indication of late catch-up at 2 years
  - Significantly higher primary patency rate observed in the Stellarex cohort , 75.2% vs. 61.2%, p=0.004 (per KM) Significantly lower rate of CD-TLR 12.1% vs. 30.5% (p<0.001)
- Functional outcomes maintained at a similar level, with 60% fewer reinterventions in the Stellarex cohort
- Stellarex is the first low-dose DCB to demonstrate a statistically significant treatment effect at 2 years

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