Safety & Effectiveness of the Stellarex DCB with Low Dose Paclitaxel: ILLUMENATE Pivotal Trial Four Year Results

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Disclosure

Speaker name: Sean P. Lyden, MD

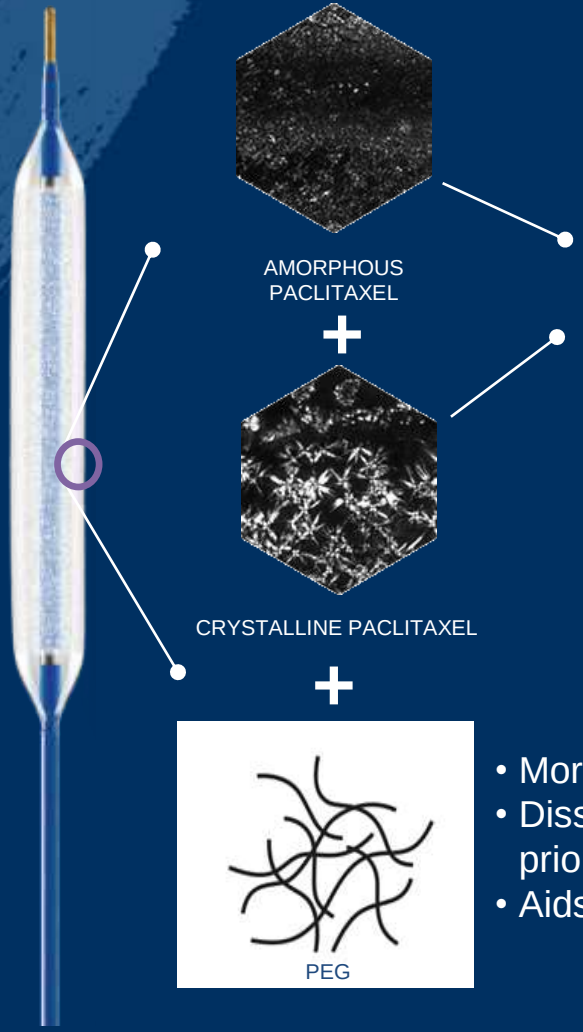
I have the following potential conflicts of interest to report:

- [x] Consulting: PQ Bypass, Intact Vascular, Philips, Medtronic Boston Scientific, Endologix, Shockwave, VIVA Physicians
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

Stellarex Coating: Designed to maximize efficiency of Ptx delivery & clinical performance

DCB design goals
- Limited drug dose
- Limited drug loss
- High drug transfer
- High deliverability
- Clinical performance



- Prompt availability
- Optimized tissue residency with anti-proliferative effect

- More durability during handling, tracking, inflation
- Dissolves slowly to protect paclitaxel from loss prior to balloon inflation at target site
- Aids in keeping dose level low

1. Mark, J. et al. Physical Properties of Polymers – Cambridge University Press 3rd edition, 2004
2. Data on file at Philips

Stellarex Clinical Program

- Stellarex data analyses have confirmed its efficacy and safety: ILLUMENATE trials met their Primary Safety/Efficacy Endpoints
- Over 2300 patients treated with Stellarex in ATK DCB trials with independent CEC for AE adjudications

Trial	Type	ATK/ BTK	Enrollment	Sites	Region	Status
ILLUMENATE FIH	First in Man	ATK	80	3	Europe	Closed
ILLUMENATE PK	Pharmacokinetic	ATK	25	2	Europe	Closed
ILLUMENATE EU RCT	Pivotal	ATK	328	18	Europe	Follow Up
ILLUMENATE Pivotal	Pivotal	ATK	300	43	US/Europe	Follow Up
ILLUMENATE Global	Post Market	ATK	371	37	Europe, AUS, NZ	Follow Up
ILLUMENATE Global-ISR	Labeling Expansion	ATK	129	26	Europe, AUS, NZ	Follow Up
SAVER	Real World Evidence	ATK/BTK	~1700	42	Europe	Enrolling
ILLUMENATE BTK PM	Post Market	BTK	17/75	9	Europe	Enrolling
ILLUMENATE BTK IDE	Label expansion	BTK	53/354	17	US/Europe	Enrolling

ILLUMENATE Pivotal Study Design

Circulation

American Heart Association.

Stellarex Drug-Coated Balloon for Treatment of Femoropopliteal Disease: Twelve-Month Outcomes From the Randomized ILLUMENATE Pivotal and Pharmacokinetic Studies

Prakash Krishnan, Peter Faries, Khusrow Niazi, Ash Jain, Ravish Sachar, William B. Bachinsky, Joseph Cardenas, Martin Werner, Marianne Brodmann, J. A. Mustapha, Carlos Mena-Hurtado, Michael R. Jaff, Andrew H. Holden and Sean P. Lyden

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12-Month primary Endpoints Met and Published

Objective: Demonstrate safety and effectiveness of the Stellarex DCB vs. standard PTA for treatment of arterial disease in the SFA and/or popliteal arteries	
N Patients	300
Multicenter (N sites)	43 (US & EU)
Enrollment	Dec 2012 – Apr 2015
Follow Up	5 Years (through PAS)
Randomization	2:1
Pre-dilatation	Mandatory
Duplex Core-lab	✓
Angiographic Core-lab	✓
External Monitoring with 100% SD Verification	✓
Clinical Event Committee	✓
Data Safety Monitoring	✓

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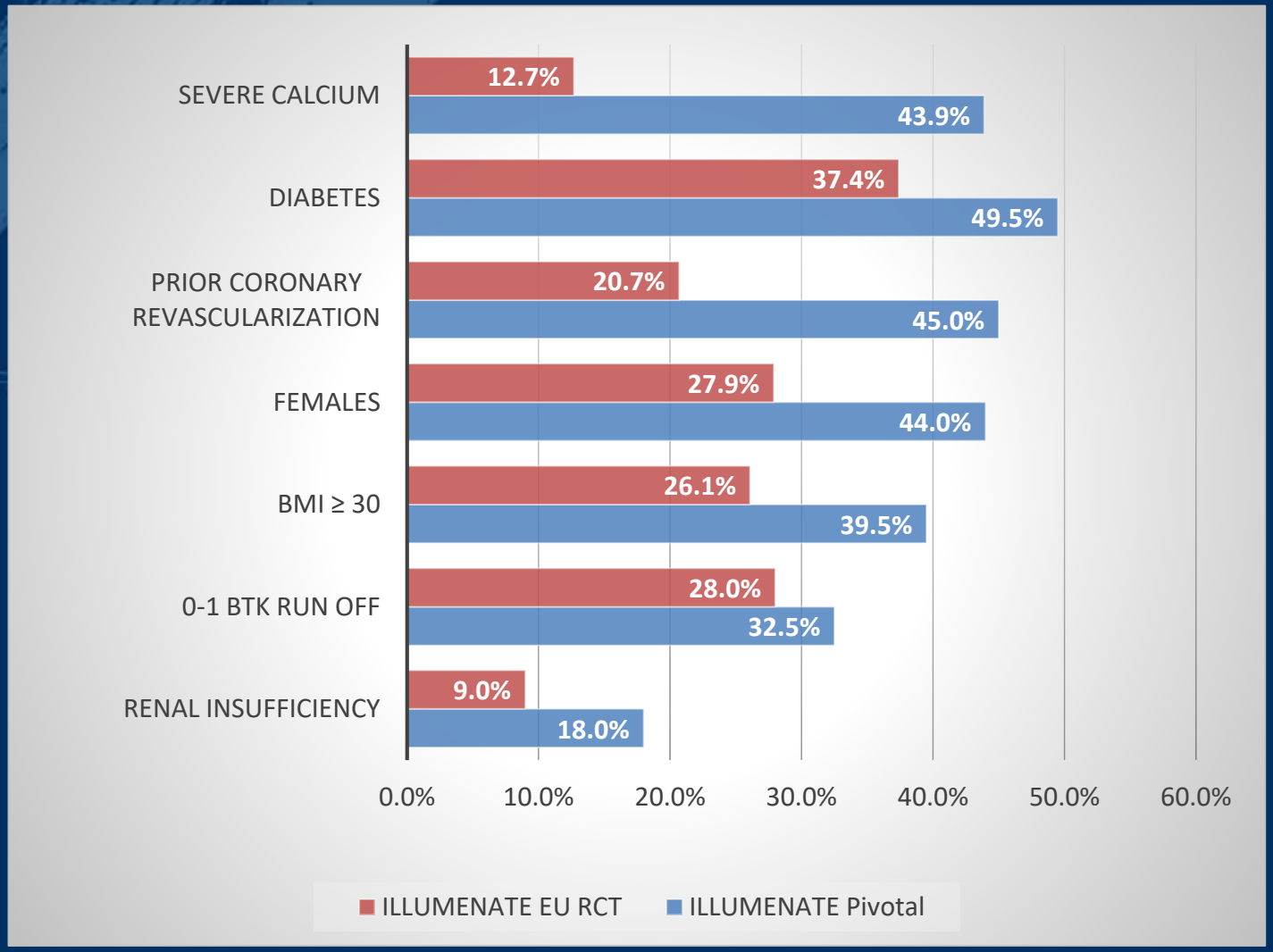
Baseline Characteristics

Patient Characteristics	Stellarex	PTA	p
Age (years)	68.3 ± 10.3 (200)	69.8 ± 9.8 (100)	0.225
Female	44% (88/200)	36% (36/100)	0.185
Rutherford Clinical Category			0.735
2	31.5% (63/200)	35.0% (35/100)	
3	64.5% (129/200)	60.0% (60/100)	
4	4.0% (8/200)	5.0% (5/100)	
ABI	0.75 ± 0.21 (193)	0.76 ± 0.2 (100)	0.508
Hypertension	93.5% (187/200)	94.0% (94/100)	0.867
Hyperlipidemia	88.0% (176/200)	90.0% (90/100)	0.606
Previous or Current Smoker	84.0% (168/200)	75.0% (75/100)	0.061
Diabetes	49.5% (99/200)	52.0% (52/100)	0.683
Renal Insufficiency	18.0% (36/200)	17.0% (17/100)	0.830

Patient Characteristics	Stellarex	PTA	p
Lesion Length (cm)	8.0 ± 4.5 (199)	8.9 ± 4.6 (100)	0.105
Total Occlusion	19.0% (38/200)	18.0% (18/100)	0.834
Restenotic	9.5% (19/200)	18.0% (18/100)	0.035
Severe Calcification	43.9% (87/198)	43.0% (43/100)	0.877
Baseline Diameter Stenosis (%)	73.9 (200)	74.8 (100)	0.673

Higher Patient Complexities in ILLUMENATE Pivotal



No Differences in All-Cause Mortality through 4 Years including Vital Status

4 Year Vital Status Compliance Update

Reporting Period	Vital Status Compliance
December 2019	95% (284/300)

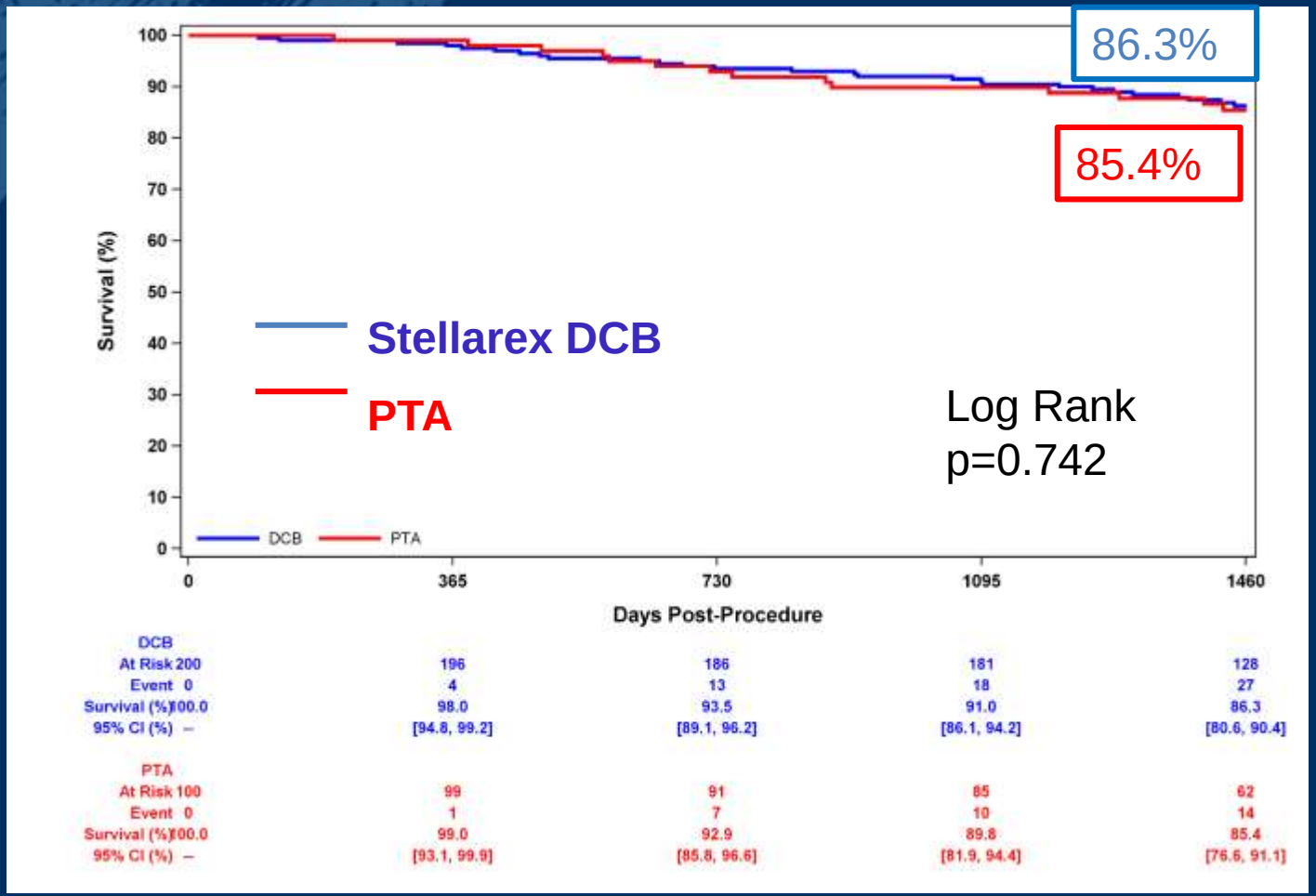
ILLUMENATE Pivotal Cumulative Mortality (Exact Rates): Post hoc analysis

All Cause Mortality	DCB	PTA	p Value
12 months	2.5% (5/200)	2.0% (2/100)	1.000
24 months	6.5% (13/200)	8.1% (8/99)	0.615
36 months	9.5% (19/199)	10.4% (10/96)	0.814
48 months	**15.6% (30/192)**	**15.2% (14/92)**	**0.929**

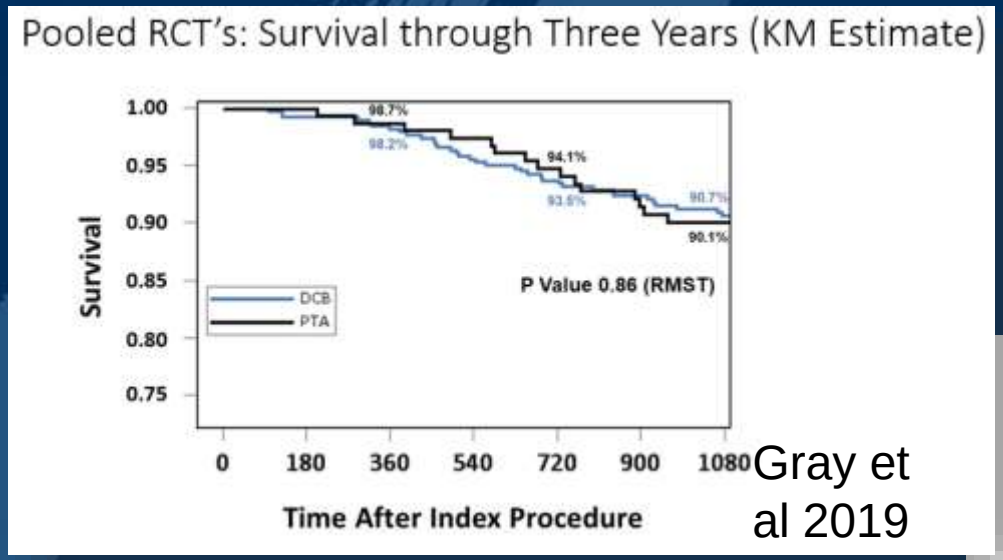
Survival through 4 years (KM Estimate)

ILLUMENATE Pivotal: Post hoc analysis

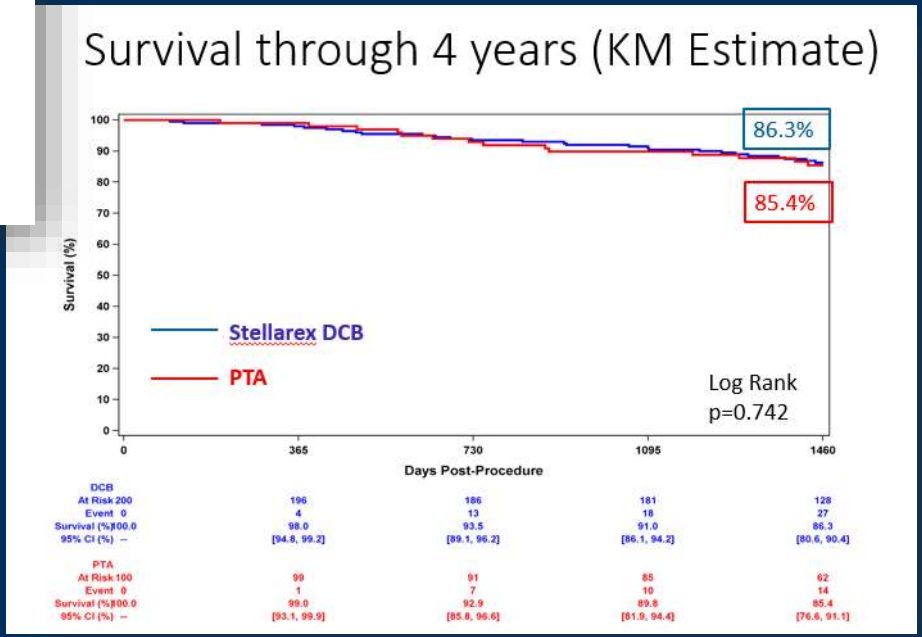
Overlapping survival curves for Stellarex DCB and PTA through 4 years (ITT)



4 Year Survival Consistent with Pooled Stellarex 3 Year Data



Gray et al 2019



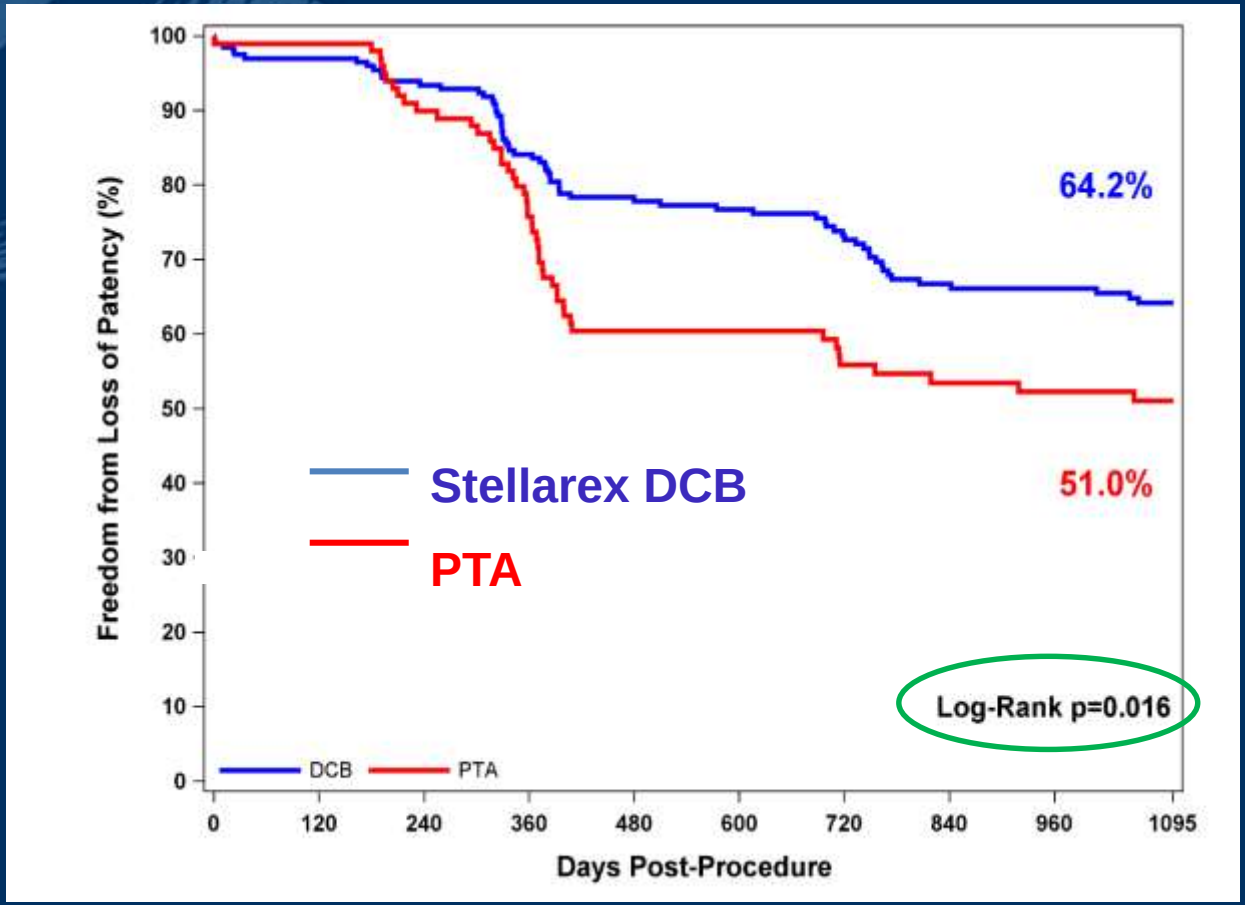
Survival rates between Stellarex and control are consistently overlapping over time

Circulation 2019;140:1145–1155. DOI: 10.1161

Primary Patency Through 3 Years

Significant difference in patency between Stellarex DCB and PTA

Primary patency defined as the absence of target lesion restenosis determined by DUS and freedom from CD-TLR during an office visit.



Four Year Outcomes

Key Endpoints @ 4 Years*	Stellarex	PTA	p Value
All Cause Mortality (Post Hoc Data)	15.6% (30/192)	15.2% (14/92)	0.929
Cardiovascular Mortality	5.6% (9/161)	8.3% (7/84)	0.409
Composite Safety Endpoint**	71.2% (111/156)	65.9% (54/82)	0.399
Target Limb Major Amputation	0.7% (1/153)	0.0% (0/77)	1.000
CD-TLR	28.2% (44/156)	34.1% (28/82)	0.343

* 4 Year follow up determined by phone call

** Defined as composite of freedom from device and procedure-related death through 30 days post-procedure and freedom from target limb major amputation and clinically-driven target lesion revascularization (CD-TLR) through 48 months post-procedure.

Conclusions

- Survival curves of Stellarex DCB and PTA continue to overlap through 4 years with similar all-cause mortality rates
- Stellarex DCB has high safety profile and sustained treatment effect through 4 years
- 4 year data demonstrates clinically relevant difference with lower CD-TLR rate in Stellarex DCB group compared with PTA
- Stellarex is the only low-dose DCB supported by head-to-head 4 year randomized data with favorable safety and efficacy within an extensive complex patient cohort
- ILLUMENATE Pivotal 4 year data builds on the robust, consistent long-term data of the Stellarex program

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