Final Long-Term Mortality Results of Paclitaxel-Coated DCBs from the ILLUMENATE RCTs: 5-Year Data from EU RCT and Pivotal studies

Prof Marianne Brodmann

Medical University of Graz

Graz, Austria

Disclosure

Speaker name:

Brodmann Marianne, MD

I have the following potential conflicts of interest to report:

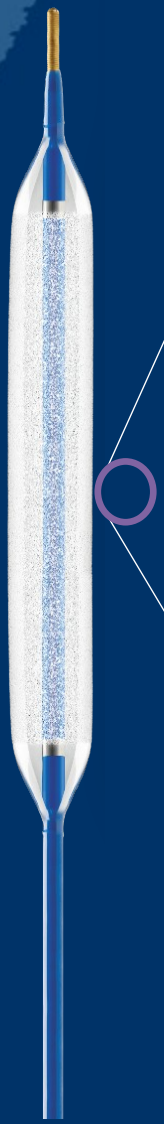
- [x] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

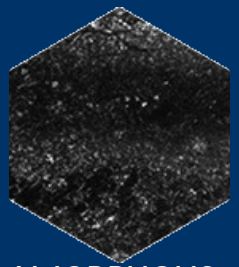
- [ ] I do not have any potential conflict of interest

Stellarex DCB Design

DCB design goals

- Limited drug dose
- Limited drug loss
- High drug transfer
- High deliverability
- Clinical performance





AMORPHOUS PACLITAXEL

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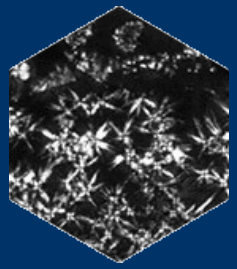

CRYSTALLINE PACLITAXEL

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- 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

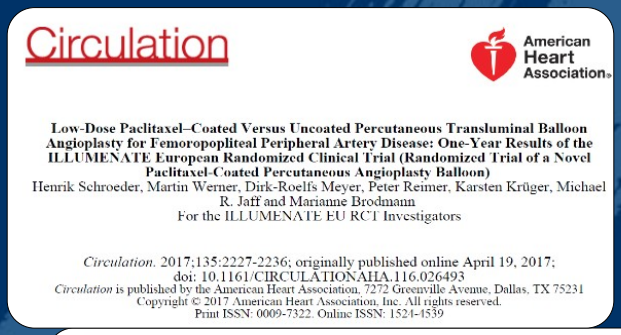
1. Mark, J. et al. Physical Properties of Polymers – Cambridge University Press 3rd edition, 2004
2. Data on file at Philips

Stellarex Clinical Program

- Stellarex DCB has been extensively evaluated in 9 studies
- ILLUMENATE trials met their Primary Safety/Efficacy Endpoints
- Over 3000 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	~2000	42	Europe	Follow Up

ILLUMENATE EU RCT & Pivotal


Circulation

American Heart Association

Low-Dose Paclitaxel–Coated Versus Uncoated Percutaneous Transluminal Balloon Angioplasty for Femoropopliteal Peripheral Artery Disease: One-Year Results of the ILLUMENATE European Randomized Clinical Trial (Randomized Trial of a Novel Paclitaxel-Coated Percutaneous Angioplasty Balloon)

Henrik Schroeder, Martin Werner, Dirk-Roelfs Meyer, Peter Reimer, Karsten Krüger, Michael R. Jaff and Marianne Brodmann
For the ILLUMENATE EU RCT Investigators

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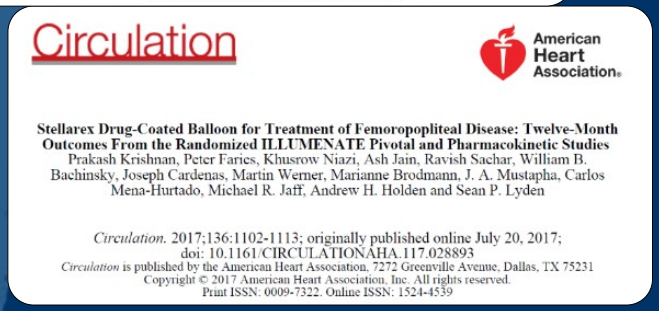
Circulation

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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- 2 robust RCT's with ~600 patients
- Similar design, same rigor
- 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

	ILLUMENATE EU RCT	ILLUMENATE Pivotal (IDE)
N Patients	**294**	**300**
Multicenter (N sites)	**18 (EU)**	**43 (US & EU)**
Enrollment	**Dec 2012 – Apr 2015**	**Dec 2012 – Apr 2015**
Follow Up	**5 years**	**5 Years**
Randomization	**3:1**	**2:1**
Pre-dilatation	**Mandatory**	
Duplex Core-lab	✓	
Angiographic Core-lab	✓	
100% Source Data Monitoring	✓	
Clinical Event Committee	✓	
Data Safety Monitoring	✓	

1. Schroeder H et al. Low-dose Paclitaxel-coated Versus Uncoated Percutaneous Transluminal Balloon Angioplasty for Femoropopliteal Peripheral Artery Disease: 1-year Results of the ILLUMENATE European Randomized Clinical Trial. Circulation. 2017 Apr 19. pii: CIRCULATIONAHA.116.026493
2. Krishnan P et al. Stellarex Drug-Coated Balloon for Treatment of Femoropopliteal Disease: Twelve-Month Outcomes From the Randomized ILLUMENATE Pivotal and Pharmacokinetic Studies. Circulation. 2017 Sep 19;136(12):1102-1113

Baseline Characteristics

ILLUMENATE EU RCT Data Set*

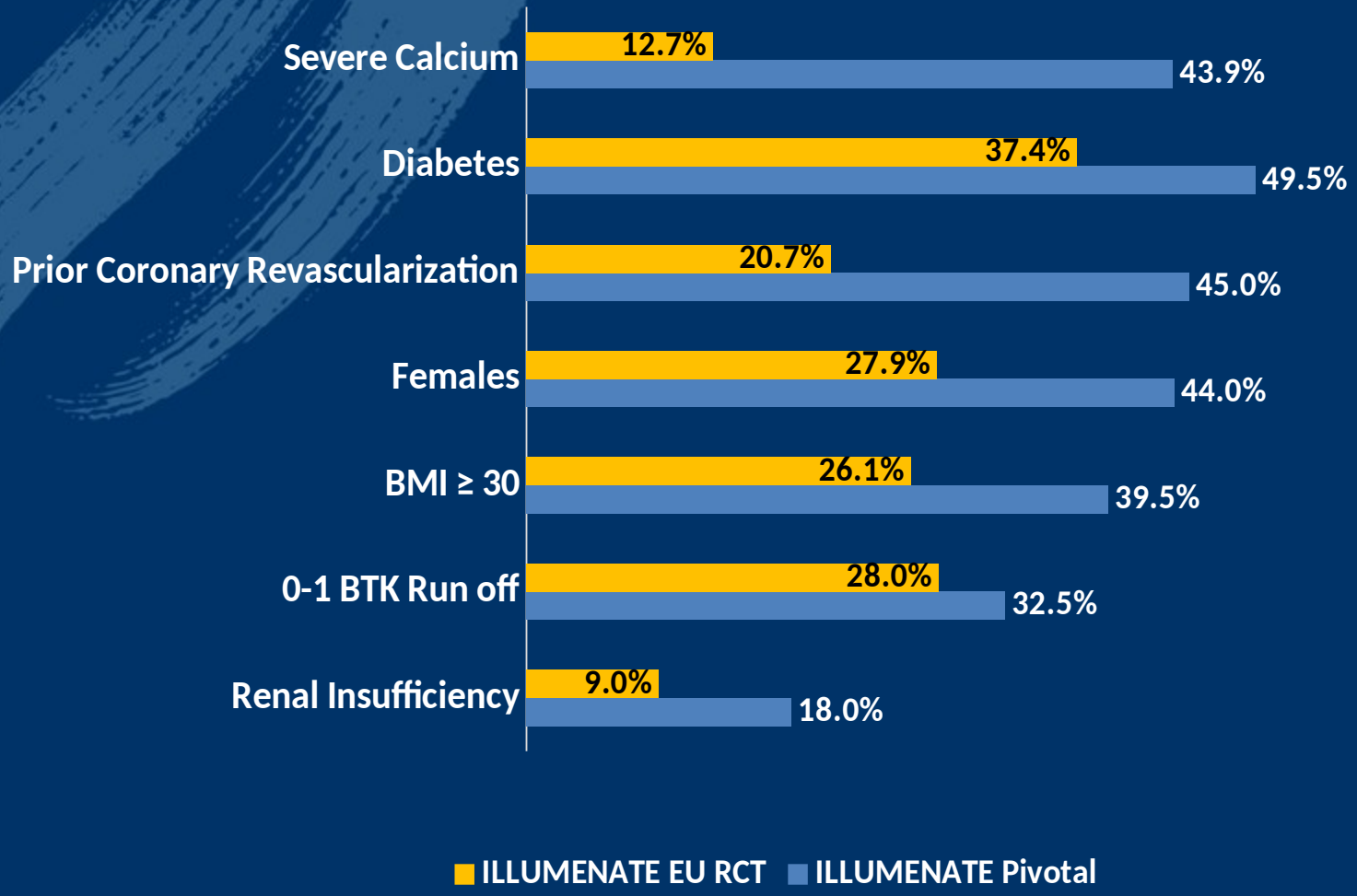
PATIENT CHARACTERISTICS	Stellarex	PTA	p
Age (years)	66.8 ± 9.2 (222)	69.0 ± 8.6 (72)	0.079
Female	27.9% (62/222)	31.9% (23/72)	0.514
Rutherford Clinical Category			0.525
2	15.4% (34/221)	21.1% (15/71)	
3	82.8% (183/221)	77.5% (55/71)	
4	1.8% (4/221)	1.4% (1/71)	
ABI	0.72 ± 0.21 (212)	0.69 ± 0.26 (68)	0.250
Hypertension	77.9% (173/222)	83.3% (60/72)	0.326
Hyperlipidemia	61.7% (137/222)	68.1% (49/72)	0.332
Previous or Current Smoker	89.2% (198/222)	83.3% (60/72)	
Diabetes	37.4% (83/222)	36.1% (26/72)	0.846
Renal Insufficiency	9.0% (20/222)	8.3% (6/72)	0.861
LESION CHARACTERISTICS	**Stellarex**	**PTA**	**p**
Lesion Length (cm)	7.2 ± 5.2 (250)	7.1 ± 5.3 (79)	0.878
Total Occlusion	19.2% (48/250)	19.0% (15/79)	0.967
Restenotic	7.9% (20/254)	10.1% (8/79)	0.529
Severe Calcification	12.7% (32/251)	10.1% (8/79)	0.533
Baseline Diameter Stenosis (%)	79.5% (250)	83.0% (79)	0.297

ILLUMENATE Pivotal Data Set**

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)	16.0% (16/100)	0.666
LESION 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

* Randomized Cohort IIT set ** Randomized Cohort IIT set

Higher patient complexities in ILLUMENATE Pivotal



Two Stellarex RCTs with no differences in All-Cause Mortality through 5 years

ILLUMENATE EU RCT

Vital Status Compliance
93.2% (274/294)

All Cause Mortality	DCB	PTA	p Value
12 months	2.8% (6/215)	1.5% (1/66)	1.000
24 months	7.5% (16/214)	4.6% (3/65)	0.578
36 months	11.3% (24/212)	9.2% (6/65)	0.707
48 months	17.7% (36/203)	14.1% (9/64)	0.494
60 months	**19.3% (40/207)**	**19.4% (13/67)**	**0.989**

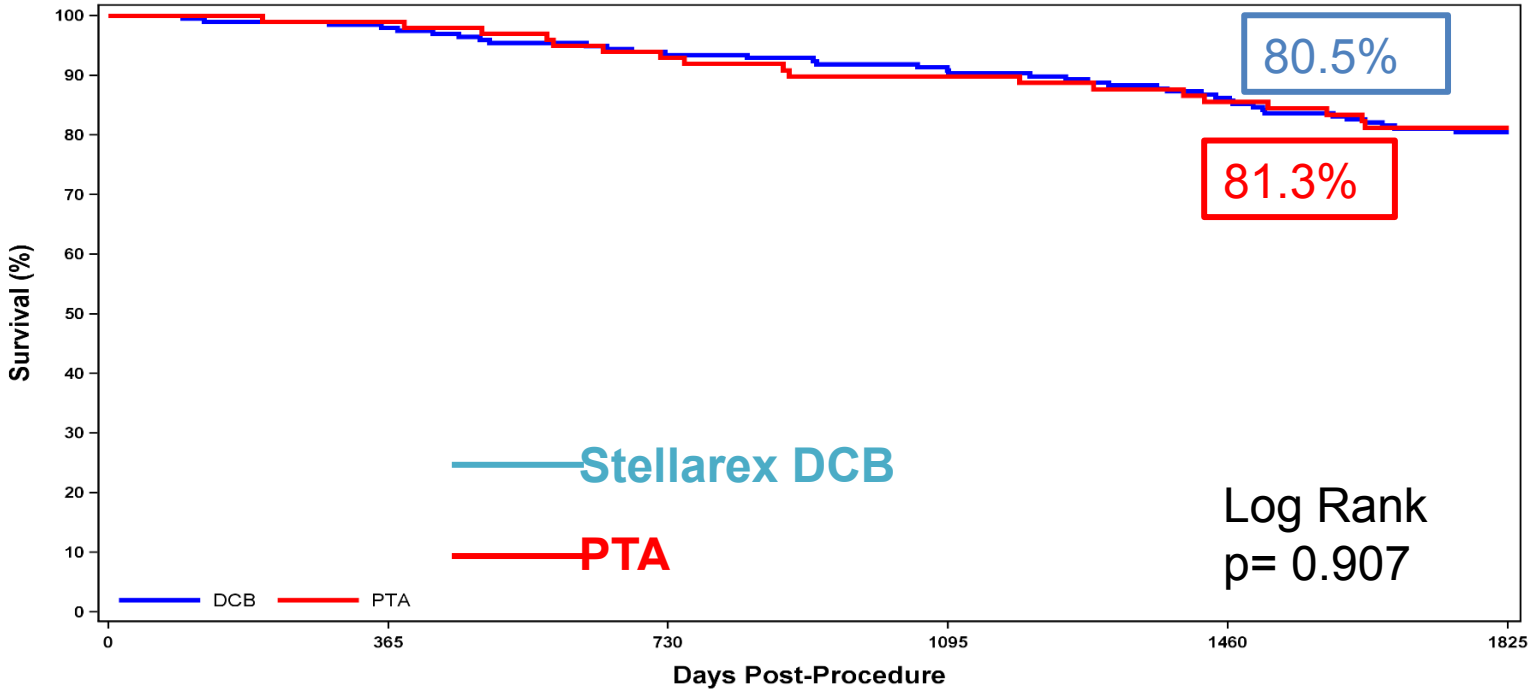
ILLUMENATE Pivotal

Vital Status Compliance
91.0% (273/300)

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
60 months	**21.2% (39/184)**	**20.2% (18/89)**	**0.853**

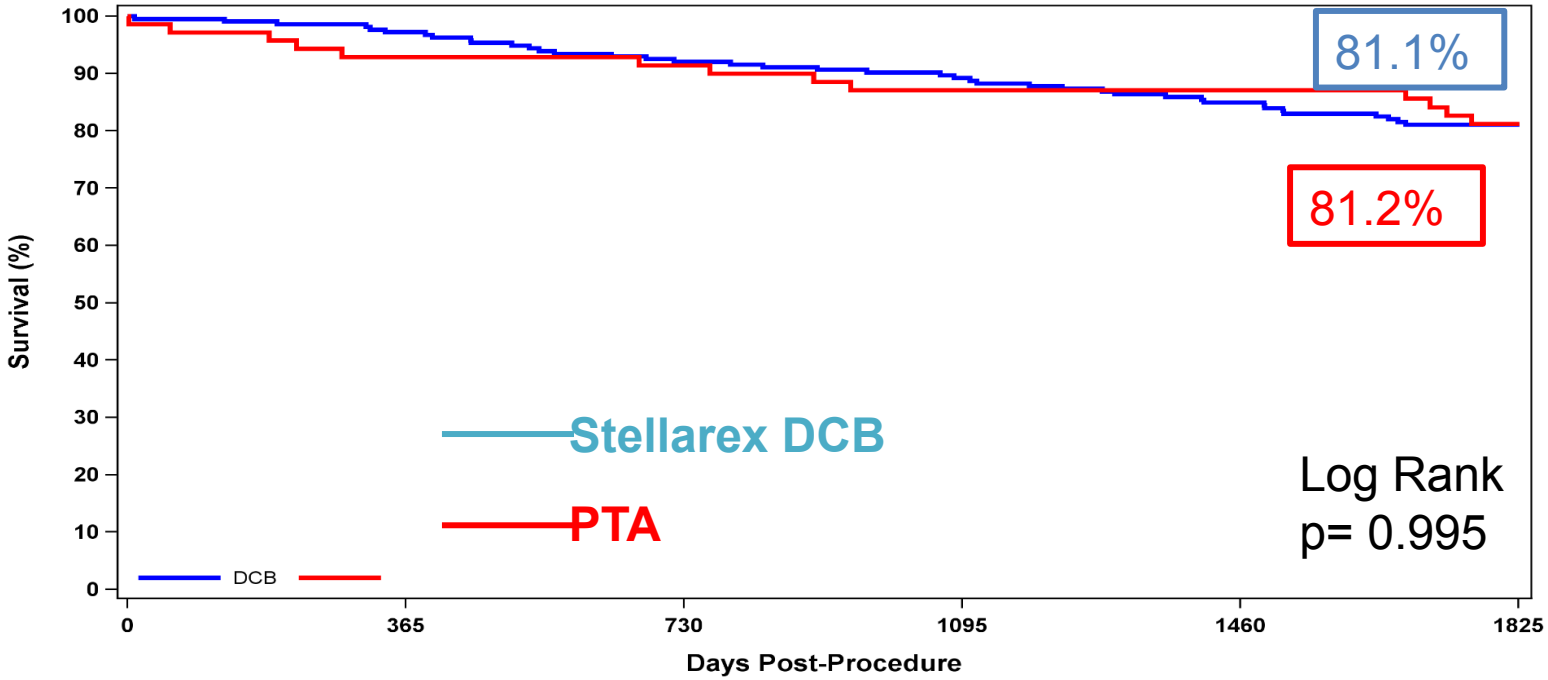
ILLUMENATE EU RCT & Pivotal: Post hoc vital status analysis

Pivotal RCT: Survival curves overlap through 5 years



DCB						
At Risk	199	194	184	178	167	62
Event	0	4	13	18	27	38
Survival (%)	100.0	98.0	93.4	90.9	86.3	80.5
95% CI (%)	--	[94.7, 99.2]	[89.0, 96.1]	[85.9, 94.2]	[80.6, 90.4]	[74.2, 85.4]
PTA						
At Risk	100	99	91	85	80	30
Event	0	1	7	10	14	18
Survival (%)	100.0	99.0	92.9	89.8	85.5	81.3
95% CI (%)	--	[93.1, 99.9]	[85.8, 96.6]	[81.9, 94.4]	[76.8, 91.2]	[71.9, 87.8]

EU RCT: Survival curves overlap through 5 years



DCB						
At Risk	220	208	196	189	177	112
Event	0	6	17	23	32	40
Survival (%)	100.0	97.2	92.1	89.2	84.9	81.1
95% CI (%)	--	[93.9, 98.7]	[87.5, 95.0]	[84.2, 92.7]	[79.4, 89.1]	[75.1, 85.8]
PTA						
At Risk	72	65	63	60	60	36
Event	0	5	6	9	9	13
Survival (%)	100.0	92.9	91.4	87.1	87.1	81.2
95% CI (%)	--	[83.8, 97.0]	[81.9, 96.1]	[76.7, 93.1]	[76.7, 93.1]	[69.8, 88.6]

Conclusions

- The 5-year data from two independent RCTs, ILLUMENATE Pivotal and EU RCT, build on the robust, consistent long-term data of the Stellarex program
- High vital status compliance for both RCTs: Over 90% of LTFU/Withdrawn patients found
- Survival curves of Stellarex DCB and PTA continue to overlap through 5 years with similar all-cause mortality rates, and are applicable within an extensive complex patient cohort
- Stellarex RCT data demonstrate comparable mortality rates between DCB and PTA cohorts at each time point through 5 years
- The ILLUMENATE RCTs present the strongest long-term safety data from an individual DCB
- Following the recent findings from SWEDEPAD and Voyager, these data further reinforce not only the long-term safety of Stellarex DCB, but DCBs as a class

Thank You! Stellarex Program: Sites & Investigators

ILLUMENATE EU RCT

294 subjects enrolled
18 EU sites

Dr. Henrik Schroeder :Jewish Hospital, Berlin

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

ILLUMENATE Pivotal IDE

300 subjects enrolled
43 US & EU sites

P. Faries, NY

K. Niazi, GA

A. Jain, CA

R. Sachar, NC

W. Bachinsky, PA

J. Cardenas, AZ

M. Werner, Vienna, Austria

M. Brodmann, Graz, Austria

C. Mena-Hurtado, CT

J. Mustapha/ L. Diaz, MI

J. Ricci, MI,

M. Khuddus, FL

W. Crowder, MS

M. Laiq Raja, TX

G. Ansel, OH

C. Joels, TN

J. Sandhu, PA

L. Lopez, IN

N. Farhat, OH

E. Kang, GA

C. Metzger, TN

J. Henretta, NC

C. Bosarge, FL

O. Rosales, TX

M. Shishehbor/ L. Kirksey, OH

G. Al-Khoury, PA

M. Goodwin, IL

J. Angle, VA

J. Park, TX

M. Mewissen, WI

E. Korngold, OR

P. Desai, NC

M. Ghani, OK

W. Miller, CO

C. Pollock, TN

D. Paolini, OH

D. Fry, IA

T. Gensler, VA

R. Kovach, NJ

G. Schultz, SD

G. Mayeda, CA

B. Katzen, FL

A. Nanjundappa, WV