Stellarex DCBs at 5 Years Data from the ILLUMENATE US And European RCTs

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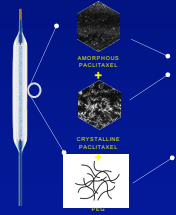
Disclosures

- Consultant: BD, Boston Scientific, Contego Medical, Cordis, Endologix, Inspire MD, Medtronic, Rapid Medical, Shockwave, Penumbra, Vivasure, Nectero, Reflow
- Stock options: Inspire MD and Centerline Biomedical, Reflow
- VIVA Physicians, Board Member
- Research Studies: Abbott, Endologix, Surmodics, W.L. Gore, Terumo Aortic, NIH, Boston Scientific, Merit, Contego Medical, Inspire MD, Reva Medical, Penumbra, Medalliance, Nectero

Stellarex DCB Design

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 DCB has been extensively evaluated in 7 SFA ATK studies
- ILLUMENATE trials consistently met their primary safety/efficacy endpoints
- >3000 patients treated with Stellarex in SFA 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	Closed
ILLUMENATE Pivotal	Pivotal	ATK	300	43	US/Europe	Closed
ILLUMENATE Global	Post Market	ATK	371	37	Europe, AUS, NZ	Closed
ILLUMENATE Global-BR	Labeling Expansion	ATK	129	26	Europe, AUS, NZ	Closed
SAVER	Real World Evidence	ATK/BTK	1960	60	Europe	Closed

ILLUMENATE EU RCT & Pivotal

2 robust RCT's with ~600 patients
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 Pivotal	ILLUMINATE EU RCT
N Patients	300	204
Multicenter (N sites)	43 (US & EU)	18 (EU)
Enrollment	June 2013 – July 2015	Dec 2012 – Apr 2015
Follow Up	5 Years (through PAS)	5 years
Randomization	2:1	2:1
Pre-dilatation	Mandatory	
Duplex Core-lab	✔	
Angiographic Core-lab	✔	
100% 1D Monitoring	✔	
Clinical Event Committee	✔	
Data Safety Monitoring	✔	

1. Schroder 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. Jun 6;135(23):2227-2236
2. Brodmann et al. Sustainable Antirestenosis Effect With a Low-Dose Drug-Coated Balloon. J Am Coll Cardiol Intv. 2018;11:2357-64
3. 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
4. Lyden et al. Six Mortality Signal with Stellarex Low-Dose Paclitaxel DCB: ILLUMENATE Pivotal 4-Year Outcomes. J Endovasc Ther. 2022 Dec;29(6):928-938
5. Lyden et al. Five-Year Independent Patient-Level Mortality Analysis of the Pooled ILLUMENATE Pivotal and EU Randomized Controlled Trials J Soc Cardiovasc Angiogr Interv. 2023 Jul 12;2(4):100534

Baseline Characteristics

ILLUMENATE EU RCT Data Set*

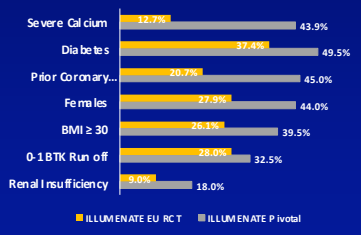
Patient Characteristics	Stellarex	PTA	P
Age (years)	66.8 ± 9.2 (222)	69.5 ± 8.8 (72)	0.079
Female	27.9% (62/222)	31.9% (23/72)	0.514
Rutherford Clinical Category			0.525
2	15.4% (34/221)	21.1% (15/71)	
3	82.8% (183/221)	77.5% (55/71)	
4	1.8% (4/221)	1.4% (1/71)	
ABI	0.72 ± 0.21 (212)	0.68 ± 0.26 (68)	0.250
Hypertension	77.3% (173/222)	83.3% (60/72)	0.326
Hyperlipidemia	61.7% (137/222)	68.1% (49/72)	0.332
Previous or Current Smoker	88.2% (196/222)	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)	66.1 ± 10.3 (200)	68.8 ± 9.6 (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)	0.79 ± 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)	8.9 ± 4.5 (190)	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	43.5% (87/168)	41.6% (41/100)	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



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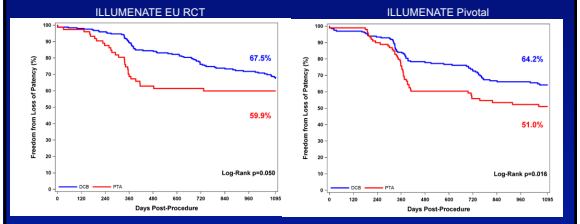
Significant Difference in Primary Patency between Stellarex DCB and PTA through Three Years



NCVH 2019 Scientific Sessions. S. Jay Mathews, MD "Stellarex in the Treatment of the SFA and Popliteal: Late-Breaking 3-Year Data"

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Two Stellarex RCTs with No Difference in All-Cause Mortality through Five Years

ILLUMENATE EU RCT[1]

Vital Status Compliance: 93.2%

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[1]

Vital Status Compliance: 94.3%

All Cause Mortality	DCB	PTA	P value
12 months	3.0% (6/199)	2.0% (2/100)	0.723
24 months	7.0% (14/199)	8.1% (8/99)	0.745
36 months	10.2% (20/197)	10.4% (10/96)	0.944
48 months	15.7% (31/197)	14.9% (14/94)	0.853
60 months	**20.6% (39/189)**	**20.2% (19/94)**	**0.934**

ILLUMENATE EU RCT & Pivotal: Post hoc analysis

1.J Soc Cardiovasc Angiogr Interv. 2023 Jul 12;2(4):100634

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Pooled Stellarex RCTs: No Difference in Crude All-Cause Mortality through Five Years

All Cause Mortality	DCB	PTA	P Value
12 months	2.2% (9/405)	1.2% (2/165)	0.5240
24 months	7.6% (29/383)	5.0% (8/159)	0.3516
36 months	10.8% (40/370)	10.9% (16/147)	>0.9999
48 months	17.0% (59/348)	16.4% (23/140)	>0.9999
60 months	**25.2% (80/317)**	**24.8% (32/129)**	**>0.9999**

ILLUMENATE EU RCT & Pivotal: Post hoc analysis

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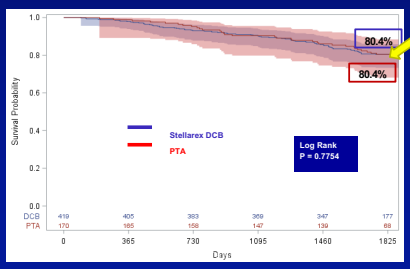
Pooled Stellarex RCTs: No Difference in Survival through Five Years



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Conclusions

- ILLUMENATE Pivotal and EU RCT all-cause mortality rates between Stellarex DCB and PTA continue to be similar out to five years
- Two Stellarex RCTs consistently show no statistically significant difference in long-term, all-cause mortality rates at each annual follow-up out to five years
- ILLUMENATE RCT data show favorable overall safety and efficacy of the Stellarex low-dose paclitaxel DCB, even within an extensive complex patient cohort
- Stellarex is the only low-dose DCB supported by five-year randomized data with favorable safety and efficacy to date

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