Long-Term Safety of Stellarex DCB Across Two ILLUMENATE RCTs: Five-Year Results from a Patient-Level Meta-Analysis

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Background

- A summary-level meta-analysis reported a long-term safety signal in patients treated with paclitaxel-coated devices for PAD
- The purpose of this study was to assess the long-term five-year safety of the Stellarex drug-coated balloon (DCB) compared with percutaneous transluminal angioplasty (PTA) for symptomatic femoropopliteal peripheral artery disease (PAD) in a patient-level meta-analysis of the ILLUMENATE randomized controlled trials (RCTs)

Methodology and Design

- Individual patient-level meta-analysis of two RCTs conducted by a 3rd party
  - ILLUMENATE Pivotal and ILLUMENATE EU RCT
- Pre-specified, systematic assessment of mortality for patients treated with Stellarex DCB for ATK lesions
- Test for homogeneity (I^2 = 0%)
- Meta analysis to compare mortality through five years between Stellarex DCB and control (PTA) cohorts (N = 589)
  - DCB: 419 and PTA: 170
- Both studies included independent AE adjudication by CECs
- Over 90% vital status compliance

Results

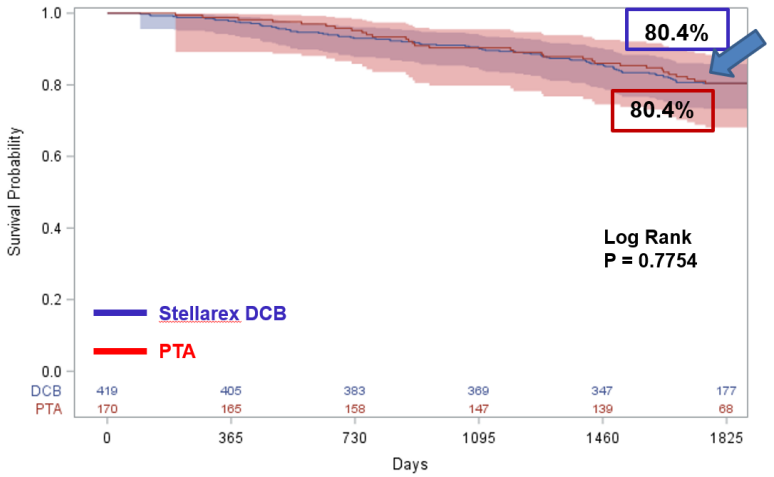
Pooled RCT Baseline Characteristics

Patient Characteristics	DCB N=419	PTA N=170	P value (for DCB RCTs vs. PTA RCTs)*
Median Age [IQR] (years)	67	69	**0.02**
Sex			
Men	64.2%(269)	65.3% (111)	**0.85**
Women	35.8% (150)	34.7% (59)	
Hypertension	85.2% (357)	89.4% (152)	**0.19**
Hyperlipidemia	74.2% (311)	81.2% (138)	**0.09**
Myocardial infarction	16.9% (71)	20.0% (34)	**0.41**
Angina	10.7% (45)	14.7% (25)	**0.21**
Congestive heart failure	9.1% (38)	8.2% (14)	**0.87**
Renal insufficiency	13.4% (56)	13.5% (23)	**>.0.99**
Chronic obstructive pulmonary disease	16.0% (67)	16.5% (28)	**0.90**
Diabetes	43.0% (180)	45.3% (77)	**0.65**
Prior Peripheral Revascularization	32.2% (135)	36.5% (62)	**0.34**
Smoking	86.6% (363)	78.8% (134)	**0.02**
Calcification	54.4% (227)	57.1% (97)	0.58

*P values were calculated using two-tailed Fisher's exact tests

Results

Pooled Stellarex RCTs: No Difference in Survival through Five Years



ILLUMENATE EU RCT & Pivotal: Post hoc analysis

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

Results

Neither Paclitaxel, Nor Paclitaxel Dose, is a Predictor of Death in Stellarex Analysis

Multivariate Cox Proportional Hazards Model for Mortality

Covariate	Hazard Ratio (95% CI)	P value
With paclitaxel exposure forced into the model		
Renal insufficiency	2.380 (1.540, 3.677)	<0.0001
Age	1.053 (1.031, 1.075)	<0.0001
Length	1.005 (1.001, 1.009)	0.0069
Reference vessel diameter	1.250 (1.022, 1.527)	0.0295
Paclitaxel	**1.149 (0.761, 1.734)**	**0.5085**
With paclitaxel dose forced into the model		
Renal insufficiency	2.390 (1.546, 3.695)	<0.0001
Age	1.053 (1.031, 1.075)	<0.0001
Length	1.005 (1.001, 1.009)	0.0258
Reference vessel diameter	1.244 (1.018, 1.520)	0.0325
Paclitaxel dose (mg)	**1.027 (0.959, 1.100)**	**0.4423**

ILLUMENATE EU RCT & Pivotal: Post hoc analysis

Conclusions

- Stellarex DCB continues to consistently demonstrate no difference in mortality compared with PTA cohort year-over-year through five years both within individual RCTs and pooled analysis
- This patient level meta-analysis represents the highest level of evidence to determine long-term mortality of a single DCB
  - Largest homogenous prospective RCT dataset to show no difference in mortality[1,2]
  - No evidence of paclitaxel (exposure or dose) as a predictor of mortality
- This independent meta-analysis confirms and reinforces the consistent and durable long-term safety profile of low dose Stellarex DCB in final five-year dataset

1. Katsanos et al. Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *JAHA*. 2018 Dec 8.
2. Schneider et al. Paclitaxel exposure: Long-term safety and effectiveness of a drug-coated balloon for claudication in pooled randomized trials. *Catheter Cardiovasc Interv*. Aug 24 2020.