ILLUMENATE Trial Update: 4-Year ILLUMENATE Global Stellarex DCB Data

Andrew Holden, MBChB, FRANZCR, EBIR, ONZM

Director of Interventional Radiology

Auckland Hospital

Auckland, New Zealand

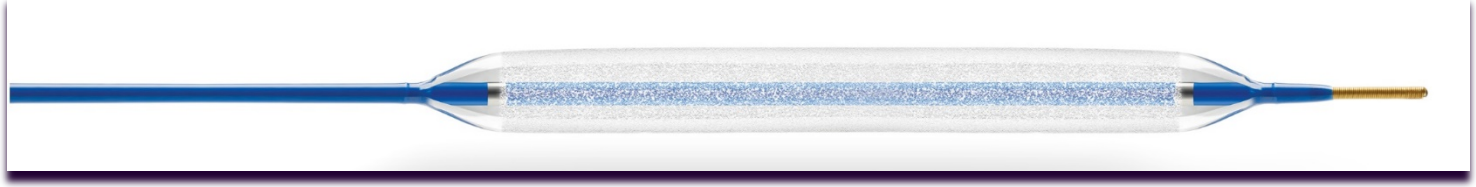
On behalf of Thomas Zeller MD,, Prof Frank Vermassen, Dr. Marianne Brodmann and the ILLUMENATE Global Investigators

Disclosures

- Dr Andrew Holden is a Clinical Investigator in the Illumenate Trials and Medical Advisory board Member for Philips
- No other relevant disclosures

Stellarex DCB Technology

Designed to perform safely with a low paclitaxel dose of 2µg/mm2 by enhancing transfer efficiency and limiting distal embolization[1,2] to minimize the effect on non-target tissues



- **Hybrid formulation: Amorphous + Crystalline Paclitaxel[3]**
  - Coating stability, prompt + sustained drug release
- **Polyethylene Glycol (PEG) excipient[3,4]**
  - High molecular weight → coating elasticity / stability
  - High affinity to hydroxyl apatite (Hap) → limited wash-out in presence of Calcium

1. Torii S, Jinnouchi H, Sakamoto A, Romero ME, Kolodgie FD, Virmani R, Finn AV. Comparison of Biologic Effect and Particulate Embolization after Femoral Artery Treatment with Three Drug-Coated Balloons in Healthy Swine Model. J Vasc Interv Radiol. 2019 Jan;30(1):103-109
2. Raphaël Coscas - Pre-dinical and histology findings from different DCBs LINC 2019 oral presentation
3. James Mark KN, William Graessley, Leo Mandelkern, Edward Samulski, Jack Koenig, George Wignall. Physical Properties of Polymers. Third ed. Cambridge, United Kingdom: Cambridge University Press 2004
4. Tanford C. Physical Chemistry of Macromolecules: John Wiley and Sons, 1961

Background: Stellarex Clinical Program

- All ILLUMENATE trials met their Primary Safety Endpoints with significantly lower MAE rates (either individual or composite) vs. either PG or PTA control arms
- Over 2300 patients treated with Stellarex DCB in ATK trials with independent CEC for AE adjudications
- No device/procedure-related mortality

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	~1900	42	Europe	Enrolling
ILLUMENATE BTK PM	Post Market	BTK	30	9	Europe	Enrolling
ILLUMENATE BTK IDE	Label expansion	BTK	79	17	US/Europe	Enrolling

ILLUMENATE Global Trial

- Prospective, OUS, multi-center, single-arm study
- Study device: Stellarex DCB:
- Patients followed for 5 years (4 and 5 year FU are phone call visits)
- Monitoring with 100% source data verification
- Same rigorous data collection process as RCT's , independent adjudication by:
  - ✓ Angiographic Core Laboratory
  - ✓ Duplex Ultrasound Core Laboratory
  - ✓ Clinical Events Committee
  - ✓ Data Safety Monitoring Board

ILLUMENATE Global Study Overview

Study Objective: Assess safety and performance of the Stellarex DCB in the SFA and/or popliteal arteries

Primary Safety Endpoint: Freedom from device- and procedure-related death through 30 days and freedom from target limb major amputation and CD-TLR through 12 months

Primary Effectiveness Endpoint: Primary patency at 12 months

Inclusion Criteria

- Rutherford class 2, 3 or 4
- SFA and/or popliteal (down to trifurcation)
- At least one patent run-off below-the-knee
- 1 or 2 target lesion(s) with cumulative length ≤ 20 cm
- Target vessel reference diameter 4-6 mm

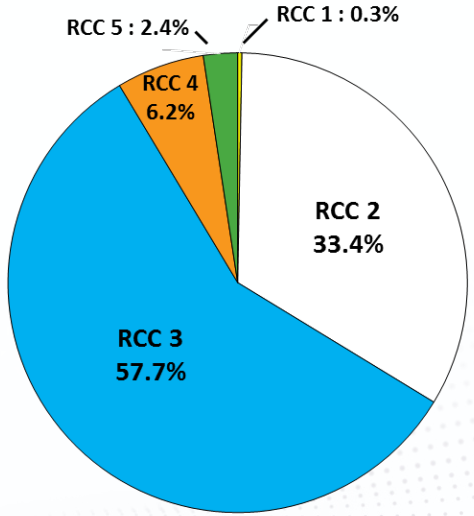
Exclusion Criteria

- Acute or sub-acute thrombus in target vessel
- Significant inflow disease not successfully treated
- In-stent restenosis
- Severe calcification that precludes adequate PTA treatment
- Use of adjunctive therapies (i.e. debulking or plaque incision)

ILLUMENATE Global: Baseline Patient Characteristics

Patient Characteristics	Stellarex N=371
Age (years)	68.2 ± 9.3 (371)
Male	73.0% (271/371)
Diabetes	33.7% (125/371)
Body Mass Index	27.0 ± 4.2 (368)
Hypertension	79.5% (295/371)
Hyperlipidemia	74.7% (277/371)
Previous or Current Smoker	81.9% (304/371)
Previous Coronary Revasc	33.4% (124/371)
ABI	0.70 ± 0.20 (347)
Renal Insufficiency	7.0% (26/371)
Previous intervention of lower limb	42.3% (157/371)

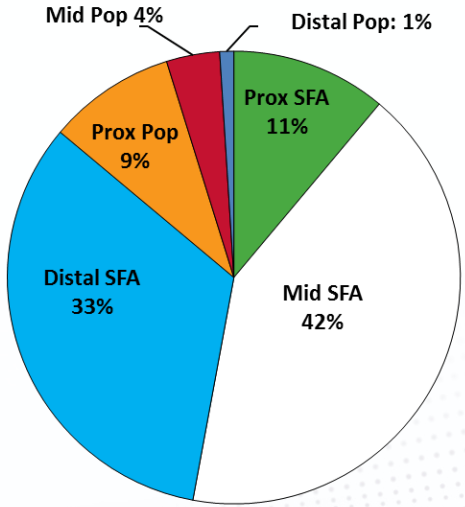
Baseline Rutherford Classes



ILLUMENATE Global: Baseline Angiographic Characteristics

Lesion Characteristics (Core Lab Assessment)	Stellarex N=417
De novo[1]	94.0% (392/417)
Lesion Length (cm)	7.5 ± 5.3 (413)
Total occlusions	31.3% (129/412)
Calcification	
None/Mild	43.0% (173/402)
Moderate	16.2% (65/402)
Severe[2]	40.8% (164/402)
Minimum lumen diameter (mm)	0.96 ± 0.87 (412)
Reference vessel diameter (mm)	4.87 ± 0.84 (412)
Baseline diameter stenosis (%)	80.3 ± 17.4 (412)
Eccentric Lesion	60.4% (249/412)

Lesion Locations



1. Site reported
2. *Severe calcification*: Radiopacities noted on both sides of the arterial wall and extending more than one cm of length prior to contrast injection or digital subtraction.

ILLUMENATE Global: Procedural Characteristics

Lesion Characteristics (Site/Core Lab Assessments)	N=417 Lesions
Pre-dilatation[1]	98.1% (409/417)
Post-dilatation[1]	28.3% (118/417)
Provisional stent[1]	31.3% (129/412)
Stent Due to Dissection[1]	8.4% (35/417)
Post-DCB Dissections	
Grade D	19.7% (81/416)
Flow-limiting (Grade E or F)	0.2% (1/416)
Post-DCB MLD (mm)	3.43 ± 0.80 (407)
Post-procedure Diameter Stenosis (%)	24.7 ± 11.8 (409)
Lesion Success[2]	97.6% (399/409)

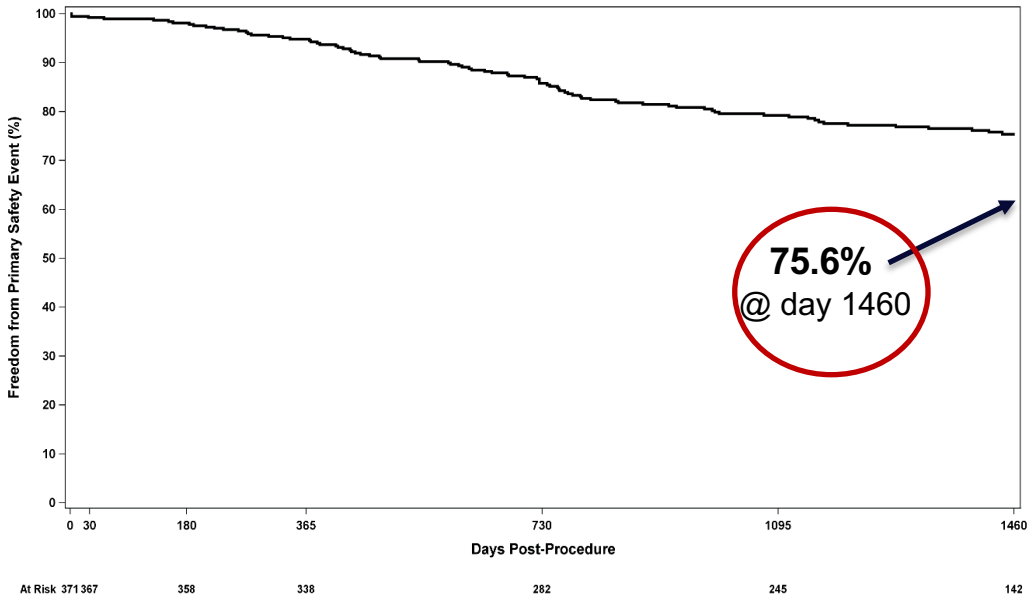
1. Site-reported data
2. Lesion success- Final residual %DS ≤ 50% (per angiographic core lab), after using the DCB

ILLUMENATE Global: 4 Year Key Safety Endpoints

Key Safety Endpoints @ 48 Months*	Stellarex N=371
Primary Safety Endpoint	77.9% (289)
Device- or procedure-related death	0
Clinically-driven TLR**	21.8% (66)
Major target limb amputation	0.8% (3)
All-Cause Mortality	8.1% (30)

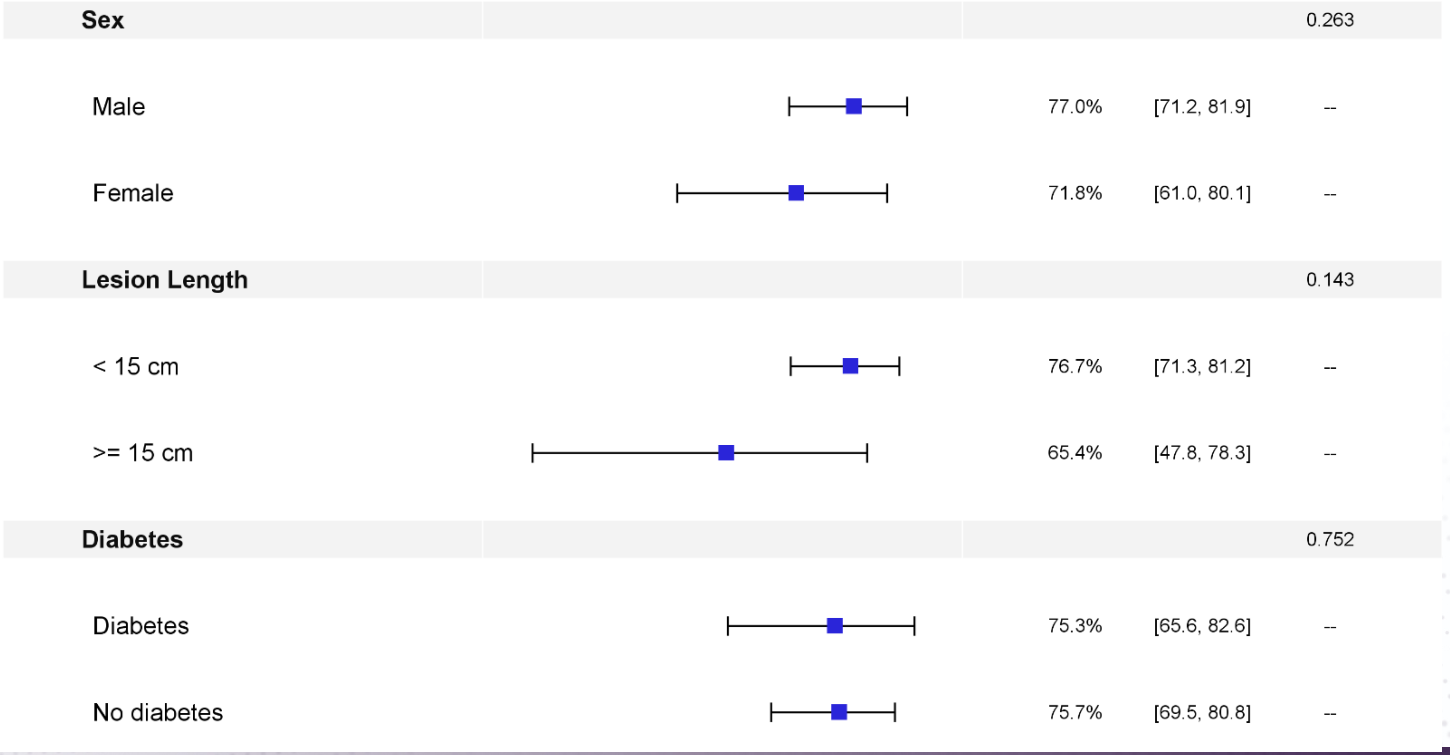
*4 Year follow up determined by phone call .Through day 1460, The denominator includes subjects with an event or those without an event having follow-up on or past the opening of the f/u window.
** Freedom from device and procedure-related death through 30 days post-procedure and freedom from target limb major amputation and clinically-driven target lesion revascularization (CD-TLR) through 48 months post-procedure.

ILLUMENATE Global: KM Freedom from CD-TLR* through 4 years

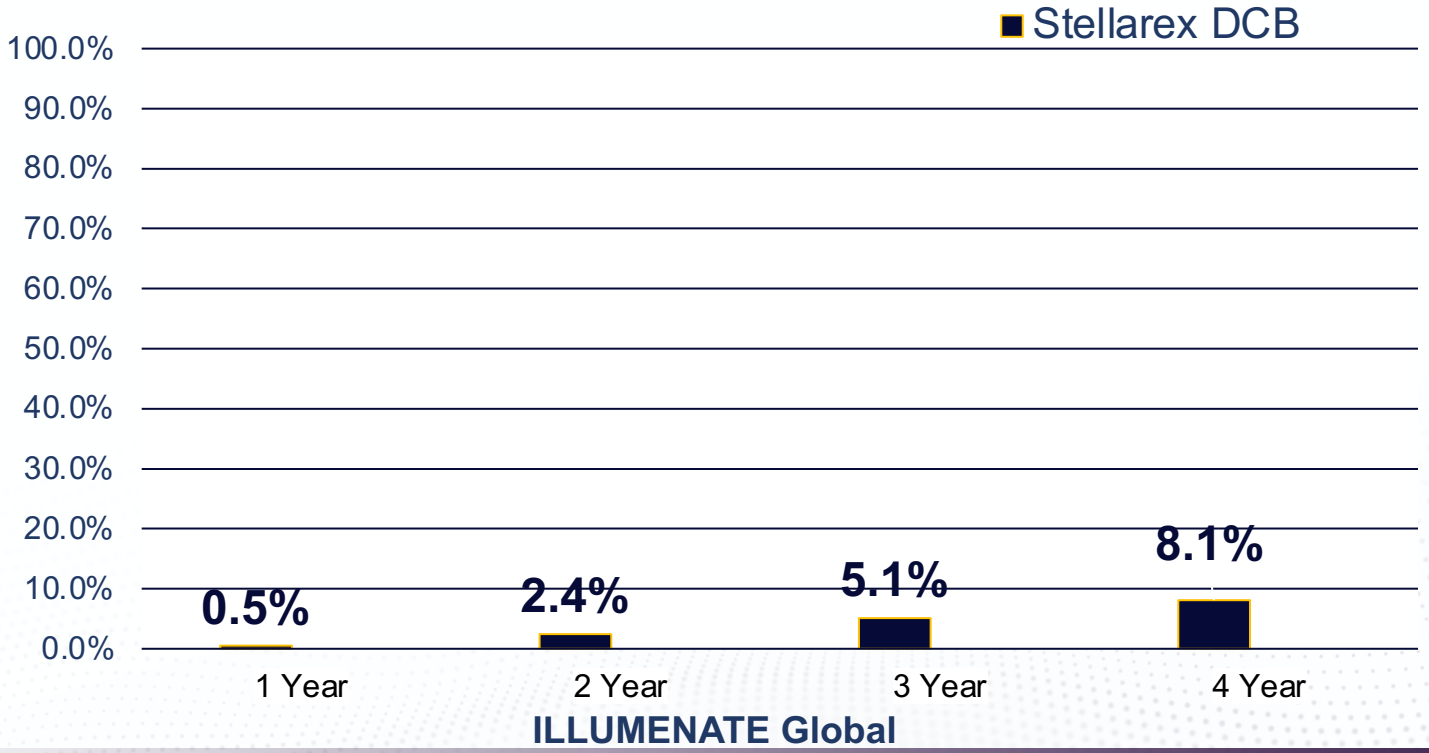


*Defined as revascularization associated with PSVR ≥ 2.5 or >50% stenosis via angiogram and worsening of RCC by more than 1 or ABI decrease of >0.15 from the maximum early post-procedure level, that is clearly referable to the target lesion by Clinical Events Committee Adjudication

Subgroup Analysis: KM Freedom from CD-TLR through 4 years: No difference in prespecified cohorts



ILLUMENATE Global: Stellarex DCB All-Cause Mortality through 4 Years



ILLUMENATE Global: Conclusions

- ILLUMENATE Global builds on the ILLUMENATE RCT program with a rigorous study on an expanded population
- 4 yr ILLUMENATE Global data shows favorable safety and efficacy consistent with the ILLUMENATE RCTs
- 4 yr ILLUMENATE Global data demonstrates similar efficacy in prespecified cohorts including gender and diabetics
- The ILLUMENATE Global study supports durable long-term outcomes with the Stellarex DCB and is applicable to a complex population

Thank you

ILLUMENATE Global Investigators!