Stellarex DCB in the SAVER Registry: Complex and BTK cohort analysis

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Disclosure

Speaker name:

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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 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-clinical 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

Stellarex Clinical Program

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	45	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

SAVER: Stellarex Vascular e-Registry

ClinicalTrials.gov Identifier: NCT02769273

Objective	Assess safety and efficacy of Stellarex DCB use in superficial femoral, popliteal, and/or infra-popliteal arteries in a broad, real-world, claudicant or critical limb ischemia patient population
Design	• Multi-center European • Imaging Core lab* • External Monitoring • Clinical Event Committee adjudication • Patient Follow up to 3 years • 12M visit (not mandated by protocol)**

*Imaging cohorts for pre-defined subsets: CTO, ISR, long lesions, Ca++
**Per institution's standard practice

SAVER: Eligibility Criteria and Primary Endpoints

Patients

- Rutherford 2-3-4-5-6 Single limb or bilateral
- Single or multiple lesions
- Fem-pop and/or BTK
- Calcium of any grade / severity
- With or without pre-dilation
- Lesion pre / post-treatment at operator's discretion

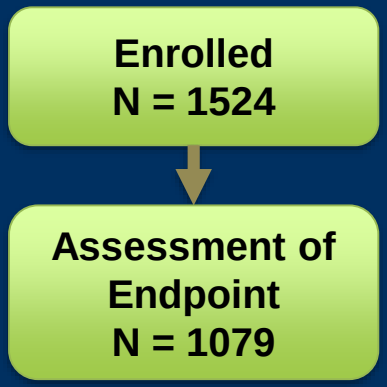
Cohorts and Endpoints

- Cohort 1: Rutherford 2 - 3
  - **Safety:** Freedom from 30-day device and procedure related death and freedom from 12-month target limb major amputation and CD-TLR
  - **Efficacy:** Freedom from 12-month CD-TLR
- Cohort 2: Rutherford 4 - 6
  - **Safety:** Freedom from Composite MALE and perioperative death through 30 days
  - **Efficacy:** Freedom from 6-month CD-TLR

Post hoc Analysis of Complex Patients: ATK Cohort in the SAVER Registry

Objective: To assess the 12-month safety and efficacy outcomes after DCB treatment for complex patients/lesions

Eligible Patients	Symptomatic stenosis of the SFA/Pop treated with the Stellarex OTW DCB
Complex Patients (N=981)	1 or more of the following: • Diabetic • Long lesion (>150mm) • Severe Calcification • Total Occlusion (CTO)



01 Feb 2016 through 31 Jan 2019

Complex ATK Cohort: Baseline Characteristics

Patient Characteristics	All Comers (N=1524 patients)
Age (years)	70.3 ± 9.9 (1076)
Male	64.8% (985/1521)
Hypertension	79.0% (1148/1454)
Hyperlipidemia	65.5% (942/1439)
Previous Intervention of the Lower Limb	52.4% (742/1415)
Previous Intervention of the Study Limb	38.6% (544/1408)
Renal Insufficiency	5.3% (75/1428)
Diabetes	**34.9% (507/1453)**
Lesion Characteristics	**All Comers (N=1789 lesions)**
CTO	**28.4% (481/1692)**
Long Lesions (>150 mm)	**19.1% (341/1786)**
Mean Lesion Length (mm)	100.7 ± 81.9
Severe Calcification	**17.5% (243/1388)**

64.3% (981/1524) of patients had at least 1 or more complex factor

ATK Cohort: Key Study Endpoints

12 Month Endpoints	All Comers	Complex Patients
CD-TLR	11.3% (122/1079)	11.5% (82/714)
Primary Safety Endpoint*	11.6% (125/1080)	11.9% (85/715)
Major Amputation	0.7% (7/1068)	0.7% (5/708)
All Cause Mortality	3.8% (42/1096)	4.5% (33/729)
Cardiovascular Death	1.8% (19/1076)	2.0% (14/713)

***Primary Safety Endpoint:** Defined as the 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 12 months post-procedure

ATK Complex Cohort: No Statistical Difference in Key Study Endpoints for Severe Calcium Lesions

12 Month Endpoints	Non Severely Calcified	Severe Calcium	p-Value
CD-TLR	8.8% (32/363)	12.9% (19/147)	0.161
Primary Safety Endpoint*	9.1% (33/364)	12.9% (19/147)	0.191
All Cause Mortality	3.5% (13/370)	5.4% (8/149)	0.332
Major Amputation	0.3% (1/363)	1.4% (2/145)	0.197

***Primary Safety Endpoint:** Defined as the 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 12 months post-procedure

BTK Cohort Interim Analysis: Baseline Characteristics

Enrolled through Dec 2019
N = 69 Patients

Patient Characteristics	Stellarex BTK N=69 patients
Female	17.4% (12/69)
Rutherford Clinical Category	
2	2.9% (2/69)
3	21.7% (15/69)
4	1.4% (1/69)
5	71.0% (49/69)
6	2.9% (2/69)
Hypertension	91.2% (62/68)
Hyperlipidemia	70.8% (46/65)
Diabetes	70.1% (47/67)
Renal Insufficiency	9.4% (6/64)

Patient Characteristics	N=92 Lesions
Lesion Length (cm)	78.1 ± 73.0 (92)
Total Occlusion	34.1% (30/88)
Restenotic	12.1% (11/91)
Severe Calcification	24.0% (6/25)
Baseline Diameter Stenosis (%)	91.2 ± 9.8 (91)

BTK Cohort: Key Procedural Characteristics

Procedural Success	N=92 Lesions
Lesion success*	**98.9% (88/89)**
Procedural Complications	**N=92 Lesions**
Dissection	4.3% (4/92)
All-Cause Mortality	0.0% (0/91)
Significant Distal Embolization	0.0% (0/91)
Thrombosis of the Target Vessel	0.0% (0/91)

* Final % Diameter stenosis<50%

BTK Cohort: Key Clinical Endpoints (Interim Analysis)

Safety at 30 Days	N=40 patients
Primary Safety*	0% (0/40)
All-Cause Mortality	2.5% (1/40)
Cardiovascular Mortality	2.5% (1/40)
Major Amputation	0.0% (0/39)
Efficacy at 6 Months	**N=39 patients**
CD-TLR	5.1% (2/39)

* Freedom from Composite MALE and POD through 30 days

Conclusions

- The Stellarex clinical program includes large datasets of complex patients treated with Stellarex DCB including SAVER
- SAVER demonstrated excellent key efficacy and safety endpoints in patients treated with Stellarex DCB which are also reflected in the complex cohort
- Interim analysis of SAVER BTK patients also demonstrates high procedural success with low rate of complications
- SAVER reinforces the safety and effectiveness profile for Stellarex in a real-world patient population including BTK patients

Thank You!

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