The LUTONIX Japan Femoropopliteal Post-Market Surveillance Trial: 6-Month Results

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Disclosure

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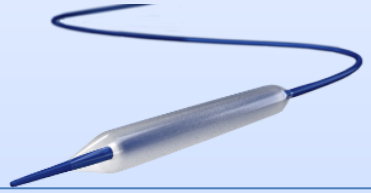
I have the following potential conflicts of interest to report:

- ☐ 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

Japan LUTONIX Study: Design & Overview

Study Design	Prospective, multi-center, single-arm study (no concurrent control)
Study Device	LUTONIX® 035 Drug Coated PTA Dilatation Catheter Active Drug: Paclitaxel (2 µg/mm2) Carrier: Polysorbate and sorbitol 
Objective	Evaluate the LUTONIX® 035 DCB (SFA-popliteal use) in a real-world setting compared to a performance goal derived from the randomized, controlled LEVANT Japan study
Primary Endpoint	Primary patency at 6 and 12 months
Number of Subjects/Sites	352 subjects 28 sites (Japan)
Data Analysis	Angiographic and DUS assessment by an independent Core Laboratory
Follow-up	Current Analysis: 6 months Ongoing through 12 months

Japan LUTONIX Study Criteria

Key Inclusion Criteria

- De novo or restenotic lesion(s) in the superficial femoral or popliteal artery
- Reference vessel diameter: ≥4 mm and ≤6 mm
- Lesion length: Single lesion or multiple lesions ≤15 cm
- Residual stenosis of <50% after pre-dilatation with uncoated balloon

Key Exclusion Criteria

- Severely calcified lesions not treatable with DCB alone
- In-stent re-stenosis
- Severe dissection (≥ Grade D*)
- Potential hypersensitivity to paclitaxel, the raw materials of the base angioplasty balloon, or contrast media
- Patients contraindicated for antithrombotic therapy

*National Heart, Lung and Blood Institute dissection classification

Japan LUTONIX Study Sites

28 Investigative Study Sites

Investigative Site	City, Prefecture
Kansai Rosai Hospital	Amagasaki, Hyogo
Tokeidai Memorial Hospital	Sapporo, Hokkaido
Morinomiya Hospital	Osaka, Osaka
Kishiwada Tokushukai Hospital	Kishiwada, Osaka,
Sendai Kosei Hospital	Sendai, Miyagi
Nara Medical University	Kashihara, Nara
Toho University Ohashi Medical Center	Meguro-ku, Tokyo
Fukuoka Sanno Hospital	Fukuoka, Fukuoka
Kasukabe Chuo General Hospital	Kasukabe, Saitama
Takatsu General Hospital	Kawasaki, Kanagawa
Kyoto Second Red Cross Hospital	Kyoto, Kyoto
Kyoto Prefectural University of Medicine	Kyoto, Kyoto
Saiseikai Yokohamashi Tobu Hospital	Yokohama, Kanagawa
Sakurabashi Watanabe Hospital	Osaka, Osaka

Investigative Site	City, Prefecture
Kobe University Hospital	Kobe, Hyogo
Kokura Kinen Hospital	Kitakyusyu, Fukuoka
Shonan Kamakura General Hospital	Kamakura, Kanagawa
Miyazaki Medical Association Hospital	Miyazaki, Miyazaki
Kakogawa Central City Hospital	Kakogawa, Hyogo
Osaka Saiseikai Nakatsu Hospital	Osaka, Osaka
Iwaki City Medical Center	Iwaki, Fukushima
Ota Memorial Hospital	Ota, Gunma
Shin Koga Hospital	Kurume, Fukuoka
Tokyo Saiseikai Central Hospital	Minato-ku, Tokyo
Kyoto Katsura Hospital	Kyoto, Kyoto
Matsuyama Red Cross Hospital	Mastuyama, Ehime
Omihachiman Community Medical Center	Omihachiman, Shiga
Chikamori Hospital	Kochi, Kochi

Japan LUTONIX Study: Patient Demographics

	Japan Lutonix Group
Number of Patients	352
Male/Female, %	72.2/27.8
Mean Age, years ± SD	73.9 ± 8.2
Mean Weight, kg ± SD	58.5 ± 10.9
Mean BMI, kg/m^2 ± SD	22.7 ± 3.4
Rutherford Classification, % (n)	
Class 2	26.7 (94)
Class 3	40.9 (144)
Class 4	7.4 (26)
Class 5-6	11.6 (41)
ABI (target limb), mean ± SD	0.71 ± 0.17

Japan LUTONIX Study: Patient Medical History

	Japan Lutonix Group
Number of Patients	352
Medical History/Risk Factors, % (n)	
Hypertension	80.1 (282)
Dyslipidemia/Hypercholesterolemia	58.8 (207)
Coronary Artery Disease	52.0 (183)
Smoker	68.5 (241)
Current	19.3 (68)
Diabetes Mellitus	61.1 (215)
Chronic Renal Failure	41.2 (145)
Hemodialysis	27.0 (95)

Japan LUTONIX Study: Lesion Characteristics

	Japan Lutonix Group
Number of Lesions*	354
Lesion Location, % (n)*	
Superficial Femoral Artery	88.4 (313)
Popliteal Artery	11.6 (41)
De Novo Stenosis/Restenosis (non-stented), %	90.4/9.6
TASC Classification, % (n)*	
TASC A	45.6 (156)
TASC B	52.1 (178)
TASC C	2.3 (8)
Calcification, % (n/N)*	64.8 (223)
Severe Calcification^	30.2 (104)
Chronic Total Occlusion, % (n/N)*	16.7 (56)
Mean Total Lesion Length (per patient), mm ± SD*	94.1 ± 46.9
Pre-Procedure % Diameter Stenosis (per patient), mean ± SD*	70.1 ± 19.4

*Evaluated per lesion by the Core Laboratory unless indicated

^Bilateral or circumferential calcification >5cm in length or >50% of lesion length

Japan LUTONIX Study: Procedural Data

	Japan Lutonix Group
Number of Drug-Coated Balloons Used	423
Balloon Transit Time < 30 seconds, % (n)	94.8 (401)
Balloon Inflation Time ≥ 120 seconds, % (n)	98.4 (416)
Balloon Inflation Pressure ≥ Nominal Pressure, % (n)	98.6 (417)
Final Angiographic Procedural Data*	
Total Treatment Length, mm ± SD	131.9 ± 45.9
% Diameter Stenosis, mean ± SD	23.0 ± 12.7
Vessel Runoff, % (n)	
1 Vessel	34.9 (123)
2 Vessel	32.7 (115)
3 Vessel	14.8 (52)
Provisional (Bailout) Stent Placement, % (n)	0.9 (3)

*Evaluated per patient by the Core Laboratory

Japan LUTONIX Study: Key Endpoint Definitions

- **Safety:** Freedom from a composite of target limb re-intervention, unscheduled amputation, or death
- **Primary Patency*:** Freedom from restenosis (> 50%) based on DUS-derived PSVR ≥2.5 (core-lab adjudicated) and freedom from TLR
- **TLR:** First revascularization procedure at the target lesion
- **Clinically-Driven TLR:** TLR based on restenosis (>50% by DUS or angiography), or return of ischemic symptoms in the target limb (e.g., worsening ABI or Rutherford classification)
- **Improvement of Ankle-Brachial Index (ABI):** Improvement from baseline ≥ 0.15
- **Improvement in Rutherford Classification:** Improvement in Rutherford category from baseline value

*Primary Endpoint: 6-Month Primary Patency

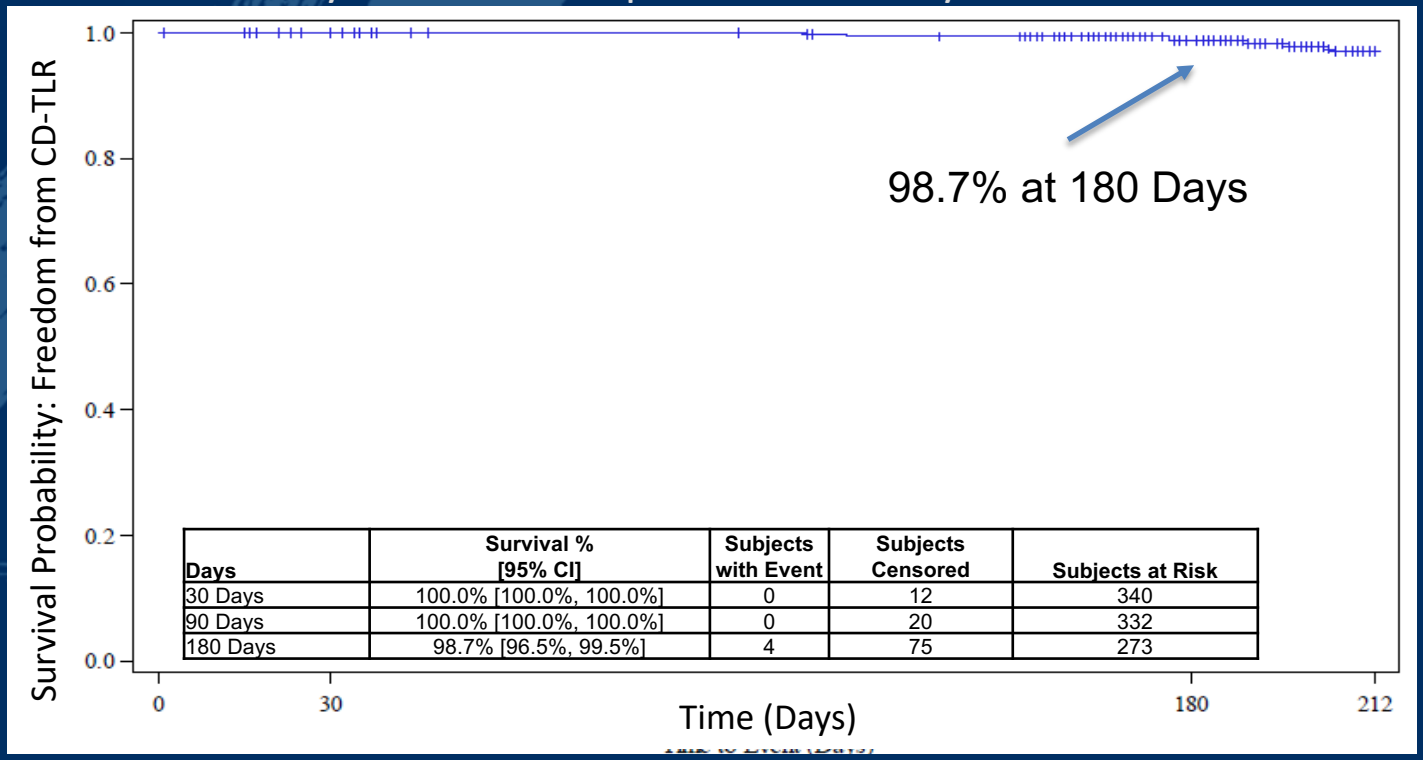
Japan LUTONIX Study: Safety Results

Freedom from a Composite* Safety Event	ITT (N=352)	[95% CI]
30-Days, % (n/N)	**97.7 (340/348)**	**[95.5%, 99.0%]**
Unscheduled target-Limb amputation	0.9% (3/348)	
Target-limb reintervention	2.0% (7/348)	
Target-limb-related death	0.0% (0/348)	
6-Month, % (n/N)	**93.6 (308/329)**	**[90.4%, 96.0%]**
Unscheduled target-Limb amputation	1.8% (6/329)	
Target-limb reintervention	5.8% (19/329)	
Target-limb-related death	0.3% (1/329)	
All-Cause Death through 6 Months, % (n/N)	**3.1 (11/352)**	

*Composite of target limb re-intervention, unscheduled amputation, or death

Japan LUTONIX Study: Efficacy Results

Clinically-Driven TLR Kaplan-Meier Analysis at 6 Months



Days	Survival % [95% CI]	Subjects with Event	Subjects Censored	Subjects at Risk
30 Days	100.0% [100.0%, 100.0%]	0	12	340
90 Days	100.0% [100.0%, 100.0%]	0	20	332
180 Days	98.7% [96.5%, 99.5%]	4	75	273

Proportion/binary analysis of primary patency at 6-months

	ITT (N=352)	[95% CI]	Performance Goal[1]	p-value[2]
Primary Patency, % (n/N)	78.4% (225/287)	[73.2%, 83.0%]	65.4%	<0.0001

Primary Patency at 6 months in the Japan LUTONIX Study was statistically better than the performance goal[1] derived from the Levant Japan Study

[1] Performance goal based on the lower confidence interval value (95% CI) for primary patency from the per-protocol LUTONIX DCB arm of the randomized, controlled Levant Japan study. 78.4% binary primary patency compared to 65.4% performance goal ($p < 0.0001$) [2] P-value compared the computed value to the performance goal (65.4%) using a one-sided exact binomial test

Japan LUTONIX Study: Secondary Outcomes

Improvement in Ankle-Brachial Index (ABI)

	Baseline ABI	Visit	Change
30-Days, mean score ± SD	0.70 ± 0.17	0.94 ± 0.15	0.24 ± 0.18
6-Month, mean score ± SD	0.70 ± 0.17	0.90 ± 0.17	0.20 ± 0.19

Mean ABI improved from baseline to 6 months by 0.2 points – numerically greater than the performance standard of 0.15

Improvement in Rutherford Classification

Target-Limb Rutherford Classification	Baseline ABI	30 Days	6 Months
Asymptomatic (0)	0.6%	59.4%	57.3%
Mild Claudication (1)	4.3%	12.9%	15.8%
Moderate Claudication (2)	26.7%	4.1%	6.5%
Severe Claudication (3)	40.9%	2.1%	1.6%
Ischemic Rest Pain (4)	7.4%	0.6%	1.2%
Ischemic Ulceration (5)	11.4%	4.1%	3.7%
Severe Tissue Loss (6)	0.3%	0.3%	0.0%

Japan LUTONIX Study: Summary

The Lutonix® 035 Drug Coated PTA Dilatation Catheter, used in a Japanese real-world patient population, provided good clinical outcomes through 6 months for the treatment of stenotic and occlusive lesions of the SFA and popliteal artery

- Freedom from a composite safety event was 93.6% at 6 months
- Clinical Outcomes at 6 Months:
  - Primary patency: Statistically better than a performance goal derived from the randomized, controlled Levant Japan Trial
  - Freedom from CD-TLR: 98.7% (K-M-Analysis at 180 days)
  - Mean ABI improved from baseline by 0.2 points – numerically greater than the performance standard of 0.15
  - Rutherford Scores improved consistently from baseline
  - All-Cause Death: 3.1%
- Follow up is ongoing through 12 months