**The Serranator Balloon Catheter from Cagent Medical to Score Lesions, Facilitate Their Dilatation without Dissection and Possibly Improve Drug Delivery: How it Works and Results of the PRELUDE Trial**

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**CONSULTANT TO CAGENT**

**Serranator®: Mechanism of Action**

- **Serrated material is more responsive to directed energy**
- Serrations are responsive to the balloon’s energy, enabling predictable and controlled lumen expansion along the lines.

**PRELUDE Study: Overview**

- **Study Design:** Single arm, prospective, multi-center feasibility study enrolling up to 30 subjects with obstructive superficial femoral or popliteal artery lesions.  
- **Follow-up:** 30 days & 6 months  
- **Enrollment Completed:** May 2017 (n=25)  
- **Study End:** December 2017

**Investigators**

- Andrew Holden, MD (PI)  
- Marianne Brodmann, MD  
- Marek Krzanowski, MD  
- Przemyslaw Nowakowski, MD  
- William A. Gray, MD

**Core Lab Adjudicated Data**

- Angio: Yale Cardiovascular Research Group  
- DUS: Vascore Ultrasound Core Laboratory  
- OCT/IVUS: Harrington Heart & Vascular Institute  
- 100% Data Monitoring

**Serration Effect using Serranator® Bass in Cadaver**

- Clear fracturing of circumferential calcium  
- Arrows indicate superficial neointimal lacerations  
- There is a multifocal fracture of calcified segments, with dashed circles indicating some non-displaced areas.  
- Creation of “reservoirs” for potential drug-uptake
Summary: Study Objectives/Endpoints

**Objectives**

**Primary Objective**

Technical feasibility of using the Serranator in critical SFA or popliteal artery lesions.

**Secondary Objective**

Feasibility of OCT and/or IVUS in a sub-set (n=10) of subjects to evaluate the presence of serrations.

**Endpoints**

**Safety**

Composite of MAEs and Per-procedural death (POD) at 30 days post procedure.

**Efficacy**

Device success: successful delivery, balloon inflation/deflation, device retrieval with a final diameter stenosis of <50%.

Core lab assessment of pre- and post-procedure angiogram assessment.

Primary patency: absence of CD-TLR and lack of target lesion restenosis by DUS*.

TLR & TVR at 30 days, and 6 months.

**Key Secondary Endpoints**

- Core lab assessment of pre- and post-procedure angiogram assessment.
- Primary patency: absence of CD-TLR and lack of target lesion restenosis by DUS*.
- TLR & TVR at 30 days, and 6 months.

**Key Inclusion/Exclusion Criteria**

- Inclusion:
  - Rutherford 1, 5, or 6
  - Previously implanted stent
  - CTO > 6 cm
  - Evidence of acute thrombus
  - Severe calcification*
  - Atherectomy

- Exclusion:
  - *Severe calcification of target lesion described as circumferential calcium and >50% of lesion length.

**PRELUDE Demographics**

<table>
<thead>
<tr>
<th>Baseline Demographic</th>
<th>N=25</th>
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<tbody>
<tr>
<td>Male</td>
<td>18/25 (72%)</td>
</tr>
<tr>
<td>Age Avg. (range)</td>
<td>66 (50-81)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Current/Former Smoker</td>
<td>22/25 (88%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21/25 (84%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>12/25 (48%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>10/25 (72%)</td>
</tr>
<tr>
<td>Carotid Artery Disease</td>
<td>12/25 (48%)</td>
</tr>
<tr>
<td>Rutherford Clinical Category 2</td>
<td>3/25 (12%)</td>
</tr>
<tr>
<td>Rutherford Clinical Category 3</td>
<td>19/25 (76%)</td>
</tr>
<tr>
<td>Rutherford Clinical Category 4</td>
<td>3/25 (4%)</td>
</tr>
</tbody>
</table>

**PRELUDE Angiographic Descriptors and Acute Results**

<table>
<thead>
<tr>
<th>Core Lab Assessment (n=25)</th>
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<tbody>
<tr>
<td>Lesion Length (cm)</td>
</tr>
<tr>
<td>SFA lesions</td>
</tr>
<tr>
<td>PTK lesions</td>
</tr>
<tr>
<td>RVD (mm)</td>
</tr>
<tr>
<td>CTO (&lt;6cm)</td>
</tr>
<tr>
<td>Moderate/Severe Calcification</td>
</tr>
<tr>
<td>Pre Diameter Stenosis</td>
</tr>
<tr>
<td>Final Diameter Stenosis</td>
</tr>
<tr>
<td>Flow Limiting Dissections</td>
</tr>
<tr>
<td>Bailout Stent (Optal Dissection in CTO)</td>
</tr>
</tbody>
</table>

*Severe calcification of target lesion described as circumferential calcium and >50% of lesion length.

**PRELUDE Study Effectiveness**

100% Device Success

**Efficacy**

Device Success defined as the achievement of successful delivery, balloon inflation and deflation, and retrieval of the study device(s) with a final diameter stenosis of <50% by visual assessment at the intended target site using only the Serranator device.

Similar Effect in Severe Calcification

**Mean Lumen Gain**

**Mean Maximum Atmospheric Pressure**

*Severe calcification of target lesion described as circumferential calcium and >50% of lesion length.
PRELUDE Case: Right Distal SFA

Pre-Treatment
RVD: 6.12 mm
% stenosis: 94.59%
Lesion length: 30.04 mm

Post-Treatment
Residual stenosis: 24.07%
No dissection

PRELUDE Case: L Mid Popliteal

Pre-Treatment
RVD: 4.56 mm
% Stenosis: 100%
Lesion length: 30.48 mm

Post-Treatment
Residual Stenosis: 28.65%
Dissection Type: B
Occlusion

PRELUDE Safety & Effectiveness
(Preliminary data)

- 0 Major Adverse Events
- 0 Deaths
- 1 SAE reported, not related to device or procedure

<table>
<thead>
<tr>
<th>Rutherford Clinical Category</th>
<th>Pre-Treatment</th>
<th>6-Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>N/A</td>
<td>7/25 (48%)</td>
</tr>
<tr>
<td>1</td>
<td>N/A</td>
<td>9/25 (36%)</td>
</tr>
<tr>
<td>2</td>
<td>1/25 (20%)</td>
<td>6/25 (24%)</td>
</tr>
<tr>
<td>3</td>
<td>10/25 (40%)</td>
<td>3/25 (12%)</td>
</tr>
<tr>
<td>4</td>
<td>1/25 (4%)</td>
<td>0</td>
</tr>
</tbody>
</table>

PRELUDE: Case performed by Dr. Krzanowski

PRELUDE Conclusions

- Study Objectives & Primary Endpoints achieved
  - Serranator is safe and effective in treating critical femoro-popliteal lesions
  - 100% device success
  - Acute results show low residual stenosis (mean 23%)
  - 100% Patency at 30 days
  - 100% freedom from TLR at 30 days and 6 months

- 100% serration effect demonstrated in OCT and IVUS (n=10)
- Equally effective in lumen gain in both moderate and severely calcified lesions

Serranator® Bass®: In development

- Bass PTA Serration Balloon Catheter is intended for dilatation of lesions in infrapopliteal arteries. Not for use in the coronary or neuro-vascular systems.
- 2.5, 3.0, 3.5 mm diameters
- 40, 80, 100 mm length
- 0.014" guidewire compatible
- 5F sheath
- 3 strips
- Unique integrated coil designed catheter for support and flexibility for trackability

*Not available in US or OUS

Cadaver Study: Serranator® Bass in Severe Calcification

- Characterize device effectiveness: pushability, trackability,
  and effectiveness in opening diseased lesions.
- Characterize human lesion morphology in pre- and post-
  treatment with fluoroscopy.
- Evaluate the extent of plaque/mural disruption with cross
  sectional histopathology.

SUMMARY OF LESIONS TREATED

- Age/Sex/Race: 79 years old, Male, Caucasian
- Weight/BMI: 185 lbs, 25.09
- Primary Cause of Death: Acute Heart Failure; Coronary Artery Disease
- Health History: Replacement to both knees; COPD; Adult onset diabetes; Dementia; Heart Disease, Pacemaker 1-3 years
- Operator: Jihad Mustapha, MD

Serranator® Bass® PTA Serration Balloon Catheter
Histopathology Summary

Severe underlying arterial vascular disease was present:
- Marked, segmental to diffuse medial and neointimal calcification
- Regionally variable, mild to marked/occlusive neointima

Cumulative effect in treated sections was disruption of neointima and media:
- Multifoil, typically superficial neointimal scoring
  - ≤250µm (≤0.25mm), usually involving only most superficial neointima and rarely consistent with trans-medial extension
- Notable fracture/disruption of calcified segments.
  - Often included EL breaks, most often along luminal aspect of the mineralized zones.
  - Not consistently associated with luminal laceration, and therefore likely due to mechanical effects, e.g., separate effects of balloon inflation.
  - Possibility of some compressive mechanical effect, e.g., during tissue trimming, cannot be excluded in the ex vivo/postmortem model.
- No histologic indication of perforation or dissection (consistent with contrast imaging).

PRELIDE Results

Subset analysis: Serration effect n=10 (100%)

PRELIDE: Case Right Popliteal

Severe Calcification

Case performed by Dr. Holden
PRELUDE Case: Right Popliteal

| Severe Calcification |

*Case performed by: Holden*