Clinical Trial: IMPERIAL Trial - A Randomized trial coMParing Eluvia dRug-eLuting Stent vs. Zilver PTX stent for treatment of Superficial femoral and/or proximal popliteal arteries

(Lower Limb Advanced Arterial Therapeutics, Medtronic PV Lower Limb Advanced Arterial Therapeutics, Peripheral Vascular Therapeutics - In Development)

Companies/Sponsors:
- Boston Scientific Corporation, Inc.
- Cook Medical, Inc

Product:
- Eluvia Peripheral Vascular Drug-Eluting Stent System
- Zilver® PTX Drug Eluting Peripheral Stent

Objective:
To evaluate the safety and effectiveness of the Boston Scientific Corporation (BSC) ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 140 mm in length.

Long Lesion Substudy: to evaluate the safety and effectiveness of the Boston Scientific Corporation (BSC) ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions >140 mm and ≤ 190 mm in length.

Trial Design:
Global, prospective, multi-center 2:1 randomized single-blind, non-inferiority trial (RCT) with a concurrent non-blinded, non-randomized, single-arm PK, long lesion substudy. Approximately 524 subjects between Dec 2015 to Feb 2017 the enrollment was 465 patients (309 for ELUVIA and 156 for ZILVER, 12-20 for the PK substudy) will be enrolled at up to 75 study centers worldwide in the RCT or the PK substudy but not both. Regions participating include the United States, Canada, European Union, Japan and New Zealand. The experimental arm will receive the Eluvia Drug-Eluting Stent while the active comparator arm will receive the Zilver PTX Peripheral Drug-Eluting Stent. Follow-up at 1 month, 6 months, 1 year, 2 years and 5 years post-procedure.

Patient Demographics:

<table>
<thead>
<tr>
<th>Results Have Been Published - 1 year LLL for FP lesions, 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
</tr>
<tr>
<td><strong>Male (%)</strong></td>
</tr>
<tr>
<td><strong>Body Mass Index</strong></td>
</tr>
<tr>
<td><strong>Current Smoker (%)</strong></td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
</tr>
<tr>
<td><strong>Pre procedural ABI</strong></td>
</tr>
<tr>
<td><strong>Post procedural ABI</strong></td>
</tr>
<tr>
<td><strong>Rutherford Category 2/3/4</strong></td>
</tr>
<tr>
<td><strong>TASC classification A/B/C/D</strong></td>
</tr>
<tr>
<td><strong>Lesion Length (mm)</strong></td>
</tr>
<tr>
<td><strong>Reference diameter (mm)</strong></td>
</tr>
<tr>
<td><strong>CTO (%)</strong></td>
</tr>
<tr>
<td><strong>PACSS grade (%) 0/1/2/3/4</strong></td>
</tr>
<tr>
<td><strong>Stent Diameter (mm)</strong></td>
</tr>
<tr>
<td><strong>IVUS Usage (%)</strong></td>
</tr>
</tbody>
</table>

NOTE: P Values reported as available

1 year Patient Demographics Have Been Published - VIVA 2018

<table>
<thead>
<tr>
<th><strong>Group</strong></th>
<th><strong>Result</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions</td>
<td>8 cms</td>
</tr>
</tbody>
</table>
Exclusion Criteria:

1. Previously stented target lesion/vessel.
2. Target lesion/vessel previously treated with drug-coated balloon <12 months prior to randomization/enrollment.
3. Subjects who have undergone prior surgery of the SFA/PPA in the target limb to treat atherosclerotic disease.
4. Use of atherectomy, laser or other debulking devices in the target limb SFA/PPA during the index procedure.
5. History of major amputation in the target limb.
6. Documented life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject’s ability to participate in the clinical trial, limit the subject’s compliance with the follow-up requirements, or impact the scientific integrity of the clinical trial.
7. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated.
8. Known hypersensitivity/allergy to the investigational stent system or protocol related therapies (e.g., nitinol, paclitaxel, or structurally related compounds, polymer or individual components, and antiplatelet, anticoagulant, thrombolytic medications).
9. Platelet count <80,000 mm3 or >600,000 mm3 or history of bleeding diathesis.
10. Concomitant renal failure with a serum creatinine >2.0 mg/dL.
11. Receiving dialysis or immunosuppressant therapy.
12. History of myocardial infarction (MI) or stroke/cerebrovascular accident (CVA) within 6 months prior to randomization/enrollment.
13. Unstable angina pectoris at the time of randomization/enrollment.
14. Pregnant, breast feeding, or plan to become pregnant in the next 5 years.
15. Current participation in another investigational drug or device clinical study that has not completed the primary endpoint at the time of randomization/enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then)

Results:

NOTE: P Values reported as available
16. Septicemia at the time of randomization/enrollment.
17. Presence of other hemodynamically significant outflow lesions in the target limb requiring intervention within 30 days of randomization/enrollment.
18. Presence of aneurysm in the target vessel.
19. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to randomization/enrollment.
20. Perforated vessel as evidenced by extravasation of contrast media prior to randomization/enrollment.

**Primary Endpoints:**
- Primary Safety Endpoint: Major Adverse Events (MAEs) [ Time Frame: 12 Months ]
  [ Designated as safety issue: Yes ]
  MAEs defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization (TLR) through 12 months
- Primary Effectiveness Endpoint: primary patency [ Time Frame: 12 Months ]
  [ Designated as safety issue: No ]
  Primary patency of target lesion at 12-months assessed by duplex ultrasound as adjudicated by an independent core laboratory

**Secondary Endpoints:**
- Technical success of the stenting procedure [ Time Frame: During Procedure ]
  [ Designated as safety issue: No ]
  Technical Success is defined as delivery and deployment of the assigned study stent to the target lesion to achieve residual angiographic stenosis no greater than 30% assessed visually
- Procedural success of the stenting procedure [ Time Frame: Within 24 hours of stenting procedure ]
  [ Designated as safety issue: No ]
  Procedural Success is defined as technical success with no MAEs noted within 24 hours of the index procedure
- MAE rate [ Time Frame: 1 Month ]
  [ Designated as safety issue: Yes ]
  MAE rate is defined as all causes of death, target limb major amputation and/or TLR
- Clinically-driven TLR Rate
  [ Time Frame: 1 Month, 6 Months, 12 Months, 24 Months, 36 Months, 48 Months and 60 Months ]
  [ Designated as safety issue: No ]
  TLR is defined as any surgical or percutaneous intervention to the target lesion(s) after the index procedure
- Clinically-driven Target Vessel Revascularization (TVR) Rate
  [ Time Frame: 1 Month, 6 Months, 12 Months, 24 Months, 36 Months, 48 Months and 60 Months ]
  [ Designated as safety issue: No ]

**VEITH 2016**

<table>
<thead>
<tr>
<th>Group</th>
<th>12 months</th>
<th>24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>96.1%</td>
<td>74.8%</td>
</tr>
<tr>
<td>TLR</td>
<td>3.8%</td>
<td>86.6% (Zilver PTX)</td>
</tr>
<tr>
<td>Stent fracture</td>
<td>0 (Eluvia)</td>
<td>8% TLR (Eluvia), 16.1% TLR (Zilver)</td>
</tr>
</tbody>
</table>
TVR is defined as any surgical or percutaneous intervention to the target vessel(s) after the index procedure.

- **Adverse Event Rates**
  - (unanticipated, major, serious, device/procedure-related)
  - [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months, 36 Months, 48 Months and 60 Months]
  - [Designated as safety issue: Yes]

- **Non-serious non-device/procedure-related Adverse Event Rates**
  - [Time Frame: Through 12 months]
  - [Designated as safety issue: Yes]

- **Stent Fracture Rate**
  - [Time Frame: 12 Months, 24 Months and 60 Months]
  - [Designated as safety issue: No]
  - Stent fracture is defined as a break in one or more places of the stent. The following definitions will be used to determine the type and extent of stent fracture (to be assessed by the x-ray core laboratory):
    - Grade 0: No Strut fractures
    - Grade I: single strut fracture
    - Grade II: multiple strut fractures
    - Grade III: stent fracture(s) with preserved alignment of the components
    - Grade IV: stent fracture(s) with mal-alignment of the components
    - Grade V: Stent fracture(s) in a trans-axial spiral configuration

- **Distribution of Rutherford Classification**
  - [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months]
  - [Designated as safety issue: No]
  - Rutherford Classification:
    0. Asymptomatic Normal Treadmill/stress test
    1. Mild claudication
       Completes treadmill exercise; ankle pressure (AP) after exercise <50mm Hg, but >25 mm Hg less than BP
    2. Moderate claudication
       Between categories 1 and 3
    3. Severe claudication
       Cannot complete treadmill exercise and AP after exercise <50 mm Hg
    4. Ischemic rest pain
       Resting AP <40 mm Hg, flat or barely pulsatile ankle or metatarsal pulse volume recording (PVR); toe pressure (TP) <30 mm Hg
    5. Minor tissue loss - nonhealing ulcer, focal gangrene with diffuse pedal edema
       Resting AP <60 mm Hg, ankle or metatarsal (MT) PVR flat or barely pulsatile; TP <40 mm Hg
    6. Major tissue loss - extending above MT level
       Same as Category 5
• Rate of Primary Sustained Clinical Improvement as assessed by changes in Rutherford Classification [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months] [Designated as safety issue: No]
Endpoint determined to be a success when there is an improvement in Rutherford classification of one or more categories as compared to pre-procedure without the need for repeat TLR

• Rate of Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months] [Designated as safety issue: No]
Endpoint determined to be a success when there is an improvement in Rutherford classification of one or more categories as compared to pre-procedure including those subjects with repeat TLR

• Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index (ABI) [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months] [Designated as safety issue: No]
Hemodynamic improvement defined as Improvement of ABI by ≥0.1 or to an ABI ≥ 0.90 as compared to the pre-procedure value without the need for repeat revascularization

• Walking Improvement assessed by change in Six Minute Hall Walk (6MHW) from baseline [Time Frame: 12 Months] [Designated as safety issue: No]
The 6MHW measures the maximal walking distance that a patient achieves on a flat, hard surface in a period of 6 minutes (the 6MWT). It evaluates the global and integrated responses of all the systems involved during exercise, including the pulmonary and cardiovascular systems, systemic circulation, blood, neuromuscular units, and muscle metabolism

• Walking Improvement assessed by change in Walking Impairment Questionnaire (WIQ) [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months] [Designated as safety issue: No]
The WIQ is a functional-assessment questionnaire that evaluates walking ability with regard to speed, distance and stair climbing ability as well as the reasons that walking ability might be limited. Range of scores is between 0% and 100% with 100% being the best and 0% being the worst score

• Patient Utility Values by change in EQ-5D [Time Frame: 1 Month, 6 Months, 12 Months, 24 Months and 60 Months] [Designated as safety issue: No]
The EQ-5D is a descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care,
usual activities, pain/discomfort, anxiety/depression) each of which can take one of five responses. The responses record five levels of severity (no problems/slight problems/moderate problems/severe problems/extreme problems) within a particular EQ-5D dimension.

PI:
- Gray, William, MD, wgray@crf.org,
  +1.212.342.0947

PI Study Site:
- New York-Presbyterian Hospital, Columbia University Medical Center, New York, New York

Enrollment:
- 524

Trial Start Date:
- December 2015

**Please Note:** All links will open in the current window - to open a link in a new window please right click the link and select "Open in New Window" or "Open in New Tab"

Conclusion:
- In conclusion, the study demonstrated that one-year LLL in the Eluvia group was significantly lower than that in the Zilver PTX group.
- In conclusion, in the long lesion subset of the IMPERIAL trial, the device maintained its safety and efficacy profiles similar to the main IMPERIAL study, demonstrating no decrement in this more complex patient cohort - VIVA 2018.
- This study is active but not recruiting with a primary completion date of December 28, 2017 and a final study completion date of March 2020.
- Based on these findings, physicians in TCT 2018 believe that the Eluvia stent can be a preferred therapy option when treating patients with arterial blockages in the superficial femoral or proximal popliteal arteries.

**Additional PI Sites:**
- United States
  - Arizona
    - Arizona Yuma Regional Medical Center, Yuma
  - California
    - California Veterans Affairs Medical Center, Los Angeles
    - University of California, Davis Medical Center, Sacramento
  - Florida
    - Florida Research Network, LLC, Gainesville
    - First Coast Cardiovascular Institute, Jacksonville
    - Mount Sinai Medical Center, Miami Beach
    - Baptist Cardiac and Vascular Institute, Miami
    - MediQuest Research at Munroe Regional Medical Center, Ocala
    - Baptist Hospital, Pensacola
  - Georgia
    - Georgia University Hospital, Augusta
  - Illinois
    - Illinois Advocate Christ Medical Center, Oak Lawn
    - St. Francis Medical Center, Peoria
  - Indiana
    - St. Joseph Hospital, Fort Wayne
  - Massachusetts
    - Steward St. Elizabeth’s Medical Center of Boston, Inc., Boston
  - Michigan
    - Northern Michigan Hospital, Petoskey
  - Minnesota
    - Mercy Hospital, Coon Rapids
    - Mayo Clinic Foundation, Rochester
  - Nebraska
    - Alegent Creighton Health Bergan Mercy Medical Center, Omaha
  - New Hampshire
    - Dartmouth Hitchcock Medical Center, Lebanon
  - New Jersey
    - Hackensack University Medical Center, Hackensack
  - New Mexico
    - New Mexico Heart Institute, PA, Albuquerque
  - New York
    - Maimonides Medical Center, Brooklyn
    - New York University Medical Center, New York
    - New York Presbyterian Hospital-Columbia University Medical Center, New York
  - North Carolina
    - Carolinas HealthCare System NorthEast, Concord
    - Rex Hospital, Raleigh
  - Ohio
    - Aultman Hospital, Canton
    - University of Toledo Medical Center, Toledo
    - LakeWest Hospital, Willoughby
  - Oregon
This study has a primary completion date of January 2018 and a final study completion date of January 2022.

Sources:

June 29, 2019 --- "Results & patient demographics" - Late Lumen Loss data --- "Conclusion" --- "Source"  

April 17, 2019 --- "Results" - 12 months sub analysis group results were presented at Charing Cross Symposium 2019 --- "Source"  
<https://vascularnews.com/imperial-eluvia-sub-analyses-cx2019/>

November, 2018 --- "Patient Demographics" --- "Results" --- "Conclusion" - 1 year VIVA 2018 data --- "Source"  
<https://vivaphysicians.org/news-article?id=415>

October 2, 2018 --- "Results" --- "Source"  

October 1, 2018 --- "Trial status" --- "Enrollment" --- "Conclusion" --- "Source"  
<https://clinicaltrials.gov/ct2/show/NCT02574481>

September 22, 2018 --- "Results" - 1 year results presented in TCT 2018 --- "Conclusion" - data presented in TCT 2018 --- "Source"  

November 23, 2016 --- "Results" field - Updated VEITH 2016 results -- "Sources" field -  

February 15, 2016 --- "Enrollment" field - Updated enrollment --- "Trial Design" field -Updated trial design text and image --- "Sources" field -  

January 11, 2016 --- "Trial Name" field - Added trial name --- "Objective" field - Added objective --- "Trial Status" field - Added trial status --- "Trial Phase" field - Added trial phase --- "Enrollment" field - Added enrollment --- "Trial Start Date" field - Added trial start date --- "Trial Publication Date" field - Added publication date --- "Trial Design" field - Added trial design text and image --- "PI" field - Added PI --- "PI Study Site" - Added PI study site --- "Inclusion Criteria" field - Added inclusion criteria --- "Exclusion Criteria" field - Added exclusion criteria --- "Primary Endpoints" field - Added primary endpoints --- "Secondary Endpoints" field - Added secondary endpoints --- "Conclusions" field -added study completion dates --- "Sources" field -  

Last Update: July 10, 2019

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