Update on the Chocolate PTA Balloon: Mode of Action, Advantages and Clinical Results

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Disclosures
Consultant:
• Abbott Vascular
• Bard Peripheral Vascular
• Boston Scientific
• Cardiovascular Systems, Inc.
• Cook Medical
• Covidien
• Medtronic
• Spectranetics
• Terumo Medical

Chocolate Balloon Design

Constraining Structure

Uniform Inflation

Modulated Dilatation

Chocoalte Design Concept & Mechanism of Action

Grooves allow for plaque channeling, and provide area for stress relief

Advantage: Chocolate PTA Uniform Inflation

Advantage: Chocolate PTA Low Secondary Profile
The Next Step: Drug-Coated Chocolate
Chocolate balloon catheter + Paclitaxel Drug-Coating
Combines:
• Acute & clinical performance benefits of the Chocolate Balloon AND
• The sustained, long-term drug effect of Paclitaxel
  - Paclitaxel in an anti-mitotic agent with proven ability to inhibit neointimal thickening when delivered by a balloon.
  - Nominal dose density of paclitaxel on Chocolate balloon is approximately 3.0 µg/mm², similar to other drug coated balloons

• Chocolate Touch PTA Paclitaxel Coated Balloon: ATK and BTK sizes now CE marked
• Chocolate Heart PTA Paclitaxel Coated Balloon: Coronary Balloon in early feasibility study

Advantages of Drug-Coated Chocolate Platform
- The constraining structure (CS) is designed to cover the coated balloon during insertion, delivery through tortuosity, and balloon unfolding
- The inflated Chocolate has a larger surface area vs. POBA
- The inflated balloon opens the vessel by angioplasty, while passively transferring the vessel wall to paclitaxel
- Upon deflation, the CS and balloon are removed from the vessel; no part of the device remains

Data from the Chocolate BAR BTK Cohort
Sponsored by TriReme Medical

Patient Characteristics
<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n=226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>72 ± 10</td>
</tr>
<tr>
<td>Male gender</td>
<td>150 (66%)</td>
</tr>
<tr>
<td>Diabetes history</td>
<td>209 (93%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>186 (82%)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>151 (67%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>133 (59%)</td>
</tr>
<tr>
<td>Coronary artery</td>
<td>129 (57%)</td>
</tr>
<tr>
<td>Obesity</td>
<td>38 (17%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>24 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (4%)</td>
</tr>
<tr>
<td>Length, cm</td>
<td>88 ± 7.7</td>
</tr>
<tr>
<td>Diameter, mm</td>
<td>8.7 ± 0.9</td>
</tr>
<tr>
<td>Ankle circumference</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
</tr>
<tr>
<td>Study Schedule</td>
<td></td>
</tr>
<tr>
<td>Number of Sites</td>
<td>33</td>
</tr>
<tr>
<td>Total Patients Enrolled</td>
<td>490</td>
</tr>
<tr>
<td>BTK Cohort</td>
<td>226</td>
</tr>
<tr>
<td>ATK Cohort</td>
<td>264</td>
</tr>
</tbody>
</table>

Lesion Characteristics
<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (n=226 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target lesion</td>
<td>97±27 lesion</td>
</tr>
<tr>
<td>Diameter, mm</td>
<td>8.7±0.9 mm</td>
</tr>
<tr>
<td>Stenosis, %</td>
<td>82.9±17.3%</td>
</tr>
<tr>
<td>Chronic total occlusion</td>
<td>71 (26%)</td>
</tr>
<tr>
<td>Moderate/Severe calcification</td>
<td>136 (60%)</td>
</tr>
<tr>
<td>No/Poor run-off</td>
<td>189 (84%)</td>
</tr>
</tbody>
</table>

Chocolate BAR BTK Cohort Clinical Outcomes

Procedural Outcomes
- Balloon stent placement: 4.9% vs 9.9%
- 30-Day Outcomes
  - Target lesion revascularisation: 2.2% vs 8.1%
  - Major amputation: 1.3% vs 4.4 - 6.6%
  - Mortality: 0.9% vs 1.7 - 3.3%
- 6-Month Outcomes
  - Target lesion revascularisation: 9.0% vs 16.0%
  - Major amputation: 3.2% vs 11.8%
  - Mortality: 2.9% vs 7.7%
Early Data from the ENDURE Study

An Evaluation of the Drug-Coated Chocolate Touch PTA Balloon

Study Centers and Core Labs

Investigator / Institution | Patients
---|---
Prof. Gunnar Tepe | 20
Dr. Andrew Holden | 17
Prof. Thomas Zeiler | 16
Dr. Sebastian Sixt | 14

Total: 87 patients

Core Labs:

Angiographic:
- Yale University School of Medicine Core Lab - New Haven, CT
- Duplex Ultrasound: VASCORE - Vascular Ultrasound Core Lab - Boston, MA

Population Overview

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Our patients (N=70)</th>
<th>Total Patient Population Data (N=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Range)</td>
<td>69 years (18-90 years)</td>
<td>69 years (18-90 years)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>30.5% (21/69)</td>
<td>38.6% (26/68)</td>
</tr>
<tr>
<td>History of diabetes</td>
<td>46.6% (32/69)</td>
<td>56.8% (39/68)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>30.5% (21/69)</td>
<td>40.5% (27/67)</td>
</tr>
<tr>
<td>History of hyperlipidemia</td>
<td>33.3% (23/69)</td>
<td>43.1% (30/69)</td>
</tr>
</tbody>
</table>

Lesion Characteristics

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>Core Lab Adjudicated Data (N=70)</th>
<th>Total Patient Population Data (N=70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal Lumen Diameter</td>
<td>3.97 mm ± 0.97</td>
<td>3.97 mm ± 0.97</td>
</tr>
<tr>
<td>Stenosis</td>
<td>1.19 mm ± 0.57</td>
<td>1.19 mm ± 0.57</td>
</tr>
<tr>
<td>Length (N=69)</td>
<td>7.1 cm (1.5 – 16.5 cm)</td>
<td>7.1 cm (1.5 – 16.5 cm)</td>
</tr>
</tbody>
</table>

Procedural Review

Core Lab Adjudicated Data (N=69)

- Adjudicated Flow Limiting Dissections: 89 (69%)
- Adjudicated >50% Diameter Stenosis: 1% (1/69)
- Adjudicated Bail-out Stent: Per protocol stent was permitted with flow-limiting dissection or >50% stenosis: 1.4% (1/69)

- This study did not require pre-dilatation. The IN.Pact global registry, which also did not require pre-dilatation, reported 24.7% provisional stenting.
- Many other DCB studies exclude suboptimal pre-dilatation outcomes from enrollment.

- Additional non-ball-out stents were placed per operator discretion. In all cases in which these stents were placed, the Chocolate Touch balloon was adjudicated to be undersized less than 1:1.

- Interim 6 Month Results

- Major Adverse Events
  - Per Protocol: Clinically-driven TLR 1, Amputation 0, Death 0
  - Other: TLR (Asymptomatic) 3*, Thrombosis 0

- Patency
  - N=54
  - All Patients: 88.9% (48/54)
  - Patients Treated per Protocol: 90.0% (45/50)

* Interventions performed during 6-month follow-up angiogram with no reported clinical symptoms.
**Chocolate Heart FIH Study Overview**

**Objective:** To evaluate the feasibility, safety, and performance of the Paclitaxel Drug-Coated Chocolate Heart Balloon Catheter in de-novo coronary artery lesions.

**Design:**
- Prospective, single-arm, Interventional, Single-center, Open-label study
- Up to 30 patients

**Study Center:** Santo Domingo, Dominican Republic

**Study Investigators:**
- Dr. Carlos Garcia Lithgow
- Dr. Julian Javier
- Dr. Jihad Mustapha
- Dr. Carlos Garcia Lithgow

**Follow-Up:**
- 1 Month
- 6 Months
- 12 Months
- 24 Months

**Chocolate Heart FIH Study Design**

**Inclusion/Exclusion Overview:**
- Target lesion cannot have evidence of excessive tortuosity or calcification preventing access
- Target lesion cannot be CTO, ISR, Restenotic, Unprotected LMCA lesion, or Calcified with arc >90 degrees
- Outcome must be attained prior to target vessel treatment
- Non-target lesion located in another major epicardial vessel can be treated, first with optimal medical therapy
- The target vessel RVD is 2.0 mm to 3.0 mm
- Lesion complexity: Type B, Type C
- Lesion length: ≤30 mm
- Lesion diameter: ≥2.5 mm or ≤3.5 mm

**Procedural Outcomes**

<table>
<thead>
<tr>
<th>Procedural Complications in this study</th>
<th>Historical PTCA Balloon Procedural Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bail out stent placement 0% (0/19)</td>
<td>Bail out CABG 2.7 – 10.1%</td>
</tr>
<tr>
<td>Significant Dissection 0% (0/19)</td>
<td>Dissections 29.0 – 35.0%</td>
</tr>
<tr>
<td>Abrupt Closure 0% (0/19)</td>
<td>Sub-Acute closure 5% (0/19)</td>
</tr>
</tbody>
</table>

**Population**

A total of 19 patients have been enrolled between April & Aug 2015.
6 month visits for the study will be in November 2015

In-hospital / 30 Day MACE Reported
Chocolate Heart FH Study:

<table>
<thead>
<tr>
<th></th>
<th>Death</th>
<th>MI</th>
<th>TLR</th>
<th>Overall MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

One patient missed 30 day visit

Historical PTA Balloon In-Hospital Outcomes:

<table>
<thead>
<tr>
<th></th>
<th>Death</th>
<th>Q-wave MI</th>
<th>Re-intervention</th>
<th>MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.1 – 1.1%</td>
<td>1.1 – 3.0%</td>
<td>10.1 – 12.1%</td>
<td>4.1 – 9.0%</td>
</tr>
</tbody>
</table>

Conclusions

1. Chocolate’s “low trauma” mechanism achieved excellent procedural outcomes resulting in a low rate of bail-out stent use in three studies presented here.
2. In BTK lesions, treatment with the Chocolate PTA Balloon shows improved outcomes for TLR, amputation and survival when compared to the use of traditional PTA balloons.
3. The combination of the Chocolate platform with paclitaxel (neointimal suppression for good long-term results) offers the potential to avoid stents almost entirely.
4. In ENDURE, the Drug-Coated Chocolate Touch:
   - achieved a low residual diameter stenosis and no flow limiting dissections resulting in an extremely low rate of per protocol bail-out stenting
   - shows promising evidence of the drug effect by way of high patency and low late lumen loss at 6 months
5. Early data with the drug-coated chocolate coronary balloon show promising early results, especially compared to historical PTA balloon results.

Thank You

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