

# Final Results of the Feasibility Study for the Drug-coated Chocolate Touch PTA balloon of Femoropopliteal lesions: (The ENDURE Trial)

Andrew Holden

Principal Investigator - ENDURE Study

Auckland Hospital

LINC 2017 - January 25<sup>th</sup> 2017

# Disclosure

Speaker name:

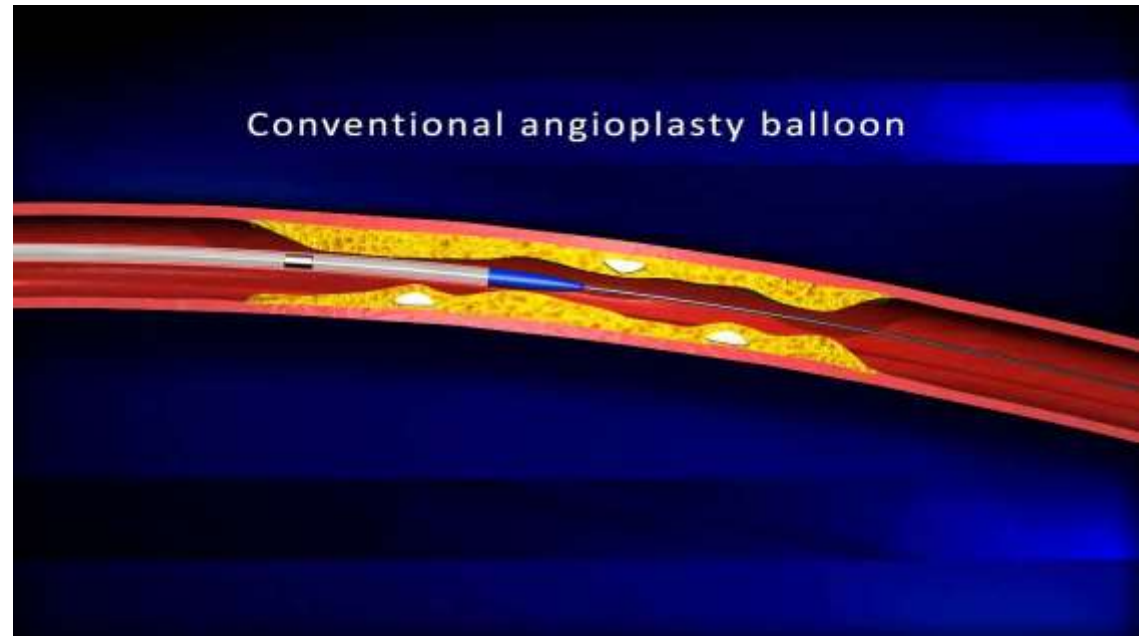
**Andrew Holden**

I have the following potential conflicts of interest to report:

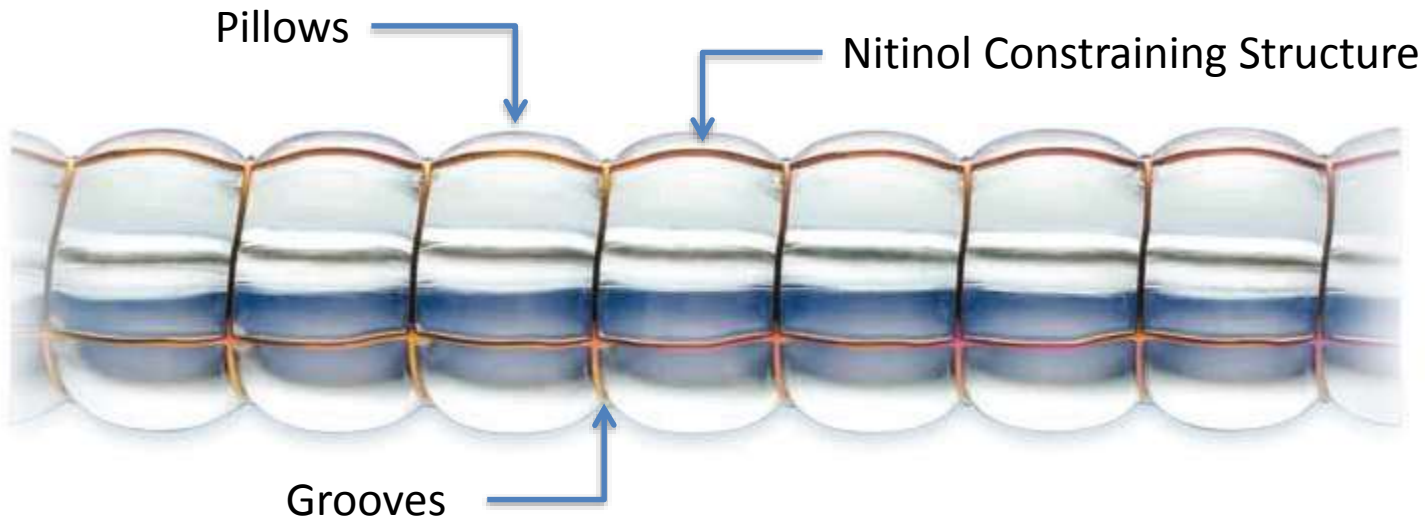
- Consulting – Clinical Investigator for Trireme Medical**
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)
  
- I do not have any potential conflict of interest

# Challenge: Acute vessel trauma with POBA

- POBA can cause dissection, vessel wall trauma, and edge injury through a combination of torsional, radial and longitudinal stress



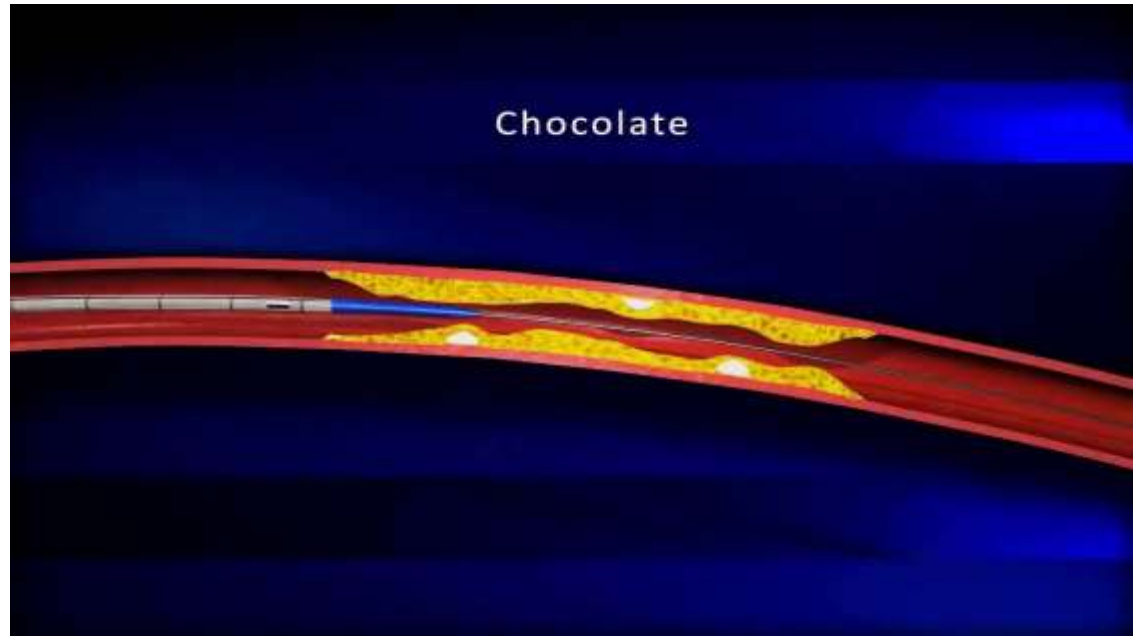
# Chocolate platform for controlled inflation



- **Uniformly distributes circumferential forces**
- **Shields vessel wall from torsional shear stress caused by balloon unfolding**
- **Modifies plaques via pillows and grooves (stress relief)**

# Chocolate: Platform for controlled inflation

- Controlled dilatation to help reduce dissections, minimize vessel wall trauma and edge injury



- <sup>1</sup> Predictable: less dissection and less bailout stenting
- <sup>2</sup> Chocolate BAR interim results
- <sup>3</sup> Cadaver data on file at TriReme Medical, LLC

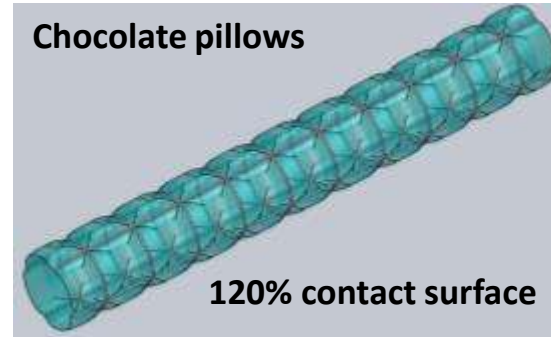
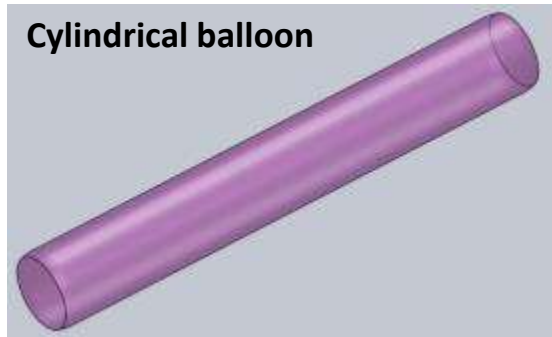
# The Next Step: Drug-Coated Chocolate™



- Controlled, predictable dilatation with unique pillows and grooves design
- Low rates of dissection and bail out stenting
- 20% greater drug-coated surface on Chocolate pillows, compared to same-sized conventional balloon

- Paclitaxel, anti-proliferative agent clinically proven to inhibit neointimal hyperplasia
- 3  $\mu\text{g}/\text{mm}^2$  paclitaxel dose
- Crystalline paclitaxel coating with hydrophilic excipient, developed in collaboration with InnoRa GmbH

# Potential advantages of Drug-Coated Chocolate Platform



- The CS is designed to cover the coated balloon during insertion, delivery through tortuosity, and balloon unfolding
- 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

## **Chocolate Touch™ PTA Paclitaxel Coated Balloon:**

- ❖ **CE Mark approved in Europe**
- ❖ **ENDURE Study data**
- ❖ **IDE Study Approved in US**

## **Chocolate Heart™ PTCA Paclitaxel Coated Balloon:**

- ❖ **CE Mark approved in Europe**
- ❖ **Early first in human data**



# Data from the ENDURE Study

*An Evaluation of the Drug-Coated Chocolate Touch™ PTA Balloon*



# ENDURE Study Design

## 4 sites in Germany and New Zealand; Single-Arm Study

- Single or Tandem *de novo* lesion
- Total lesion length  $\leq$  150 mm
- RVD 4.5 – 6.0 mm
- Rutherford Grade 3-5



### Treatment Strategy:

- No Pre-dilatation required
- Additional PTA balloon required if  $>30\%$  residual stenosis, or, Type C or worse dissection
- Bail-out Stent permitted if  $>50\%$  residual stenosis, or, flow-limiting dissection

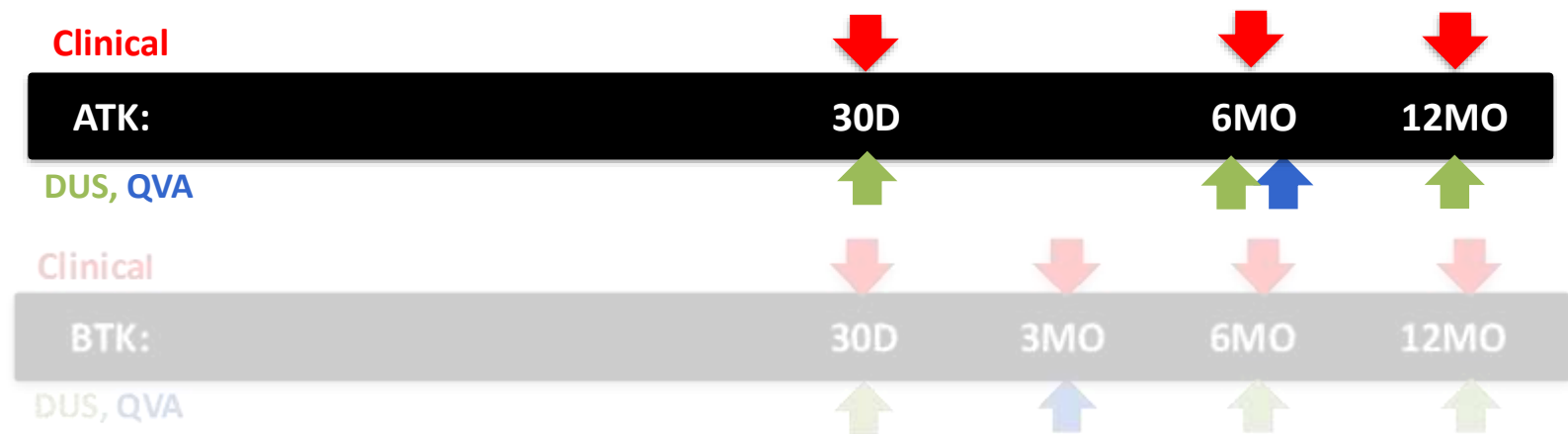
### Study Endpoints:

- Late Lumen Loss
- Patency Rate
- Rate of Clinically Indicated TLR
- Survival Rate
- Amputation Rate
- Clinical Improvement

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### Study Endpoints:

- **Late Lumen Loss – 6 month angiography**
- Patency Rate
- Rate of Clinically Indicated TLR
- Survival Rate
- Amputation Rate
- Clinical Improvement

# ENDURE: Study Centers & Core Labs

<b>Investigator / Institution</b>	<b>Patients</b>
<b><i>Prof. Gunnar Tepe</i></b> Rosenheim Medical Center, Germany	20
<b><i>Dr. Andrew Holden</i></b> Auckland City Hospital, New Zealand	17
<b><i>Prof. Thomas Zeller</i></b> Universitäts-Herzzentrum Freiburg Bad Krozingen GmbH, Germany	16
<b><i>Dr. Sebastian Sixt</i></b> Hamburg University Cardiovascular Center, Germany	14
<b>Total</b>	<b>67 patients</b>
<b>Patients with two Target Lesions = 3</b>	<b>70 lesions</b>

## Core Labs:

### ***Angiographic:***

Yale University School of Medicine Core Lab - New Haven, CT

### ***Duplex Ultrasound:***

VASCORE - Vascular Ultrasound Core Lab - Boston, MA

- Interim Data are representative of available information as of 17 Sep 2015
- Monitoring /data clean-up are incomplete
- Follow-up is ongoing

# ENDURE: Population Overview

## Patient Characteristics

Per patient	
Age Average (Range)	69 years (53-92 years)
Male	60.6% (40/66)
Diabetes	34.3% (23/67)
Tobacco Use	78.5% (51/65)
Calculated BMI Average (Range)	28.1 (17.7 – 42.2)
History of Hypertension	86.6% (58/67)
History of Hyperlipidemia	68.2% (45/66)
History of Coronary Intervention (PTCA or CABG)	29.9% (20/67)
Intermittent Claudication	95.5% (64/67)
ABI (average)	0.66 ± 0.28
Rutherford Category *	
Rutherford 3	92.6% (62/67)
Rutherford 4	3.0% (2/67)
Rutherford 5	4.5% (3/67)

## Lesion Characteristics

Core Lab Adjudicated Data (N=70)		
<b>Pre-Dilatation Conducted</b>	28.6% (16/56)	
<b>Superficial Femoral Artery</b>	92.9% (65/70)	
<b>Popliteal Artery</b>	7.1% (5/70)	
<b>Calcification</b>	None to Mild	45.7% (32/70)
	Moderate	31.4% (22/70)
	Severe	22.9% (16/70)
<b>RVD</b>	Proximal	5.3±0.67
	In lesion	5.1±0.62
	Distal	5.1±0.73
<b>Lesion Length (N = 69<sup>+</sup>)</b>	7.3 cm ( 1.5 – 16.5cm)	
<b>% DS (N=69<sup>+</sup>)</b>	76.3% ± 19.1	
<b>Total Occlusions</b>	33.3% (23/69 <sup>+</sup> )	
	<b>Pre-treatment (N=69<sup>+</sup>)</b>	<b>Post Treatment (N=70)</b>
<b>Minimum Lumen Diameter</b>	1.19 mm ± 0.97 ( 0 – 3.2 mm)	3.97 mm ± 0.57 ( 2.5 – 5.6 mm)

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**Severe calcifications and CTOs significantly higher than other DCB trials**

# ENDURE: Procedural Review

Core Lab Adjudicated Data (N=70)	
Adjudicated Flow Limiting Dissections	(0 / 69 <sup>^</sup> )
Adjudicated >50% Diameter Stenosis	1.4% (1/69 <sup>^</sup> )
Adjudicated Bail-out Stenting* <i>Per protocol stent was permitted with flow-limiting dissection or &gt;50% stenosis</i>	1.4% (1/69 <sup>^</sup> )

- **Technical Success** (ability to deliver and inflate Chocolate Touch balloon) – **100%**
- **Device Success** (<30% residual stenosis without flow limiting dissection) – **77%\***
- **Procedural success** (device success without protocol driven bailout stenting) – **98.6%**
  - *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*

\* Undersizing of Chocolate Touch (<1:1, DCB:RVD) contributed in cases where device success was not achieved

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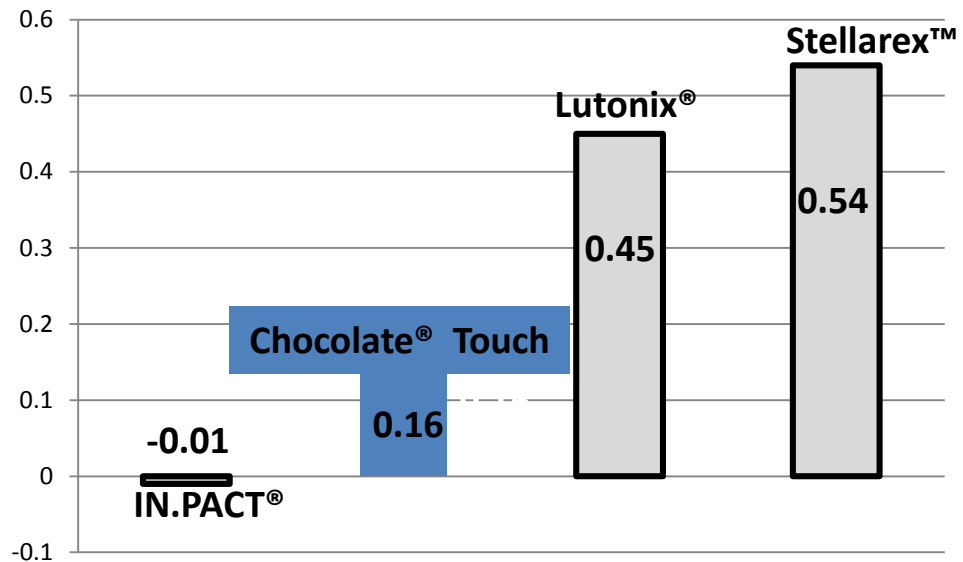


# ENDURE: Primary Endpoint LLL at 6 Month

N=49	
Mean	0.16
Std Dev	±0.72

Based upon Angiogram QVA  
analysis by the QVA Corelab (Yale  
University, New Haven, CT )

**Late Lumen Loss**  
*Compared to other Drug-Coated Balloons*



**Based on:**

- PACIFIER Study (IN.Pact)
- ENDURE Study (Chocolate Touch )
- LEVANT I Study (Lutonix)
- ILLUMENTAE Study (Stellarex)

# ENDURE: Major Adverse Events

## 6 Months (Cumulative)

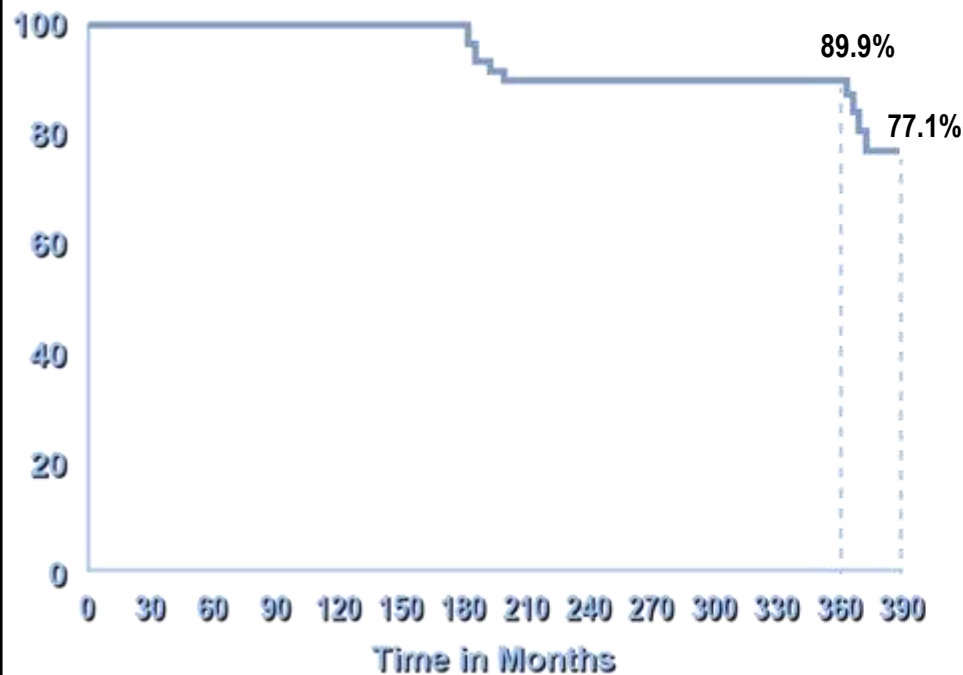
Per Protocol	
Clinically driven TLR	4
Amputation	0
All-cause Death	0
Total MAE	4

## 12 Months (Cumulative)

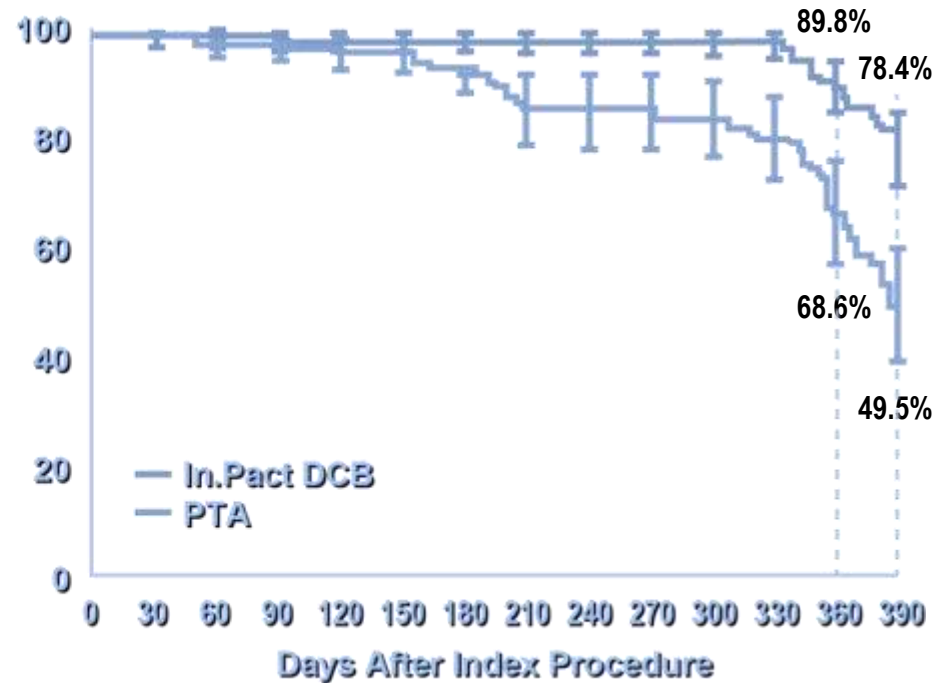
Per Protocol	
Clinically driven TLR	4
Amputation	0
All-Cause Death	1
Total MAE	5

# ENDURE: 12 Month Patency

**Chocolate Touch DCB IDE Study 12 Month Patency**

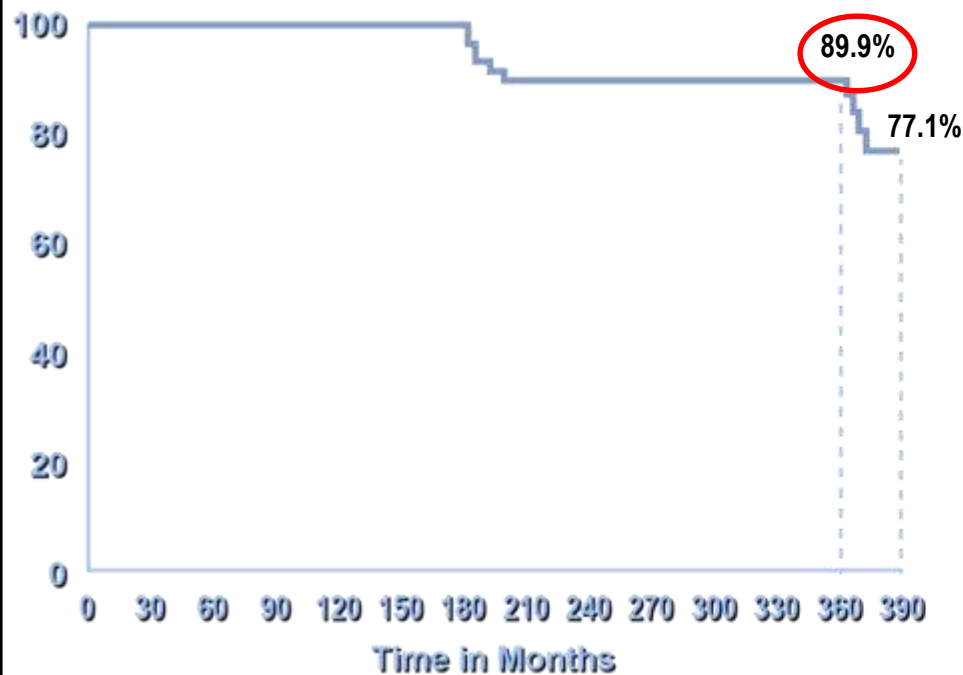


**In.Pact DCB IDE Study 12 Month Patency**

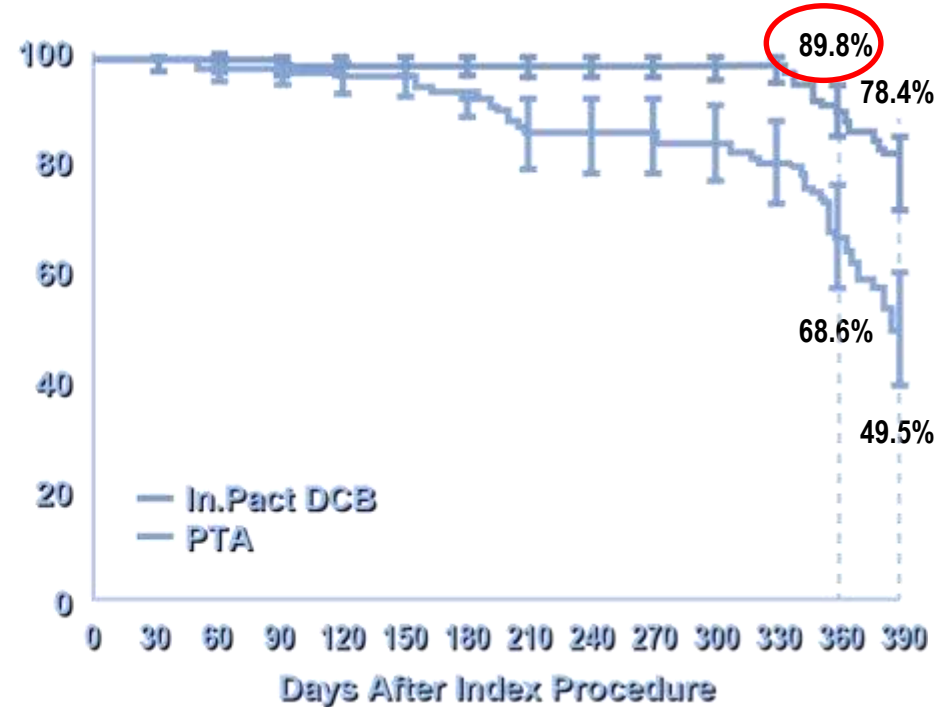


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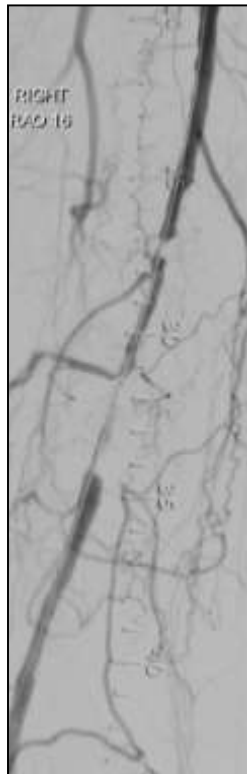


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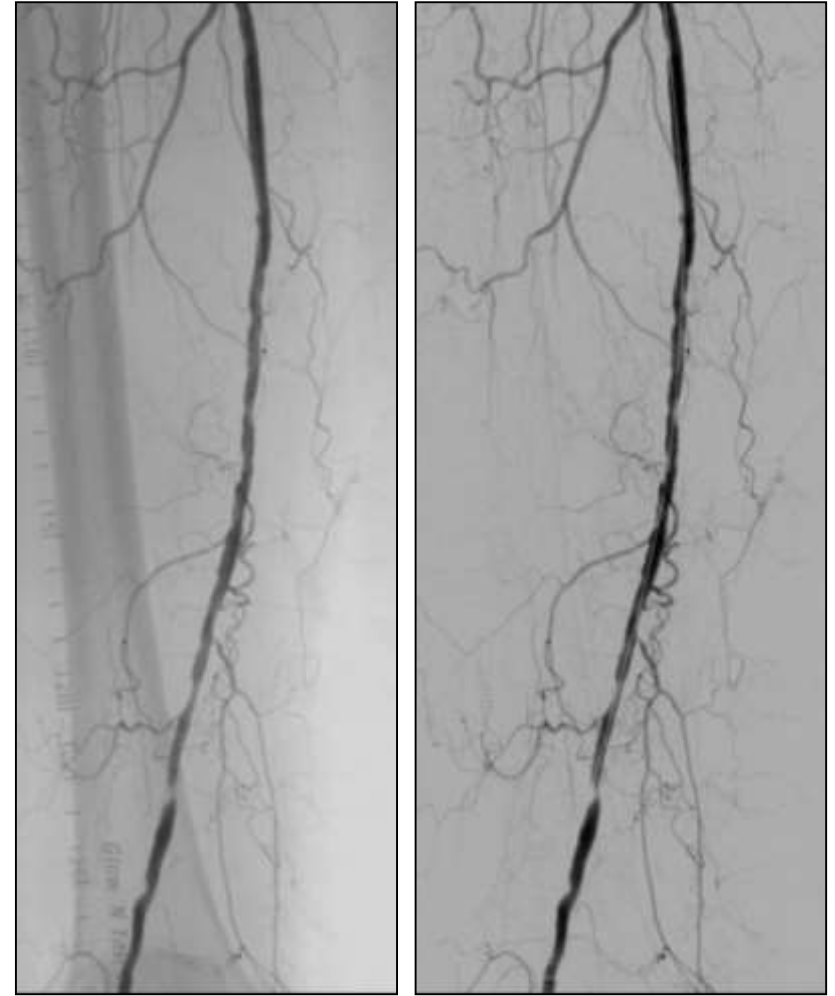
## Case Study # 1

- 69 year old male
- Right leg claudication, Rutherford 3
- 95mm long CTO/critical stenosis
- “Stent-like” appearances after primary treatment with 6.0mm X 120mm Chocolate Touch DCB



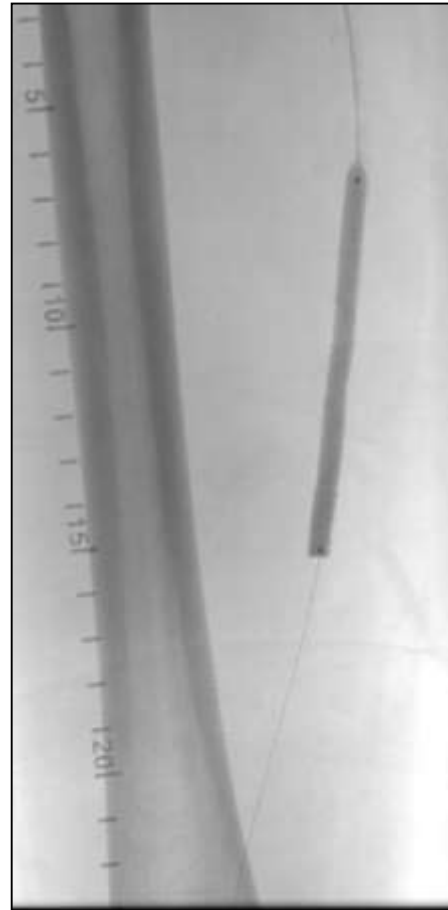
## Case Study # 2

- 82 year old female
- Right leg rest pain, Rutherford 4
- Diffuse RSFA and above knee popliteal artery stenotic disease
- RVD 4.0-4.5mm



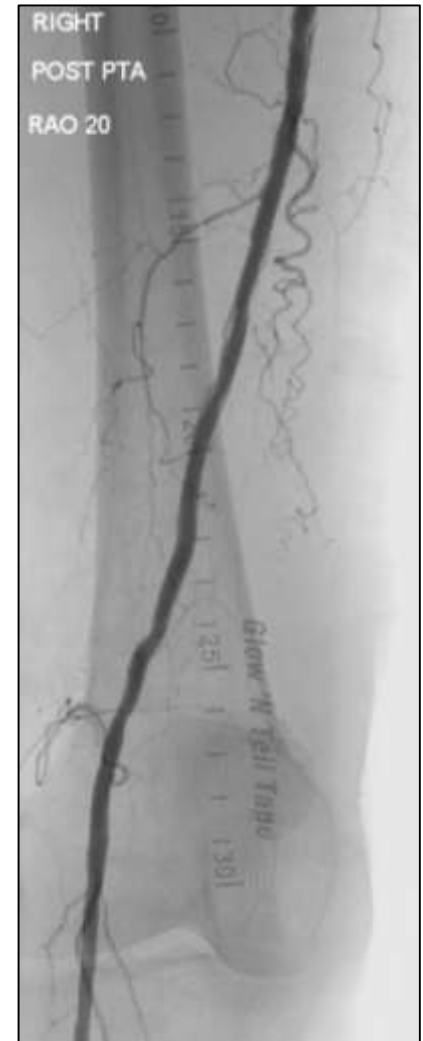
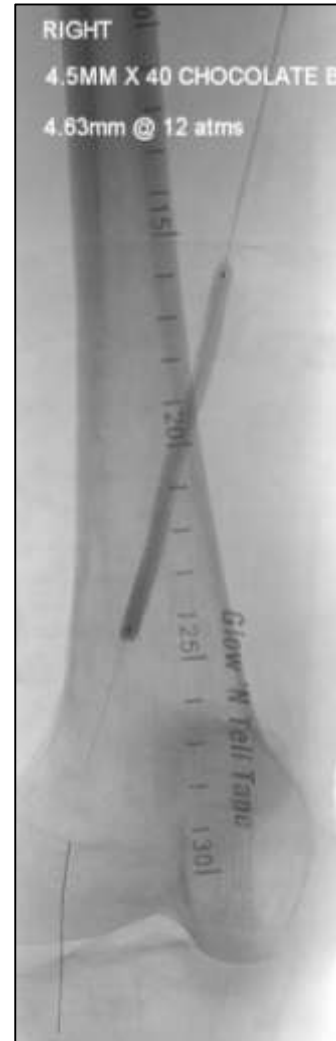
## Case Study # 2

- Proximal lesion primarily dilated with 5.0mm X 80mm Chocolate DCB
- Excellent result



## Case Study # 2

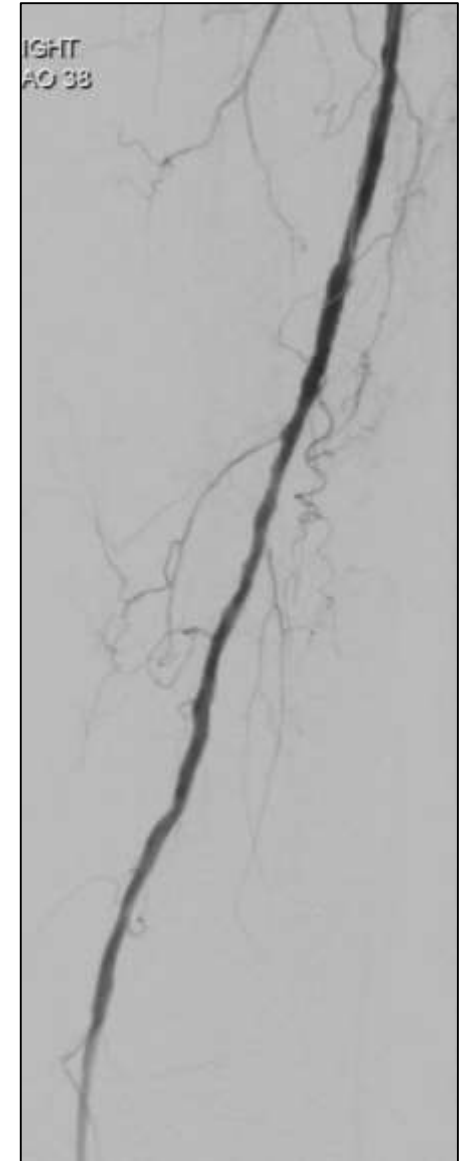
- Distal lesion primarily dilated with 4.5mm X 80mm Chocolate DCB
- Excellent result





## Case Study # 2

- Patient doing well clinically @ 6 months
- No significant re-stenosis on 6 month DSA



# Conclusions

- Chocolate's "low trauma" mechanism achieves excellent procedural outcomes resulting in a low rate of bail-out stent use
- The combination of the Chocolate platform with paclitaxel (neointimal suppression for good long-term results) offers the potential to avoid stents almost entirely
- 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 12 month patency and low late lumen loss at 6 months

# What's Next?

## Randomized Pivotal IDE Trial for Chocolate Touch

- FDA approval received Sept 16, 2016
- 30 Multi-National Centers currently undergoing start-up activities

***This will be the first head-to-head DCB study in the US***

- Randomized (1:1) to the Lutonix Drug-Coated Balloon
- Effectiveness endpoint will include bail-out stenting as a failure; Success is therefore limited only to cases in which the DCB actually treats the lesion

***Study PIs:***

***Mehdi Shishehbor (Cleveland Clinic)***

***and***

***Thomas Zeller (Univ of Freiburg-Bad Krozingen)***

## Feasibility Study for BTK Lesions Treated with Chocolate Touch

- Planned to start in early 2017
- Multi-Center International Study with up to 5 clinical Sites
  
- Designed for up to 75 patients with Rest pain or Critical Limb ischemia
- Intended to demonstrate Late Lumen Loss and Patency for Chocolate Touch in BTK Lesions

***Study PIs:***

***Andrew Holden (Auckland City Hospital)***

***and***

***Dierk Scheinert (University of Leipzig)***

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