

# BTK Intervention with Drug-Coated Balloons: Past Lessons and Future Exploration

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- **IMPORTANT INFORMATION:** These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician's professional judgment in light of all available information for the case at hand.
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# Disclosure

Speaker name:

...M Sapoval .....

I have the following potential conflicts of interest to report:

- Consulting (Boston Scientific)
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)
  
- I do not have any potential conflict of interest

# First Experience With Drug-Eluting Balloons in Infrapopliteal Arteries

A Schmidt et al JACC 2011

- 109 limbs (lesion length 177 mm).
- 3 m angiography at showed a restenosis in 27.4% (19.1% had restenosis of more than 50%, and 8.3% were totally occluded)
- Only in 9.5% of all angiographically followed up arteries was the entire treated segment re-stenosed or re-occluded.
- At 1 year (91 limbs)
  - Complete wound healing occurred in 74.2%,  
Limb salvage of 95.6%

# IN.PACT DEEP trial

- Increased amputation rate in DEB group .....
- Early stop of the trial

# Drug-Coated Balloons for Revascularization of Infrapopliteal Arteries: A Meta-Analysis of Randomized Trials

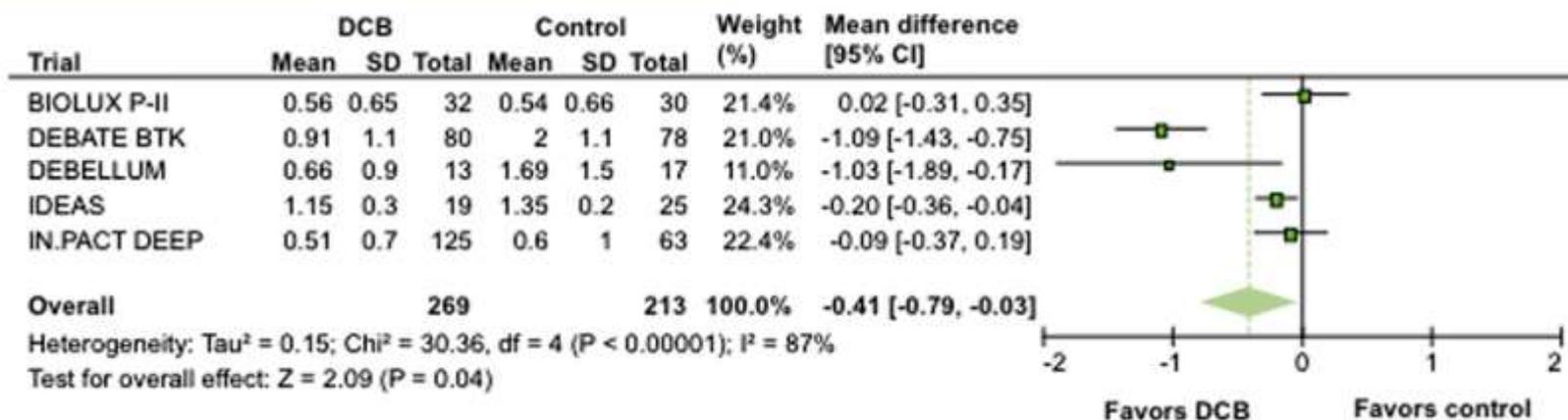
S. Cassese, et al JACC 2016

- A total of 641 patients in 5 trials received DCBs (or control therapy)
- Median follow-up : 12 months.
- Patients treated with DCBs had:
  - Similar risk for target lesion revascularization
  - Similar risk for amputation
  - Similar risk for death
  - Similar risk for major adverse events
- Lesions treated with DCBs showed lower late lumen loss (weighted mean difference 0.41; 95% CI: 0.79 to 0.03;  $p = 0.04$ ) compared with those treated with control therapy.

# Reduction of Late Lumen Loss?

**FIGURE 6** Risk Estimates of Late Lumen Loss for Drug-Coated Balloon Versus Control Therapy

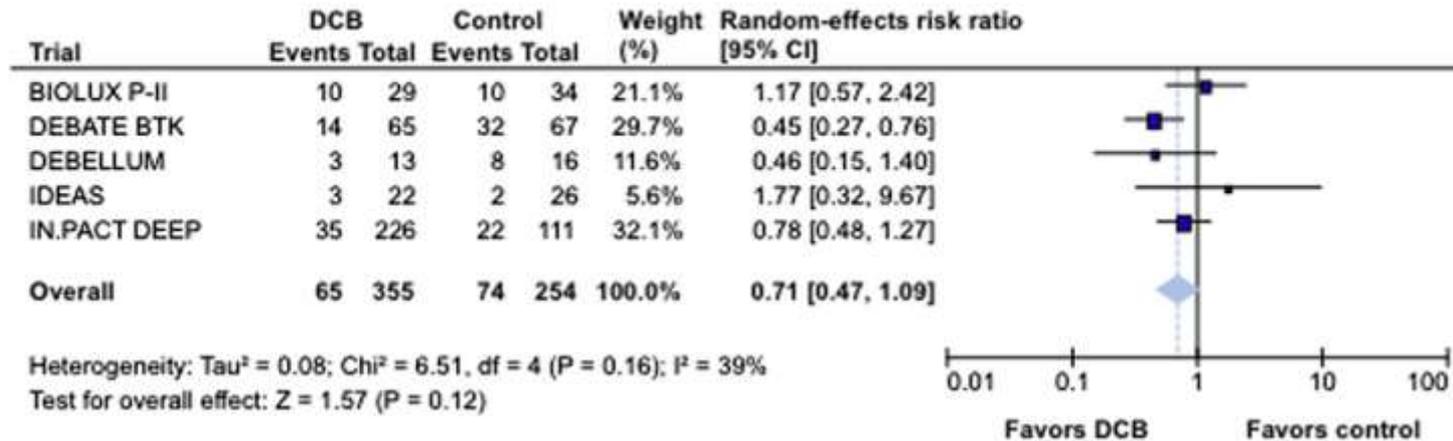
## Late lumen loss



Plots of weighted mean difference for late lumen loss associated with drug-coated balloon (DCB) versus control therapy. The **diamond** indicates the point estimate, and the **left and right ends of the line** indicate the 95% confidence interval (CI). Trial acronyms are defined in [Table 1](#).

**FIGURE 1** Risk Estimates of Target Lesion Revascularization for Drug-Coated Balloon Versus Control Therapy

### Target lesion revascularization



Plots of risk ratio for target lesion revascularization associated with drug-coated balloon (DCB) versus control therapy. The **diamond** indicates the point estimate, and the **left and right ends of the line** indicate the 95% confidence interval (CI). Trial acronyms are defined in [Table 1](#).

Favorable Angiographic Outcome  
After Treatment of Infrapopliteal Lesions With Drug-Coated  
Balloons Without Clinical Benefit  
What We Learn From a Meta-Analysis\*

Thomas Zeller, MD, Michael R. Jaff, JACC 2016

- Only the 3 uncontrolled studies using the IN.PACT Amphirion DCB resulted in superior LLL outcomes (13–15)
- Both independently core laboratory adjudicated and fully industry funded studies found identical LLL outcomes for the DCB and PTA cohorts

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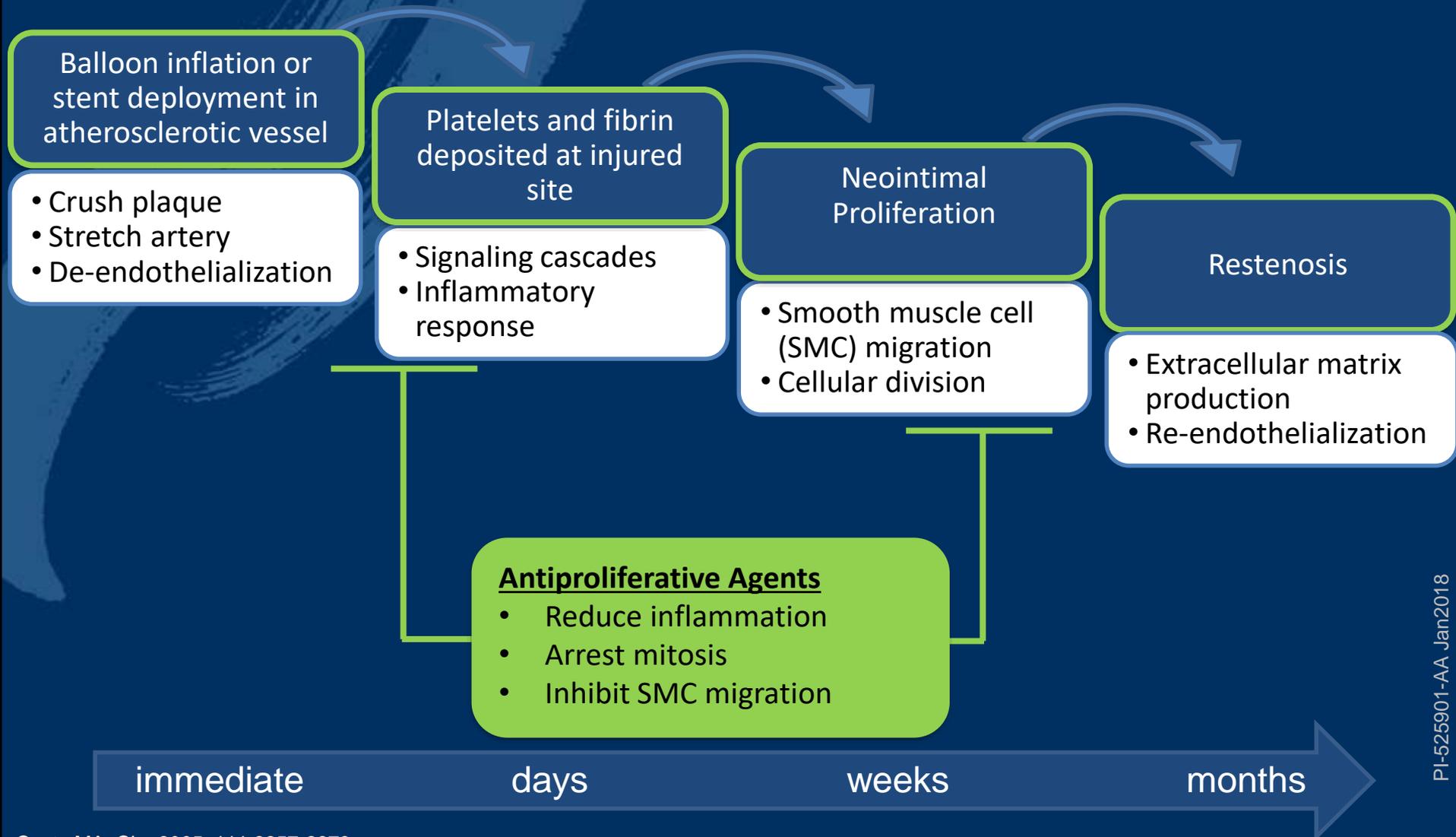
Thomas Zeller, MD, Michael R. Jaff, JACC 2016

- In summary, despite the superior angiographic outcome defined as LLL in this meta-analysis the performance of DCB in infra-popliteal lesions remains controversial.
- In particular the independently controlled studies did not result in any proof of efficacy of short-term balloon-based paclitaxel release to the wall of infra-popliteal arteries.

# DEB are still a controversy at this level

- Need for new approaches ...

# Restenotic Cascade



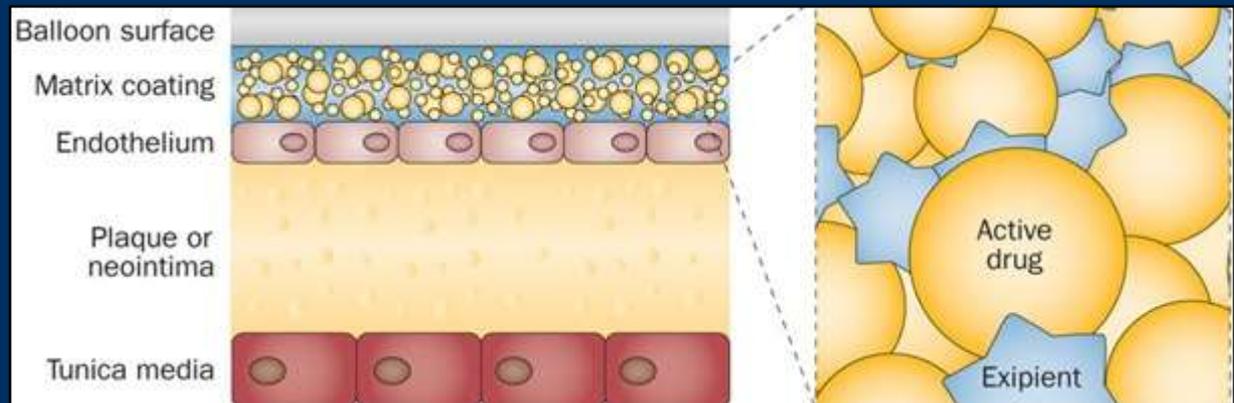
# Architecture of DCB

## Drug-coated Balloon Coating Characteristics

<b>Polymer matrix coating:</b>	drug molecules diffuse through a matrix
<b>Porous coating:</b>	drug molecules diffuse through pores
<b>Resorbable polymer matrix coating:</b>	drug molecules are encapsulated in the polymer and are released with resorption
<b>Surface deposition:</b>	imprinting of the drug on the balloon surface

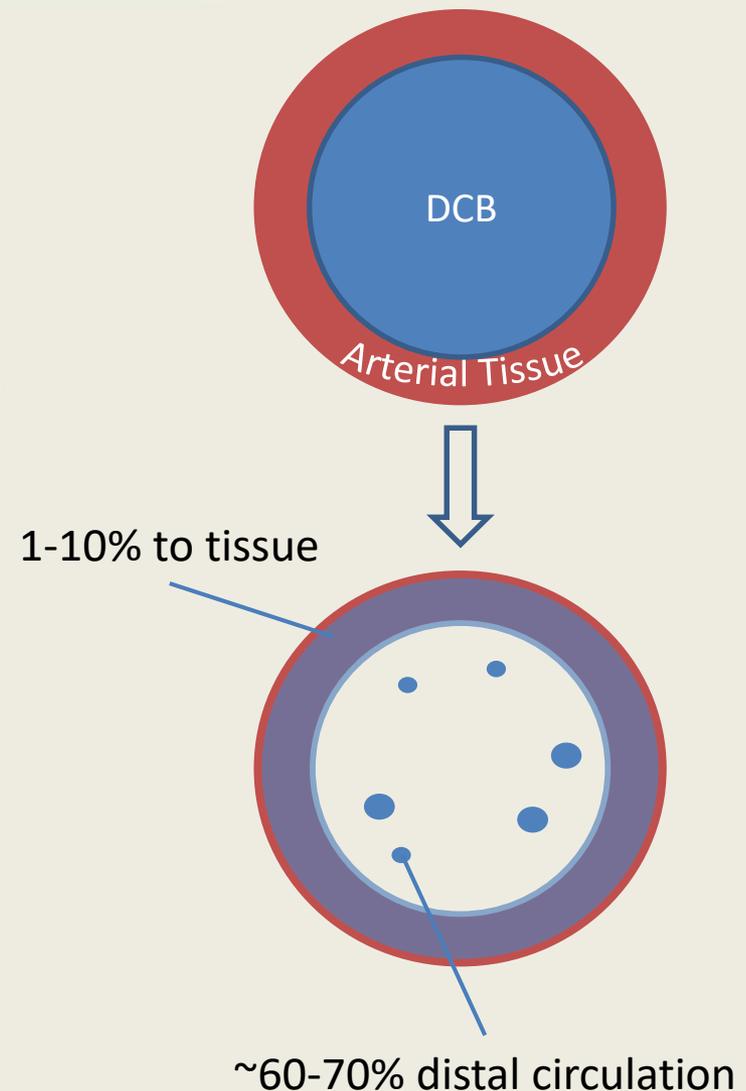
**Drug-balloon surface bonding:** strong enough to maintain drug integrity during transit while allowing efficient drug transfer:

- Minimal drug loss during transit
- Rapid and efficient drug transfer (<60 seconds)



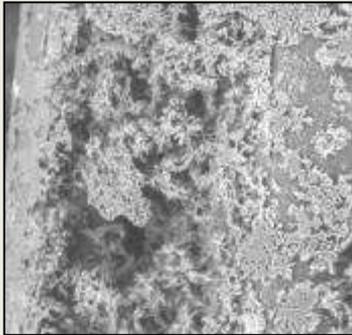
# Determinants of DCB Biological Effect

- Antiproliferative agent (Paclitaxel)
- Initial dose/dose density
- Tissue transfer efficiency
  - Coating characteristics (eg, hydrophobicity/hydrophilicity, crystallinity/amorphous morphology)<sup>1-4</sup>
  - Excipient<sup>5</sup>
  - Coating technique<sup>6</sup>
- Loss to circulation (Insertion-Transit-Inflation)<sup>1</sup> and risk of:
  - Particulate embolization
  - Systemic effects
- Paclitaxel tissue residency
  - Presence in tissue during restenotic cascade<sup>7</sup> (duration of retention)
  - Homogeneity of distribution

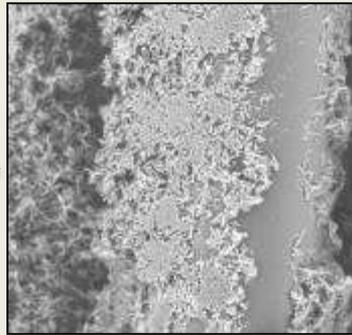


# Coating Integrity: Adherence During Hydration

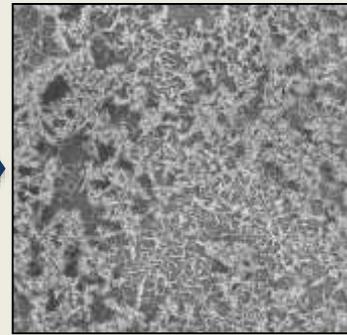
**TransPax™  
Coating**



**T = 0 min**



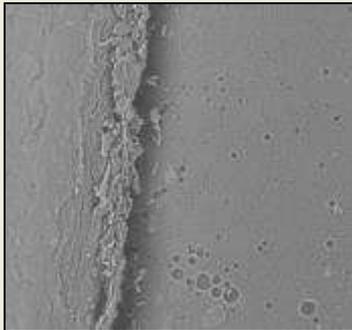
**3 min**



**10 min**

**TransPax coating  
remained adhered  
to the balloon  
during hydration**

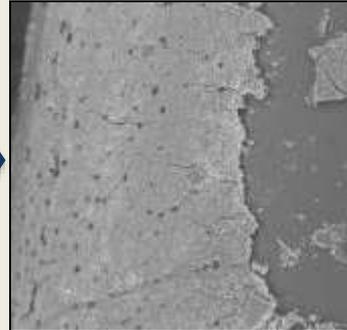
**IN.PACT™  
Coating**



**T = 0 min**



**3 min**

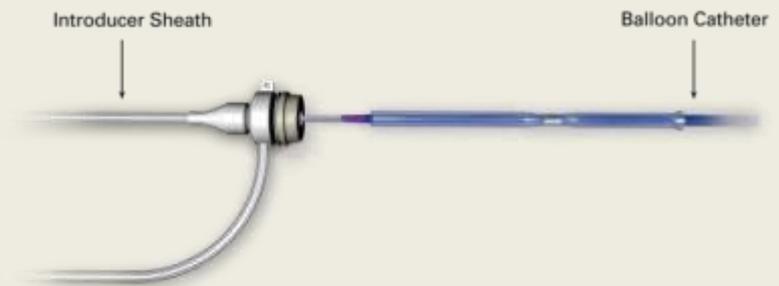


**10 min**

**IN.PACT coating  
started to crack  
and flake off after  
a few minutes of  
hydration**

# Next Generation DCB: Boston Scientific Ranger™

- Sterling balloon platform
- TransPax™ coating technology
  - Paclitaxel 2  $\mu\text{g}/\text{mm}^2$
- Ranger™ DCB Loading Tool
  - Designed to protect the drug coating
- Size matrix:
  - SFA: 4-8 mm; 30-200 mm
  - BTK: 2-4 mm; up to 150 mm

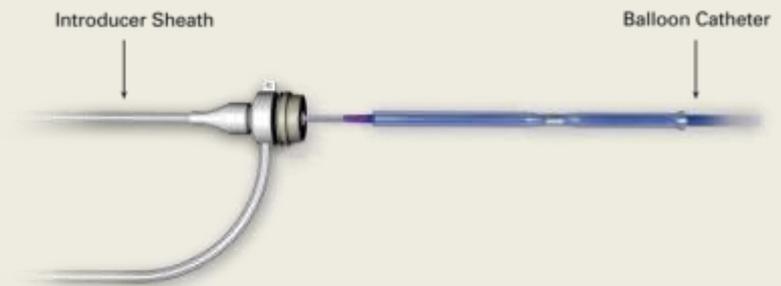


# The Ranger BTK study

- Open label prospective trial Investigator sponsored study (Boston Scientific)
- Independant Sponsoring Assistance Publique Hôpitaux de Paris (APHP)
- Angiographic and clinical results of the Ranger balloon BTK to treat patients with critical limb ischemia
- 30 consecutive patients in a single Center (Pompidou H , Paris )
- Last 6 months angiographic follow up March 2018
- Results Q 3 2018

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# Inclusion and Exclusion criteria

- Patient has documented chronic CLI in the target limb prior to the study procedure with Rutherford Category 4, 5 or 6
- Single or multiple lesions with  $\geq 70\%$  diameter stenosis (DS) or total occlusion in at least one BTK vessel
- Reference vessel reference diameter comprised between 2 and 4 mm
- Intraluminal recanalization of the target vessel with successful crossing of the target lesion and placement of the guidewire into the distal true lumen

# Primary Endpoint 6 months

- **Efficacy : Primary patency (no stenosis >50%) of the Target Lesion measured by Quantitative Vascular Angiography (QVA) at 6 months**
- **Safety : Composite of all death and major amputation at 6 months**

## Secondary Endpoints (6 and 12 Months)

- Late Lumen Loss (LLL)
- Quantitative Vascular Angiography (QVA) at 6 months (Core Lab)
  
- Clinically driven TLR
- Amputation Free Survival
- Rate of Wound Healing
- Ulcer diameter in the target limb

# As of January 2018

- 30 consecutive patients included (inclusion completed)
- Male/female 24/6
- Mean Age 68,8 Years
- Diabetes No ( n= 11) , Type 2 (n=18) Type 1 (n=1)
- Rutherford Rutherford 6 (n=1) Rutherford 4 (n =1) Rutherford 5 (n=28)
- Leg ulcer 29/30

# Lesion type

- Anterior tibial artery (n=14)
- Posterior tibial artery (n=7)
- Peroneal artery (n=2)
- Combined (n=7)

# Conclusion

- Need for more evidence in DES for BTK lesions
- The Ranger BTK will be a first step toward more evidence and design of a prospective randomized controlled trial with the Ranger BTK balloon
- Results expected Q3-Q4 2018

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