Novel Strategies For Drug-Delivery And Scaffolding For Treating Lesions In BTK Arteries

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Disclosures
Consulting/Honoraria
- Medtronic
- BARD
- Spectranetics
- Intact Vascular
- Sound Medical
- Biotronik
- Bayer
- Daiichi
- Boehringer Ingelheim
- Astra Zeneca

Drug Delivery BTK: What lies ahead?
Inconsistent data so far from trials comparing DCB/PCDBA in BTK
RCTs changed the landscape
Equivalent or inferior results

Biolux II

- Not equivalent to DCB
- Higher adverse events
- More dissections
- More pseudoaneurysms
- More stent fractures

Impact Deep

- Less angiographic follow-up compliance (~50%)
- PTA Patients showed better than expected

Past-generation DCB Technologies?

- In.Pact Amphirion and Passeo 18 Lux DCBs both coated in a deflated (folded) state

Lessons learned

- Limited generalizability of single-center studies
- Role of confounders and center: Appropriate specific symptomatic errors (i.e. balloon size, inflations pressure)
- Risk of amplification of random error due to imperfect randomization and small sample size
- Watch out study design and study execution (design a doable trial)
  - Selection of endpoints: too subjective: number of DCB vs. other mode
  - Randomization: only 1:1 (In.Pact DEEP vs. PTA)

In.Pact DEEP findings

- Some important differences at baseline:
  - Pre-intervention: In.Pact DEEP 41.7%, PTA 27.1% (p=0.047)
  - In.Pact DEEP 33.9%, PTA 17.5% (p=0.035)
- Procedure complications (DCB vs. PTA): 9.7% vs. 3.4% (p=0.035)
- Very low angiographic follow-up compliance (~50%)
- PTA Patients did better than expected

Past-generation DCB Technologies?

- As In.Pact DEEP did better than expected

In.Pact DEEP was Flawed!

- In.Pact DEEP was Flawed!
- Oral presentation TCT 2014

Drug Delivery BTK: PAST

Ongoing Trials
Lutonix DCB IDE
- RCT or Lutonix DCB vs. PTA
- Primary endpoint: limb salvage and primary patency at 6 months
- Originally designed as a 1:1 patient:primary patency at 6 months
- First patient enrolled in June 2013 (~300 patients enrolled as of April 2017)
- Protocol recently amended to include claudication symptoms

In the horizon: New Trials, New DCBs
ILLUMINATE BTK IDE
- RCT of Stellarex BTK vs. PTA
- 354 patients, in up to 45 sites in EU, Asia
- Primary endpoint: limb salvage and primary patency at 6 months
- Originally designed as a 1:1 patient:primary patency at 6 months

NEW In.Pact BTK FIH
- RCT of In.Pact BTK vs. PTA + EU centers
- Primary endpoint: limb salvage and primary patency at 6 months
- Originally designed as a 1:1 patient:primary patency at 6 months
- First patient enrolled in April 2015 (~300 patients enrolled as of April 2017)
Different drugs will give better results? _ Temsirolimus

**TANGO**
- April 26th 1st patient enrolled
- Incorporates temsirolimus (TORISEL)

Different drugs will give better results? _ Nano-encapsulated Sirolimus

**Caliber Virtue™** sirolimus-eluting angioplasty balloon and formulation

Feasibility of delivery, long-term retention and vascular effects of sirolimus nanoparticles delivered through a novel porous angioplasty balloon in normal porcine arteries.

The use of sirolimus and its analogues in balloon-based delivery technologies has been limited by their inherent instability in solution and inability to achieve long-term tissue retention when delivered into local arterial tissue.

Nanoencapsulation technologies have recently emerged as an alternative method of formulating antiproliferative agents that may overcome many of the barriers limiting the use of sirolimus.

Different drugs will give better results? _ Improved Paclitaxel DCBs

**SurVail™ Drug Coated Balloon Catheter**

- Improved delivery
- Long-term drug effect
- Reduced procedural time
- Reduced radiation exposure
- Reduced contrast dye use
- Increased patient comfort
- Safety margin demonstrated

Different drugs will give better results? _ Better uptake of drug

**OPTIMIZE**: Orbital vessel Preparation to Maximize DCB Efficacy in calcified below the knee (BTK) lesions

- Pilot study for endpoint selection
- Prospective, i.i Randomization
- 2-year follow-up

Sites in:
- Austria (Prof. Brodmann & Wiener)
- Germany (Prof. Zeller & Tepel)
- Switzerland (Prof. Broyia)

Purpose: Demonstrate the ability of the OAS to prepare catchers, BTK lesions for optimal DCB deployment

Different drugs will give better results? _ Get rid of calcium

**Lithoplasty in BTK Arteries: Study Design**
- Safety and feasibility of Lithoplasty in calcified, stenotic, infrapopliteal Arteries
- Device: 2.5 to 3.5 x 90 mm Lithoplasty
- 20 patients treated at 5 sites
- Population: RIC ≥ 5 infrapopliteal disease
- Target lesion: 2.5 – 3.5 mm, <50% stenosis, ≥150 mm length, single/multiple targets allowed
- Safety – Major Adverse Events at 30 day including death, MI, revascularization and amputation
- Efficacy - % reduction in diameter stenosis
Drug Delivery BTK: AHEAD

Different drugs will give better results? Additional drug application

A Phase 1, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Deep-Excavation Study of Vasiopentamine Administered Following Angioplasty of a Distal Popliteal, Tibial or Peroneal Artery in Patients With Peripheral Artery Disease

Purpose: Therapeutic angiogenesis, a recombinant human-platelet, for use as a reconstructive agent in peripheral arterial disease (PAD)

The research study is designed to assess the technical feasibility and safety of a percutaneous injection of vasiopentamine delivered via micro-injection catheter to the distal popliteal, tibial or peroneal arteries immediately following successful angiography.

The multicenter, randomized, double-blind, placebo-controlled, dose-escalation Phase 1 study will enroll up to 40 patients with PAD undergoing angioplasty of an artery below the knee. Immediately following angioplasty, patients will receive a single administration of either vasiopentamine or placebo via a drug-delivery catheter, the Balloon-Infused Microinflation Device developed and manufactured by Merck/A MedSystems.

First Patient enrolled on November 10th 2016 by Dr. Jhagal Mustafa

Scaffolding BTK: Ahead

Dissection Repair Below the Knee

- Prolonged inflammation
  - No data for BTK arteries
  - Longer inflation times appear to lower the rate of SPA dissection
  - Does not prevent 100% of SPA dissections

- Stenting:
  - BTK arteries are susceptible to externalosphering force, especially the posterior tibial artery
  - Chronic inflammation from high-metal burden
  - In-stent restenosis (difficult to treat)
  - Limited future treatment options

Ideal BTK Dissection Repair Would...

- Leave minimal metal behind
- Minimize vessel inflammation
- Preserve options for future treatment

Scaffolding BTK: Ahead

TOBA BTK

- Percutaneous angioplasty of iliac and superficial femoral arteries
- Angioplasty in US, Europe and New Zealand

TOBA II BTK

- Percutaneous angioplasty with stenting
- Population: Subjects with CLI, RCI or LCI and angiographic evidence of a dissection post-BTA requiring repair in the distal popliteal and/or tibial arteries
- No vessel length or number maximum

What is Next?

TOBA BTK

- Pilot IDE study of the Tack Endovascular System in the treatment of patients with critical limb ischemia

- Study Design
  - Percutaneous angioplasty with stent
  - Population:
    - Subjects with CLI, RCI or LCI and angiographic evidence of a dissection post-BTA requiring repair in the distal popliteal and/or tibial arteries
    - No vessel length or number maximum
  - Safety:
    - MLE at 90 days
  - Efficacy:
    - MLE at 6 months + POC at 30 days

Scaffolding BTK: Ahead

- New drugs (Sorilimus/everolimus instead of paclitaxel)
- Additional treatment technologies
- Debunking: Trying to get rid of calcium as a barrier
- New ways of applying the drug (Limbo)