A New Concept For Local Drug Delivery To Arteries Using The Bullfrog Catheter Technology From Mercator

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Potential conflicts of interest

Speaker's name: Andrej Schmidt
✓ I have the following potential conflicts of interest to report:

Consulting:
- Medtronic, Abbott, Boston Scientific, Cook, Cordis, C.R.Bard, Intactvascular, ReFlow Medical, Spectranetics, Upstream Peripheral

The Bullfrog® Micro-Infusion Device

• Microneedle is 34 Ga (0.007") diameter; smaller than most suture needles, so insertion does not injure the vessel.
• Needle is constantly sheathed during manipulation to prevent scratching the vessel.
• Balloon self-adjusts to a range of vessel diameters (2-4 mm, 3-6 mm or 4-8 mm)
• Balloon inflation limited to 2 atm to prevent barotrauma
• Contrast co-delivered with drug confirms real-time procedural success

Bullfrog Device Features

Bullfrog Infusion (DANCE Trial of Adventitial Dexamethasone)

Pre-Revascularization
Post-Revascularization
Post-Infusion Without Angio With Angio
20% contrast, 80% drug

Revascularization Injures the Deep Layers of the Artery

• What is seen during vascular intervention
• What is affected during vascular intervention
Restenosis Summary

INJURY

Recoil

Leukocyte adherence

Neointima

Inflammation

Stretching

Denudation

Progenitor cell differentiation

Myofibroblast proliferation

INJURY response programs

Phenotypic switch: quiescent → proliferative and synthetic

Fibrosis

Negative remodeling

Adventitia

Media

Lumen

Perivascular tissue

Restenosis Begins with Inflammation

INFLAMMATION, RECRUITMENT, PROLIFERATION, MIGRATION, FIBROSIS, HYPERPLASIA

Timeframe:

Hours to Days

Weeks

Months

Agents:

Dexamethasone

Platelet-activating compounds

DANCE-Pilot

DANCE: Dexamethasone to the Adventitia to eNhance Clinical Efficacy after fem-pop revascularization

Clinical Hypothesis:

Adventitial delivery of dexamethasone at the time of peripheral artery endovascular revascularization reduces inflammation and improves long-term patency*

DANCE-Pilot study results

- 20 patients with average lesion length 8.8cm
- 6-month primary patency: 88% (17/19)
- 1-year primary patency: 81% (13/16)

DANCE Pilot (Owens)

In.PACT SFA (Tepe, MEET 2014)

LEVANT 2 (FDA Panel 2014)

390 Day (1 year ± 1 month) Primary Patency Rates in SFA-POP Trials

Treatment

Control

N=220

N=111

N=264

N=135

N=20

N=20

Lesion length (cm) 8.9 8.9 8.8 6.3 6.3
% total occlusions 50% 26% 20% 21% 22%
% popliteals 45% 7% 7% 5% 4%
% R2 15% 38% 57% 5% 38%
% R3 65% 56% 5% 38% 63%
% R4 15% 8% 5% 15% 8%

DANCE Trial

- SFA and Popliteal
- Advential Dexamethasone added to PTA or atherectomy
- Current enrollment 280 out of 300 patients
- PI: Chris Owens, MD, UCSF, San Francisco, CA
- Co-PI: Mahmood Razavi, MD, St. Josephs, Orange, CA

Biomarker Indicators for Restenosis

- Circulating levels rise in response to inflammatory cytokines (e.g. IL-6) expressed in response to local triggers (e.g. inflammation)
- Physiologic role: bind to dead or dying cells to activate the complement system via C1Q complex
- Elevations tied to restenosis

C-Reactive Protein (CRP)

- Recruits monocytes, memory T cells, and dendritic cells to the sites of inflammation produced by either tissue injury or infection
- Dexamethasone destabilizes the mRNA that codes for MCP-1, shutting off its production
- Elevations tied to restenosis

Monocyte Chemoattractive Protein-1 (MCP-1)
DANCE Atherectomy Biomarker Results: CRP

C-Reactive Protein [mg/L] Change from Baseline to 24 Hours (Median and interquartile Range)

- Pre-Revascularization
- Post-Revascularization
- Post-Infusion

Bullfrog Adventitial Infusion BTK

Pre-Revascularization Post-Revascularization Post-Infusion

20% contrast, 80% drug

LIMBO Trials

- **Below-The-Knee**
- **2 trials**: Adventitial Dexamethasone added to PTA (Germany) or atherectomy (U.S.)
- Anticipated start: Q1 2016
- **LIMBO-PTA PI**: Dierk Scheinert, MD, University Hospital Leipzig, Germany
- **LIMBO-ATX PI**: George Adams, MD, UNC-Rex, Raleigh, NC