

# Temsirolimus Adventitial Delivery to Improve ANGiographic Outcomes Below the Knee (TANGO)

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# Disclosure

Speaker name: Ehrin Armstrong

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I have the following potential conflicts of interest to report:

- Consulting: Abbott Vascular, Boston Scientific, Cardiovascular Systems, Gore, Medtronic, Philips, PQ Bypass, Shockwave
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

I do not have any potential conflict of interest

# Presented on Behalf of Enrolling Sites

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- Mehdi Shishehbor, DO, MPH, PhD, University Hospital, Cleveland, OH, USA

# Background

- Current infrapopliteal treatments lack long-term durability
- Drug-coated balloons continue to show poor or no results in BTK
- Failure of DCB in BTK region may be inherent to heavy thrombus, plaque and calcium burden
- Direct adventitial delivery provides a shortcut through the disease
- Temsirolimus is an ideal agent to reduce restenosis
- As interventionalists, we need to be stewards of new technology and make decisions based on high quality trials and positive RCT data

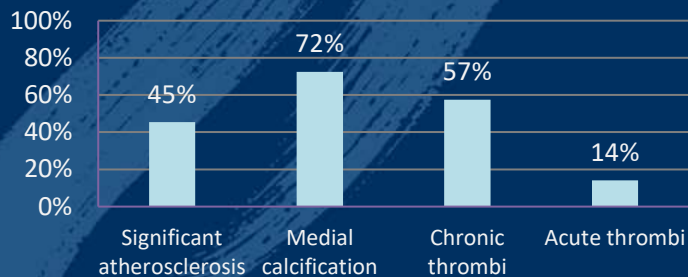
# DCB in BTK

## *A Series of Negative Studies*

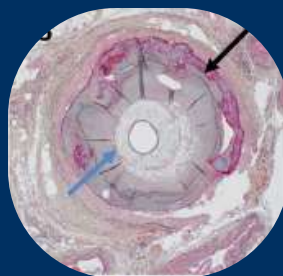
Study	Endpoint Measure	DCB Group	PTA Group	Difference	Outcome
In.PACT DEEP (JACC 2014;64:1568-76)	12-month Freedom from Restenosis	59.0%	64.5%	-5.5%	Further studies discontinued due to safety concerns
	12-month Freedom from CD-TLR	88.1%	86.5%	1.6%	
	12-month Freedom from Major Amp	91.2%	96.4%	-5.2%	
BioLUX P-II (JACC Intv 2015;8:1614-22)	6-month Freedom from Restenosis	46.9%	58.6%	-11.7%	Negative efficacy result
Lutonix BTK (J Inv Cardiol 2019;31:205-11)	6-month Primary Efficacy Endpoint*	74.5%	63.5%	11.0%	Did not meet primary endpoint, signal dropout at 12 months
	12-month Primary Efficacy Endpoint	60.4%	60.9%	-0.5%	
*Composite of freedom from major amputation, target lesion occlusion, or CD-TLR					

# BTK Challenge for Intimal Drug Delivery: Barrier Tissue

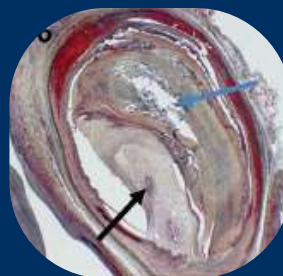
Makeup of typical BTK lesions  
(Narula, 2018)



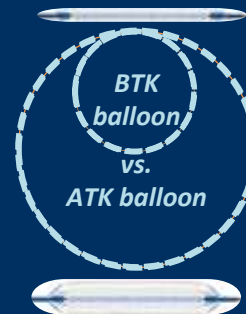
*Plaque burden and medial calcification*



*Luminal thrombus*



*Lower payload than ATK*



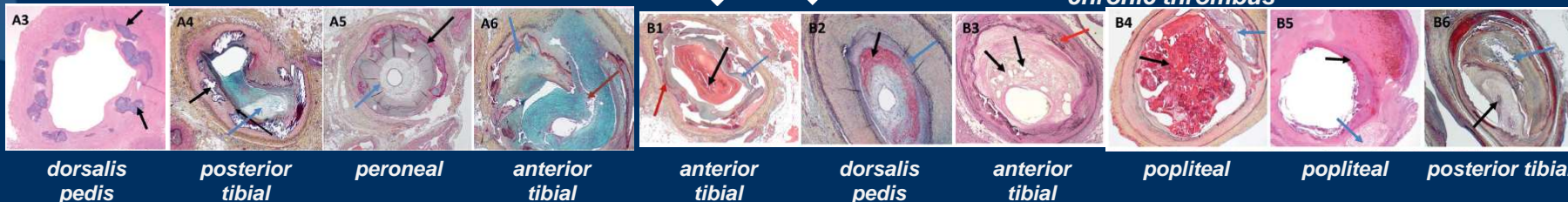
*Transit time leads to wash-out*



*medial calcification*

*fibrocalcific or fibroatheromatous plaque  
acute thrombus*

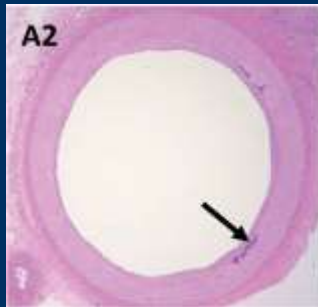
*chronic thrombus*



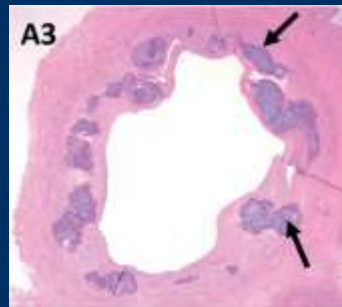
Narula, et al. JACC 2018;72:2152-63.

# Adventitia/Perivascular Tissue is Key Driver of Restenosis

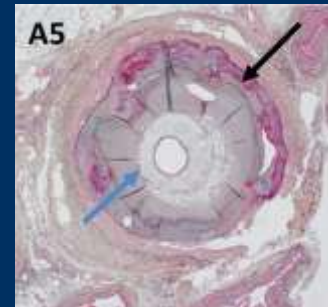
- “Am I looking forward to new DCB BTK results?”
- We all are familiar with the adventitia by now
- Can DCB still work in BTK?



**Yes**



**Maybe**

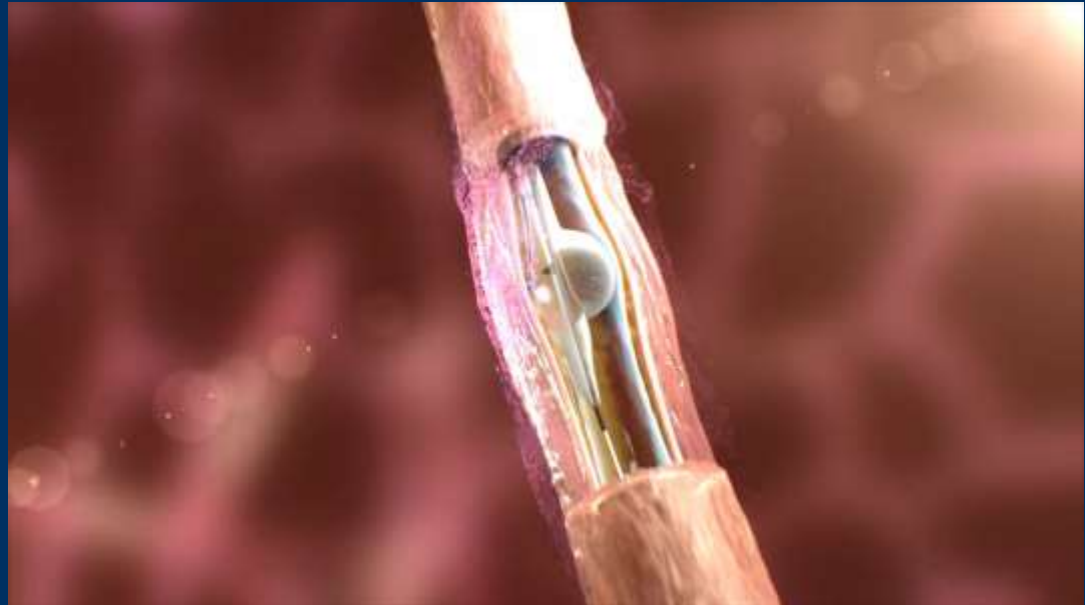


**How?**

*Images: Narula, et al.  
JACC 2018;72: 2152-63.*

# The Bullfrog<sup>®</sup> Micro-Infusion Device

- Adventitial delivery confirmed with contrast medium
- Dose control: Inject from separate syringe only after needle is engaged
- Unlimited payload: Not limited to the tiny surface area and thickness of a drug coating
- Multiple injections with one device – no need to swap out balloons for long lesion treatment





# TANGO Trial Design and Enrollment

- TANGO: Temeirolimus adventitial delivery to improve ANGIOgraphic Outcomes below the knee
- Phase II prospective, multi-center, randomized, double-blinded, dose-escalation trial
- FDA IND-regulated
- Randomized 2:1 for treatment vs. control

*Temeirolimus 0.1 mg/mL (n=20)*  
*Temeirolimus 0.4 mg/mL (n=21)*

vs.

*Saline control (n=20)*

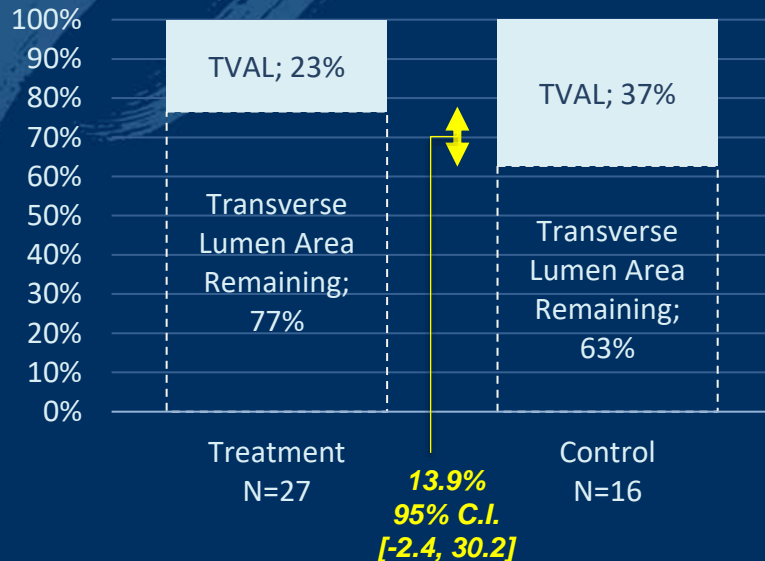
- Primary endpoint (biologic signal)
  - 6-month angiographic TVAL – Transverse View Area Loss
- Key secondary endpoint (primary endpoint for Phase 3)
  - 6-month composite freedom from Clinically Relevant Target Lesion Failure (CR-TLF):
    - CD-TLR
    - Ischemia-related major amputation
    - Clinically relevant target lesion occlusion

Characteristic	Treatment				Control			
N	41				20			
Age (years)	72.4 ± 9.4				73.2 ± 7.9			
Male	63%				60%			
Black or African Descent	32%				30%			
Caucasian	68%				60%			
Obesity (BMI ≥ 30 kg/m <sup>2</sup> )	34%				25%			
CAD	51%				70%			
Diabetes Mellitus	59%				70%			
Hyperlipidemia	90%				85%			
Hypertension	85%				85%			
Tobacco Use (Current)	10%				20%			
Rutherford 3   4   5	42%	17%	42%	45%	10%	45%		
ABI	0.8 ± 0.41				0.9 ± 0.36			
Lesion Length (cm)	10.9 ± 7.8				12.7 ± 7.8			
TASCII A   B   C   D	32%	17%	22%	29%	20%	25%	10%	45%
Severe Calcification	13%				10%			
Total Occlusion at Baseline	32%				45%			

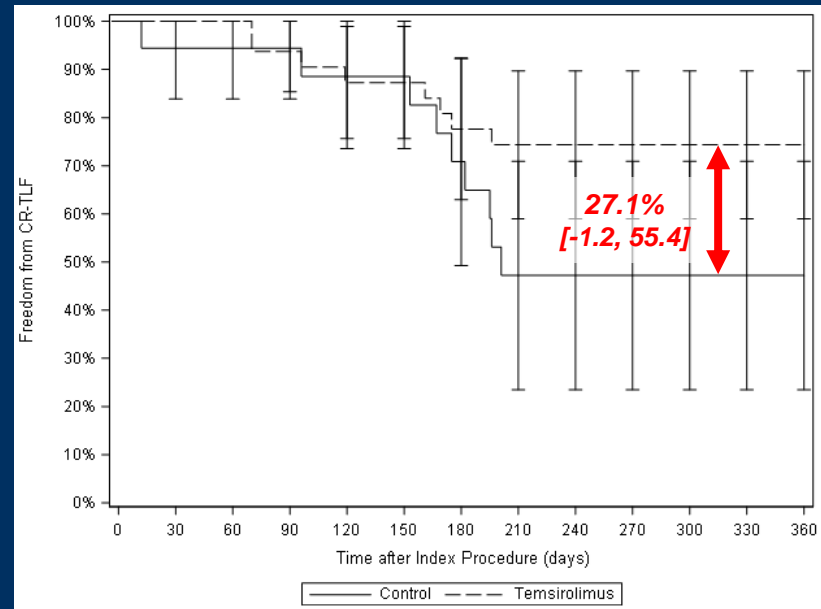
P=NS for each category

# TANGO Efficacy Results

Mean 6-month Transverse-View Area Loss (TVAL) in PP Group, Relative to Transverse Lumen Area Remaining



Kaplan-Meier Freedom from Clinically Relevant Target Lesion Failure in PP Group

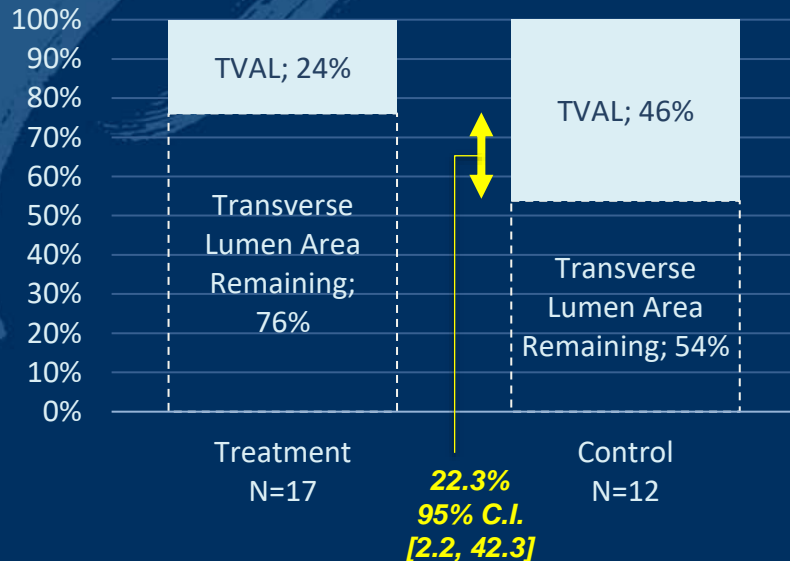


**Treatment**  
**74.4%**  
**(N=35)**

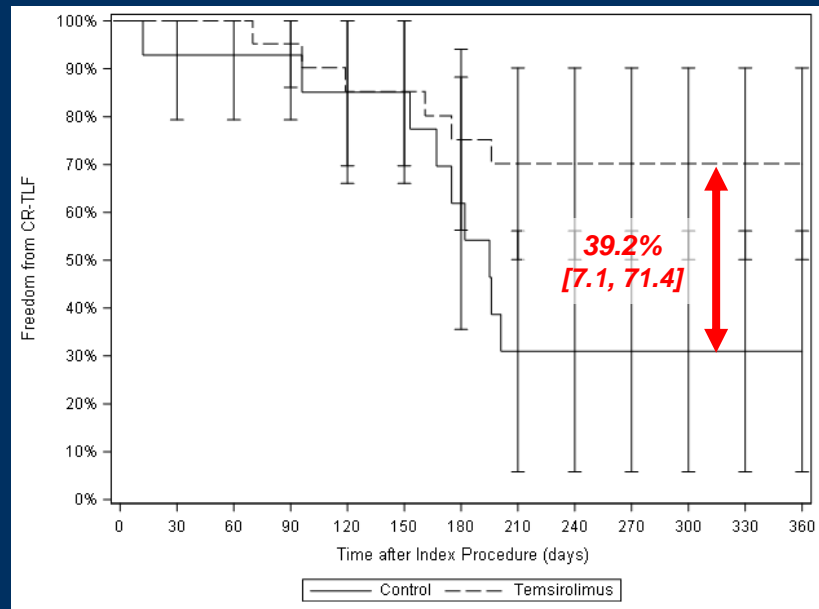
**Control**  
**47.2%**  
**(N=18)**

# TANGO Efficacy Results Excluding TASC A Lesions

Mean 6-month Transverse-View Area Loss (TVAL) in TASC B-D Group, Relative to Transverse Lumen Area Remaining



Kaplan-Meier Freedom from Clinically Relevant Target Lesion Failure in PP Group



**Treatment**  
**70.2%**  
**(N=22)**

**Control**  
**31.0%**  
**(N=14)**

# Conclusions

- BTK disease has been more difficult to achieve positive improvement with drug-enhanced therapy than ATK
- BTK drug treatment must pass through excessive tissue barriers
- While new DCB and DES are in development, positive results have been limited to short, focal segments
- Adventitial drug delivery has provided robust outcomes in a multicenter, dual-blinded Phase 2 RCT
- A sizable effect has been seen in more complex lesions with adventitial temsirolimus delivery