Where do we stand with DCB therapy in BTK arteries?

Francesco Liistro

Chief of Cardiovascular Intervention

San Donato Hospital, Arezzo, Italy

Disclosure

Speaker name: Francesco Liistro

I have the following potential conflicts of interest to report:

x Consulting: Medtronic, Boston Scientific, ACOTEC Ltd, Biotronic

Employment in industry

Stockholder of a healthcare company

Owner of a healthcare company

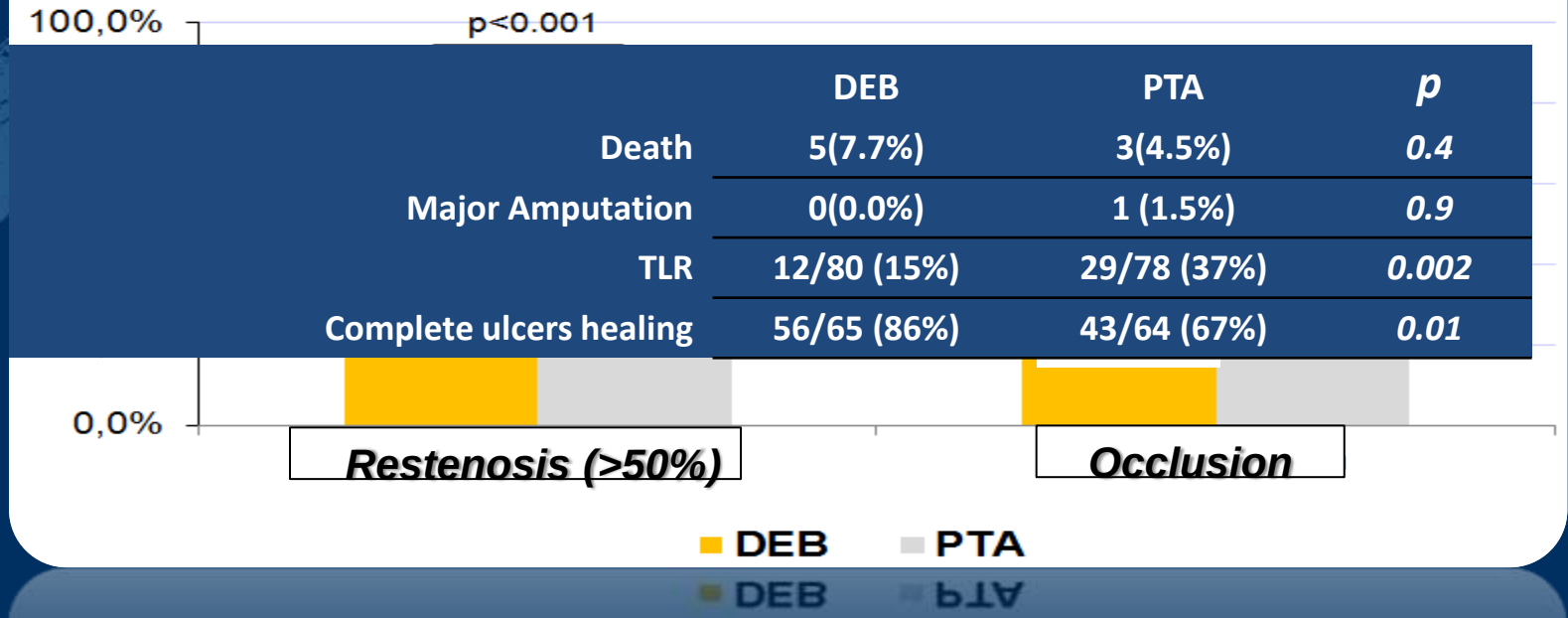
Other(s)

I do not have any potential conflict of interest

Past experience with DCB in BTK

DEBATE BTK (2013)

12-month Restenosis and Occlusion rates



	DEB	PTA	*p*
Death	5(7.7%)	3(4.5%)	*0.4*
Major Amputation	0(0.0%)	1 (1.5%)	*0.9*
TLR	12/80 (15%)	29/78 (37%)	*0.002*
Complete ulcers healing	56/65 (86%)	43/64 (67%)	*0.01*

Nr eligible Lesions	74 (92.5%)	74 (94.9%)
Lesion Assessment: ANGIO	67 (90.5%)	68 (91.9%)

Liistro et al, Circulation 2013

Inpact Deep

Angio Cohort

	DEB	PTA	*p*
LLL	0.51±0.66	0.60±0.97	*0.5*
Restenosis	41(25/61)	35.5 (11/31)	*0.9*
Angio follow-up	61/113(54%)	31/53(57%)	

All Patients

TLR (non amputees)	9.2%(18/196)	13.1%(14/107)	*0.29*
12-month Major Amputation	8.8% (20/227)	3.6% (4/111)	0.08
12-month Wound Healing	73.8% (121/164)	76.9% (70/91)	0.57

Difference in study design, completion, wound care program and procedural strategy

Anphirion In.Pact technology not optimal

Key points for DCB in BTK

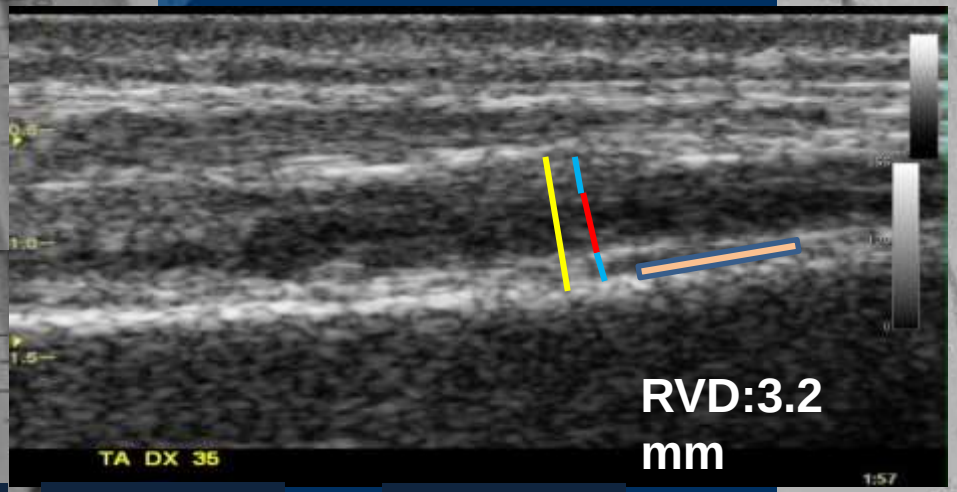
- OBA before DCB
- RVD and DCB sizing
- Balloon Technology

(Transfer and Action)

- Target vessel flow in the 24h post
- Diabetic foot management until healing
- Fast track strategy for re-intervention

Reference Vessel Diameter and Balloon/Artery Ratio: Is Angio enough?

POBA2.5x150mm



RVD:3.2 mm

RVD:2.6mm

Vessel size

Vessel lumen

Plaque burden

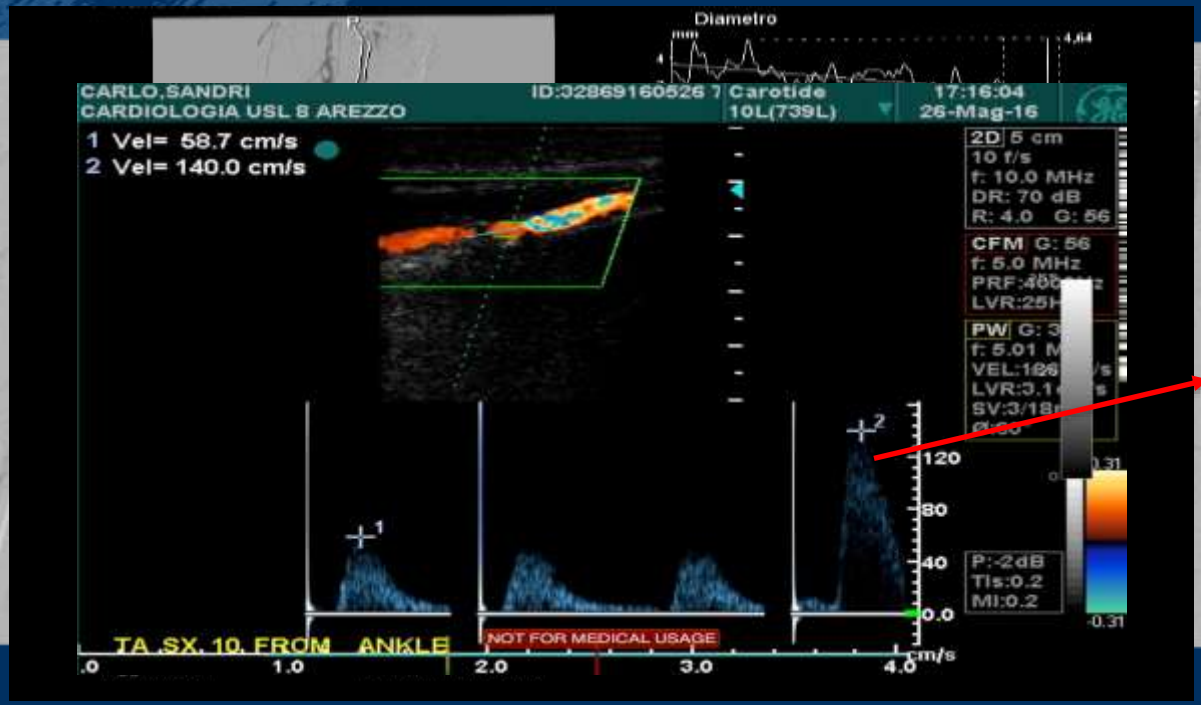
Media

Balloon angioplasty is often undersized in BTK

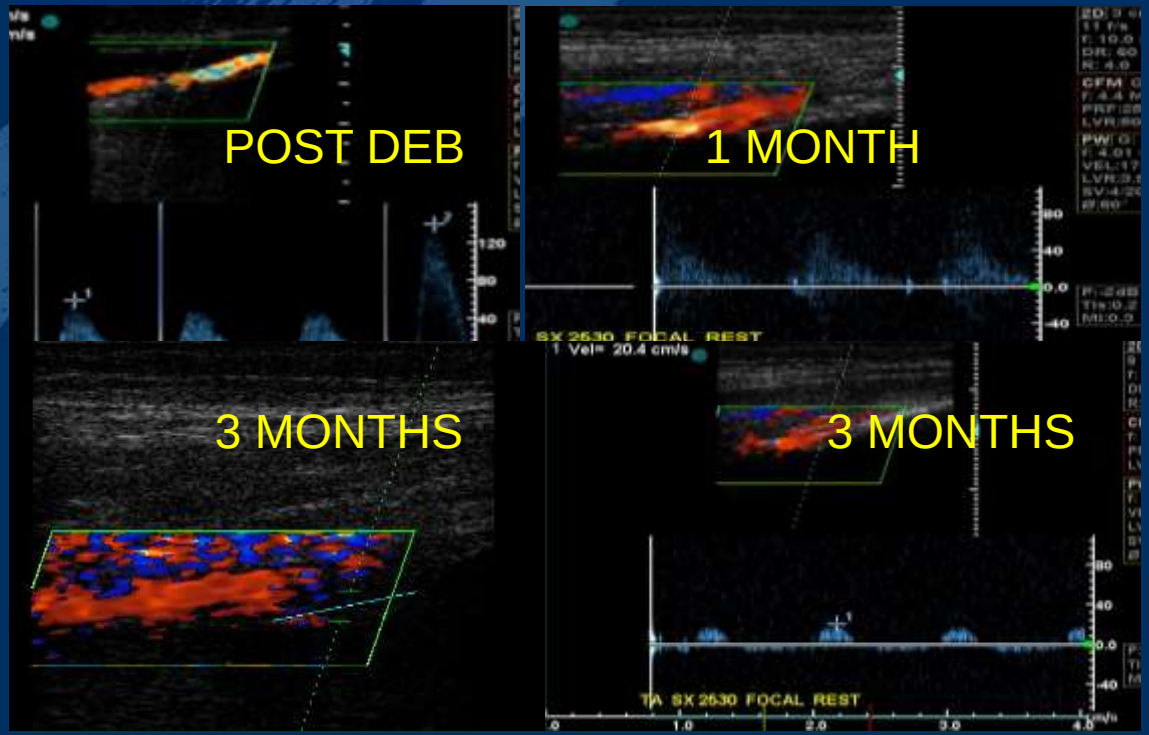
Duplex is more accurate for RVD and Balloon size

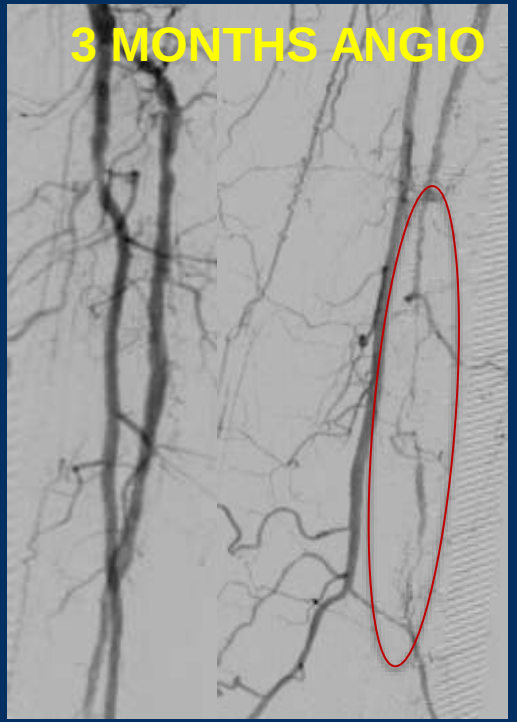
Balloon underzized and reocclusion

Residual significant narrowing

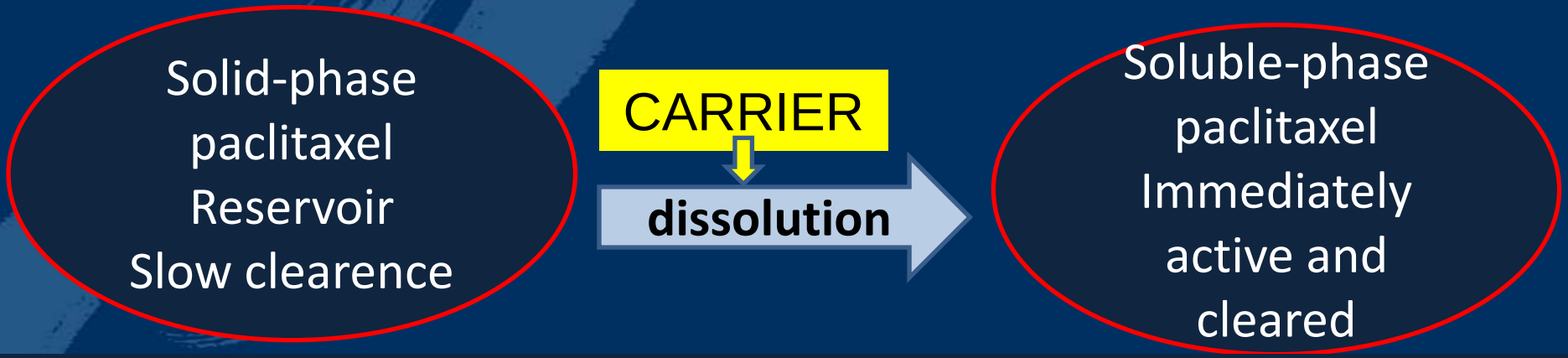


Residual significant narrowing: HIgh risk of reocclusion





Action Phase



The carrier my accelerate or slow down the dissolution of paclitaxel. Hydrophilic carriers do not emulsionate paclitaxel (hydrophobic)

Coating formulation and technology (drug dose+excipient) is key in sustaining therapeutic levels of Paclitaxel in the tissue

Recent data show efficacy od paclitaxel DCB

	AcoartBTK	Acoart II	InPact BTK
Patients/lesion	105/128	120/131	53
Mean age	75.±8.6	70.7±7.4	73±7.4
Male gender	76%	60%	78%
Diabetes	100%	72%	86%
Number of limb	109	120	*53*
Rutherford class 4	7%	42%	*12%*
5-6	93%	58%	*88%*
Lesion length	180±110	180±80	215±60
CTO	68%	77%	100
F.Up angio (months)	6	6	9

Patients Clinical Characteristics

	AcoartBTK	Acoart II	InPact BTK
RVD pre	2.7±0.30	2.55±0.34	*2.8*±0.5
DS% pre	91%	92%	*98%*
Balloon Diameter	2.9	2.9	3.0
Inflation pressure	14	13	12
Inflation Time	>2min	>2min	>2min
MLD post	1.9	1.6	1.8

Acoart BTK 6/12 month Outcome

	LITOS	POBA	p value
Lesion available	58/62(93.3)	62/66(93.9)	0.9
LLL	0.51±0.60	1.31±0.72	<0.001
TVA (mm^2)	440.75±308.83	217.34±.236.34	<0.001
TVAL(%)	5.87±23.16	51.37±36.27	<0.001
Occlusion	5(8.6)	30(48.4)	<0.001
TLR*	6/58(10)	27/59(46)	<.001
Major Amputation*	0	0	-

*12 months

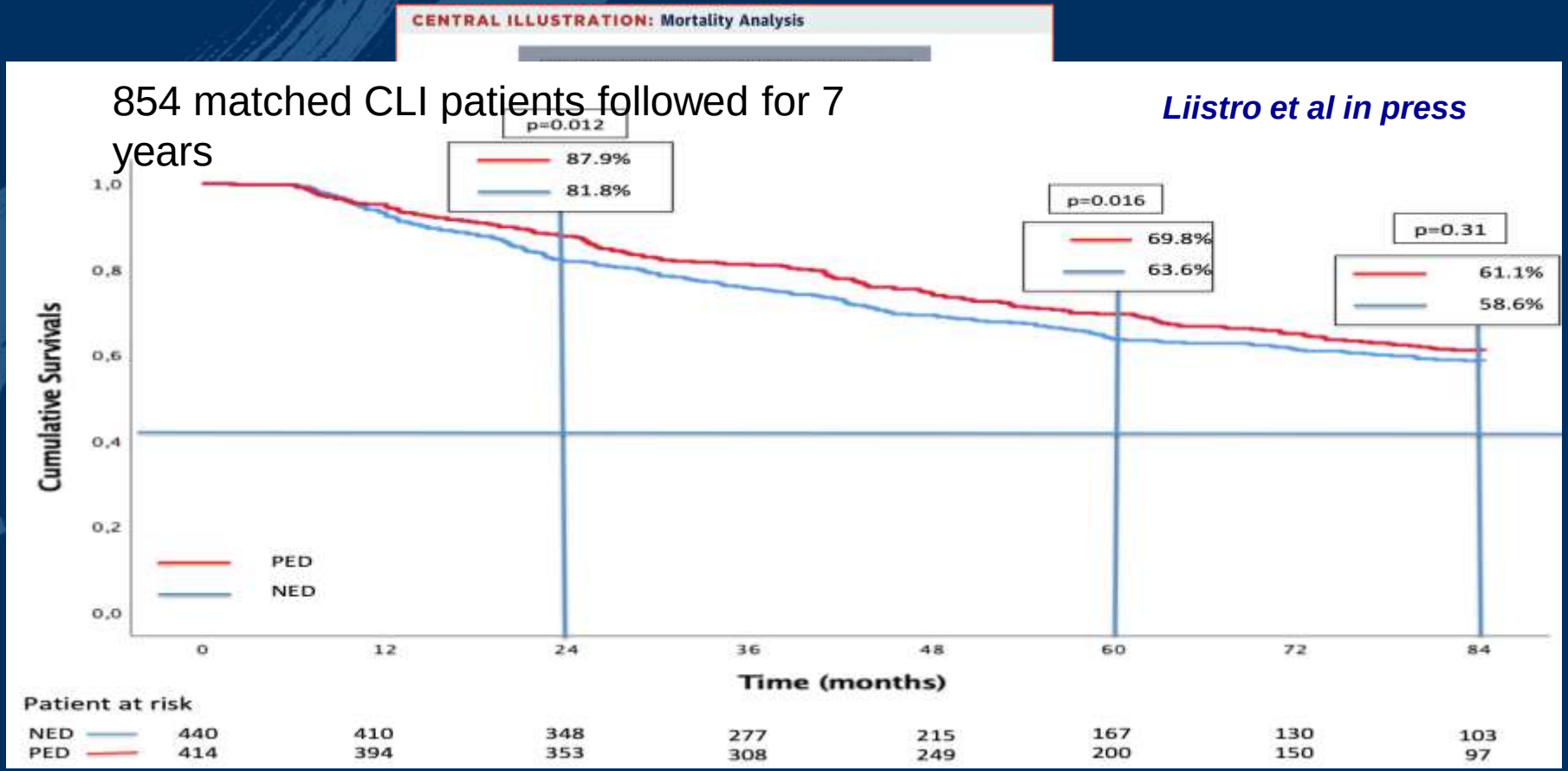
Acoart II

	DCB	PTA	P-value
Angiographic:			
MLD			
post procedure	1.66±0.41	1.56±0.35	0.13
6-month	1.33±0.78	0.49±0.59	<0.001
LLL	0.35±0.74	1.08±0.62	<0.001
Major amputation	1.6% (1/61)	1.7% (1/59)	0.98
CD-TLR	4.9% (3/61)	20.3% (12/59)	0.01

In.Pact BTK Outcome 9 months

	DCB (N=24)	PTA (N=29)	P value
Classic LLL	0.89±0.77	1.31±0.72	0.07
Sub-Segmental LLL	0.59±0.94	1.26±0.81	0.017
Reocclusion	**84.6% (11/13)**	**60.0% (6/10)**	0.341
Safety Composite Endpoint[1] %(n)	**91.3% (21/23)**	**87.5% (21/24)**	**1.000**
Device- and Procedure-related Death through 30 Days %(n)	**0.0% (0/23)**	**3.7% (1/27)**	**1.000**
Target Limb Major Amputation within 270 Days %(n)	**0.0% (0/23)**	**0.0% (0/23)**	**>0.99**
Clinically-driven TLR within 270 Days %(n)	**8.7% (2/23)**	**8.7% (2/23)**	**1.000**
All-cause Death %(n)	**4.3% (1/23)**	**8.0% (2/25)**	**1.000**

Paclitaxel Eluting Devices and Mortality

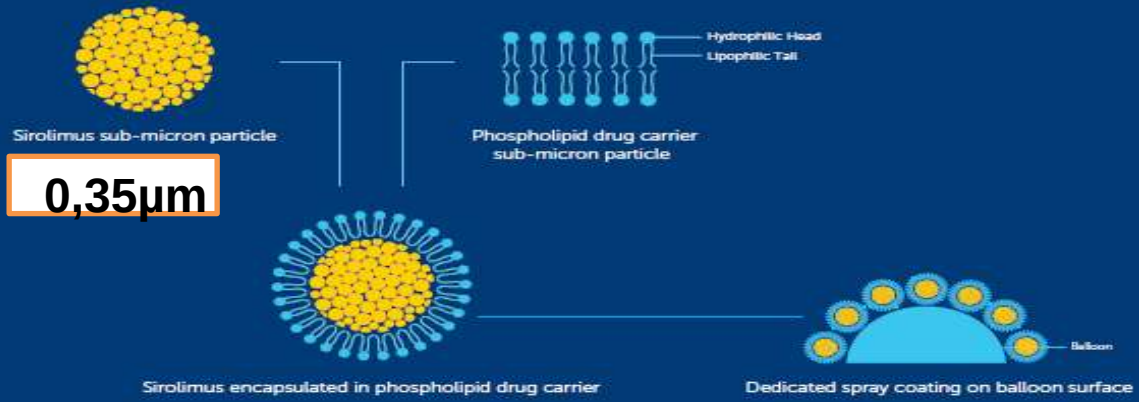


Sirolius eluting Balloon for BTK

Company	Product	Drug	Concentration	Delivery Agent
Abbott Vascular	NA	zotarolimus	6-7 µg/mm^2	iopromide matrix
Caliber Therapeutics	Virtue DCB	sirolimus nanoparticles	3 mg	porous balloon
Concept Medical	Magic Touch DCB Xtreme Touch DCB	sirolimus nanoparticles	1.3 µg/mm^2 3.0 µg/mm^2	phospholipid excipient
MedAlliance SA	Selution DCB	sirolimus nanoparticles	1.0 µg/mm^2	CAT-cell adherence technology
Sahajanand Medical Technologies	NA	sirolimus	0.7 µg/mm^2	PLGA/PVP 50-50 coating

NANOLUTE TECHNOLOGY

- Conversion of Sirolimus drug into sub-micron sized particles.
- Encapsulation of sub-micron sized Sirolimus drug into highly biocompatible drug carrier – Phospholipid.
- Phospholipid comprises of one hydrophilic head and two lipophilic tails, which improves adhesion property of encapsulated Sirolimus.
- Upon inflation of MagicTouch SCB at target site, drug carrier with Sirolimus drug inside gets transferred to the vessel wall following the principle of co-efficient diffusion.
- Upon body PH variation, drug carrier mimics the body lipids and liberates Sirolimus.
- The sub-micron sized Sirolimus drug particles penetrate the deepest layer of the vessel over a period.



ADVANTAGES OF NANOLUTE TECHNOLOGY

- Facilitates better adhesion of Sirolimus on the balloon surface
- Circumferential coating
- Effective drug transfer to the deepest layer of the vessel
- Better in-tissue bioavailability of Sirolimus

WHY SIROLIMUS

Attribute	Paclitaxel	Sirolimus
Drug Nature	Cytotoxic	Cytostatic
Drug Therapeutic Range	Narrow	Wide
Margin of Safety	100 fold	10,000 Fold
Tissue Absorption	Fast	Slow
Tissue Retention	Long	Short

DEBATE BTK DUELL

172 CLI Patients
4 centers in Tuscany

Optimal angioplasty
evus+angio

random (1:1)

Aspirin + Clopidogrel
3 months

6-month Angiograph

12-month Duplex&Clinical follow-up

Key Exclusions

- Allergy to Paclitaxel
- Contraindication for combined antiplatelet treatment
- Life expectancy <1 year
- Lack of consent
- Need for BTA angioplasty

Key Inclusions

- RC 4-5-6
- Stenosis / occlusions >40 mm
- Distal run-off (Kawarada 1-2a-2b)
- Popliteal (P3) segment patent
- No flow-limiting dissection

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PACLITAXEL Litos DCB (Acotec Ltd)

86
SIROLIMUS Magic Touch DCB (Concept Medical)

Secondary Endpoints:
12-month TLR;
TL occlusion
major amputation

Primary Endpoint:
6-month LLL

Conclusions

- DCB is the potential antiproliferative tool to match BTK disease
- A dedicated interventional strategy is required for transfer the drug into the vessel wall.
- New Studies highlight the patency advantage of Paclitaxel DCB over POBA
- Sirolimus eluting balloon started a CLI programm and results are awaited

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