Leave Nothing Behind and Suppress Restenosis: Drug-Coated Balloons

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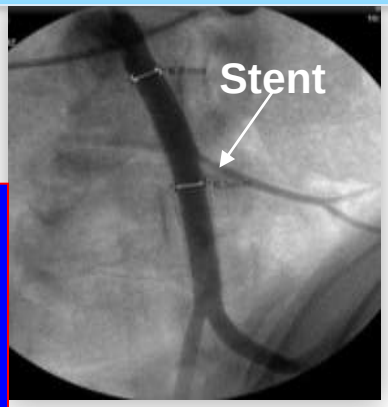
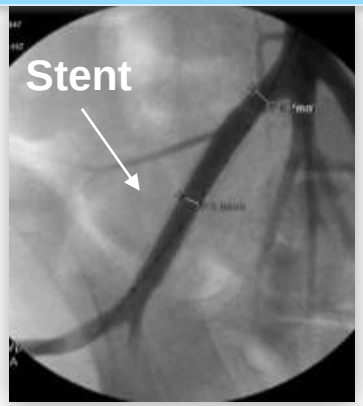
Limitations of Stents in SFA

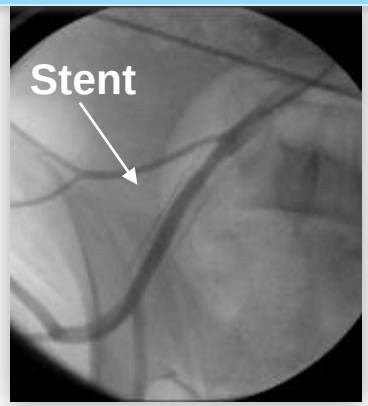
- Stent strut motion during vessel movements
- Chronic outward force by stents

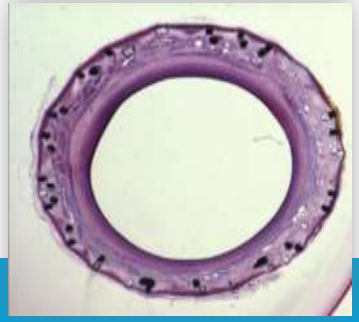
8 mm stent compressed to:	7.3 – 6.2 mm	6.2 – 5.0 mm	5.0 – 4.2 mm

Stent design & oversizing impact patency









Potential advantages of a fully resorbable stent

- Reduction/elimination of late stent thrombosis
- Improved lesion imaging using CTA or MRA
- Facilitate repeated treatments at same site
- Elimination of strut fracture induced restenosis
- Eliminate strut obstruction of side-branches
- Restoration of vasomotion
- Pediatric interventional application

Challenges in bioabsorbable stent construct

- Sufficient radial strength
- Stent retention on delivery balloon
- Adequate flexibility
- Minimizing strut thickness
- Allows for drug delivery
- Acceptable inflammation associated with degradation
- Degradation does not result in macro-embolization

Bioresorbable Scaffold Status Update

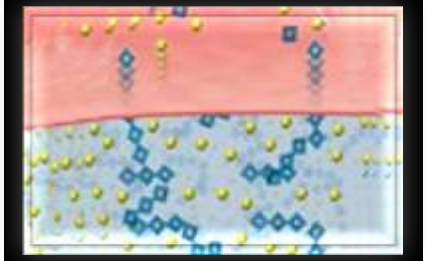
Bioresorbable scaffold, Manufacture	Target Vessel	Strut Material	Drug Coating Material	Drug	Radiopacity	Strut Thickness (μm)	Duration of radial support	Time to Resorption	Current status
Igaki-Tamai (Kyoto Medical)	SFA/Coronary	PLLA	None	None	Gold markers	170	6 mo	2-3 yrs	CE approved (PAD)
STANZA DRS (480 Biomedical)	SFA	PLGA	PCL	Paclitaxel	Platinum markers	175	6 mo	12-15 mo	FIM Initiated
Esprit (Abbott Vascular)	SFA	PLLA	PDLLA	Everolimus	Platinum markers	157?	6 mo?	2-3 yrs	FIM Initiated
BVS 1.0 (Abbott Vascular)	Coronary	PLLA	PDLLA	Everolimus	Platinum markers	157	Weeks	2-3 yrs	FIM completed
Absorb BVS 1.1 (Abbott Vascular)	Coronary/SFA	PLLA	PDLLA	Everolimus	Platinum markers	157	6 mos	2-3 yrs	CE approved
AMS-1.0 (Biotronik)	Coronary	Mg	None	None	None	165	Days or weeks	<4 mo	FIM completed
AMS-3.0 (Biotronik)	Coronary	Mg	None	Paclitaxel	None	125	Weeks	>4 mo	FIM completed
AMS-4.0 (Biotronik)	Coronary	Mg	PLLA	Sirolimus	Metalic markers	N/A	N/A	N/A	FIM Initiated
REVA (Reva Medical)	Coronary	Poly-tyrosine-polycarbonate polymer	None	None	Scaffold itself	200	3-6 mo	>4 yrs	FIM completed
ReZolve (Reva Medical)	Coronary	Poly-tyrosine-polycarbonate polymer	None	Sirolimus	Scaffold itself	114-228	4-6 mo	>4 yrs	FIM planned in 2014
DESolve (Elixir Medical)	Coronary	PLLA	PLLA	Mvolimus	Metalic markers	150	N/A	<2 yrs	FIM completed
Ideal BioStent (Xenongenics)	Coronary	Polymer salicylate+linker	Salicylate	Sirolimus	None	175	3 mo	>12 mo	FIM completed
ART 18Z (Arterial Remodeling Technologies	Coronary	PDLLA	None	None	None	170	3-6 mo	18 mo	FIM Initiated
Xinsorb (Huaan Biotechnology)	Coronary	PLLA+PCL+PLGA	None	Sirolimus	Metalic markers	160	N/A	N/A	Preclinical underway

Muramatsu et al Rev Esp Cardiol; 66(6): 483-

Esprit Drug Eluting Bioresorbable Vascular Scaffold Components

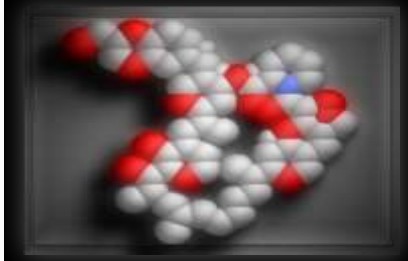
Bioresorbable Scaffold

- Poly(L-lactide) (PLLA)
- Naturally resorbed, fully metabolized
- Designed for SFA and iliac arteries



Bioresorbable Coating

- Poly(D,L-lactide) (PDLLA) coating
- Naturally resorbed, fully metabolized



Everolimus

- 100 µg/cm2

Delivery System

- Balloon-expandable delivery system
- 035” OTW platform

Esprit BVS is currently in development and is not approved or available for sale.

Stanza™ Scaffold Characteristics

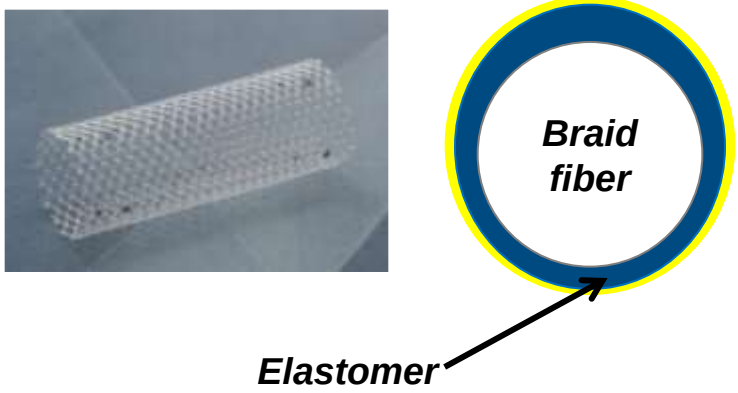
- Composite structure of PLGA fibers + bioresorbable elastomer coating
- Flexible, self-expanding design
- Radial resistive force similar to nitinol stents
- Fully resorbs in 12-15 months
- Readily formulated with Paclitaxel to achieve sustained drug delivery

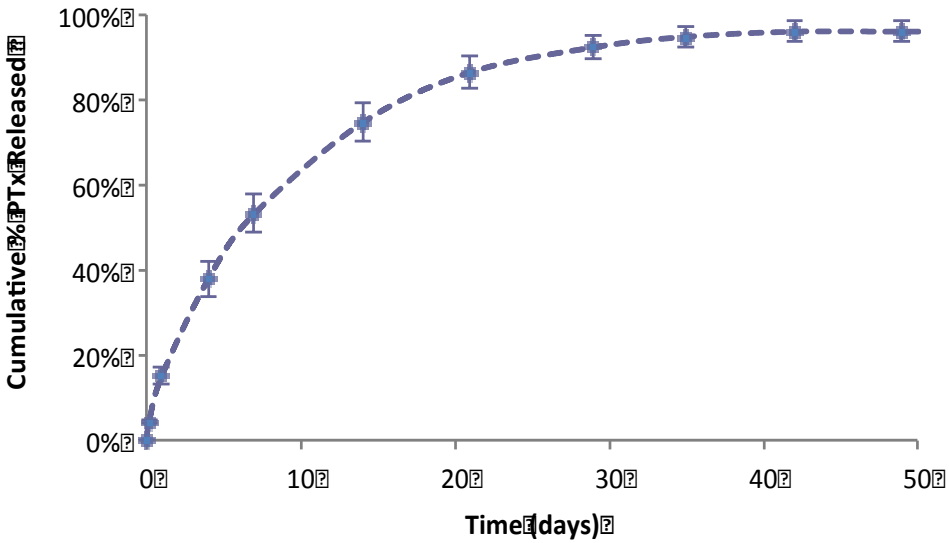
Courtesy: 480 Biomedical Inc

Stanza™ DRS offers the advantage of sustained Paclitaxel release

Paclitaxel/polymer coating

- **Thin layer, 2-3 µm thick**
- **Conformal coating**
- **Controlled drug release**

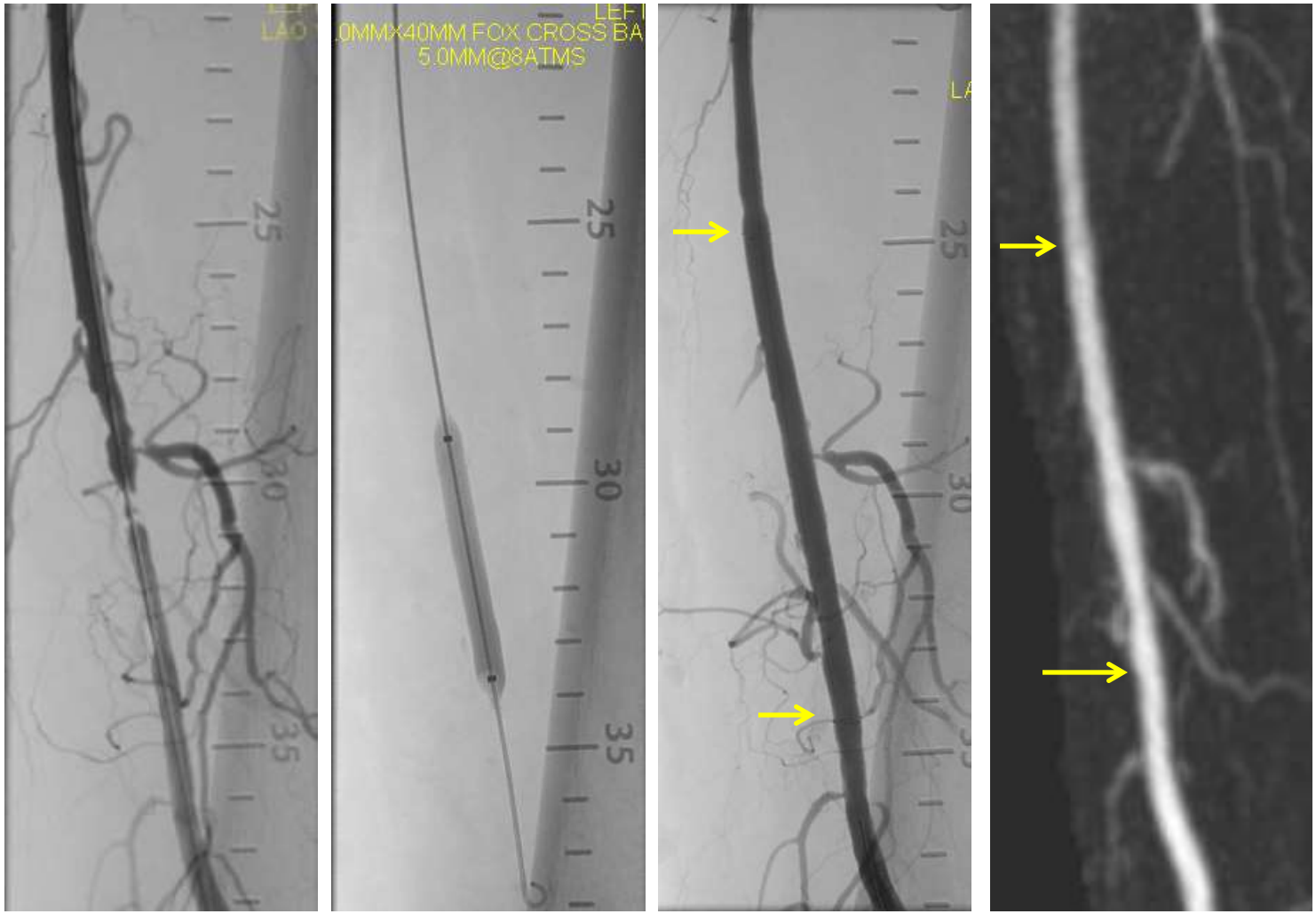




SPRINT Trial : Assess the controlled release of Paclitaxel from the Stanza™ platform

Assessment	Post-Procedure	1m	3m	6m	12m	24m
Clinical: RB, ABI, WIQ	✔	✔	✔	✔	✔	✔
Duplex Ultrasound	✔	✔	✔	✔	✔	✔
Angiography	✔				✔	
OCT/IVUS (sub-study)	✔				✔	
MRA (sub-study)	✔			✔	✔	✔
Blood PK (sub-study)	✔					

SPRINT: 65yr Male, Intermittent Claudication



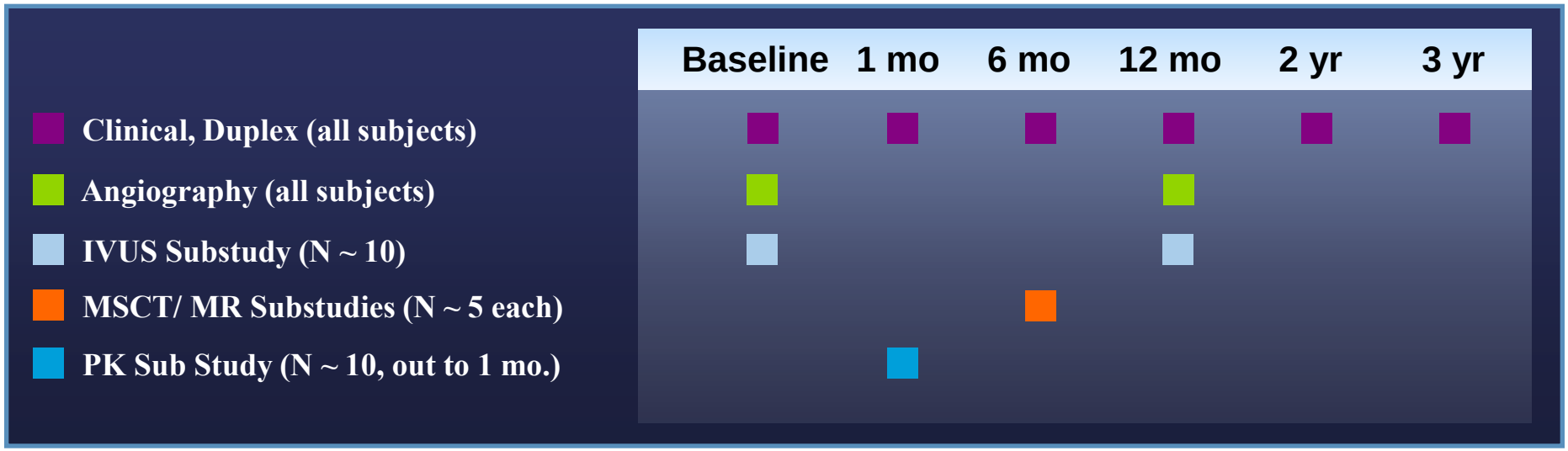
88% Stenosis

2% Residual Stenosis

ESPRIT I – Trial Design

A single *de novo* lesion in the superficial femoral (SFA) or iliac arteries in patients with symptomatic claudication (Rutherford Becker Category 1-3)

- Prospective, Single Arm, Multi-Center OUS trial evaluating the Esprit BVS (N=35)
- One target lesion treated with a single 6.0 x 58 mm Esprit BVS
- Vessel diameter from ≥ 5.5 – ≤ 6.5 mm, segment length ≤ 50 mm



Key Inclusion and Exclusion Criteria

Key Inclusion Criteria

- RB Clinical Category 1-3
- Single *de novo* lesion of the SFA or common or external iliac arteries
- Lesion length ≤ 50 mm
- Vessel diameter from ≥ 5.5 mm to ≤ 6.5 mm

Key Exclusion Criteria

- Unable to walk
- Ulcers or lesions on either foot
- Minor or major amputation of either lower extremity
- Totally occluded ipsilateral inflow artery to target lesion
- Target lesion has moderate-to-severe calcification

ESPRIT I Study Organization

Coordinating Investigator	**Johannes Lammer MD**, Medical University Vienna, Vienna, Austria
Angiographic Core Laboratory	**Jeffrey Popma MD,** BWH Boston, MA
Duplex Ultrasound Core Laboratory	**Michael R. Jaff DO**, VasCore, Boston, MA
Clinical Events Committee	Cardialysis, Rotterdam, The Netherlands
Data Safety Monitoring Board	
Study Sponsor	Abbott Vascular

ESPRIT I Patient Demographics

	Esprit BVS (N=35)
Age (yrs)	**65.3**
Male (%)	**77.1**
Family history of CAD (%)	**24.1**
Diabetes (%)	**25.7**
Dyslipidemia (%)	**85.7**
Hypertension (%)	**71.4**
Smoking history (%)	**82.9**

ESPRIT I Lesion Characteristics

	Esprit BVS (N=35)
External Iliac (%)	**11.4**
SFA (%)	**88.6**
Proximal	14.3
Mid	31.4
Distal	54.3
Target lesion length (mm)	**35.7**
Total occlusions (%)	**22.9***
Occlusion length (mm)	**30.6***

* Site-reported value. All other data reported are from angiographic core laboratory

Summary ESPIRIT-I Results

	Esprit BVS (N=34*) 1-Month	Esprit BVS 6-Month	Esprit BVS 12-Month
Target lesion revascularization (TLR) (%)	**0.0**	**0.0**	**8.8% (3/34)**
Scaffold thrombosis (%)	**0.0**	**0.0**	**2.9% (1/34)**
Angio in-segment stenosis (%)	**80.0**	**14.0**	**35.3**
Binary restenosis (Duplex)	**NA**	**0%**	**12.9% (4/31*)**

ESPRIT I Angiographic Results
Impact of vessel size on outcomes

	All 1-year F/U patients (N=27)	Patients with D_{max}* ≤ median (N=14)	Patients with D_{max}* > median (N=13)
In-scaffold %DS post-procedure	8.7%	8.9%	8.5%
		+11.2% ↓	+35.9% ↓
In-scaffold %DS 1 year	31.8%	20.1%	44.4%

* D_{max} = largest diameter within the scaffolded segment by core lab assessment (median 5.57 mm)

Outcomes are better in smaller vessels appropriately sized to the scaffold

ESPRIT I 1-Year

- Angiographic restenosis at 1 year is lower in smaller vessels where scaffold is matched appropriately to vessel diameter.
  - Suggests that everolimus controls neointimal formation in the SFA when scaffold is well apposed to vessel wall.

Conclusion

- Results promising so far but …
- Too early to judge if the technology meets its promise