A proposed treatment algorithm for focal and complex femoropopliteal disease implementing DCB, DES, atherectomy and uncoated devices
Faculty Disclosure

Thomas Zeller, MD

For the 12 months preceding this presentation, I disclose the following types of financial relationships:

• **Honoraria received from:** Abbott Vascular, Angioslide, Bard Peripheral Vascular, Veryan, Biotronik, Boston Scientific Corp., Cook Medical, Cordis Corp., Covidien, Gore & Associates, Medtronic, Spectranetics, Straub Medical, TriReme, VIVA Physicians

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Femoro-Popliteal TASC II A&B lesions
Fair Outcomes for „Optimal POBA“

Actual Enrollment Pattern

PTA Only Control Arm
n=72 (81 lesions)

PTA Only
n=43

PTA + Stent
n=29

Cross Over bailout + Stent
n=29 (40.2%)
(34 lesions)

n=206 patients randomly allocated 1:2

Intention to Treat -ITT Analysis

12-Month Results

40.2% patients in the PTA group underwent bail-out stenting and were included as PTA-failures at day 0!
1-year Restenosis Rates SFA

*Is BMS the final solution?*

**Chart:**
- **Y-axis:** Binary restenosis @ 12 months (%)
- **X-axis:** Length of the lesion (cm)
- **Legend:**
  - PTA plus provisional stent
  - Stent
  - RESILIENT
  - FAST
  - ASTRON
  - ABSOLUTE
  - SCIROCCO (2 yrs.)

**Graph Data Points:**
- PTA plus provisional stent: High restenosis rate initially, then decreases.
- Stent: Lower restenosis rates compared to other options, especially at longer lesion lengths.
- RESILIENT: Moderate restenosis rates, relatively consistent across lesion lengths.
- FAST: Initial high restenosis rate, decreases with longer lesions.
- ASTRON: Moderate to low restenosis rates, consistent across lesion lengths.
- ABSOLUTE: Low restenosis rates, consistent across lesion lengths.
- SCIROCCO (2 yrs.): Lower restenosis rates, consistent across lesion lengths.
Limitation of Bare Metal Stents

*Neo-intimal Hyperplasia*

Frequency: 30-60% of cases following stent placement depending on lesion length within 3 – 9 months.
At 5 years, Zilver PTX demonstrates a 41% reduction in restenosis compared to standard care.
DEB in SFA Evidence
Proof-of-Concept

7 Trials / 6 DEB Technologies; 6-month LLL (Primary Endpoint)

Evidence from DEB Trials

Significant and sustained TLR reduction up to 5 years

FEMPAC 2Y

THUNDER 5Y
DCB vs. PTA
IN.PACT SFA & Levant II Pivotal RCTs

Freedom from loss of Primary Patency

Freedom from clinically driven TLR

Tepe G et al. Circulation 2014  Rosenfield K et al. NEJM 2015
TASC A Lesions

**Directional Atherectomy vs. BMS vs. POBA**

De novo lesions, 4.5cm length

- Zeller et al. JACC 2006;48:1573-1578
DEFINITIVE LE

Primary Patency by Lesion Length

- < 4 cm: 81%
- 4-9.9 cm: 83%
- ≥ 10 cm: 67%

Mean length:
- < 4 cm: 2.2 cm
- 4-9.9 cm: 6.5 cm
- ≥ 10 cm: 14.4 cm

Number of lesions:
- < 4 cm: 220
- 4-9.9 cm: 307
- ≥ 10 cm: 214
Femoro-Popliteal TASC II C&D lesions
TASC II C&D Lesions
SIA
Recanalization of Chronic SFA-Occlusions

Subintimal Angioplasty

Sidhu et al.: 120 patients with TASC II C/D lesions
- Technical success: 91%
- Primary 6 months patency: 90%
- Primary 12 months patency: 73%
- Secondary 12 months patency: 85%
- 1-year limb salvage: 98%
- No relevant complications

Kim et al.: 63 consecutive procedures / 54 pats (TASC C 21%, TASC D 79%)
- Technical success: 94%
- Primary 12 months patency: 52%
- Independent predictors of patency:
  - Short occlusion length (p=0.04)
  - Distal SFA segment not involved (p=0.006)
  - Number of patent outflow arteries post-procedural (p=0.018)
DEFINITIVE LE

Primary Patency by Lesion Length

- < 4 cm: 81% Patency
- 4-9.9 cm: 83% Patency
- ≥ 10 cm: 67% Patency

Mean length:
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PSVR ≤ 2.4
IN.PACT in long SFA lesions: Leipzig Registry

Real world 260-Patient Registry

- High primary patency rates achieved overall in the full cohort and subsets
- 23.3% provisional stent rate

1-year freedom from loss of Primary Patency (PSVR < 2.4)

- 77.6% (all fem-pop)
- 82.4% (SFA only)
- 85.2% (ISR only)

Lesions ~24 cm
IN.PACT vs. DES in long SFA lesions

- 228-Patients Retrospective, Propensity score analysis
  - Non significant difference between IN.PACT DCB and Zilver PTX in long SFA lesions
  - Provisional stent rate post DCB = 18.3%

Prospective: □
Multicenter: ✓
Randomized: □
Corelab: □
Peer-rev. Published: □
Zilver Stent Clinical Program

Pre-Market

- RCT
  - PTA
    - Optimal n=118
    - Sub-optimal
      - Zilver Flex n=56
      - Zilver PTX n=63
  - Zilver PTX n=242

SAS
  - Zilver PTX n=787

Post-Market Includes

- Longer Lesions
  - Zilver PTX n=45
- Longer Lesions
  - Zilver Flex n=54
Zilver® PTX® DES
in *de novo* lesions > 15 cm

Lesions: n=133
Lesion length: 226±44mm

Primary patency
94.3% at 6 months
77.0% at 12 months

Dake et al. JEWV 2012
12-Month Primary Patency (PSVR < 2.0) in Longer Lesions (avrg. 22cm)

- Zilver PTX: 86.1%
- Zilver Flex: 70.5%
The Supera Vascular Mimetic Implant

The Supera implant mimics the natural structure and movement of the anatomy\(^1\).\(^2\)

- An innovative, interwoven nitinol design creates an implant that supports rather than resists the vessel
- Resists kinking and fracture with minimal chronic outward force\(^3\)
- Supports the natural movement of the vessel for high patency rates\(^1\)

Angio image courtesy of Dr. Hans Biemans, Rivas Hospital Gorinchem, the Netherlands.
Results Are Consistent Across Lesion Lengths

Percent of Lesions without Restenosis by Lesion Length
(12 months SUPERB IDE TRIAL)

TASC II C&D SFA Lesions

Viabahn

- Achilles' heel of SFA stenting: Neo-intimal hyperplasia
VIASTAR Trial

1-Year Primary Patency Stratified to Lesion Length

Primary patency rate >20 cm vs. ≤20 cm lesion length

Lammer et al. JACC 2013
25cm Viabahn

12M Data – Primary Patency & Freedom from TLR

Mean lesion length 26.5cm
Total occlusions 93%
Subacute Occlusions
(potentially thrombotic)
Acute & Subacute SFA-Occlusions
Mechanical Thrombectomy
Herz-Zentrum Bad Krozingen
20 Oct 2006 80 Y.O. male
Herz-Zentrum Bad Krozingen
20 Oct 2006  80 Y.O. male
Calcified Lesions
SFA-Stent Deployment Evaluation

Stent Compression - Leipzig Data

Angio AP projection

Angio LAO projection
SUPERA Stent (Abbott)

Interwoven nitinol stent design – Leipzig Experience
<table>
<thead>
<tr>
<th></th>
<th>Standard (n=20)</th>
<th>SUPERA (n=20)</th>
<th>p</th>
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<tbody>
<tr>
<td>Av Min Diam (mm)</td>
<td>4.45 +/- 0.6</td>
<td>4.92 +/- 0.75</td>
<td>0.06 (ns)</td>
</tr>
<tr>
<td>Residual Stenosis %</td>
<td>23 +/- 9</td>
<td>13 +/- 7</td>
<td>0.006 (s)</td>
</tr>
<tr>
<td>Residual Stenosis &gt;30%</td>
<td>8</td>
<td>0</td>
<td>0.00001 (s)</td>
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**Supera Has Strong Clinical Outcomes in Calcification**

<table>
<thead>
<tr>
<th>SUPERB Data - Severe Calcification</th>
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<tr>
<td>Patency (VIVA 12 months)</td>
<td>88.9%</td>
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<tr>
<td>Freedom from TLR at 1 year (K-M)</td>
<td>94.5%</td>
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<tr>
<td>Freedom from TLR at 2 years (K-M)</td>
<td>91.6%</td>
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% of Lesions with Severe Calcification (SUPERB Trial) | 45% (n=118)

Data on file at Abbott Vascular.
IN.PACT DEB and Calcium (F. Fanelli LINC 2013)

Registry to assess the effect of Calcium on DEB efficacy

Prospective✓  Multicenter  Randomized  Corelab Adj.  Peer-rev. Published

# Patients 60
Subject Population Claudicants + RC4
Major Indication Fem-pop de-novo
Primary Endpoint 12-LLL
Key baseline / proced. characteristics
• Mean l. length: 6 cm; CTO: 31.7%
• pre-dilat with std PTA

Key Findings:
• Calcium presence proportionally influence restenosis
• Influence seems higher with circumferential vs. longitudinal distribution
DEF AR suggests DAART better than DCB alone in long or calcified lesions.
Challenges in the SFA

Instant Restenosis

Stent-struts

Neo-intimal hyperplasia
Treatment of Femoropopliteal In-Stent Restenosis With Paclitaxel-Eluting Stents

Thomas Zeller, MD,* Michael D. Dake, MD,† Gunnar Tepe, MD,‡ Klaus Brechtel, MD,‡ Elias Noory, MD,* Ulrich Beschorner, MD,* Patricia L. Kultgen, PhD,§ Aljoscha Rastan, MD*

Bad Krozingen and Rosenheim, Germany; Stanford, California; and West Lafayette, Indiana

Zilver PTX*
No in-stent restenosis

Zilver PTX*
In-stent restenosis

Freedom from Event

0% 20% 40% 60% 80% 100%

0 3 6 9 12 Months

In-stent Restenosis
Non-ISR

Zeller et al. J Am Coll Cardiol Intv 2013
DEB in SFA In-Stent-Restenosis

**IN.PACT ISR**
(E.Stabile et al. JACC 2012)

39-Patient Registry
92.2% Primary Patency
92.2 freedom from TLR

**DEBATE ISR**
(F.Liistro et al. JEVT 2014)

44-Patient Registry vs. historical PTA cohort
Restenosis
19.5% (DEB) vs. 71.8% (PTA) (p<0.001)

**FAIR**
(H.Krankenberg LINC 2014)

119-Patient RCT
Freedom from TLR:
90.8% (DEB) vs. 52.6% (PTA) (p=0.0001)

12-month freedom from TLR
12-month TLR and restenosis

- ISR length: 8.3 cm
- ISR length: 13.2 cm
- ISR length: 8.2 cm
The Reline Trial
2-Year Primary Patency & Freedom from TLR

The RELINE trial:
24M Primary Patency: VIABAHN vs. PTA

The RELINE trial:
24M Freedom from TLR: VIABAHN vs. PTA
Lesion Specific Treatment Options for SFA Disease

**Summary I**

- A variety of different interventional tools are available for the treatment of particular lesion characteristics
  - Short lesions (TASC A&B)
    - DES
    - DEB
    - Atherectomy
    - BMS
  - Long lesions (TASC C&D) and CTOs
    - DES
    - DEB
    - Viabahn
A variety of different interventional tools are available for the treatment of particular lesion characteristics

- Subacute occlusions
  - Rotarex (not approved in the US)
  - Jetstream
- Calcified lesions
  - Supera Stent
  - Atherectomy & DEB
- ISR
  - DES
  - DEB
  - Viabahn
Fem-pop treatment algorithm

1. **de-novo, short (<4 cm), no-CTO?**
   - **YES**: standard PTA
   - **NO**: DEB

2. **Restenosis**
   - **YES**: Post-Dilatation: Success?
     - **YES**: NO
     - **NO**: Stent
   - **NO**: DEB

3. **Flow-limit Dissection or residual stenosis >50%?**
   - **YES**: Pre-Dilatation at least for CTO / sub-occl. / Ca++
     - **YES**: DEB
     - **NO**: Stent
   - **NO**: Post-Dilatation: Success?
A proposed treatment algorithm for focal and complex femoropopliteal disease implementing DCB, DES, atherectomy and uncoated devices