# XPEDITE Clinical Study
# PaclitaXel-coated Peripheral StEnts useD In the Treatment of FemoropoplitEal Stenoses

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# Disclosure

Speaker name: Thomas Zeller

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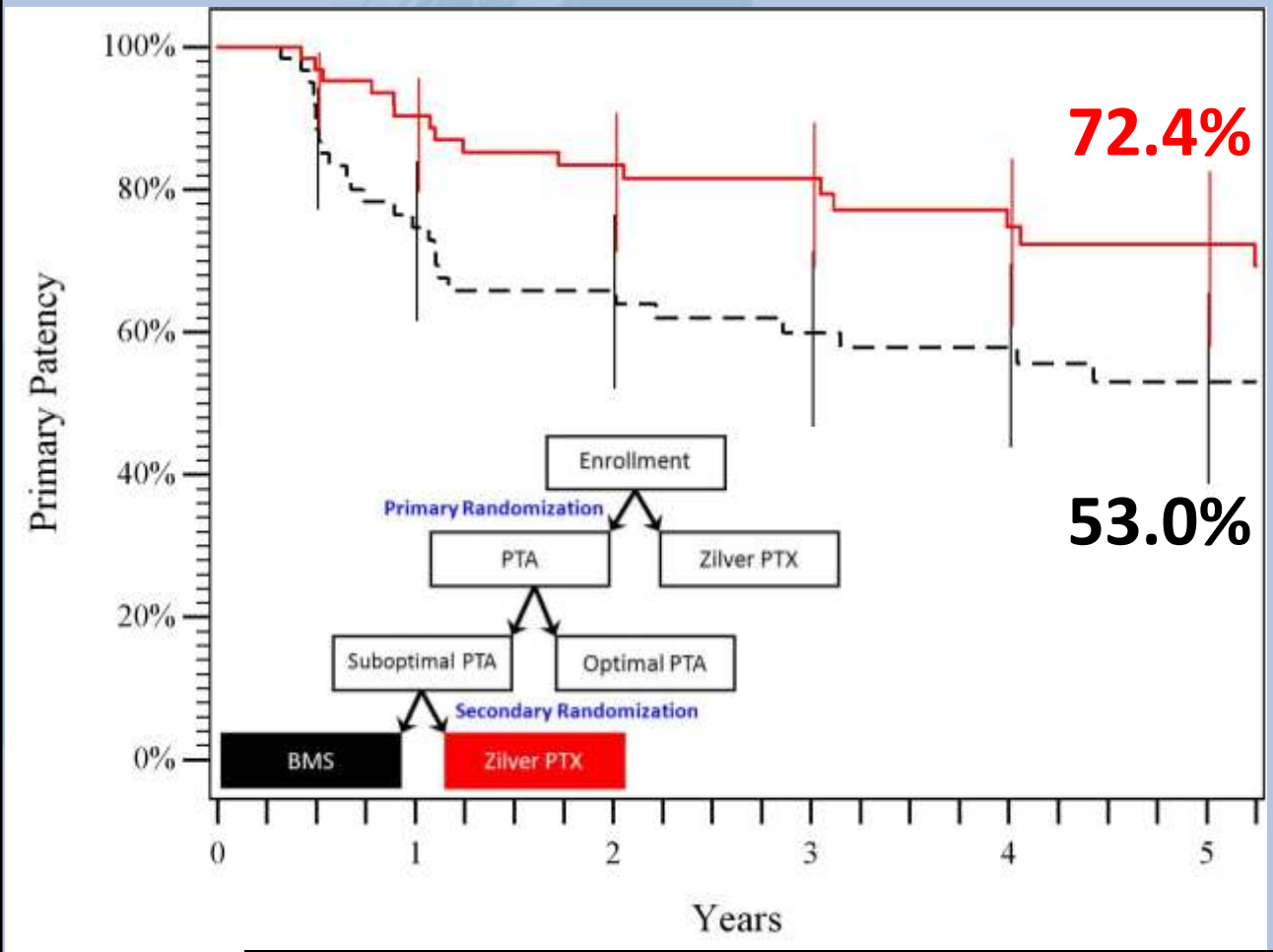
I have the following potential conflicts of interest to report:

- [X] Consulting
- [ ] Employment in industry
- [X] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest

# RCT: 5-year Primary Patency (PSVR < 2.0)
# Provisional Zilver PTX vs. BMS




**72.4%** Provisional Zilver PTX

**53.0%** Provisional BMS

*p* = 0.03
log-rank

At 5 years, Zilver PTX demonstrates a
41% reduction in restenosis compared to BMS

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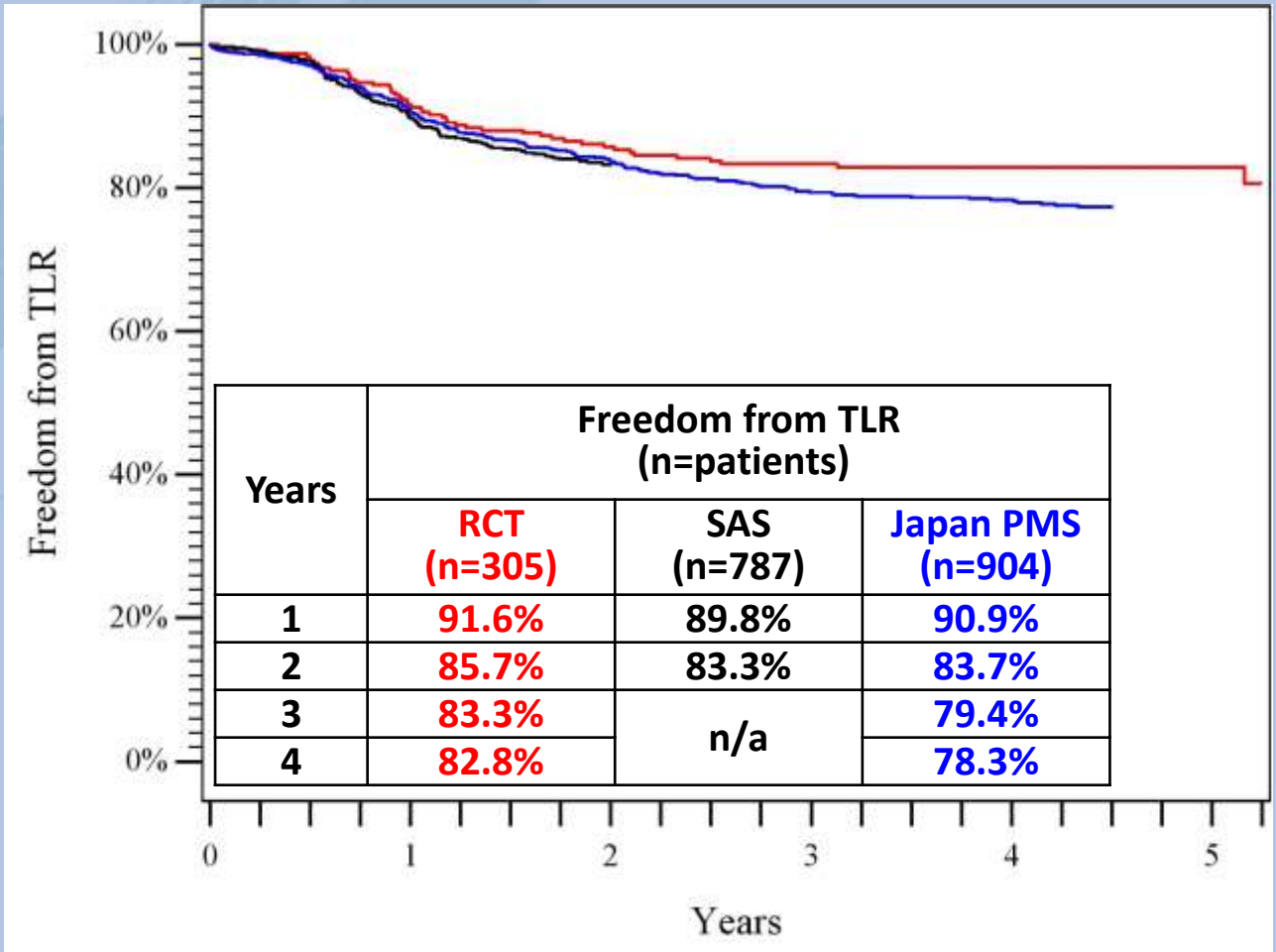
# 4-year Freedom from TLR Across Studies




| Years | Freedom from TLR (n=patients) | | |
|---|---|---|---|
| | RCT (n=305) | SAS (n=787) | Japan PMS (n=904) |
| 1 | 91.6% | 89.8% | 90.9% |
| 2 | 85.7% | 83.3% | 83.7% |
| 3 | 83.3% | n/a | 79.4% |
| 4 | 82.8% | | 78.3% |

TLR rate remains consistent despite more complex lesions

# Why Consider a New Polymer-free Paclitaxel Coating?

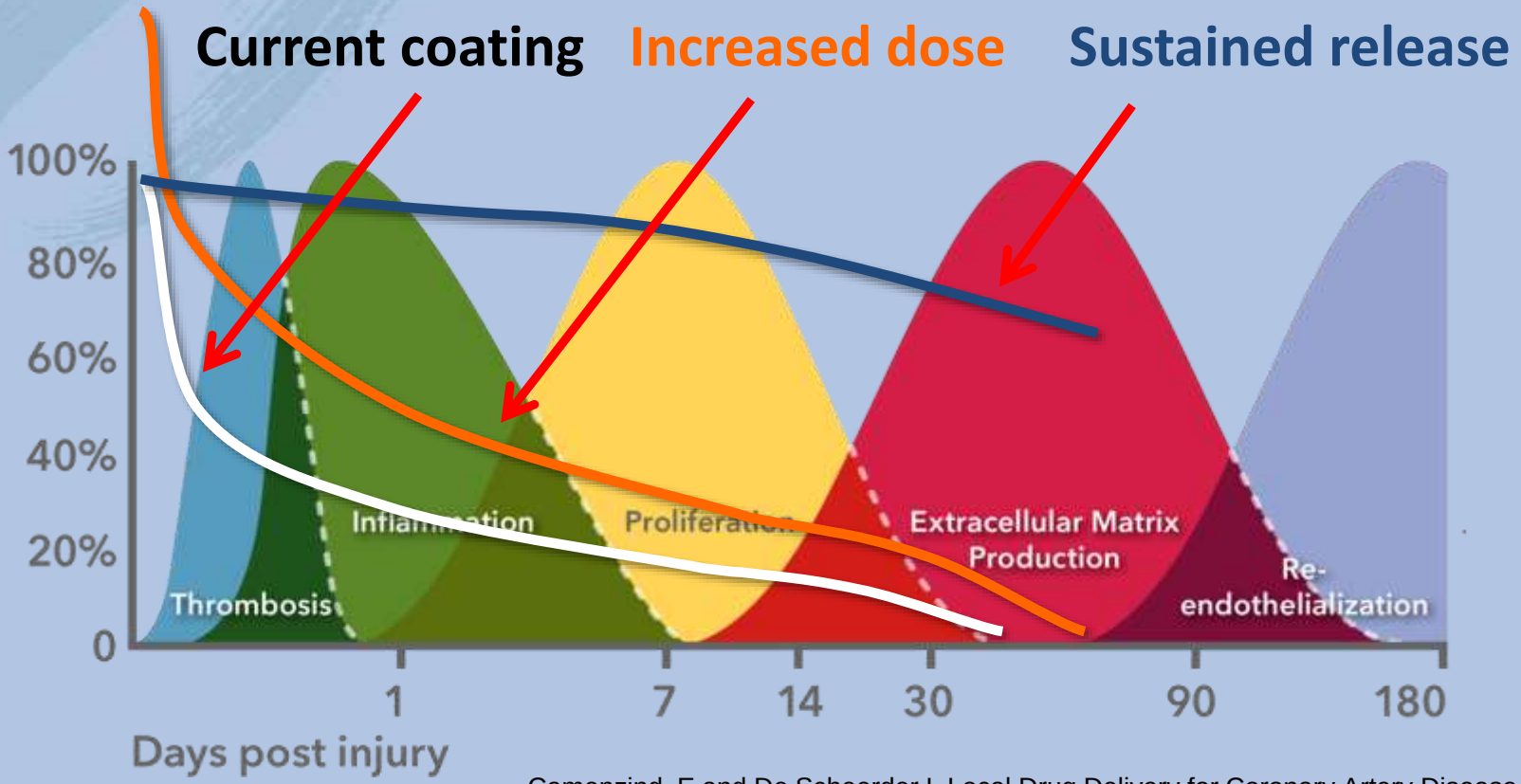
- Excellent results with current Zilver PTX
- But…can we ***further*** reduce restenosis and reintervention with a new polymer-free paclitaxel coating with:
  1. Increased dose

     or

  2. Sustained release
- XPEDITE will generate clinical evidence with new polymer-free paclitaxel coatings compared to the current Zilver PTX coating

# Selection of New Polymer-free Paclitaxel Coating

- The response to vessel injury has multiple phases
- **Proliferation is the major contributor to restenosis**
  - Paclitaxel is an anti-proliferative drug
- Re-endothelialization is necessary for vessel healing




Camenzind E and De Scheerder I. Local Drug Delivery for Coronary Artery Disease. 2005.
Nikol S, *et al. Atherosclerosis.* 1996; 123:17-31

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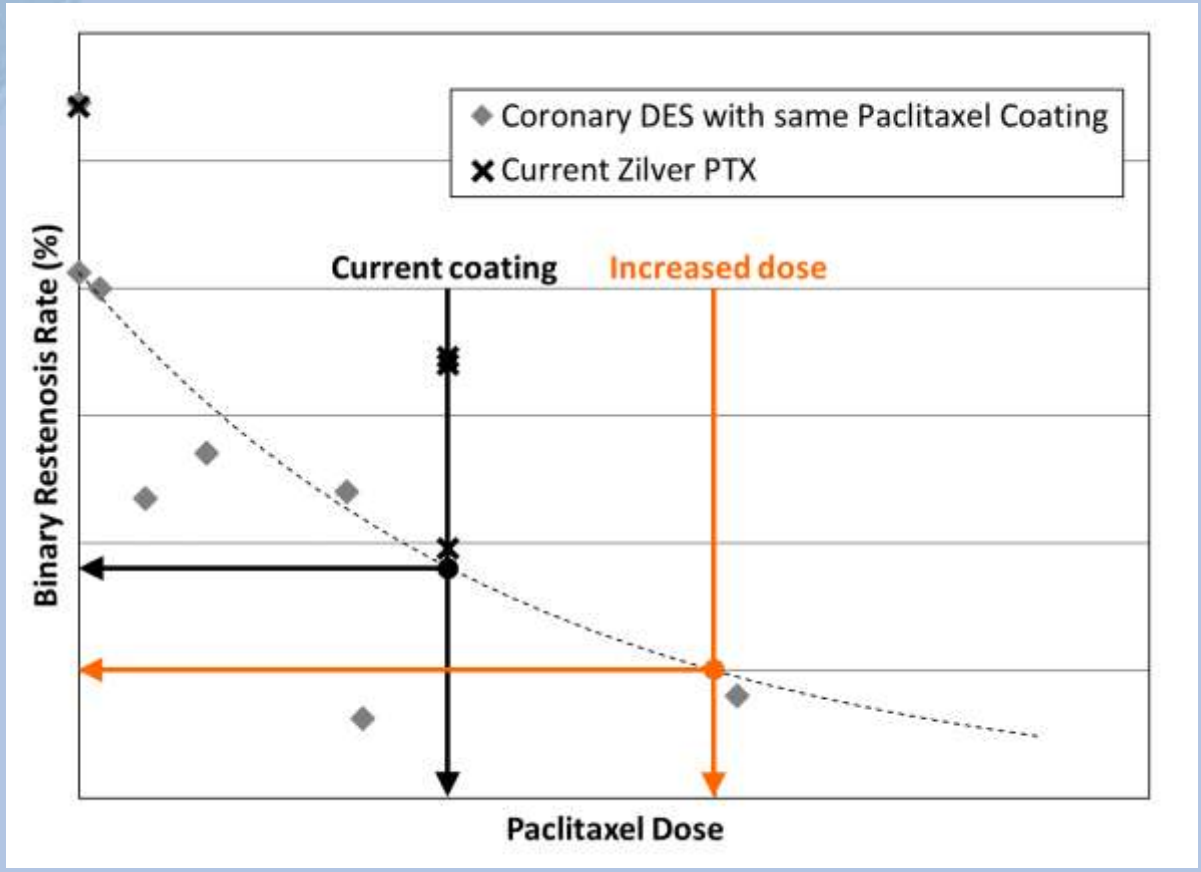
# Clinical Data Supporting Increased Dose

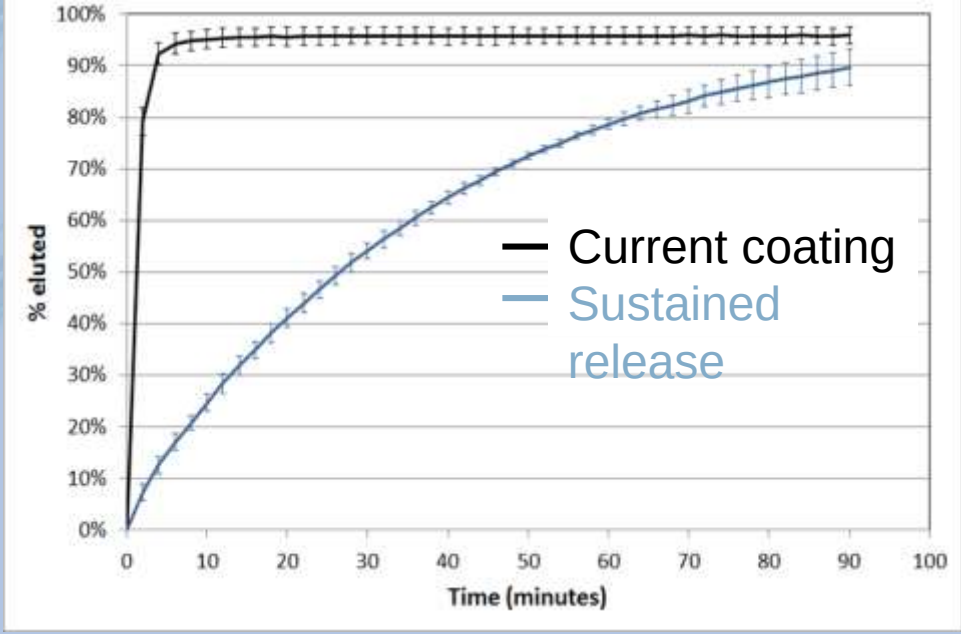
- In addition to Zilver PTX data, Coronary DES data are also available for various paclitaxel doses (ASPECT and ELUTES studies)
- These data suggest that increasing the paclitaxel dose should further reduce restenosis rates




Park *et al*., N Engl J Med, 2003;348:1537-45 Gershlick *et al*., Circulation, 2004;109:487-93

# Non-clinical Data Supporting Sustained Release

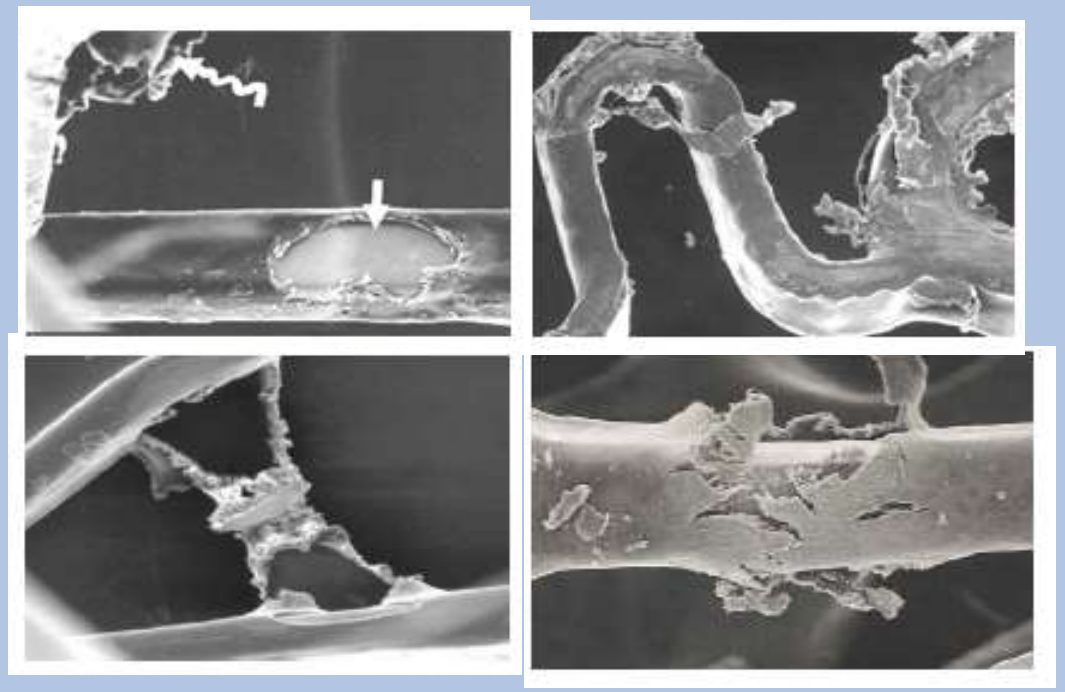
- *In vitro* dissolution testing demonstrates sustained release with polymer-free formulation compared to current coating




- Animal data support safety and prolonged biologic effect from 1 month to 6 months
  - Increased smooth muscle cell loss compared to current coating
  - Endothelial coverage maintained

# Why No Polymer:
# Polymer Coating May Have Imperfections

- Many polymers were not designed to be biodegradable or resorbable and will persist indefinitely, well beyond the duration of total drug release
- The observations included bridging, cracking, peeling, and fragmenting



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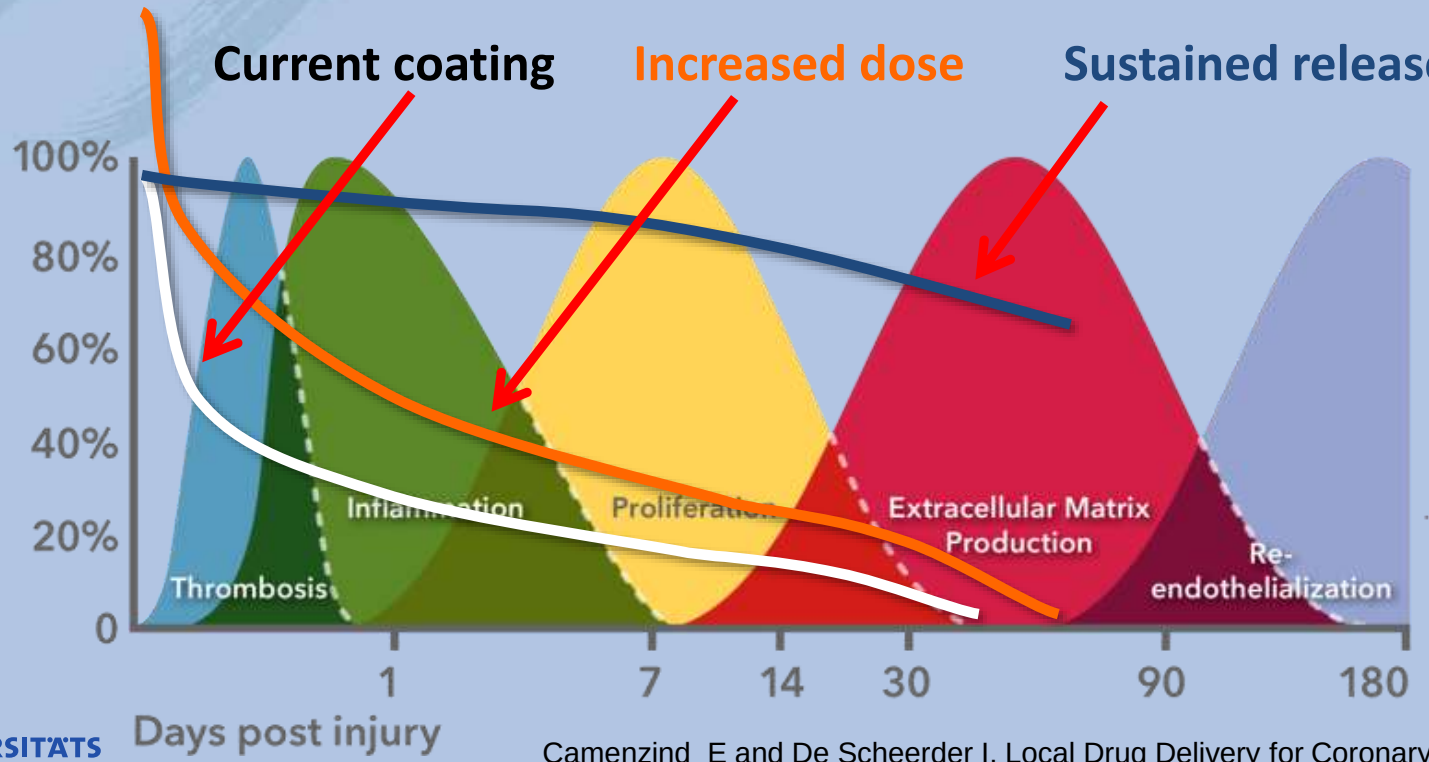
# XPEDITE Clinical Study Design

- **Objective:** compare the performance of two investigational paclitaxel coatings (**increased dose** or **sustained release**) to the current commercially-available Zilver PTX Stent in the treatment of symptomatic vascular disease of the above-the-knee femoropopliteal artery

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# XPEDITE Clinical Study Design

- Multicenter, prospective, randomized (1:1:1)
- 150 patients (50 per arm)
- Lesion lengths 40 mm to 140 mm
- Multiple clinical sites in Germany and one in New Zealand
- 24-month follow-up
- Core Lab blinded

# Study Hypothesis and Primary Endpoint

- **Hypothesis:**
  - Patients treated with stents coated with either a sustained release or increased dose polymer-free paclitaxel coating will have lower percent diameter stenosis at 6 months compared to the current polymer-free paclitaxel coating
- **Primary Endpoint:**
  - Percent diameter stenosis (%DS) within the study lesion evaluated angiographically 6 months post-procedure

# Study Follow-up

| | Pre-Procedure | Procedure | Within 7 days after procedure | Follow-up | | | | Prior to re-intervention |
|---|---|---|---|---|---|---|---|---|
| | | | | 1 month | 6 months | 12 months | 24 months | |
| Informed Consent | X | | | | | | | |
| History | X | | | | | | | |
| Walking Impairment Questionnaire (WIQ) | X | | | X | X | X | X | X |
| Study limb ABI | X | | X | X | X | X | X | X |
| Rutherford Classification | X | | | X | X | X | X | X |
| Medications | X | X | X | X | X | X | X | X |
| Adverse events | | X | X | X | X | X | X | X |
| Angiography | | X[1] | | | X | | | X |
| Duplex ultrasonography | | | | | | X | X | |

[1]Angiography performed pre- and post-stent placement.

# Additional Outcomes through 24 Months

- Procedural success (reported post-procedure only)
- Event-free survival
- Freedom from TLR
- Primary patency
- Study limb Rutherford classification
- Study limb ABI

# XPEDITE Clinical Sites and Enrollment Status

| Site | | Principal Investigator |
|---|---|---|
| Germany | Universitäts-Herzzentrum Freiburg – Bad Krozingen | Prof. Zeller |
| | Marienhospital, Stuttgart | Prof. Zähringer |
| | Uniklinikum Wurzburg Institute fur Rontgendiagnostik | Prof. Kickuth |
| | SRH Klinikum Karlsbad- Langensteinbach GmbH | Prof. Blessing |
| | Universitätsklinikum Leipzig AoR | Prof. Scheinert |
| | Universitätsklinikum, Jena | Prof. Teichgräber |
| | St. Josefskrankenhaus, Heidelberg | Dr. Jakob |
| | Medino Kliniken, Sonneberg | Dr. Thieme |
| | Klinikum Arnsberg GmbH | Dr. Lichtenberg |
| | Krankenhaus Buchholz | Dr. Hertting |
| New Zealand | Auckland City Hospital | Dr. Holden |

**Current Enrollment 97/150**

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# Summary

- Excellent results with current Zilver PTX
- XPEDITE will evaluate if a new polymer-free paclitaxel coating with either increased dose or sustained release may provide improved outcomes compared to the current Zilver PTX coating
- Study is currently enrolling (97/150)
- Primary endpoint completion projected by end of 2018

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