FIRST@CIRSE 2019

# Zilver® PTX® Drug-Eluting Peripheral Stent

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# Overview

## Actual Treatment

Analysis of mortality must consider known treatment with paclitaxel devices

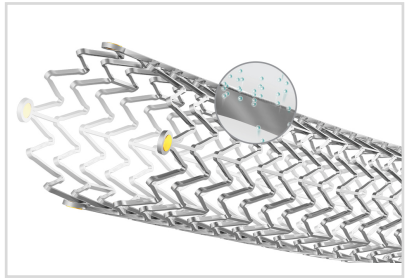
## Current Status

Cook will continue working collaboratively with regulatory authorities, clinicians, and our industry partners to provide the data needed to make informed decisions for patient treatment

## Patient Impact

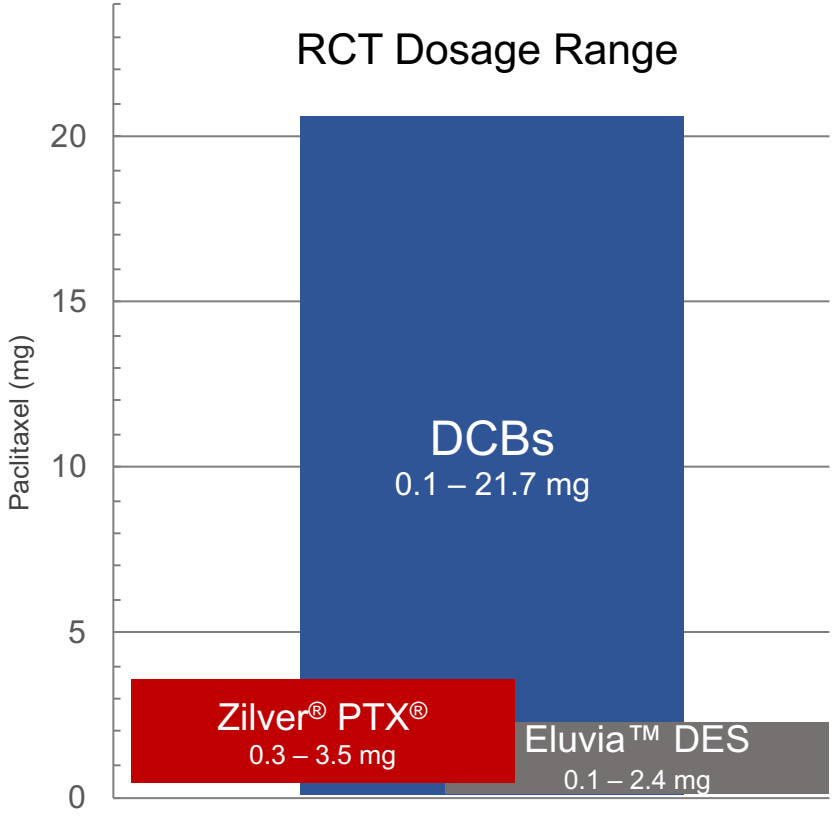
There is no mortality signal with Zilver PTX and the current situation is limiting patient access to the proven benefits of paclitaxel devices

# Zilver PTX Stent Overview



- **Coating**

  Low dose, amorphous coating with no polymer or excipient



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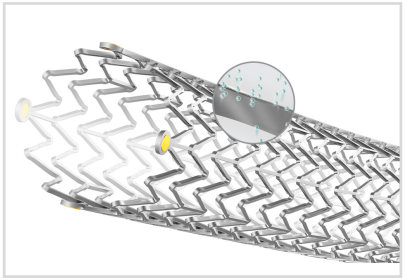

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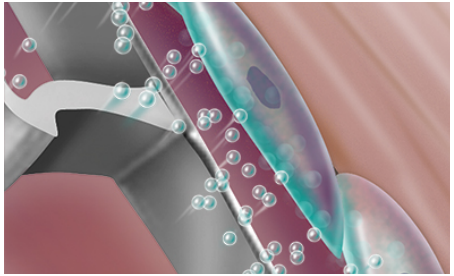

## Local Drug Delivery

Short-term drug delivery, no long-term paclitaxel exposure, only BMS remains

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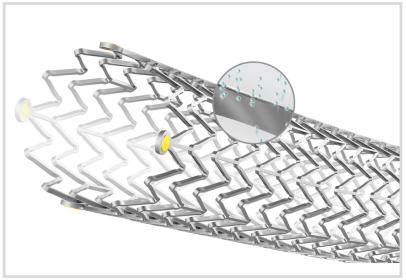

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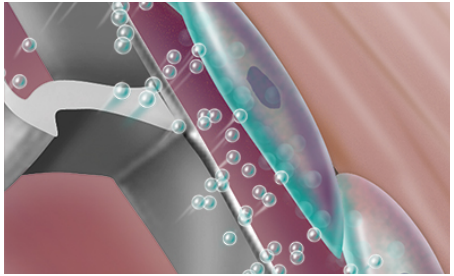

## Local Drug Delivery

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## Long-term data

Only peripheral DES with long-term safety data

# Zilver PTX Clinical Program

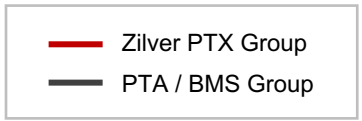
| Study | Device | Follow-up | # of Patients |
|---|---|---|---|
| RCT | Zilver PTX | 5 years | 336 |
| | PTA/BMS | | 143 |
| Japan PMS | Zilver PTX | 5 years | 904 |
| | BMS | 3 years | 190 |
| EU BMS | BMS | 5 years | 110 |
| US PAS | Zilver PTX | 5 years[1] | 200 |
| Single-arm Study | Zilver PTX | 2 years | 787 |
| French Reimbursement | Zilver PTX | 2 years | 119 |
| China | Zilver PTX | 1 year | 178 |
| REAL PTX | Zilver PTX | 3 years | 75 |
| | DCB[2] | | 75 |

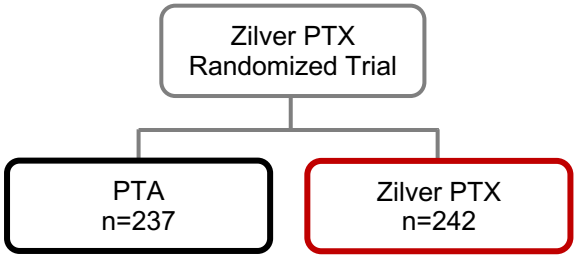
*[1] Ongoing [2] 77.3% INPact, 21.3% Lutonix, 1.4% Other.*

- Large studies
- Long-term follow-up
- Concurrent comparator groups

TRIAL DESIGN

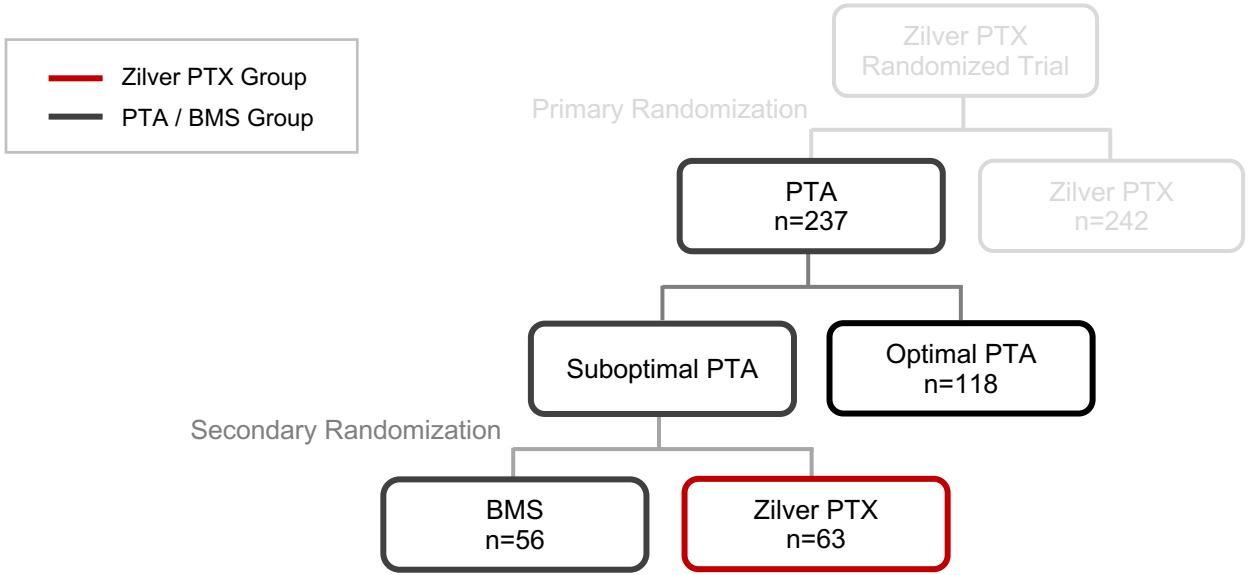
# Primary Randomization



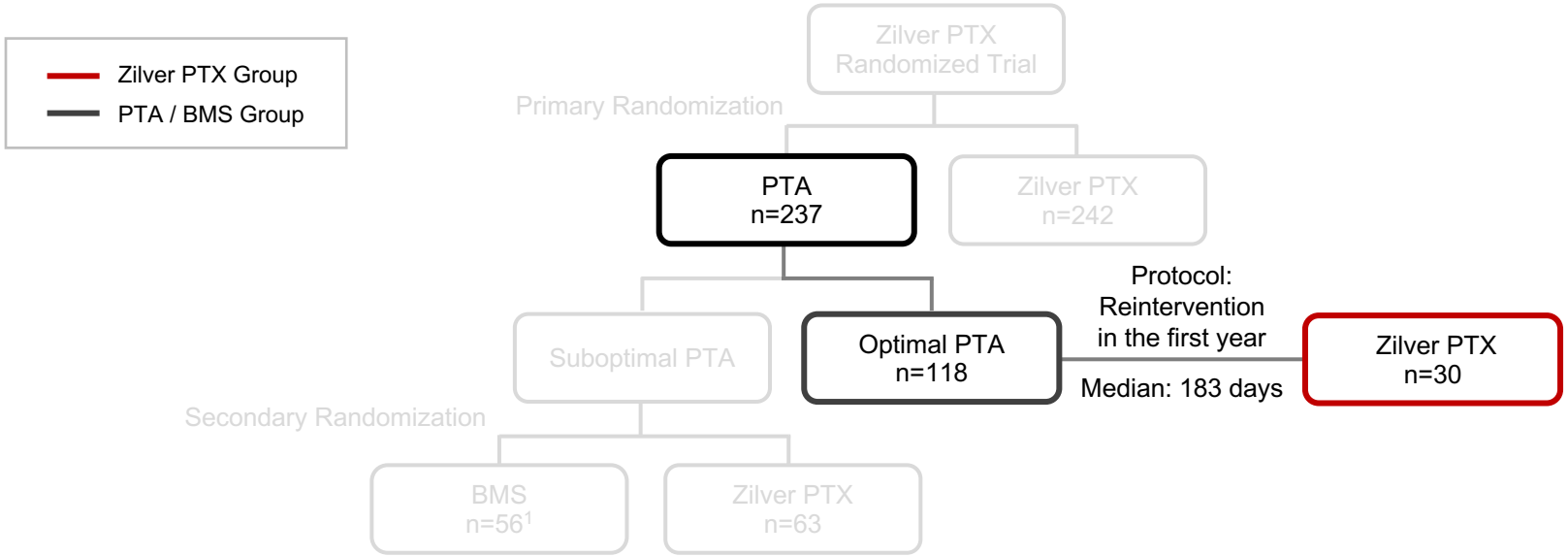
TRIAL DESIGN

# Secondary Randomization



TRIAL DESIGN

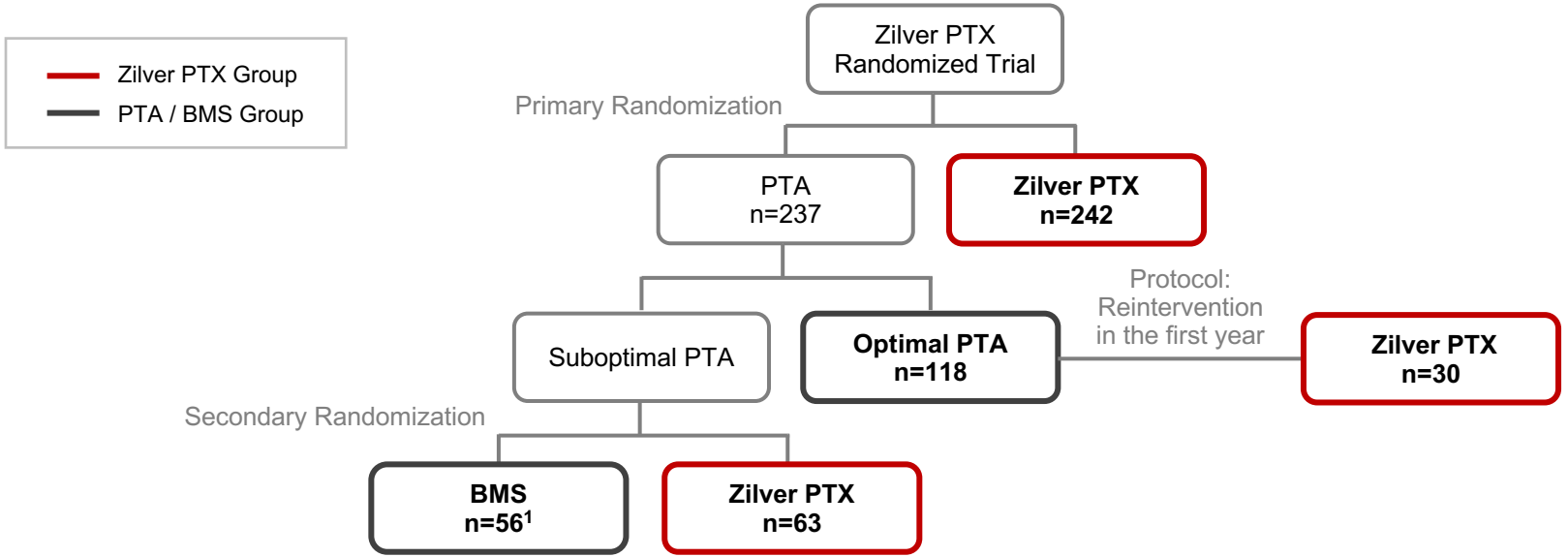
# Early Crossover




[1] *One BMS patient received Zilver PTX during reintervention within the first year.*

TRIAL DESIGN

# Actual Treatment

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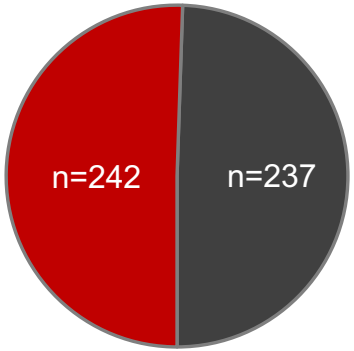
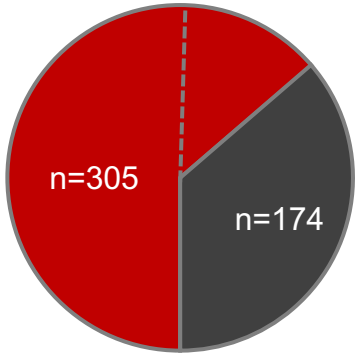
# Treatment Results

- Zilver PTX
- PTA / BMS

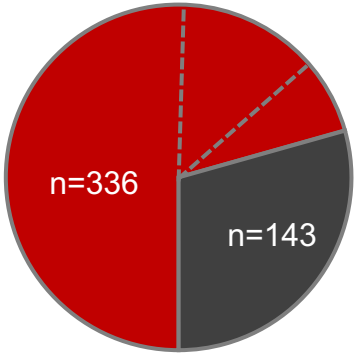
**Primary Randomization**




**Primary + Secondary Randomization**




**Actual Treatment = Primary + Secondary + Crossover**

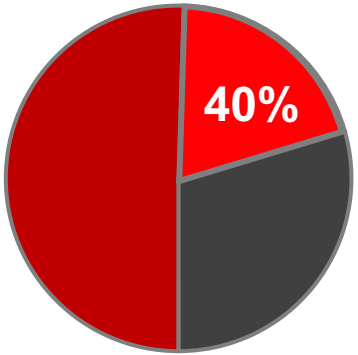


# Treatment Results

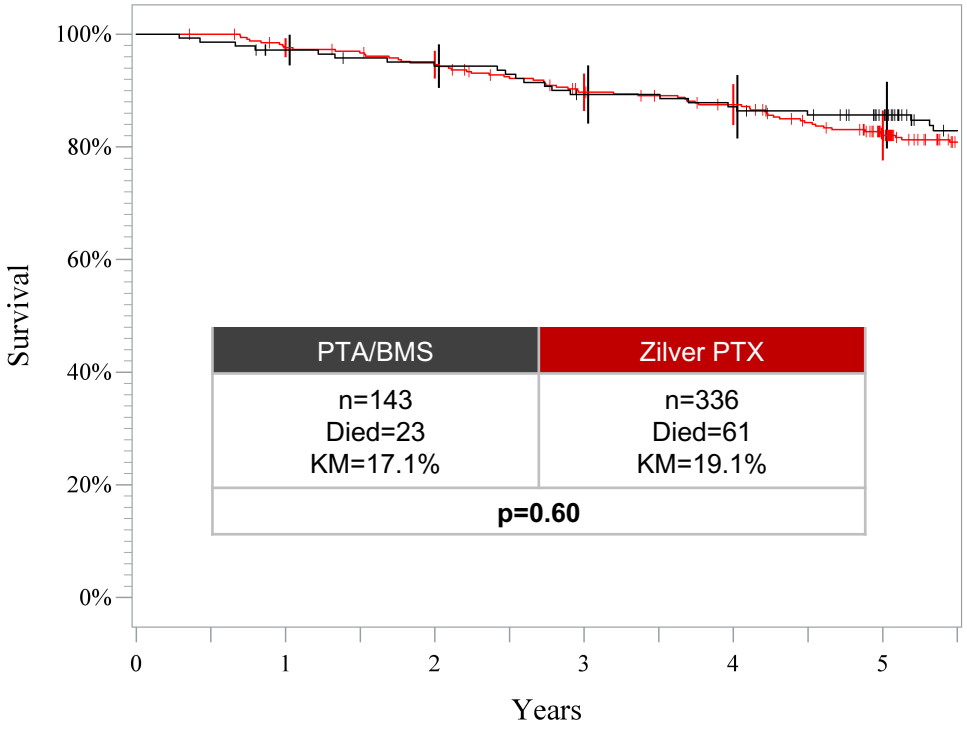
- Zilver PTX
- PTA / BMS

- 40% of patients initially randomized to PTA were actually treated with Zilver PTX

**Actual Treatment =**
**Primary + Secondary + Crossover**

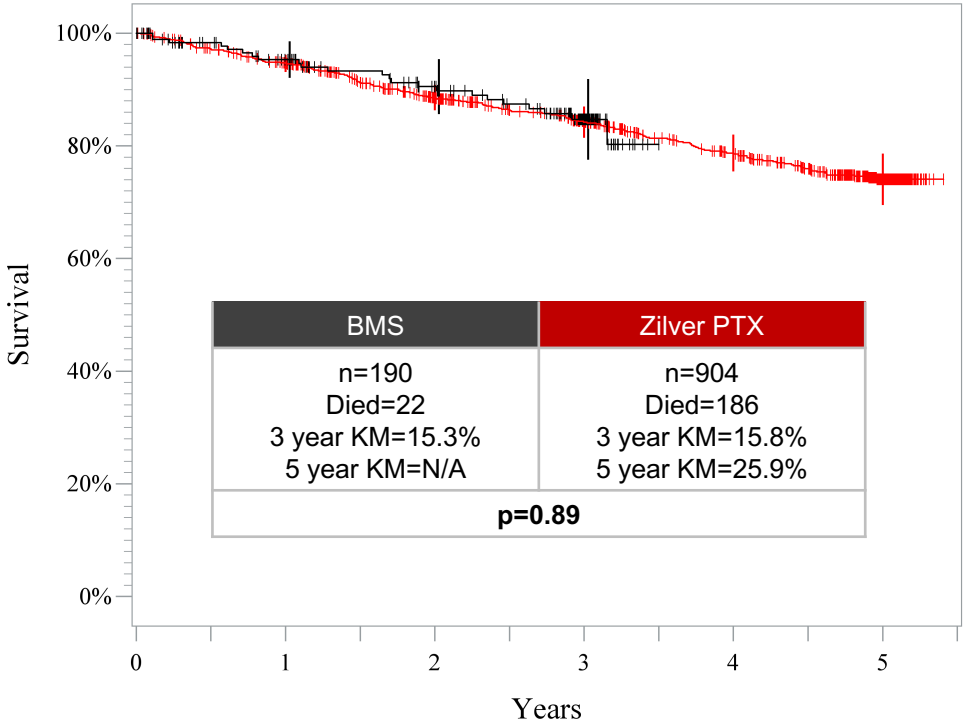


# RCT Actual Treatment




- 5-year vital status for 94% of patients
- All patients analyzed by actual treatment
- No mortality signal

# Japan Post-Market Studies



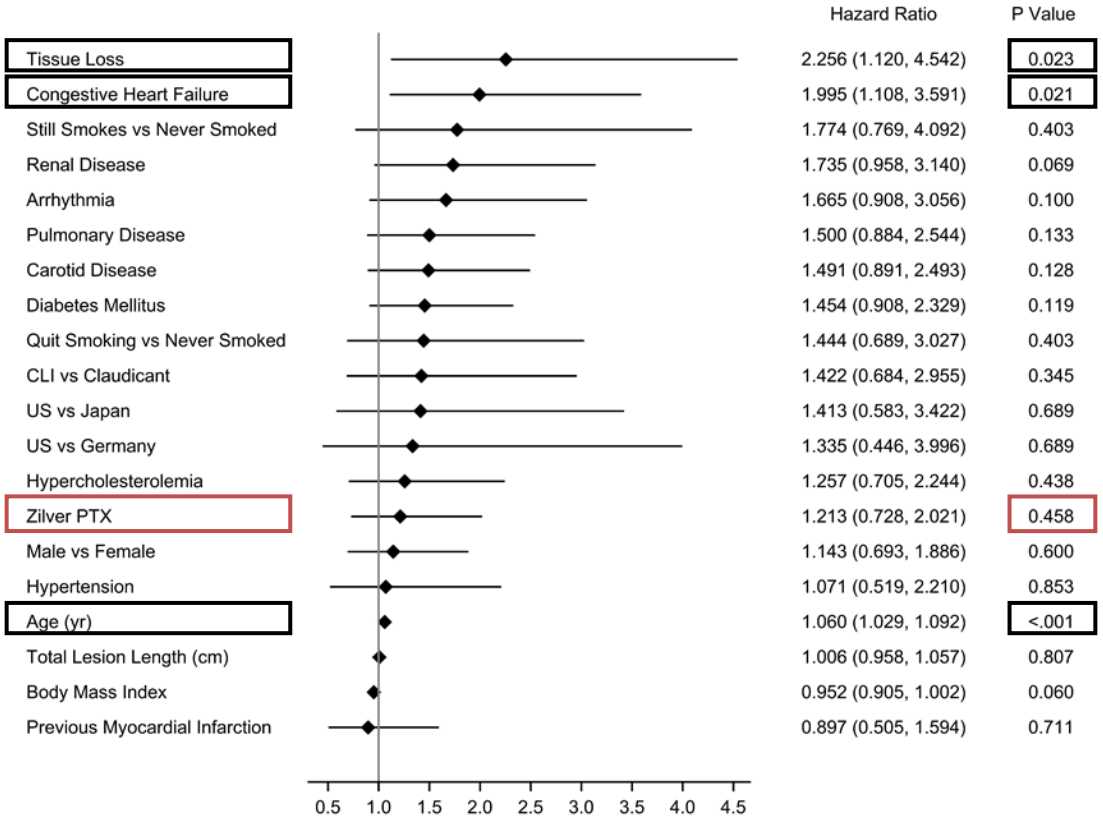

- Large, real-world; no exclusion criteria
- No increase in rate of mortality after 3 years
- No mortality signal

# Covariate Analysis

- No mortality signal for Zilver PTX when evaluating actual treatment
- What factors were associated with mortality?

ZILVER PTX RCT

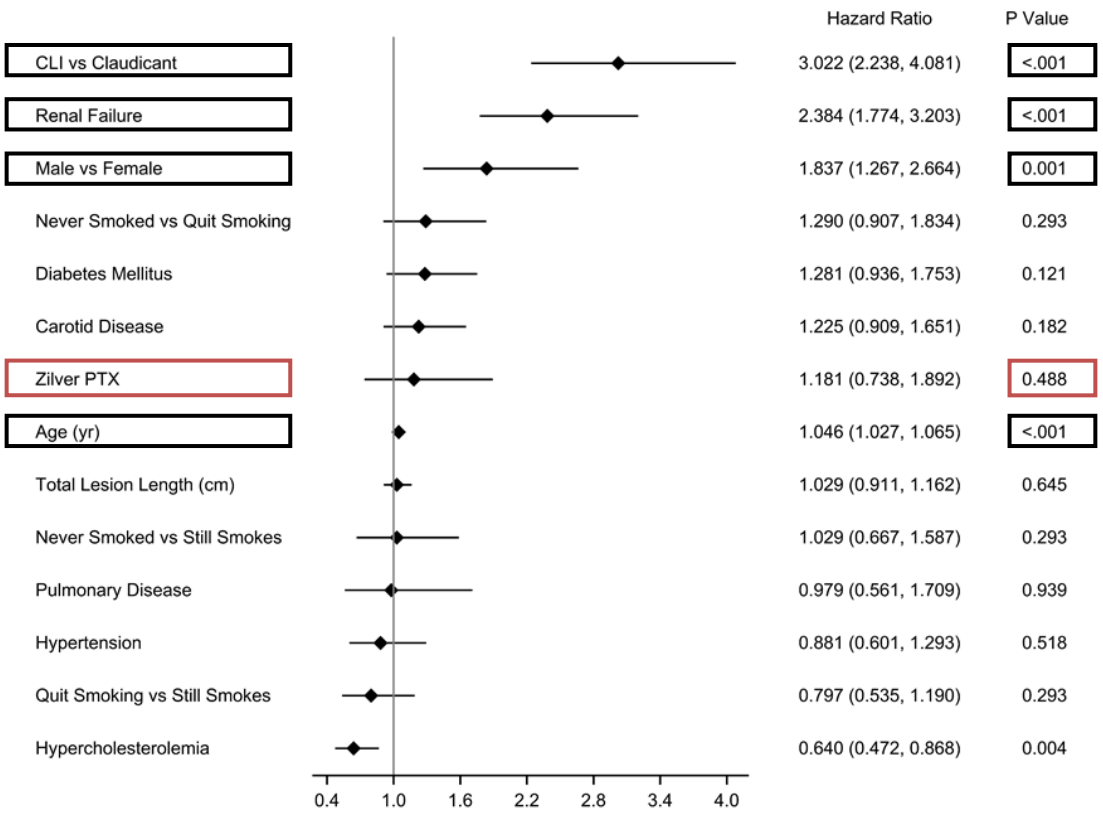
# Covariate Analysis




- Comorbidities common in PAD patients were the significant predictors of mortality
- Zilver PTX **not** a predictor of mortality

JAPAN POST-MARKET STUDIES

# Covariate Analysis




- Comorbidities common in PAD patients were the significant predictors of mortality
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# Covariate Analysis: Dose

- Paclitaxel analyzed by dose (mg) per patient
- Significant predictors same as treatment arm analysis
  - RCT: Age, tissue loss, CHF
  - Japan: CLI, renal failure, gender, age, hypercholesterolemia

| Study | Hazard Ratio | p-value |
|---|---|---|
| **RCT** | 1.034 (0.718, 1.490) | **0.86** |
| **Japan** | 1.201 (0.987, 1.461) | **0.07** |

- Paclitaxel dose **not** a predictor of mortality

# Conclusion

- **Analysis must be based on actual treatment**

  Protocol defined secondary randomization and crossover must not be ignored

- **No mortality signal with Zilver PTX**

  When data are appropriately analyzed

Cardiovasc Intervent Radiol
https://doi.org/10.1007/s00270-019-02324-4

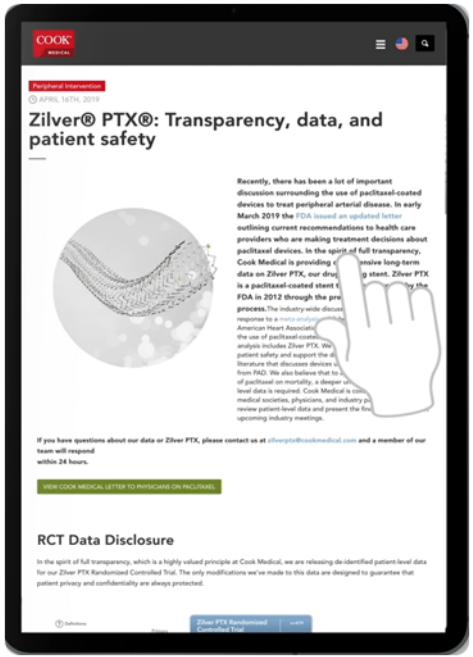
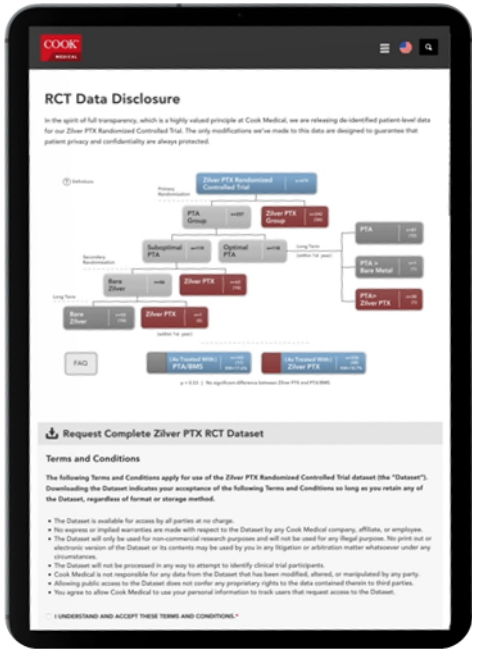
CIRSE

Check for updates

CLINICAL INVESTIGATION ARTERIAL INTERVENTIONS

# Paclitaxel-Coated Zilver PTX Drug-Eluting Stent Treatment Does Not Result in Increased Long-Term All-Cause Mortality Compared to Uncoated Devices

Michael D. Dake[1] · Gary M. Ansel[2] · Marc Bosiers[3] · Andrew Holden[4] · Osamu Iida[5] · Michael R. Jaff[6] · Aaron E. Lottes[7] · Erin E. O'Leary[7] · Alan T. Saunders[7] · Marc Schermerhorn[8] · Hiroyoshi Yokoi[9] · Thomas Zeller[10]

The patient-level data used for the analyses presented here is available on the following website:

https://www.cookmedical.com/peripheral-intervention/paclitaxel/