



Long-term Safety Information on Paclitaxel Eluting Stents: Insights from the Zilver PTX Programme

Michael D. Dake, M.D.
Senior Vice President of Health Sciences
Professor of Medical Imaging, Medicine , and Surgery
University of Arizona
Tucson/Phoenix, Arizona

Disclosure

Speaker name: **Michael Dake**

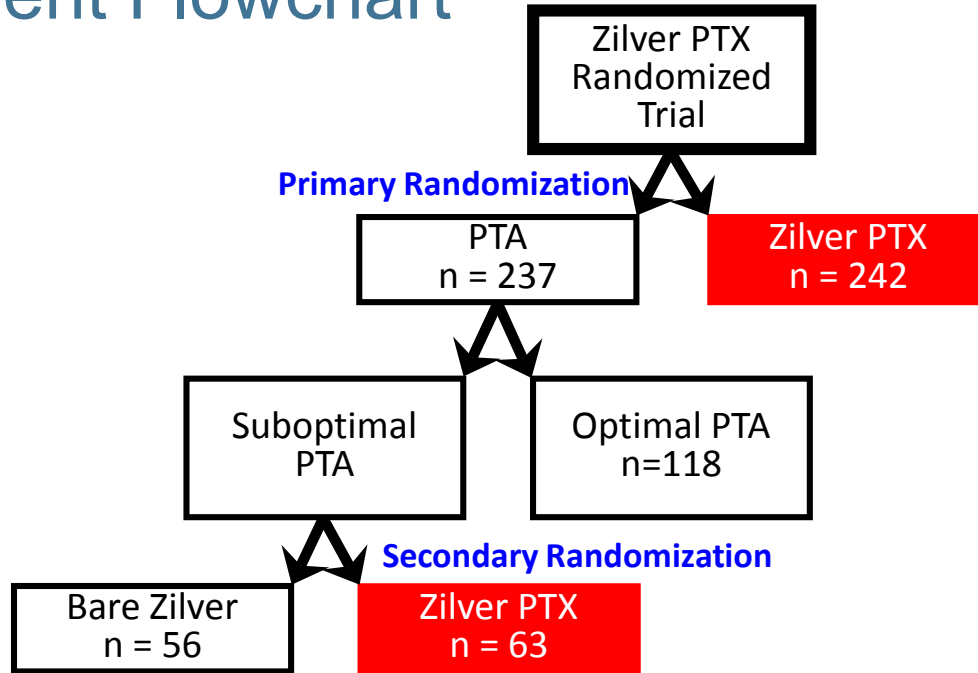
I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)
- I do not have any potential conflict of interest

Zilver PTX Key Points

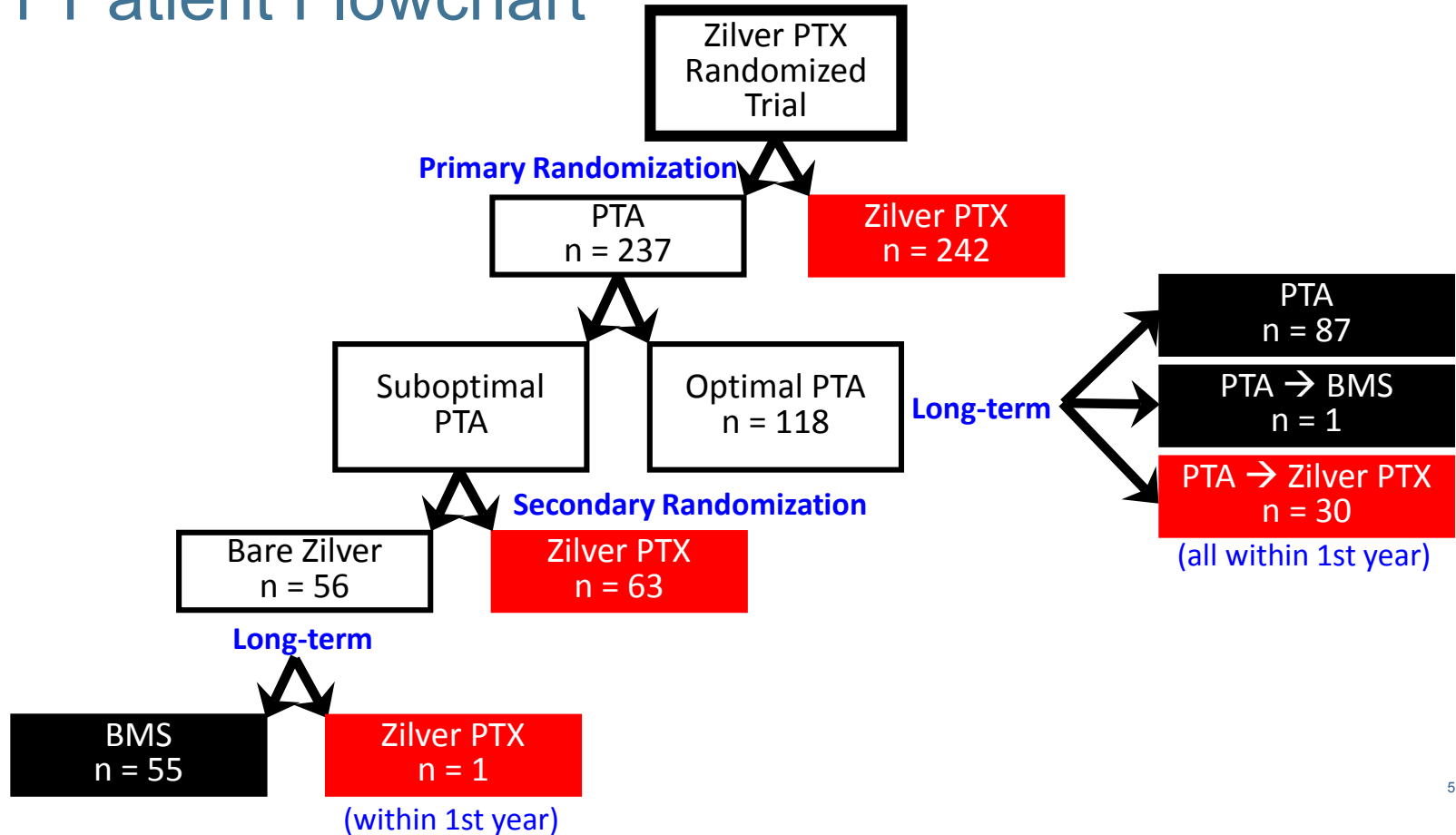
- Data used by Katsanos, et al. did not identify all patients that were treated with Zilver PTX
 - Patient-level data were not used in the analysis
 - Some patients treated with Zilver PTX were included in the control arm of the analysis
- Patient level analysis demonstrates no difference in mortality rate for Zilver PTX compared to PTA/BMS
 - Causes of death for Zilver PTX are similar to PTA/BMS

RCT Patient Flowchart

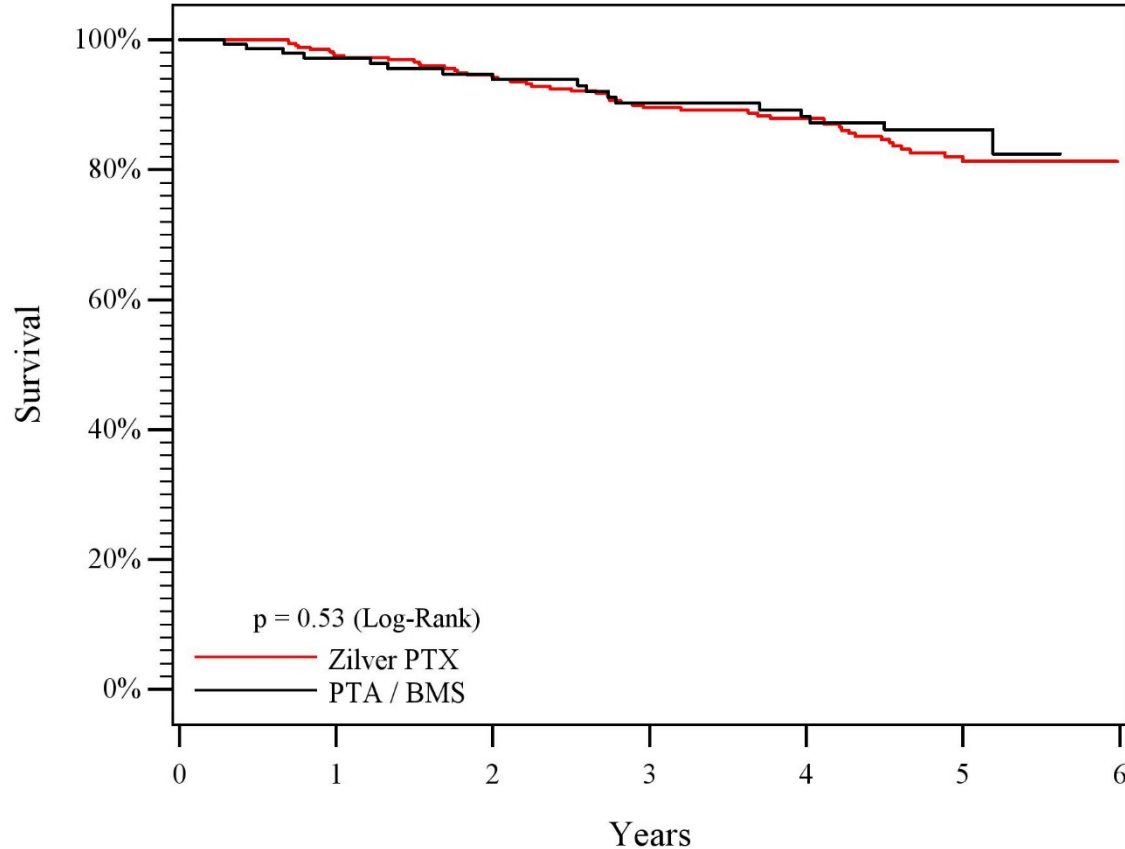


The RCT study design allowed optimal PTA patients requiring reintervention within the first year post-procedure to cross over to treatment with the Zilver PTX stent

RCT Patient Flowchart



Zilver PTX RCT Final 5-year Mortality Analysis



PTA / BMS n = 143 Died = 17 KM = 17.6%	ZILVER PTX n = 336 Died = 48 KM = 18.7%
p = 0.53	

No significant difference
between Zilver PTX
and PTA / BMS

Zilver PTX Covariate Analysis

- Cox proportional hazards model
- Included comorbidities that may be related to mortality as well as other factors of interest
- No significant difference between Zilver PTX and PTA / BMS

Covariate	Multivariate p-value
Age	0.0002
PTX vs. PTA/BMS	0.54
Hypertension	0.46
Hypercholesterolemia	0.63
Pulmonary disease	0.58
Previous MI	0.94
Diabetes	0.11
Gender	0.47
Carotid disease	0.14
Congestive heart failure	0.08
Cardiac arrhythmia	0.21
Claudication/CLI	0.15
Country	0.56
Smoking	0.17
Lesion length	0.12

Zilver PTX Dose Analysis

5-year Mortality Rate				
Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
11.5%	13.6%	13.4%	20.0%	13.2%
p=0.72				

~0.3 mg Increasing Total Paclitaxel Dose ~3 mg

No impact of Zilver PTX paclitaxel dose on mortality rate

The amount of paclitaxel on a Zilver PTX stent is approximately 10% to 20% of the amount on a DCB for the same device size and dose density

Causes of Death Through 5 Years – RCT

Cause	RCT – PTX (n=336)	RCT – PTA / BMS (n=143)
Cardiovascular	4.8%	5.6%
Cancer	4.8%	1.4%
Pulmonary	1.8%	1.4%
Stroke	0.6%	0.7%
Trauma	0.0%	1.4%
GI	0.3%	0.0%
Multiple/Unknown	2.1%	1.4%

No significant difference in cause of death, $p=0.56$

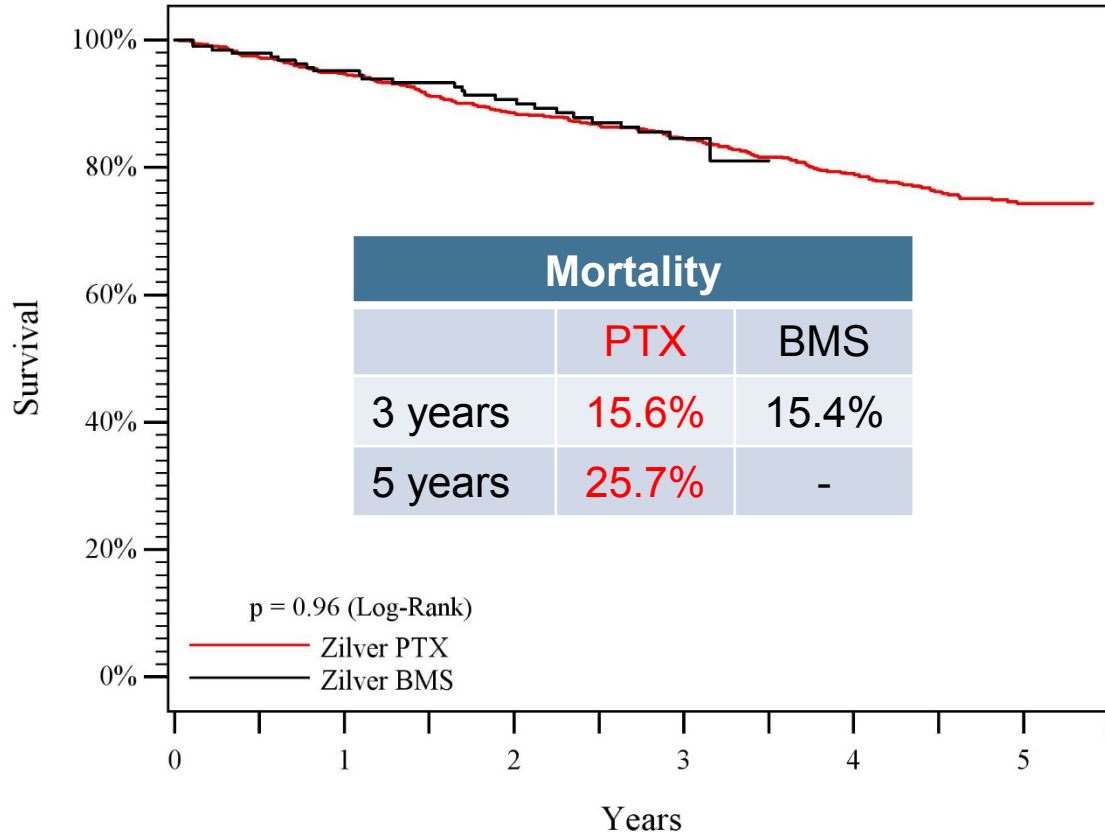
Causes of Death Through 5 Years – RCT and BMS

Cause	RCT – PTX (n=336)	RCT – PTA / BMS (n=143)	Zilver BMS Study* (n=110)
Cardiovascular	4.8%	5.6%	4.5%
Cancer	4.8%	1.4%	6.4%
Pulmonary	1.8%	1.4%	1.8%
Stroke	0.6%	0.7%	0
Trauma	0.0%	1.4%	0
GI	0.3%	0.0%	0.9%
Multiple/Unknown	2.1%	1.4%	0.9%

No increased rate of cardiovascular, cancer, or other cause of death for Zilver PTX compared to PTA or BMS

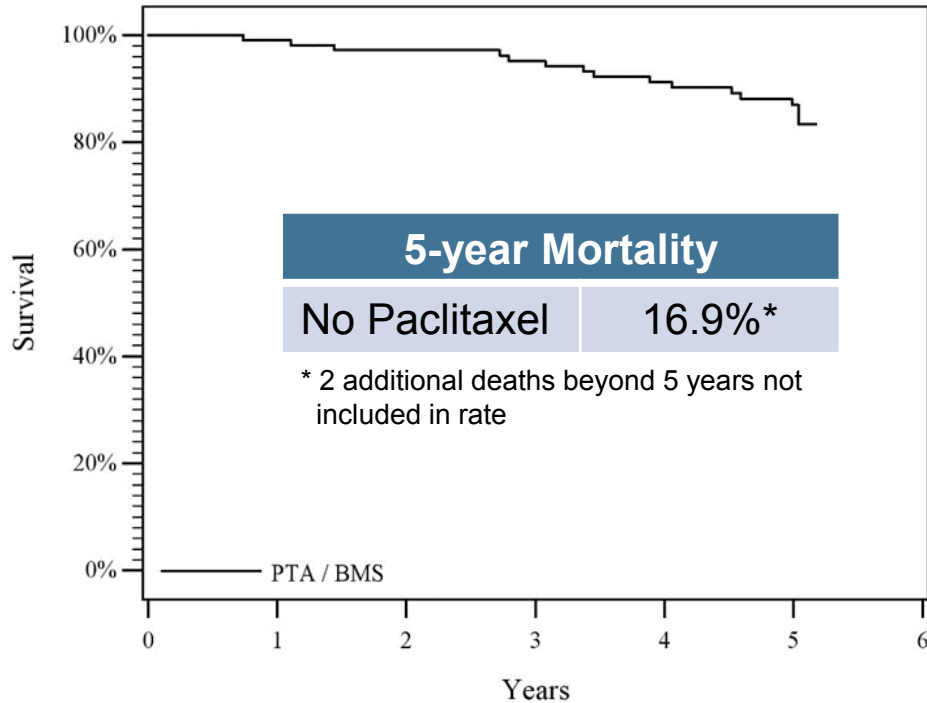
*The Zilver BMS study enrolled 110 patients with femoropopliteal artery disease for 5-year follow-up ¹⁰

Additional Zilver PTX Studies – Japan PMS



- 904 Zilver PTX patients
 - 5-year follow-up
 - No exclusion criteria; challenging patient population (21% CLI)
- 208 BMS patients
 - 3-year follow-up
- No significant difference in mortality (p=0.96)

Additional Bare Metal Stent Study



- 110 Zilver BMS patients
- 5-year follow-up
- Comparable mortality to Zilver PTX studies

Mortality Rates from Literature

- A literature review of mortality rates for PAD patients indicates:
 - 3-year mortality rates range from 9% to 29% (up to 41% for CLI patients)
 - 5-year mortality rates range from 9% to 27% (up to 51% for CLI patients)

Summary of Mortality Rates

3-YEAR MORTALITY

Cook
PTX

Cook
BMS

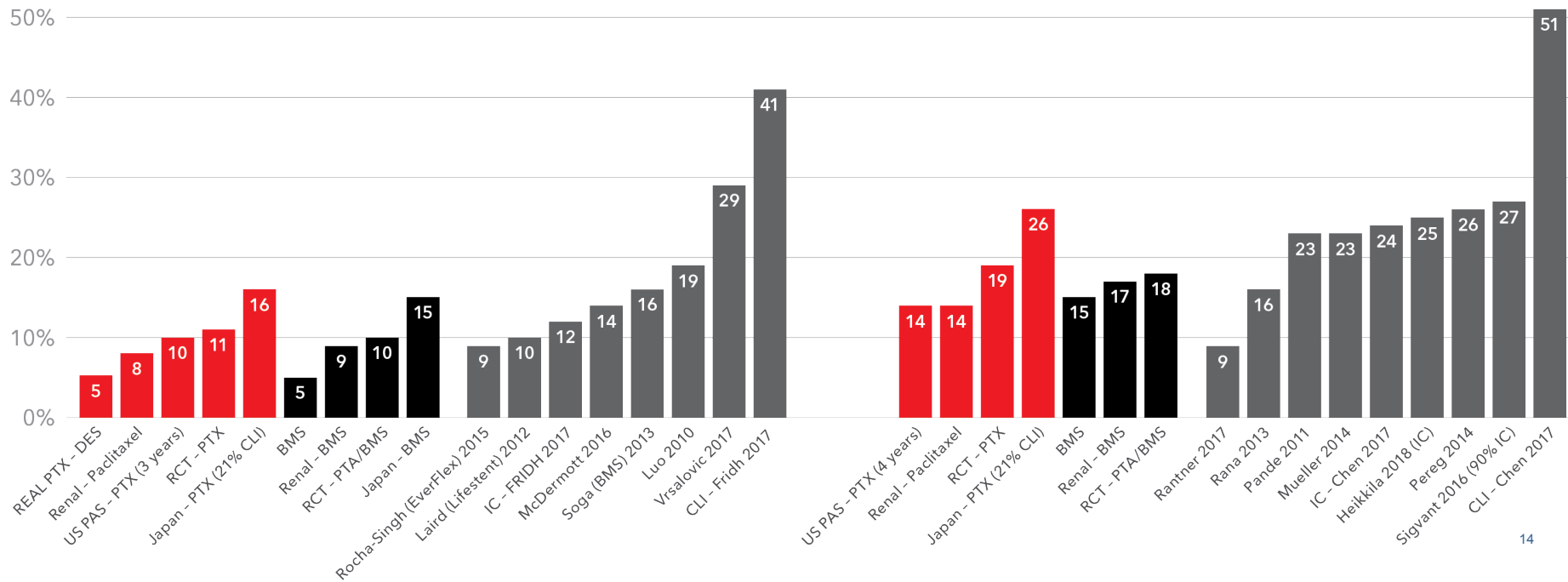
PAD Mortality
Literature Review

5-YEAR MORTALITY

Cook
PTX

Cook
BMS

PAD Mortality
Literature Review



Conclusions

- Conclusion of Katsanos, et al. was not based on patient-level data
- Patient-level analysis of RCT data shows no increased long-term mortality risk with Zilver PTX compared to PTA and BMS
 - Covariate analysis supports no significant difference
 - No impact of Zilver PTX paclitaxel dose on mortality rate
- Analysis of all global Zilver PTX data confirms RCT findings
- Mortality rates for the Zilver PTX stent are consistent with rates reported in literature for PAD patients