Site-specific Antithrombotic Therapy

DESyne BDS Plus Trial 2-Year Outcomes

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On behalf of Stefan Verheye, MD, PhD; Mark Webster, MD, and the DESyne BDS Plus RCT Investigators

Late breaking trial

2025

Potential conflicts of interest

Speaker's name: Alexandre Abizaid

☑ I do not have any potential conflict of interest to declare

Study organization

Principal Investigators and Study Centers by Country

Belgium

- Stefan Verheye, MD, PhD, ZAS Cardiovascular Center Middelheim (Study Co-PI)
- Bert Ferdinande, MD, Ziekenhuis Oost-Limburg, Campus Sint Jan
- Johan Bennett, MD, PhD, Universitaire Ziekenhuizen Leuven
- Ian Buysschaert, MD, AZ Sint Jan Brugge AV

Netherlands

- Pim A. L. Tonino, MD, PhD, Catharina Hospital

Czechia

- Tomas Kovarnik, MD, Charles University and General University Hospital

New Zealand

- Mark Webster, MD, Auckland City Hospital (Study Co-PI)
- Seif El-Jack, MD, North Shore Hospital
- Douglas Scott, MD, Middlemore Hospital
- Madhav Menon, MD, Waikato Hospital
- Gerard Wilkins, MD, Dunedin Hospital
- Dougal McClean, MD, Christchurch Hospital

Brazil

- Rodolfo Staico, MD, Instituto Dante Pazzanese
- Alexandre Abizaid, MD, PhD, Instituto do Coração

Imaging Core Lab
QCA and OCT

CERC Cardiovascular European Research Center

Pharmacokinetic Sub-study Core Lab

C42 integrated solutions in systems biology clinical research & development

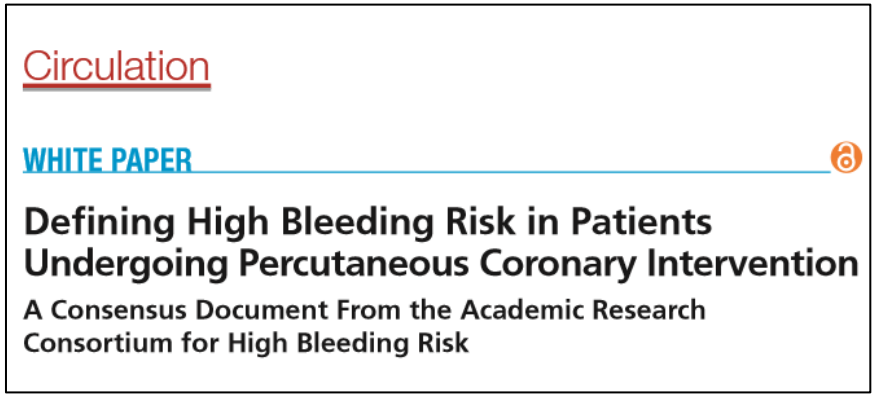
Clinical Events Committee

RARAS CRO

Unsustainable burden of managing ischemic and bleeding risk

- Balancing **ischemic** and **bleeding risk** with oral anti-thrombotic drugs **remain a significant clinical challenge,** especially in patients who are at High Thrombotic Risk (HTR) and High Bleeding Risk (HBR)

HBR Status: BARC 3 or 5 bleeding risk > 4% at 1-Year or ICH risk of >1% at 1-Year - despite shortened DAPT/SAPT with the latest gen DES[1]

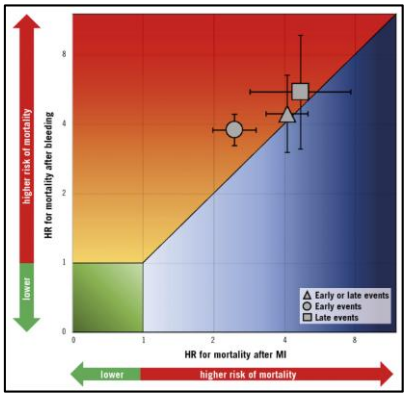

Circulation

WHITE PAPER

Defining High Bleeding Risk in Patients Undergoing Percutaneous Coronary Intervention

A Consensus Document From the Academic Research Consortium for High Bleeding Risk

Early bleeding associated with higher risk of mortality than early MI : Meta-analysis analysis including 141,059 patients[2]



Major Bleeding = MI

Early Major Bleeding >> MI

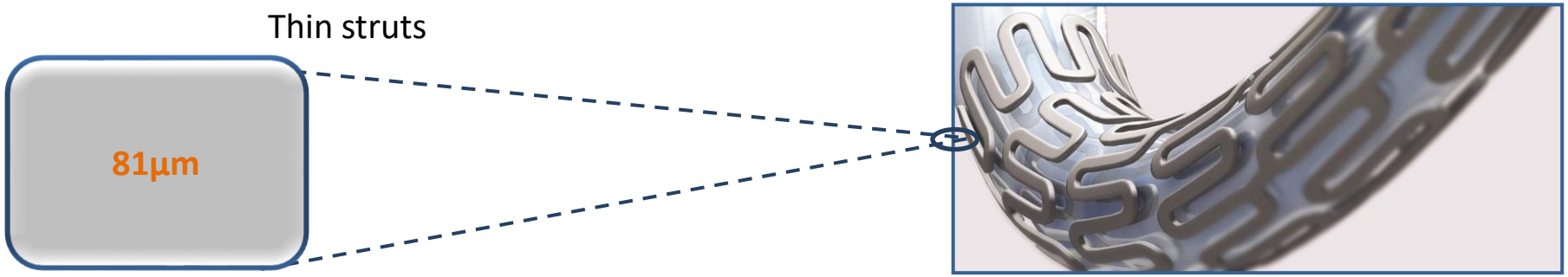
[1]Urban P et al. European Heart Journal (2019) 40, 2632–2653.
[2]Piccolo et al. EuroIntervention . 2021 Sep 20;17(7):550-560.

TRx incorporated on DESyne BDS Plus Drug Eluting Coronary Stent system*

A novel triple drug (TRx) eluting coronary stent system eluting Sirolimus along with two anticoagulants at the site of the implant is designed to deliver site-specific antithrombotic therapy

Platform

Thin struts



**DESyne BDS Plus Drug Eluting Coronary Stent System (DECSS) is for Investigational Use Only*

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Bioabsorbable Polymer

Platform

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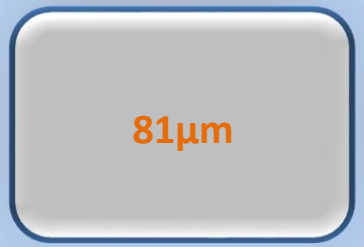


Platform

Thin struts

Bioabsorbable Polymer

Drugs:

Sirolimus	(7µg/mm)	– 4 weeks
Argatroban	(8µg/mm)	– 6 months
Rivaroxaban	(8µg/mm)	– 6 months

**DESyne BDS Plus Drug Eluting Coronary Stent System (DECSS) is for Investigational Use Only*

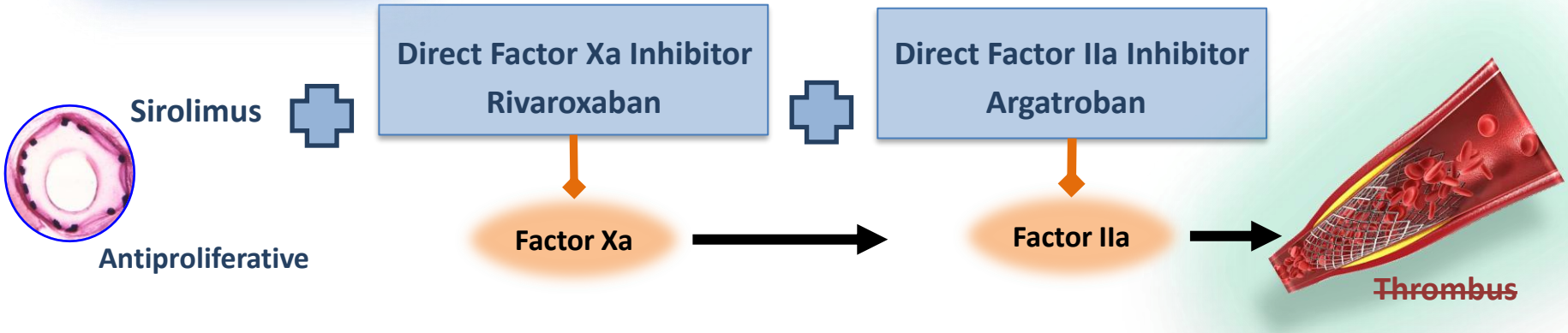
TRx blocks the critical pathway to thrombus formation (MOA)

81µm

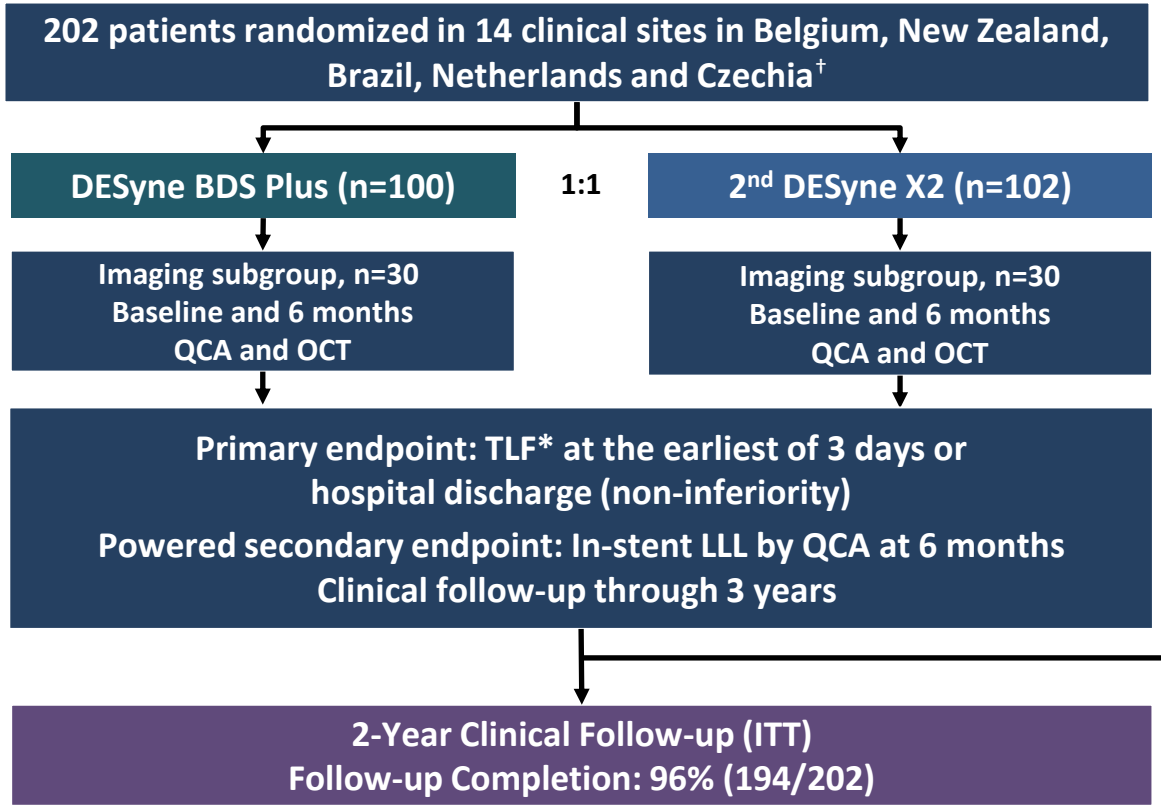
Platform

Thin struts

Bioabsorbable Polymer



DESyne BDS Plus RCT trial design



DESyne BDS Plus Pharmacokinetic (PK) sub-study† (non-randomized) n=11

PK follow-up through 7 days

Clinical follow-up through 3 years

†DAPT administration per ESC guidelines.

*Target lesion failure, defined as composite endpoint of the cardiovascular death, target vessel myocardial infarction and clinically-indicated target lesion revascularization

- Total 7 subject withdrawals:
  - 2 subjects withdrawn after randomization
  - 2 subjects withdrawn after procedure
  - 2 subjects withdrawn after 1 month
  - 1 subject withdrawn after 6 months
- 1 subject had non-CV death

Patient baseline characteristics

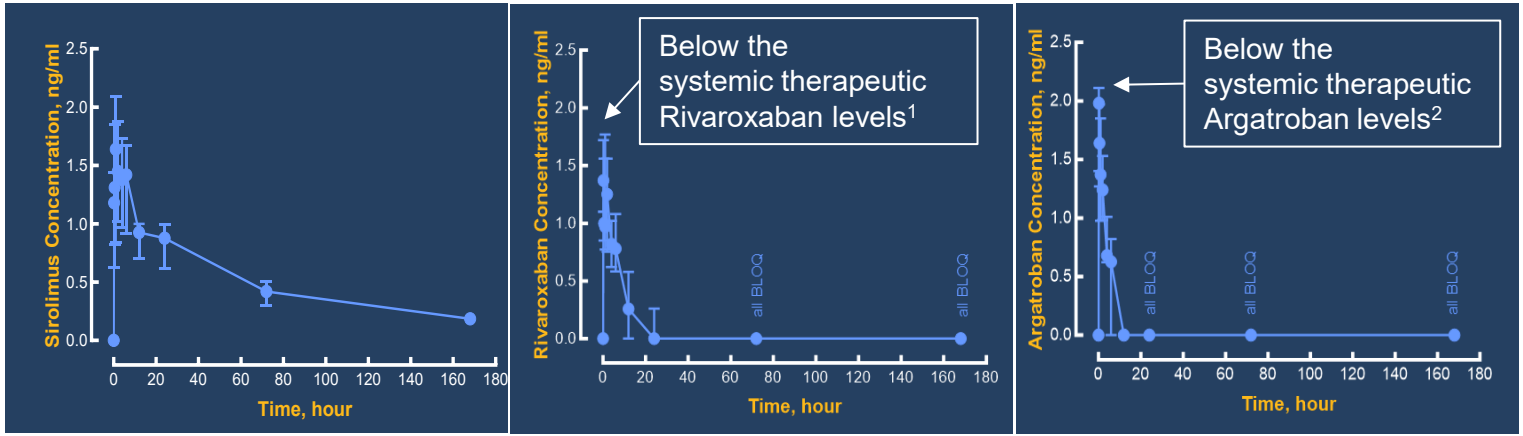
	DESyne BDS Plus n = 100	DESyne X2 n = 102[a]
Age, years	63.2 ± 9.9	62.7 ± 9.9
Female	22 (22%)	27 (26%)
Hypertension	68 (68%)	62 (61%)
Dyslipidemia	70 (70%)	73 (72%)
Diabetes mellitus[b]	28 (28%)	15 (15%)
Prior MI	24 (24%)	22 (22%)
Prior PCI	25 (25%)	26 (26%)
Prior CABG	2 (2%)	2 (2%)
Current smoking	23 (23%)	19 (19%)

	DESyne BDS Plus n = 100	DESyne X2 n = 102[a]
Clinical presentation		
Acute coronary syndrome[c]	32 (32%)	36 (36%)
Chronic/Stable coronary syndrome[d]	68 (68%)	65 (64%)
Antiplatelet Medication		
P2Y12 inhibitor	72 (72%)	73 (72%)
Aspirin	94 (94%)	92 (91%)

Note: Values are mean ± standard deviation or n (%). [a]For one patient that discontinued immediately after randomization without receiving a study stent, only demographics were reported. [b]P value<0.05. [c]Patients with unstable angina, STEMI or NSTEMI at Baseline. [d]Patients with stable angina, silent ischemia, asymptomatic post myocardial infarction or atypical chest pain at Baseline.

Systemic Subtherapeutic Levels Demonstrated in PK Study while Maintaining Therapeutic Effect at the Site Through 6 Months*

Sirolimus, Rivaroxaban and Argatroban blood concentration



Cmax, ng/mL	1.72 (1.04 to 2.12)	1.38 (1.19 to 1.82)	1.99 (1.35 to 2.11)
Tmax	2.0 hours (1.5 to 4.0)	10 min (10 to 30)	10 min (10 to 10)

Values are median (interquartile range). *Site specific therapeutic levels confirmed in pre-clinical evaluation; BLOQ, below lower limit of quantification (<0.5 ng/ml); Cmax, maximum concentration; Tmax, time to reach Cmax.

[1]Vranckx et al. Thromb Haemost. 2015;114(2): 258-267; [2]Swan et al. Pharmacotherapy. 2000;20(3):318-329

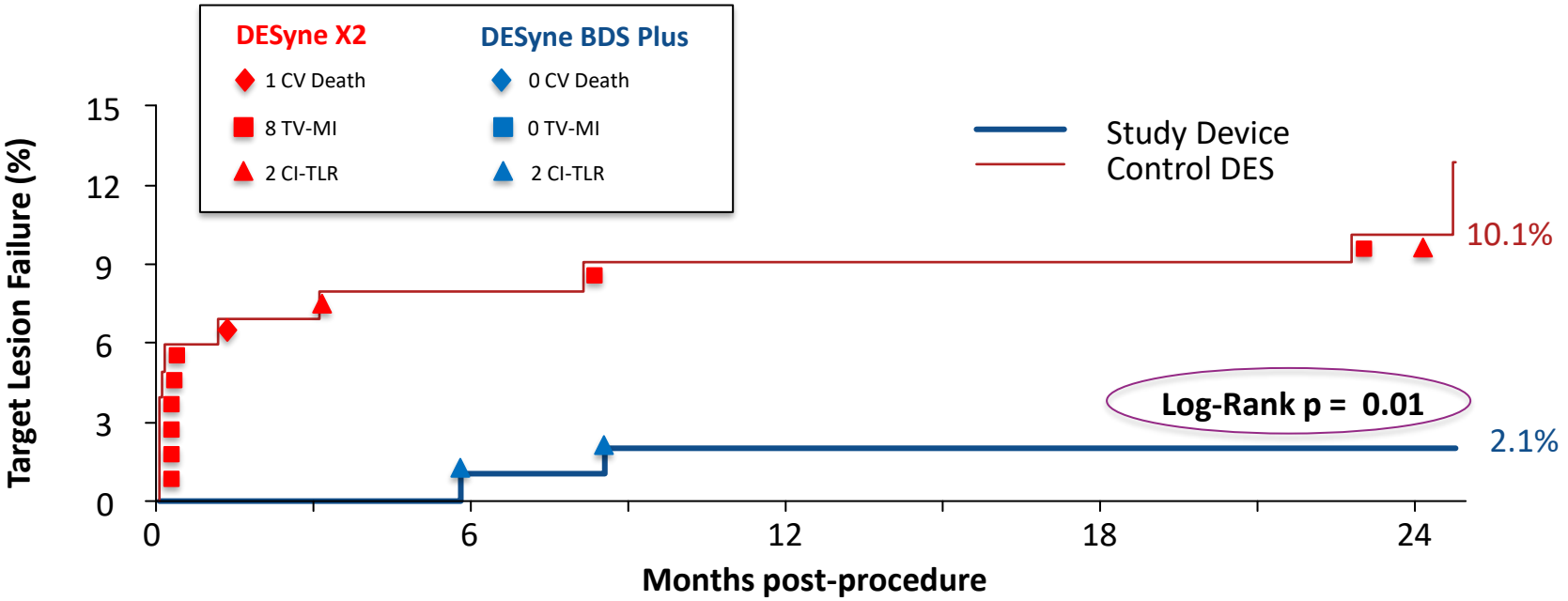
TLF primary endpoint of non-inferiority was met

Null hypothesis is rejected

	DESyne BDS Plus n = 98	DESyne X2 n = 100	Difference	P value[b]
Target lesion failure (TLF) through the earliest of 3 days or hospital discharge, %	0.0 (0.0 to 3.7)	5.0 (1.6 to 11.3)	**-5.0 (-11.8 to 1.8)[a]**	***<0.001***
CV Death, %	0.0 (0.0 to 3.7)	0.0 (0.0 to 3.6)	No Events	
TV-MI, %	0.0 (0.0 to 3.7)	5.0 (1.6 to 11.3)	-5.0 (-11.4 to -0.8)	
CI-TLR, %	0.0 (0.0 to 3.7)	0.0 (0.0 to 3.6)	No Events	

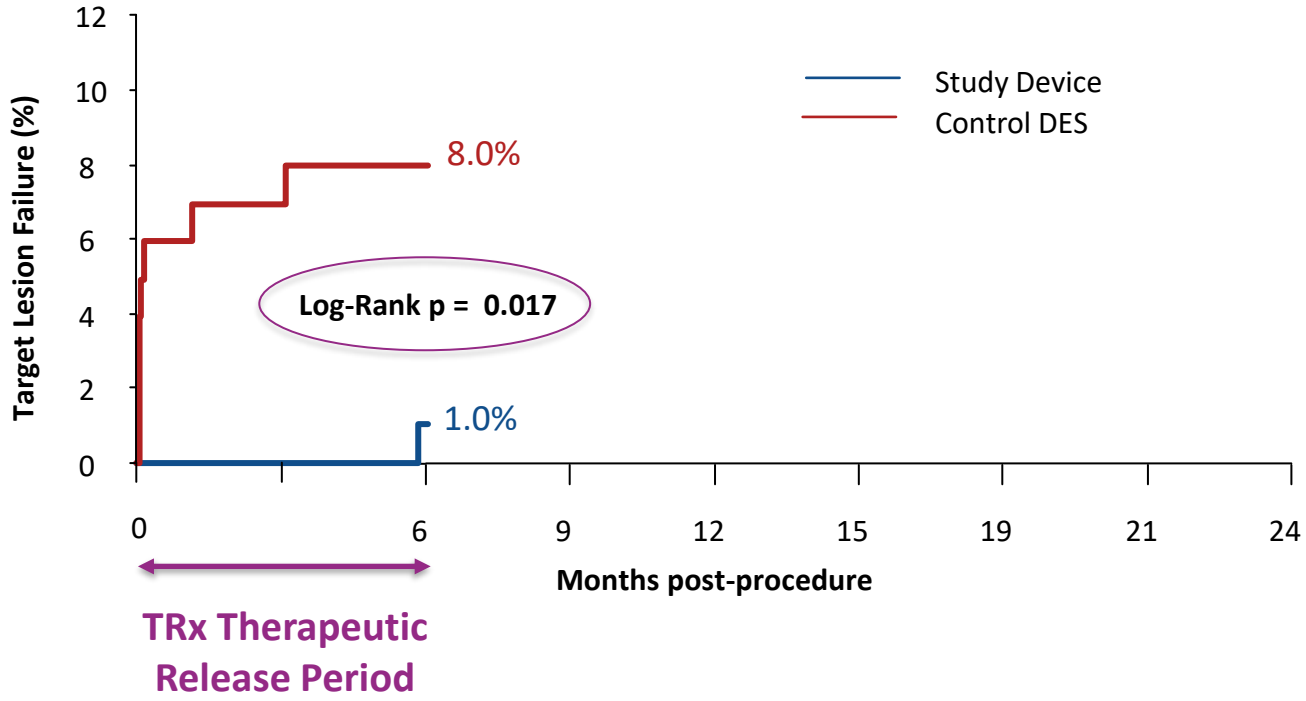
Values are event rate (95% CI). TLF, Target lesion failure; CV, Cardiovascular; TV-MI, Target vessel myocardial infarction; CI-TLR, Clinically indicated target lesion revascularization. [a]Confidence interval for target lesion failure associated with hypothesis test, all others are exact CI. [b]One-sided p value based on the Farrington-Manning test for non-inferiority with an 8% margin.

2-Year Outcomes Demonstrate Sustained Significantly Lower TLF Rate with the Study Device: no CVD, TV-MI, or Stent Thrombosis



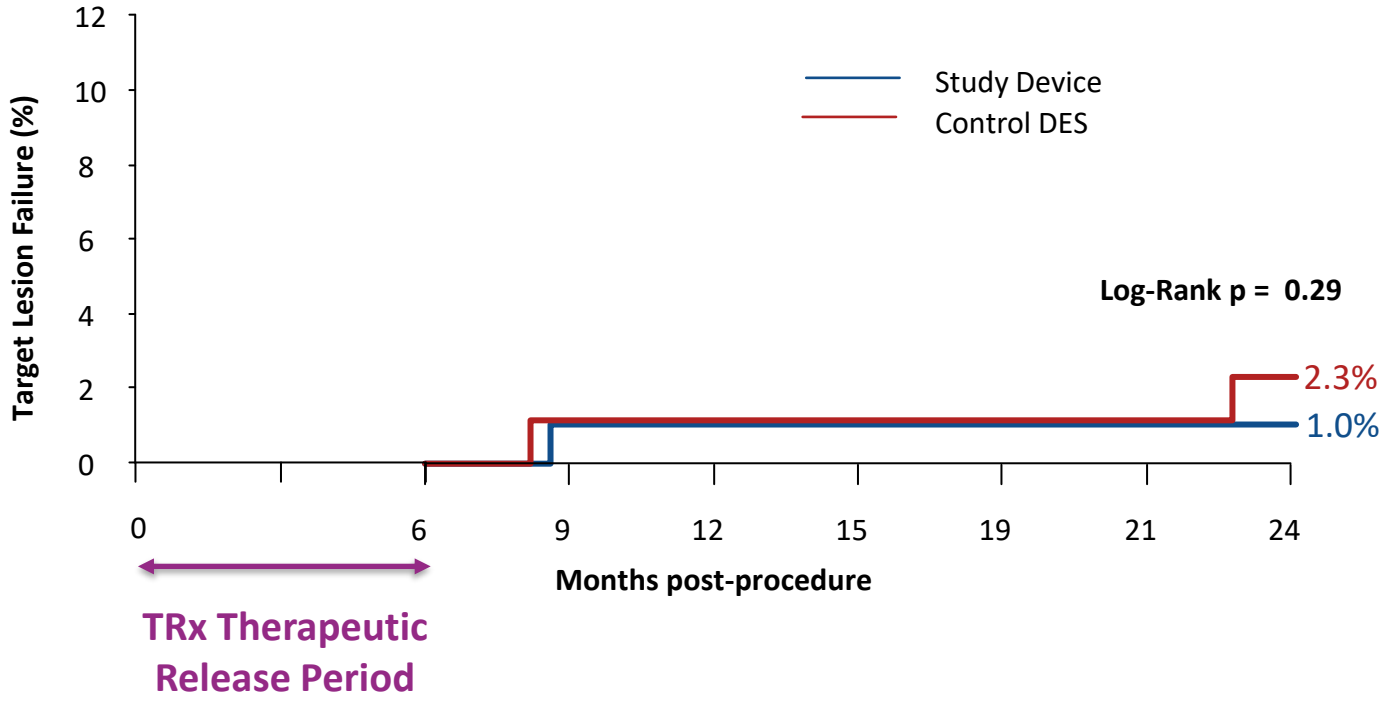
*One definite/probable stent thrombosis event in control group and none in study device through 2-year follow-up. TLF, Target lesion failure. Time to first TLF censored at 2-year follow-up visit.

Significantly Lower TLF with the Study Device Through 6 Months During TRx Release



TLF, Target lesion failure. Time to first TLF censored at 2-year follow-up visit.

Sustained Low TLF After 6 Months Through 2-Year Follow-up For Study Device and Control DES



TLF, Target lesion failure. Time to first TLF censored at 2-year follow-up visit.

Conclusions

- **2-year results from DESyne BDS Plus RCT demonstrate the sustained significantly lower adverse events with site specific anti-thrombotic drug therapy (TRx)**
  - **No stent thrombosis (definite/probable)**, CVD, TV-MI with significantly lower TLF rate (p=0.010), compared to contemporary DES, driven **by marked reduction in ischemic events in the first six months post procedure during the release of TRx.**

- **Drug pharmacokinetics results showed**
  - **Localized therapeutic levels of the two anticoagulants through 7 days and maintaining therapeutic effect through six months**

- **2-year outcomes demonstrate promising safety and effectiveness of the site specific anti-thrombotic therapeutic with DESyne BDS Plus, as a potential solution to address the compromise between bleeding and ischemic events when using systemic drugs.**

TRx Saves Lives

DESyne BDS Plus ▶ *Additional TRx applications* ▶ *Left ventricular assist device (LVAD) implants* *Left atrial appendage (LAA) implants* *Patent foramen ovale (PFO) closure implants*

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