Everolimus-eluting Bioresorbable Vascular Scaffolds in Patients with Diabetes Mellitus

The ABSORB Trial Diabetic Study

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Potential conflicts of interest

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Affiliation/Financial Relationship	Company
Study chairman of ABSORB III/IV trial program (uncompensated)	Abbott Vascular
Consultant	Reva Corp

Absorb Diabetic Study
Background

- Pts with diabetes are at high-risk for adverse ischemic events following PCI, including MI, stent thrombosis, and restenosis, due to greater vascular inflammation and a prothrombotic state, as well as more complex clinical and angiographic features
- Although recent RCTs have demonstrated comparable overall clinical outcomes with the Absorb everolimus-eluting bioresorbable vascular scaffold (BVS) compared to the Xience metallic everolimus-eluting stent (EES), diabetic subgroup analyses from individual trials have lacked the power required to provide reliable treatment effect estimates in this high-risk population

Absorb BVS

Everolimus/PDLLA (1:1) matrix coating

- 7 µm
- Conformal coating
- Controlled drug release similar to Xience CoCr-EES

PLLA Backbone

- Semi-crystalline
- Circumferential sinusoidal rings connected by linear links
- Strut thickness 150 µm
- Platinum markers in each end ring

Absorb Diabetic Study

- A pre-specified formal substudy of ABSORB III -

Objective: To evaluate the 1-year safety and effectiveness of Absorb in diabetic patients

Population: Pooled analysis of the diabetic pts from 4 Abbott Vascular sponsored studies: ABSORB Extend registry, ABSORB II RCT, ABSORB III RCT, and ABSORB Japan RCT

Analysis cohort: "As-treated" - Absorb implanted in at least 1 target lesion, regardless of treatment assignment; pts with lesion length >24 mm from Absorb Extend and Absorb II were excluded

Absorb Diabetic Study

- A pre-specified formal substudy of ABSORB III -

Primary Endpoint: Target lesion failure (TLF*) at 1 year in the Absorb BVS "as treated" diabetic cohort

Power Analysis:

- True 1-year TLF rate = 8.2%**
- Objective Performance Goal (OPG) = 12.7%***
- One-sided alpha = 0.05
- 5% loss to follow-up at 1 year
- 706 patients provide 98.6% power

* Cardiac death, target vessel-MI or ischemia-driven TLR

** 7.0% + difference (1.2%) between diabetic and all Xience patients in SPIRIT IV

*** 8.2% plus 4.5% margin ("putative placebo" preserves ≥50% Rx effect Xience vs. BMS)

Absorb (As Treated)* Diabetic Cohort

	DM Cohort			Non-DM Cohort
	ITDM Cohort	NITDM Cohort	Total DM	
ABSORB EXTEND	36	167	203	571
ABSORB II RCT	15	53	68	239
ABSORB III RCT	131	257	388	873
ABSORB Japan	24	71	95	168
Total	**206**	**548**	**754**	**1851**

*Lesion length ≤24 mm from ABSORB II and ABSORB Extend

Absorb Diabetic Cohort
Baseline Patient Characteristics

	ABSORB EXTEND (N=203)	ABSORB II (N=68)	ABSORB III (N=388)	ABSORB Japan (N=95)	Pooled (N=754)
Age (years)	61.4 ± 10.3	63.6 ± 9.5	63.8 ± 10.1	66.0 ± 9.9	63.4 ± 10.2
Male	71.9%	77.9%	61.3%	82.1%	68.3%
BMI (kg/m^2)	28.1 ± 4.7	29.1 ± 3.9	33.1 ± 6.6	24.9 ± 3.1	30.4 ± 6.3
Hypertension	79.3%	79.4%	90.7%	75.8%	84.7%
Hyperlipidemia	70.9%	72.1%	82.2%	74.7%	77.3%
Current smoker	22.7%	23.5%	18.6%	25.3%	21.0%
Prior MI	30.7%	22.4%	22.1%	20.4%	24.2%
Prior PCI	31.0%	41.2%	36.3%	35.8%	35.3%
Treated with insulin	17.7%	22.1%	33.8%	25.3%	27.3%
Treated with oral hypoglycemic	82.8%	72.1%	73.2%	78.9%	76.4%
HbA1C level >7%	69.6%	49.2%	54.6%	48.9%	57.3%

Absorb Diabetic Cohort
Baseline Lesion Characteristics

	ABSORB EXTEND (N_L=214)	ABSORB II (N_L=75)	ABSORB III (N_L=412)	ABSORB Japan (N_L=99)	Pooled (N_L=800)
# of lsns/pt	1.1 ± 0.2	1.1 ± 0.3	1.1 ± 0.2	1.0 ± 0.2	1.1 ± 0.2
- 1	94.6%	89.7%	93.8%	95.8%	93.9%
- 2	5.4%	10.3%	6.2%	4.2%	6.1%
Target lesion					
- LAD	38.3%	40.0%	44.2%	40.4%	41.8%
- LCX	28.0%	32.0%	26.9%	24.2%	27.4%
- RCA	33.6%	28.0%	28.6%	35.4%	30.8%
- LMCA	0.0%	0.0%	0.2%	0.0%	0.1%
Lsn length (mm)	12.22 ± 4.53	12.29 ± 4.64	12.56 ± 5.27	13.99 ± 5.26	12.62 ± 5.04
RVD (mm)	2.64 ± 0.37	2.61 ± 0.39	2.63 ± 0.44	2.70 ± 0.45	2.64 ± 0.42
Type B2/C lsns	43.2%	38.7%	68.9%	82.8%	60.9%
MLD (mm)	1.11 ± 0.31	1.10 ± 0.32	0.95 ± 0.38	0.96 ± 0.34	1.01 ± 0.36
%DS	57.8 ± 9.9	57.9 ± 10.6	64.0 ± 12.8	64.4 ± 10.9	61.8 ± 12.0

Absorb Diabetic Cohort
Baseline Procedural Characteristics

	ABSORB EXTEND (N=203) (N_L=214) (N_S=237)	ABSORB II (N=68) (N_L=75) (N_S=86)	ABSORB III (N=388) (N_L=412) (N_S=437)	ABSORB Japan (N=95) (N_L=99) (N_S=100)	Pooled (N=754) (N_L=800) (N_S=860)
# devices (per pt)	1.2 ± 0.5	1.3 ± 0.6	1.1 ± 0.4	1.1 ± 0.2	1.1 ± 0.4
Device length (mm, per lesion)	21.9 ± 6.5	22.5 ± 10.9	20.6 ± 7.0	20.8 ± 5.6	21.1 ± 7.2
Overlapping devices (%, per lsn)	10.7%	12.0%	5.3%	1.0%	6.9%
Bailout device (%, per lesion)	0.9%	4.0%	5.1%	1.0%	3.4%
Post-dilatation (%, per scaffold)	75.5%	55.8%	69.6%	84.0%	71.5%
Post-procedural QCA					
- % DS (in-segment)	19.3 ± 6.8	18.3 ± 6.8	19.5 ± 7.7	19.1 ± 6.7	19.3 ± 7.3
- % DS (in-device)	15.2 ± 6.5	14.6 ± 5.6	11.4 ± 8.9	11.5 ± 6.2	12.7 ± 7.9
- Acute gain (mm, in-segment)	1.00 ± 0.34	1.02 ± 0.39	1.18 ± 0.45	1.27 ± 0.42	1.13 ± 0.42
- Acute gain (mm, in-device)	1.17 ± 0.33	1.15 ± 0.38	1.38 ± 0.44	1.47 ± 0.41	1.31 ± 0.42

N = # patients; N_L= # target lesions; N_S = # scaffolds

Absorb Diabetic Cohort
One-Year Primary Endpoint

	Absorb N=754 n / N	%	Upper 1-sided 95% CL	p-value
TLF	62 / 751*	8.3%	10.1%	0.0001

*1-year follow-up in 751/754 (99.6%)

Absorb Diabetic Cohort
Independent Predictors of One-year TLF

TLF: cardiac death, TV-MI, or ID-TLR	HR [95%CI]	P value
Age (increment of 5 years)	1.23 [1.08, 1.40]	0.001
Diabetes treated with insulin (yes vs. no)	2.24 [1.34, 3.74]	0.002
Pre-procedure RVD (increment of 0.5 mm)	0.61 [0.43, 0.87]	0.007

Variables included in the Cox regression model = age (5 year increment), gender, LAD vs. non-LAD, pre-procedure RVD (0.5 mm increment), lesion length (5mm increment), insulin use, type B2/C vs A/B1 lesion, 1 vs. 2 lesions treated, Absorb III vs. non Absorb III study

Absorb Diabetic Cohort

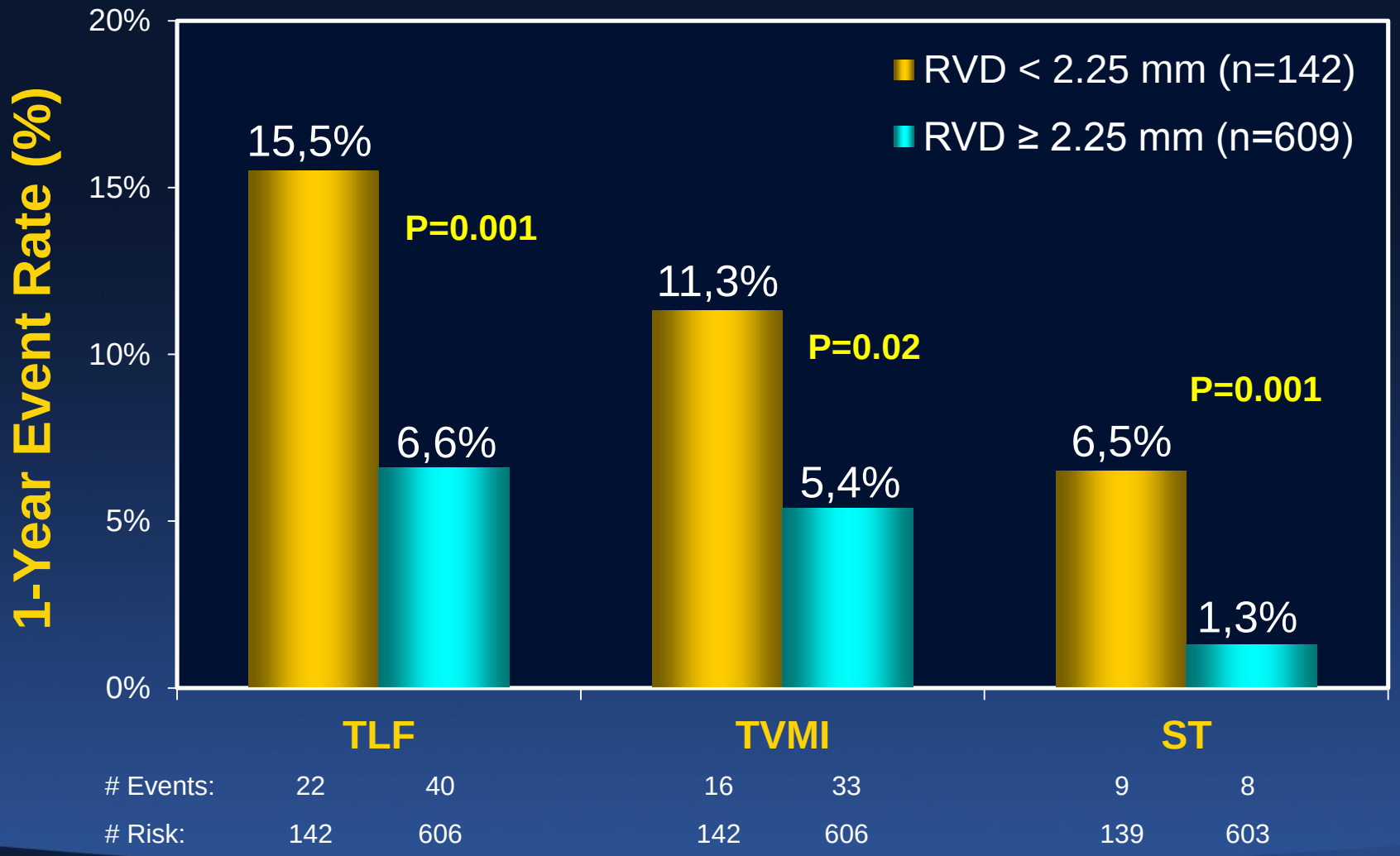
One-year Outcomes

All Patients and According to Insulin Treatment

	All pts (N=754)	NITDM (N=548)	ITDM (N=206)	P value
TLF	8.3%	6.2%	13.7%	0.001
All-cause death	0.8%	0.9%	0.5%	1.00
- Cardiac	0.4%	0.4%	0.5%	1.00
All MI	7.1%	4.9%	12.7%	0.0002
- TV-MI	6.5%	4.4%	12.2%	0.0001
ID-TLR	4.3%	3.1%	7.3%	0.01
ID-TVR	6.0%	4.6%	9.8%	0.008
Scaffold thrombosis (def/prob)	2.3%	1.5%	4.4%	0.03
- Early (≤30 days)	1.3%	0.7%	2.9%	0.03
- Late (31-365 days)	0.9%	0.7%	1.5%	0.40
- Definite	2.1%	1.3%	4.4%	0.02
- Probable	0.1%	0.2%	0.0%	1.00

Absorb Diabetic Cohort

Outcomes by QCA RVD



Absorb Diabetic Study
Limitations

- Underpowered for low frequency events such as scaffold thrombosis
- Follow-up is only available through 1-year

Absorb Diabetic Study
Conclusions

- The present prospective pooled analysis is the largest outcomes study of diabetic patients treated with Absorb
- The TLF rate at 1-year was 8.3%, nearly identical to the assumed true rate of 8.2%; the primary study endpoint was met
- The pooled Absorb diabetic analysis has demonstrated overall safety and effectiveness of Absorb in the treatment of diabetic patients with stable CAD and stabilized ACS
- Large-scale direct comparative trials of Absorb vs. Xience (with long-term follow-up) are required to determine the relative outcomes between these two devices in patients with diabetes