BIOFLOW-III

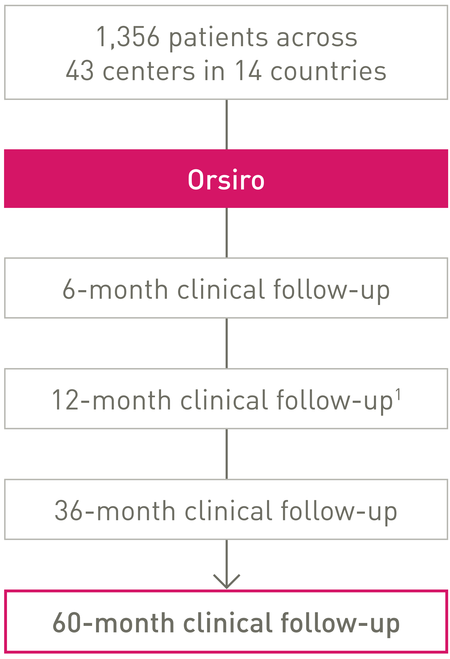
Results for total population out to 5 years

Conclusions

- In this all-comers setting a low Target Lesion Failure[1] (TLF) rate was observed out to 5 years, which implies safety and effectiveness of Orsiro®
- The low TLF rate was confirmed for pre-defined subgroups: Diabetics, Acute Myocardial Infarction (MI), Small vessels and Chronic Total Occlusion (CTO)
- Orsiro demonstrated excellent device (98.8%) and procedural (98.2%) success in total population

Study design

International, prospective, multi-center, open-label, registry of the Orsiro drug-eluting stent in daily clinical practice.



Endpoints

Primary endpoint

- TLF$^{\Delta}$ at 12 months

Secondary endpoints (selected)

- At 6 to 60 months:
  - TLF rates
  - Target Vessel Revascularization (TVR) rates
  - Stent Thrombosis§ (ST)
- Clinical device success
- Clinical procedural success

Patient characteristics[2]

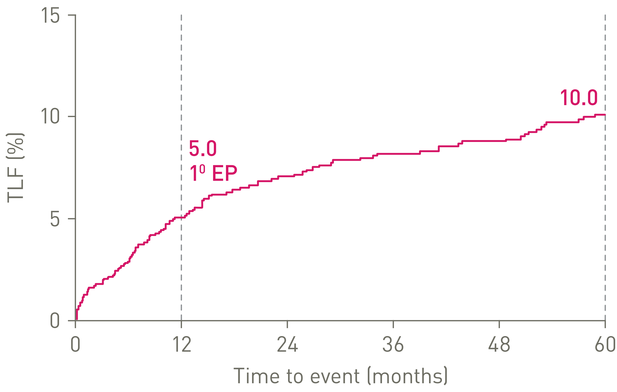
n = 1,356		
Hypertension	1,029	75.9%
Hypercholesteraemia	815	60.1%
Smoking	741	54.6%
Diabetes mellitus	402	29.6%
Insulin-dependent	137	34.1%
Non-insulin-dependent	265	65.9%
History of MI	376	27.7%
Stable angina	641	47.3%
Previous PCI	537	39.6%

Lesion characteristics[2]

n = 1,738‡		
B2/C type lesions	905	52.1%
Bifurcation	282	16.2%
Moderate calcification	411	23.6%
Severe calcification	122	7.0%
Reference vessel diameter (mm)*	3.0 ± 0.4	
Lesion length (mm)*	15.8 ± 9.1	
Diameter stenosis (%)	86.3 ± 11.1	

*Data shown as mean ± SD
‡ Number of Lesions
$^{\Delta}$ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).
§ ST as per ARC definition

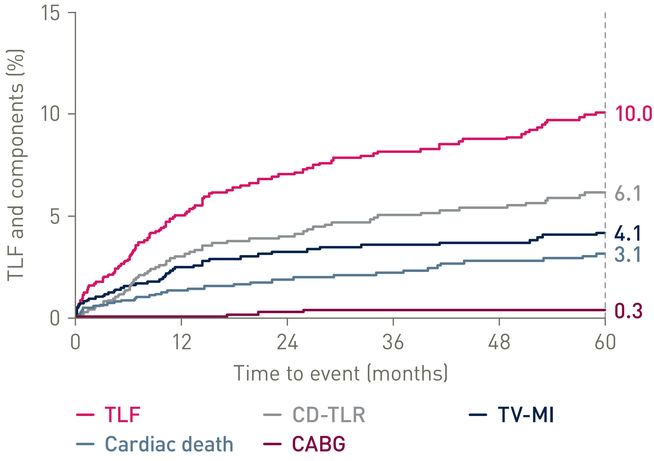
TLF rate out to 5 years[3]



10.0%
60-m TLF

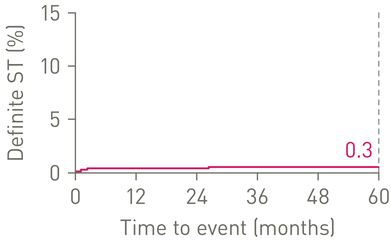
Secondary endpoints selected

TLF and its components out to 5 years total population

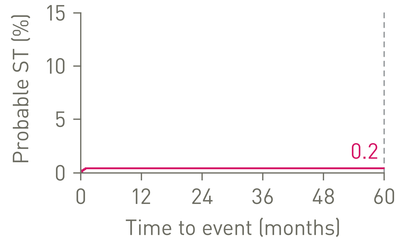


Patients may have experienced more than one component of TLF, therefore components may not sum to overall TLF rate.

Definite ST[3]



Probable ST[3]



Definite or probable ST total population[4]

0.6%
60-m ST

Device and procedural success[2]

Device success (n = 1,738)	98.8%
Procedural success (n = 1,356)	98.2%

Coordinating clinical investigator

Prof. Johannes Waltenberger, Universitätsklinikum Münster, Germany

1. Waltenberger J et al. EuroIntervention 2015; 10-online publish-ahead-of-print March 2015; 2. Waltenberger J et al. Real-world experience with a novel biodegradable polymer sirolimus-eluting stent: twelve-month results of the BIOFLOW-III registry. EuroIntervention. 2016 Feb 1;11(10):1106-0; 3. Waltenberger J. BIOFLOW-III Presentation of Five Year Target Lesion Failure Data; Presented at: EuroPCR 2018; May 24, 2018; Paris, France; ClinicalTrials.gov: NCT01553526; 4. BIOTRONIK data on file.

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BIOFLOW-III
Diabetic subgroup

Conclusions

- In this all-comers setting a low Target Lesion Failure[1] (TLF) rate was observed out to 5 years, which implies safety and effectiveness of Orsiro®
- The low TLF rate was confirmed for pre-defined subgroups: Diabetics, Acute Myocardial Infarction (MI), Small vessels and Chronic Total Occlusion (CTO)
- Orsiro demonstrated excellent device (98.8%) and procedural (98.2%) success in total population

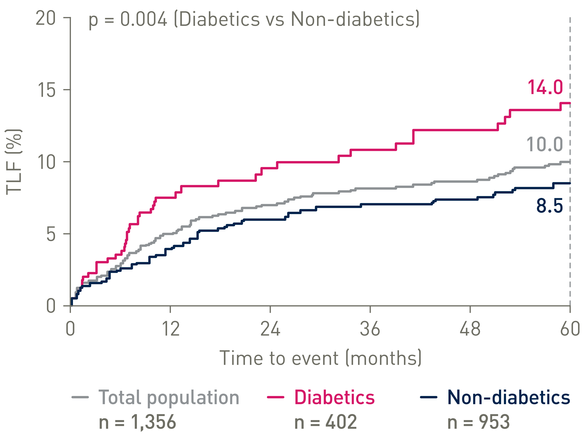
Patient characteristics[1]	Overall n = 1,356	Diabetics n = 402
Hypertension	75.9%	87.6%
Hypercholesteraemia	60.1%	63.7%
Smoking	54.6%	48.5%
Diabetes mellitus	29.6%	100.0%
Insulin-dependent	34.1%	34.1%
Non-insulin-dependent	65.9%	65.9%
History of MI	27.7%	31.6%

Lesion characteristics[1]	Overall n = 1,738‡	Diabetics n = 517
B2/C type lesions	52.1%	48.9%
Bifurcation	16.2%	13.2%
Moderate calcification	23.6%	27.3%
Severe calcification	7.0%	7.9%
Reference vessel diameter (mm)*	3.0 ± 0.4	3.0 ± 0.4
Lesion length (mm)*	15.8 ± 9.1	15.4 ± 9.3
Diameter stenosis (%)	86.3 ± 11.1	85.9 ± 11.2

Major secondary endpoints results out to 5 years[1]

	Total population n = 1,356	Diabetics n = 402	Non-diabetics n = 953	p-value**
TLF	10.0%	14.0%	8.5%	0.004
Cardiac death	3.1%	6.7%	1.7%	<0.001
TV-MI	4.1%	7.0%	3.1%	0.011
CD-TLR	6.1%	6.9%	5.7%	0.281
ST§	1.8%	4.1%	0.9%	0.0006

Diabetic subgroup TLFΔ rates out to 5 years[1]



1. Waltenberger J. BIOFLOW-III; Presentation of Five Year Target Lesion Failure Data; Presented at: EuroPCR 2018; May 24, 2018; Paris, France; ClinicalTrials.gov: NCT01553526.

* Data shown as mean ± SD
**Diabetics vs Non-diabetics
‡ Number of Lesions
Δ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).
§ ST as per ARC definition

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BIOFLOW-III
Acute MI subgroup

Conclusions

- In this all-comers setting a low Target Lesion Failure[1] (TLF) rate was observed out to 5 years, which implies safety and effectiveness of Orsiro®
- The low TLF rate was confirmed for pre-defined subgroups: Diabetics, Acute Myocardial Infarction (MI), Small vessels and Chronic Total Occlusion (CTO)
- Orsiro demonstrated excellent device (98.8%) and procedural (98.2%) success in total population

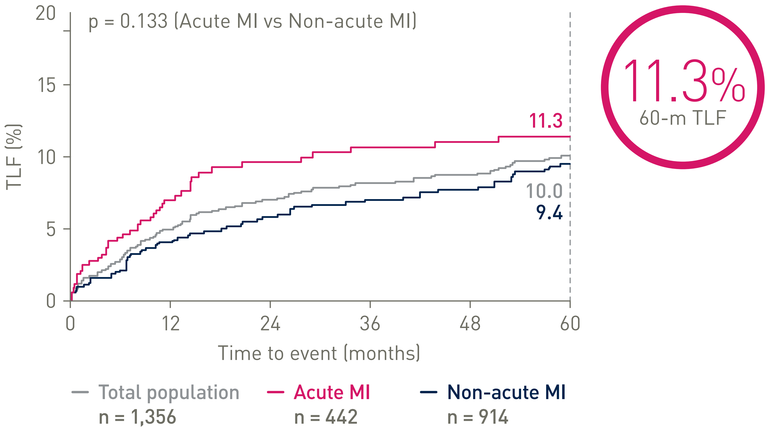
Patient characteristics[1]	Overall n = 1,356	Acute MI n = 442
Hypertension	75.9%	66.3%
Hypercholesteraemia	60.1%	50.2%
Smoking	54.6%	58.1%
Diabetes mellitus	29.6%	25.8%
Insulin-dependent	34.1%	38.6%
Non-insulin-dependent	65.9%	61.4%
History of MI	27.7%	19.7%

Lesion characteristics[1]	Overall n = 1,738‡	Acute MI n = 442
B2/C type lesions	52.1%	57.7%
Bifurcation	16.2%	16.2%
Moderate calcification	23.6%	22.0%
Severe calcification	7.0%	5.3%
Reference vessel diameter (mm)*	3.0 ± 0.4	3.0 ± 0.4
Lesion length (mm)*	15.8 ± 9.1	15.3 ± 7.6
Diameter stenosis (%)	86.3 ± 11.1	90.4 ± 10.1

Major secondary endpoints results out to 5 years[1]

	Total population n = 1,356	Acute MI n = 442	Non-acute MI n = 914	p-value**
TLF	10.0%	11.3%	9.4%	0.133
Cardiac death	3.1%	4.2%	2.6%	0.047
TV-MI	4.1%	5.6%	3.4%	0.065
CD-TLR	6.1%	4.7%	6.7%	0.391
ST§	1.8%	1.7%	1.8%	0.673

Acute MI subgroup TLFΔ rates out to 5 years[1]



1. Waltenberger J. BIOFLOW-III; Presentation of Five Year Target Lesion Failure Data; Presented at: EuroPCR 2018; May 24, 2018; Paris, France; ClinicalTrials.gov: NCT01553526.

* Data shown as mean ± SD
**Acute MI vs Non-acute MI
‡ Number of Lesions
Δ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).
§ ST as per ARC definition

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BIOFLOW-III
Small vessel subgroup

Conclusions

- In this all-comers setting a low Target Lesion Failure[1] (TLF) rate was observed out to 5 years, which implies safety and effectiveness of Orsiro®
- The low TLF rate was confirmed for pre-defined subgroups: Diabetics, Acute Myocardial Infarction (MI), Small vessels and Chronic Total Occlusion (CTO)
- Orsiro demonstrated excellent device (98.8%) and procedural (98.2%) success in total population

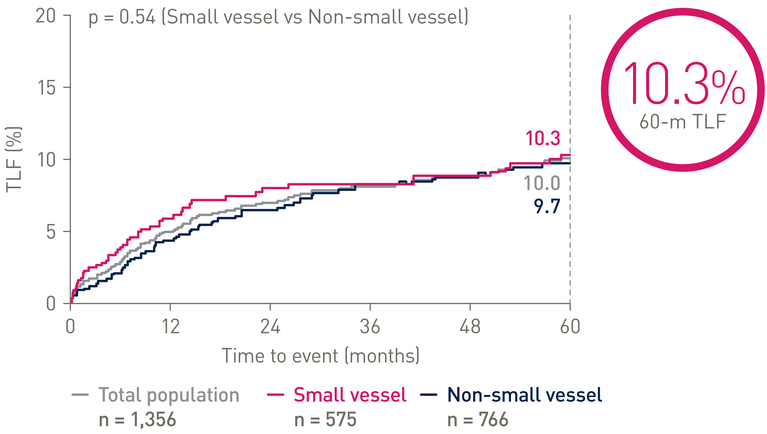
Patient characteristics[1]	Overall n = 1,356	Small vessel n = 575
Hypertension	75.9%	79.0%
Hypercholesteraemia	60.1%	61.0%
Smoking	54.6%	51.0%
Diabetes mellitus	29.6%	32.8%
Insulin-dependent	34.1%	39.9%
Non-insulin-dependent	65.9%	60.1%
History of MI	27.7%	28.5%

Lesion characteristics[1]	Overall n = 1,738‡	Small vessel n = 575
B2/C type lesions	52.1%	49.9%
Bifurcation	16.2%	17.5%
Moderate calcification	23.6%	26.1%
Severe calcification	7.0%	5.4%
Reference vessel diameter (mm)*	3.0 ± 0.4	2.7 ± 0.3
Lesion length (mm)*	15.8 ± 9.1	15.2 ± 8.4
Diameter stenosis (%)	86.3 ± 11.1	86.3 ± 10.9

Major secondary endpoints results out to 5 years[1]

	Total population n = 1,356	Small vessel n = 575	Non-small vessel n = 766	p-value**
TLF	10.0%	10.3%	9.7%	0.54
Cardiac death	3.1%	4.4%	2.2%	0.07
TV-MI	4.1%	4.9%	3.6%	0.35
CD-TLR	6.1%	5.0%	6.5%	0.46
ST§	1.8%	3.4%	0.7%	0.005

Small vessel subgroup TLFΔ rates out to 5 years[1]



1. Waltenberger J. BIOFLOW-III; Presentation of Five Year Target Lesion Failure Data; Presented at: EuroPCR 2018; May 24, 2018; Paris, France; ClinicalTrials.gov: NCT01553526.

* Data shown as mean ± SD
**Small vessel vs Non-small vessel
‡ Number of Lesions
Δ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).
§ ST as per ARC definition

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Chronic Total Occlusion subgroup

Conclusions

- In this all-comers setting a low Target Lesion Failure[1] (TLF) rate was observed out to 5 years, which implies safety and effectiveness of Orsiro®
- The low TLF rate was confirmed for pre-defined subgroups: Diabetics, Acute Myocardial Infarction (MI), Small vessels and Chronic Total Occlusion (CTO)
- Orsiro demonstrated excellent device (98.8%) and procedural (98.2%) success in total population

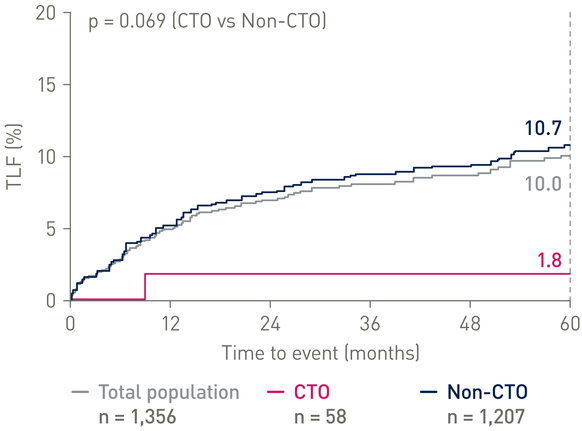
Patient characteristics[1]	Overall n = 1,356	CTO n = 58
Hypertension	75.9%	81.0%
Hypercholesteraemia	60.1%	60.3%
Smoking	54.6%	55.2%
Diabetes mellitus	29.6%	27.6%
Insulin-dependent	34.1%	37.5%
Non-insulin-dependent	65.9%	62.5%
History of MI	27.7%	27.6%

Lesion characteristics[1]	Overall n = 1,738‡	CTO n = 58
B2/C type lesions	52.1%	80.7%
Bifurcation	16.2%	26.5%
Moderate calcification	23.6%	24.1%
Severe calcification	7.0%	12.0%
Reference vessel diameter (mm)*	3.0 ± 0.4	2.9 ± 0.5
Lesion length (%)*	15.8 ± 9.1	21.8 ± 12.9
Diameter stenosis (%)	86.3 ± 11.1	95 ± 11.1

Major secondary endpoints results out to 5 years[1]

	Total population n = 1,356	CTO n = 58	Non-CTO n = 1,207	p-value**
TLF	10.0%	1.8%	10.7%	0.069
Cardiac death	3.1%	2.7%	2.9%	0.812
TV-MI	4.1%	1.8%	4.5%	0.421
CD-TLR	6.1%	1.8%	6.7%	0.227
ST§	1.8%	0.0%	1.9%	0.355

CTO subgroup TLFΔ rates out to 5 years[1]



1.8%
60-m TLF

1. Waltenberger J. BIOFLOW-III; Presentation of Five Year Target Lesion Failure Data; Presented at: EuroPCR 2018; May 24, 2018; Paris, France; ClinicalTrials.gov: NCT01553526.

* Data shown as mean ± SD
**CTO vs Non-CTO
‡ Number of Lesions
Δ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).
§ ST as per ARC definition

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BIOFLOW-III

Complex lesions subgroup

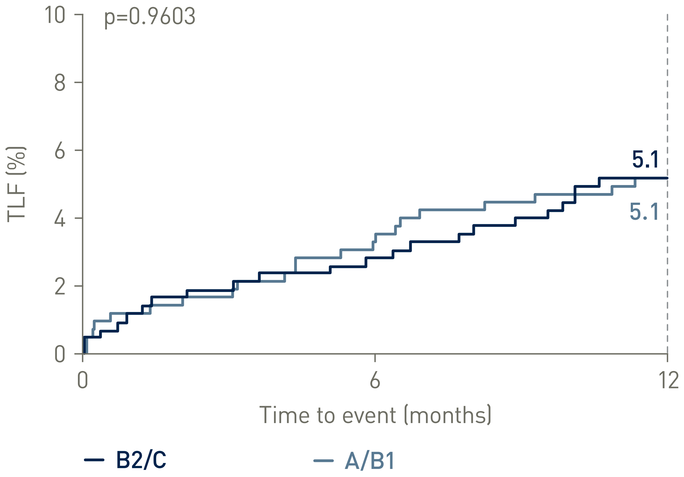
Conclusion

- The low Target Lesion Failure (TLF) rate was confirmed for pre-defined subgroups including the complex lesion subgroup. Regardless of the lesion type, Orsiro® performs equally well in both complex and non-complex lesions

Patient characteristics[1]	A/B1 n = 611	B2/C n = 743	p-value
Age, yrs (mean)	66.0	66.3	0.6256
Hypertension	76%	76%	0.7769
Hypercholesteremia	59%	61%	0.3477
Diabetes	32%	28%	0.1076
Insulin-dependent	33%	35%	0.7593
Non-insulin-dependent	67%	65%	

Lesion characteristics[1]	A/B1 n = 715	B2/C n = 1,012	p-value
Lesion length (mm)*	13.1 ± 5.8	17.6 ± 10.4	<0.0001
Reference vessel diameter (mm)*	3.0 ± 0.4	3.0 ± 0.4	0.0070
Moderate calcification	20.7%	26.0%	0.0102
Severe calcification	2.0%	10.7%	<0.0001
CTO	1.2%	6.0%	<0.0001
Tortuosity – Excessive	0.8%	4.1%	<0.0001

Complex lesion subgroup TLF$^{\Delta}$ rates out to 12 months[1]



5.1%
12-m TLF
B2/C

5.1%
12-m TLF
A/B1

ACC/AHA lesion classification[2]

1. Waltenberger J. BIOFLOW-III – One Year Safety And Performance Results; Presentation at: CRT 2015; Feb 21, 2015; Washington D.C, USA; ClinicalTrials.gov: NCT01553526; 2. Waltenberger J. BIOFLOW-III – 12 months Clinical Data; Poster presented at: TCT 2013; October 27, 2013; California, USA; ClinicalTrials.gov: NCT01553526.

* Data shown as mean ± SD

$^{\Delta}$ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).

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BIOFLOW-III

Multi-vessel disease subgroup

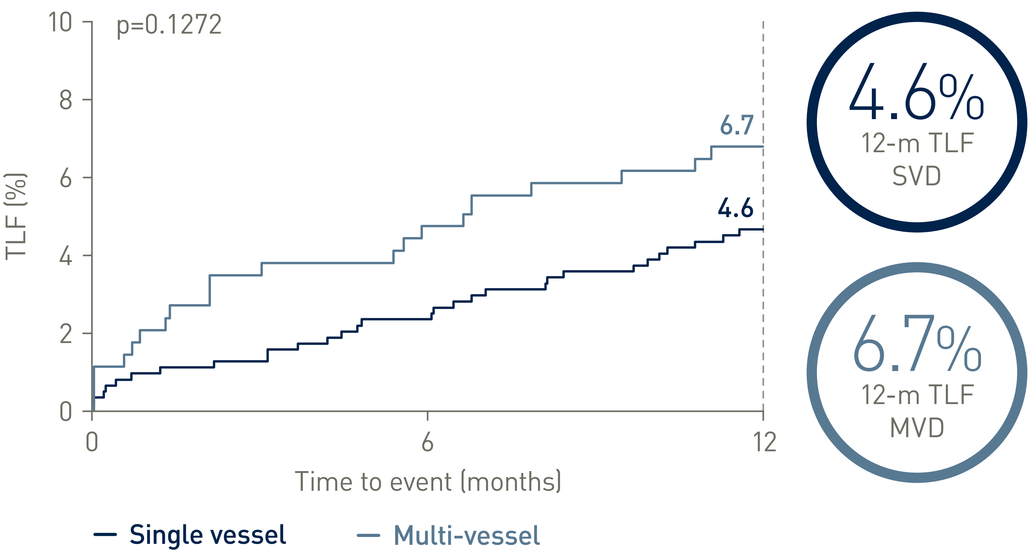
Conclusion

- The low Target Lesion Failure (TLF) rate was not only observed in the overall cohort, but also in patients with multi-vessel disease as seen in this post-hoc analysis

Patient characteristics[1]	SVD* n = 1,050	MVD** n = 305	p-value
Age, yrs‡	65.5 ± 10.8	68.0 ± 10.4	0.0003
Hypertension	75%	78%	0.3942
Hypercholesteremia	59%	63%	0.1942
Diabetes	29%	32%	0.3537
Insulin dependent	68%	59%	
Non-insulin dependent	32%	41.2%	

Lesion characteristics[1]	SVD* n = 1,050	MVD** n = 305	p-value
B2/C type lesions	50.2%	54.8%	0.4669
Lesion length (mm)‡	18.2 ± 5.7	18.0 ± 5.9	
Reference vessel diameter (mm)‡	3.0 ± 0.4	3.0 ± 0.4	

Multi-vessel disease TLF$^{\Delta}$ rates out to 12 months[1]



1. Waltenberger J. BIOFLOW-III, 1-Year TLF Data in patients with complex lesions; Presentation at: EuroPCR 2015; 19-22 May, 2015; Paris, France; ClinicalTrials.gov: NCT01553526.

* Single vessel Disease
**Multi-vessel Disease
‡ Data shown as mean ± SD
$^{\Delta}$ Composite of cardiac death, target vessel Q-wave or non-Q wave Myocardial Infarction (MI), Emergent Coronary Artery Bypass Graft (CABG), clinically driven Target Lesion Revascularization (TLR).

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