BIO-RESORT

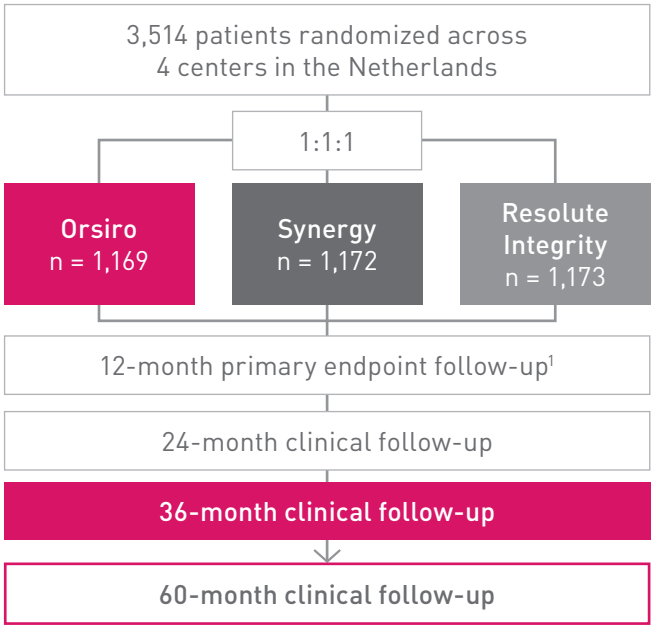
36-month primary endpoint results RCT Orsiro and Synergy vs. Resolute Integrity

Conclusions

- In this 3,514 patient large, randomized, investigator-initiated, all-comers trial, Orsiro® demonstrated non-inferiority to Resolute Integrity* while performing equally well as Synergy** (primary endpoint Target Vessel Failure (TVF) at 12 months: Orsiro 4.7%, Synergy 4.7%, Resolute Integrity 5.4%, $p_{non\text{-}inferiority} < 0.0001$).
- At 36 months, in this highly complex patient population, Orsiro has shown favorable outcomes with numerically lower event rates in TVF compared to both Synergy and Resolute Integrity.
- Additionally, there were no differences observed between Orsiro and Synergy when compared to Resolute Integrity for safety endpoints of Target Vessel-related Myocardial Infarction (TV-MI), Stent Thrombosis (ST) or Cardiac Death.

Study design

All-comers, multi-center, assessor and patient-blinded, randomized, non-inferiority trial



Endpoints

Primary endpoint

- TVF at 12 months defined as the composite of cardiac death, TV-MI or TVR

Secondary endpoints

- Individual components of the primary endpoint
- All-cause mortality
- Any MI
- Target Lesion Failure (TLF)
- Clinically indicated Target Lesion Revascularization (TLR)
- ST

Patient characteristics[1]	Orsiro n = 1,169	Synergy n = 1,172	Resolute Integrity n = 1,173
Age, yrs‡	64.2 ± 10.7	64.0 ± 10.7	63.6 ± 10.9
Male	73%	72%	72%
Smoking	30%	30%	31%
Diabetes mellitus	18%	17%	18%
Previous MI	17%	16%	21%
Previous PCI	18%	18%	17%
Previous CABG	7%	8%	8%
Clinical indication			
ST-elevation MI (STEMI)	32%	32%	28%
Non-ST-elevation MI (NSTEMI)	20%	21%	23%
Unstable angina	18%	16%	19%

Lesion characteristics[2]	Orsiro n = 1,551¤	Synergy n = 1,532¤	Resolute Integrity n = 1,580¤
De novo lesion	96.8%	97.1%	96.8%
Bifurcated lesion	28.6%	29.1%	27.7%
Severe calcification	20.4%	19.3%	20.7%
ACC-AHA lesion class (n)	1,545	1,527	1,573
A/B1	26.3%	29.0%	27.8%
B2/C	73.7%	71.0%	72.2%
Median lesion length (mm)	14.63	14.59	14.74
Minimum lumen diameter (mm)	0.71	0.71	0.70
Reference vessel diameter (mm)‡	2.75 ± 0.56	2.76 ± 0.56	2.76 ± 0.59
Stenosis (lumen diameter %)	72.8	73.8	72.5

* Resolute and Integrity are registered trademarks of Medtronic Vascular Inc.
**Synergy is a registered trademark of Boston Scientific
¤ Number of lesions
‡ Data shown as mean ± SD

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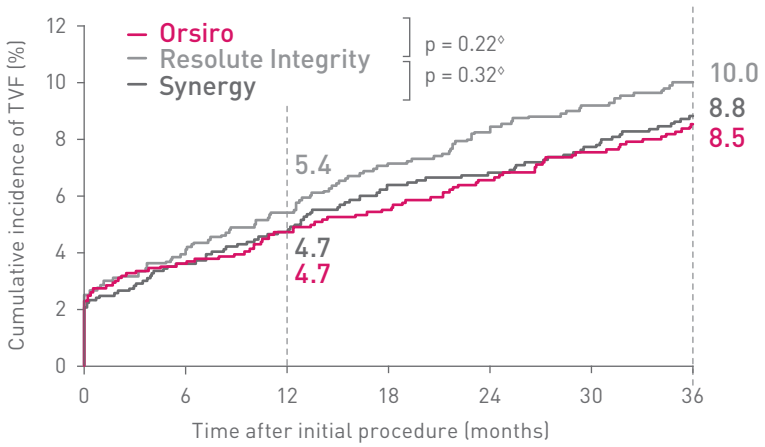
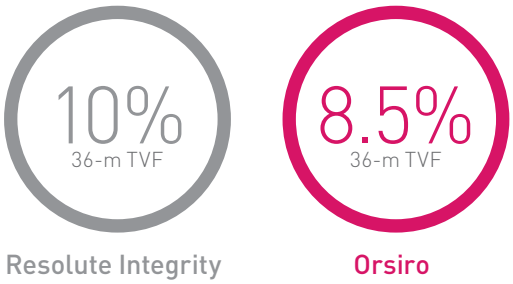
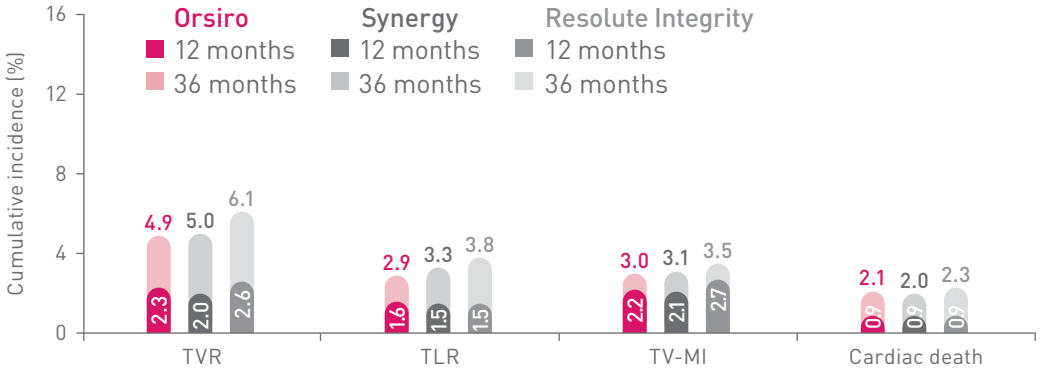
TVF at 3 years[1,3]



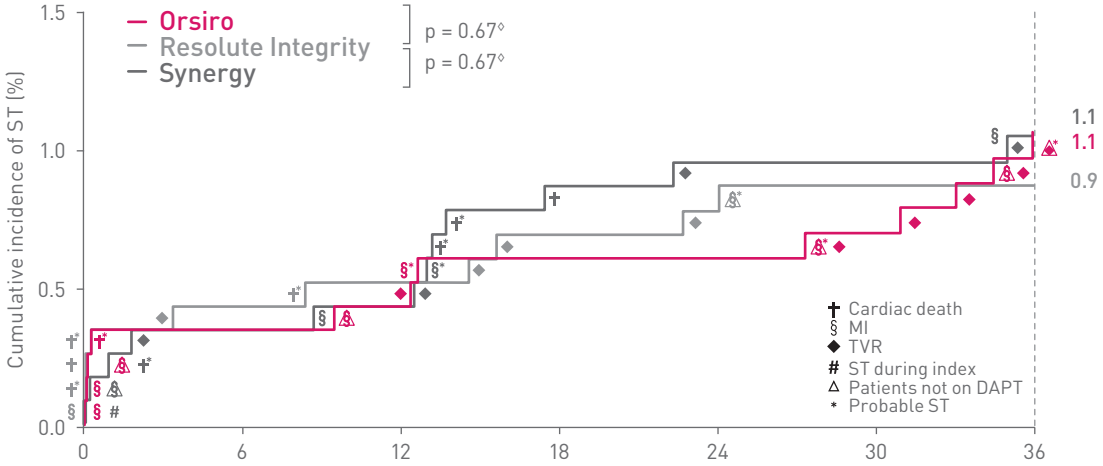


Selected clinical results up to 3 years[1,3]



Cumulative incidence (%) represent Kaplan-Meier failure estimates at 36 months; p >0.05 for all comparisons

Definite or probable ST at 3 years[3]



◊ Logrank statistical method

Principal investigator

Prof. Clemens von Birgelen, Enschede, the Netherlands

1. von Birgelen C et al. The Lancet. 2016;388(10060):2607-17; 2. von Birgelen C et al. BIO-RESORT (TWENTE III). A Prospective, Randomized Three-Arm Trial Comparing Orsiro, Synergy and Resolute Integrity in an All-Comers Population; Presented at: TCT 2016; October 30, 2016; Washington DC, USA; ClinicalTrials.gov: NCT01674803; 3. von Birgelen C et al. 3-Years BIO-RESORT: Results of the 3-Arm randomized study in all-comers, treated with contemporary biodegradable or durable polymer-coated drug-eluting stents. Presented at CRT 2019, March, 2019; Washington DC, USA; ClinicalTrials.gov: NCT01674803.

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BIO-RESORT

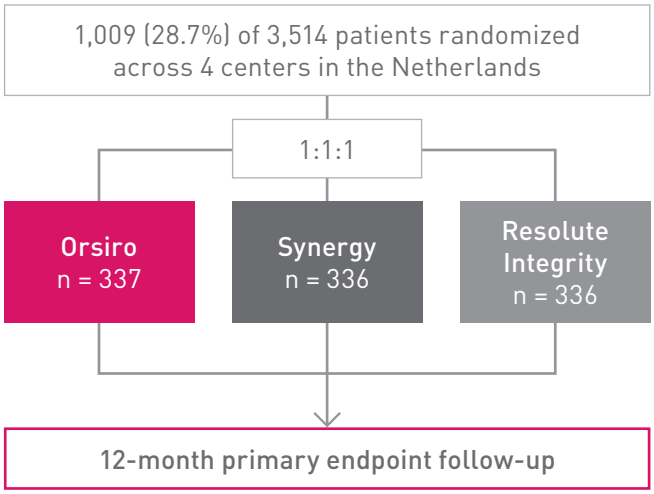
12-month High-Bleeding Risk (HBR) subgroup analysis of the BIO-RESORT trial, RCT Orsiro and Synergy vs. Resolute Integrity

Conclusions

- Almost 29% of the BIO-RESORT all-comers had a High-Bleeding Risk (HBR)
- In this subanalysis (n = 1,009), the Bioabsorbable Polymer DES (BP-DES) arm, including Orsiro®, showed numerically lower event rates of the primary composite endpoint Target Vessel Failure (TVF) compared to Durable Polymer DES (DP-DES)
- On a product level, Orsiro alone demonstrated a numerically lower TVF rate (6.0%) than Synergy* (6.9%), and Resolute Integrity** (7.3%) in HBR patients, respectively. The differences did not reach statistical significance

Study design

HBR patient stratification of an all-comers, multi-center, assessor and patient-blinded, randomized, non-inferiority trial according to defined established HBR criteria



Endpoints

Primary endpoint

- TVF at 12 months defined as the composite of cardiac death, Target Vessel-related Myocardial Infarction (TV-MI), Target Vessel Revascularization (TVR) or Target Lesion Failure (TLF)

Secondary endpoints

- Components of the primary endpoint
- All-cause mortality
- Any MI
- Clinically indicated Target Lesion Revascularization (TLR)
- Stent Thrombosis (ST)

* Synergy is a registered trademark of Boston Scientific
**Resolute and Integrity are registered trademarks of Medtronic Vascular Inc.

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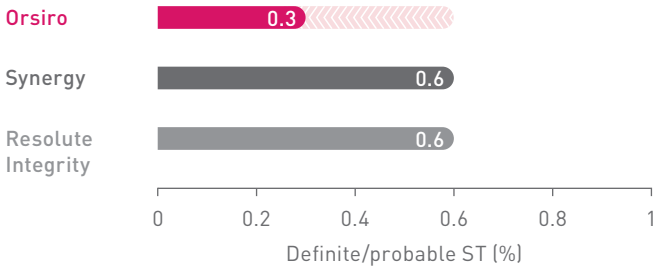
12-month clinical endpoints in HBR patients[1]

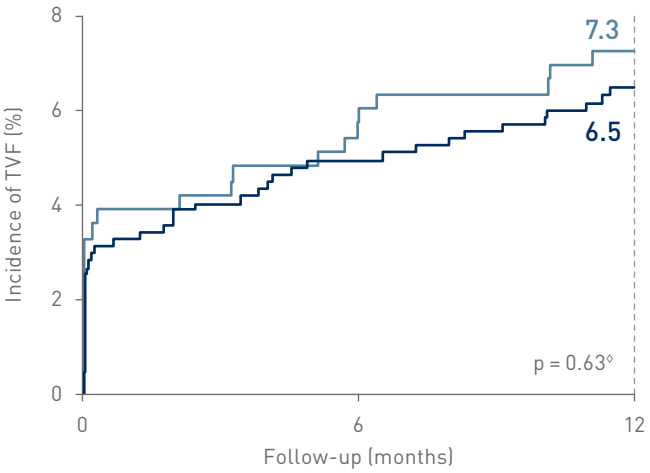
Clinical endpoints	Orsiro n = 337	Synergy n = 336	Resolute Integrity n = 336
TVF¤	6.0%	6.9%	7.3%
Cardiac death	1.5%	2.1%	2.1%
TV-MI	2.4%	3.0%	3.3%
TVR	2.4%	2.2%	3.0%
TLF	5.7%	6.6%	5.7%
Major adverse cardiac events	6.8%	8.4%	8.1%
Patient-oriented composite endpoint[2§]	10.1%	9.3%	10.5%
Definite or probable ST	0.3%	0.6%	0.6%
Major bleeding	3.0%	3.7%	3.1%

No significant difference: p >0.05



BP-DES showed numerically lower event rates in HBR patients

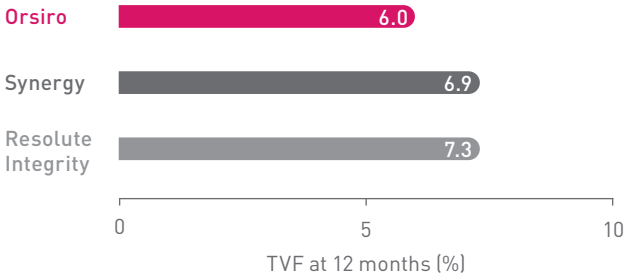
Primary endpoint TVF – at 12 months[1]



— BP-DES (Orsiro & Synergy)
— DP-DES (Resolute Integrity)

Orsiro demonstrated a numerically lower TVF[1]

Product level comparison



Differences did not reach statistical significance (Orsiro vs. Synergy p = 0.60◊, Orsiro vs. Resolute Integrity p = 0.49◊, Synergy vs. Resolute Integrity p = 0.87◊)

¤ Primary endpoint; Myocardial infarction and stent thrombosis classified according to Academic Research Consortium (ARC) criteria; Major bleeding = BARC 3 or 5 bleeding, or TIMI major bleeding. Values are n (%).
§ A composite of any death, any MI, or any revascularization.
◊ Logrank statistical method

Principal investigator

Prof. Clemens von Birgelen, Enschede, the Netherlands

1. von Birgelen C et al. High-Bleeding Risk Analysis of the BIO-RESORT Randomized Trial, Comparing 12-Month Clinical Outcome of All comer Patients Treated With Very Thin-Strut Biodegradable Polymer Versus Thin-strut Durable Polymer Drug-Eluting Stents; Presented at: CRT18; March 03, 2018 Washington DC, USA; ClinicalTrials.gov : NCT01674803;
2. Zocca P, Kok MM, von Birgelen C, et al. High Bleeding Risk Patients Treated with Very Thin-Strut Biodegradable Polymer or Thin-Strut Durable Polymer Drug-Eluting Stents in the BIO-RESORT Trial. Cardiovascular drugs and therapy. 2018 Aug 24:1-0.

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BIO-RESORT

36-month clinical follow-up results of the Small Vessel subgroup

Conclusions

- At 36 months in the small vessel subgroup, Orsiro® shows a trend towards lower rates of Target Lesion Failure (TLF) and Stent Thrombosis (ST) compared to both Resolute Integrity* and Synergy**.
- Orsiro demonstrates significantly lower rates in Target Lesion Revascularization (TLR) compared to Resolute Integrity and numerically lower rates compared to Synergy.
- Orsiro's ultrathin struts may contribute to a lower repeat revascularization risk in patients with small target vessels.

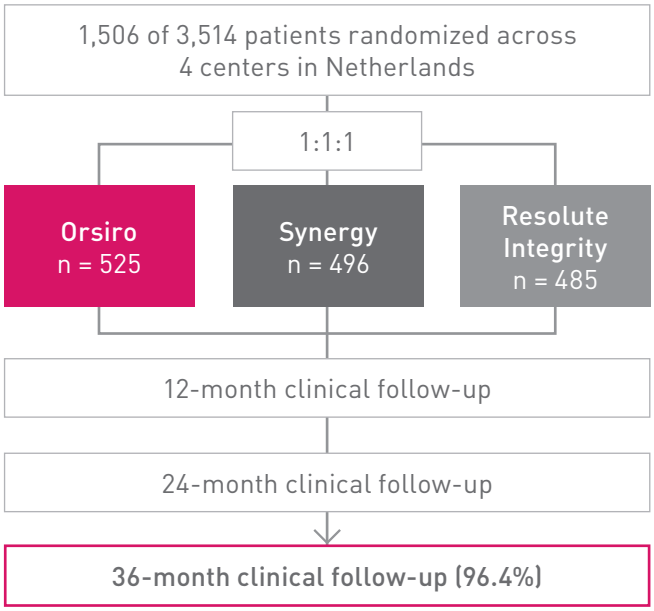
Study design

Small vessel, defined as Reference Vessel Diameter (RVD) <2.5 mm, subgroup analysis of a large-scale, all-comers, multi-center, assessor and patient-blinded, randomized, non-inferiority trial.

Endpoints

Clinical endpoints

- TLF defined as the composite of: Cardiac Death, Target Vessel-related Myocardial Infarction (TV-MI), and TLR
- ST



Patient characteristics[1]	Orsiro n = 525	Synergy n = 496	Resolute Integrity n = 485
Age,yrs‡	64.9 ± 10.2	64.0 ± 10.6	64.0 ± 10.3
Diabetes mellitus	19.2%	21.4%	21.0%
Hypertension	47.6%	46.4%	51.3%
Previous MI	18.1%	17.5%	22.5%
Clinical indication			
STEMI	27.2%	27.2%	23.3%
NSTEMI	22.5%	21.0%	22.9%
Unstable angina	19.4%	17.3%	19.2%
Stable angina	30.9%	34.5%	34.6%
Multivessel treatment	29.3%	28.4%	32.4%

Lesion characteristics[1]	Orsiro n = 636¤	Synergy n = 581¤	Resolute Integrity n = 602¤
B2/C	**71.4%**	**68.7%**	**63.3%**
Bifurcated lesion	34.9%	35.5%	34.1%
Severe calcification	17.8%	19.1%	20.9%
Reference vessel diameter (mm)‡	2.11 ± 0.28	2.12 ± 0.28	2.11 ± 0.28
Acute lumen gain‡	1.04 ± 0.49	1.08 ± 0.48	1.02 ± 0.48
Postdilation	67.3%	**74.5%**	**69.4%**

Small vessel lesions in the Orsiro group were significantly more often complex ($p_{\text{Orsiro vs. Resolute Integrity}} = 0.002$), and stent postdilation was more often performed in lesions treated with Synergy ($p_{\text{Synergy vs. Resolute Integrity}} = 0.05$).

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** Synergy is a registered trademark of Boston Scientific

‡ Data shown as mean ± SD
¤ Number of lesions

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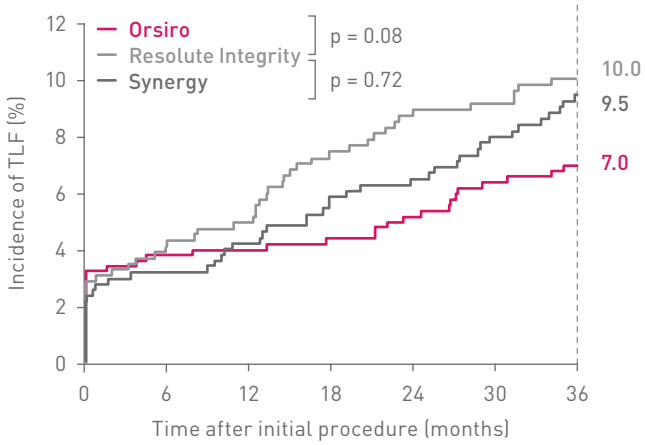
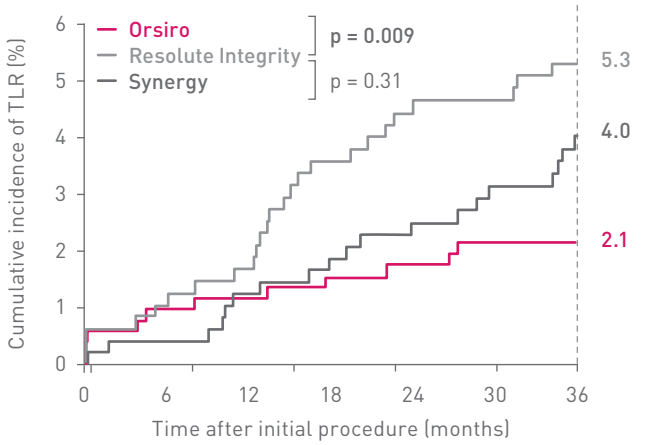
Small vessel subgroup TLF rates at 3 years[1]

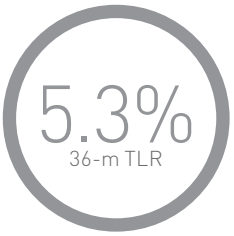


Small vessel subgroup clinical endpoints at 3 years[1]

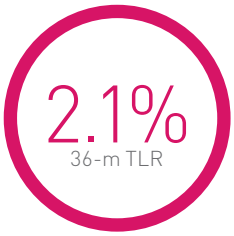
TLF components	Orsiro n = 525	Synergy n = 496	Resolute Integrity n = 485	p-value Orsiro vs. Resolute Integrity
TLF	7.0%	9.5%	10.0%	0.08
TLR	2.1%	4.0%	5.3%	**0.009**
Cardiac Death	2.4%	2.5%	2.5%	0.85
TV-MI	3.3%	3.9%	4.2%	0.46
ST				
Definite ST	0.4%	0.8%	1.1%	0.21
Def./prob. ST	0.6%	1.5%	1.5%	0.16

Small vessel subgroup TLR rates at 3 years[1]



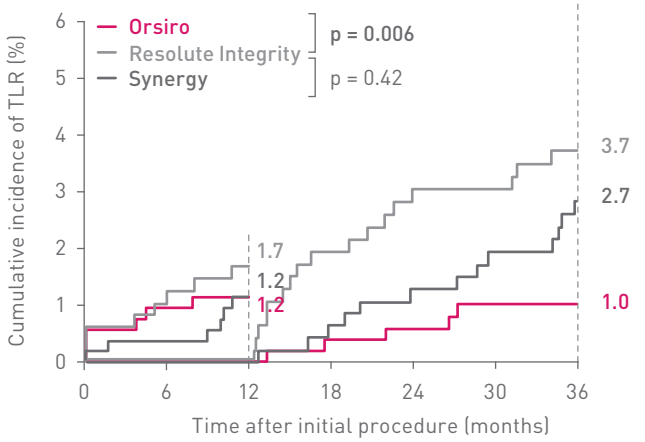


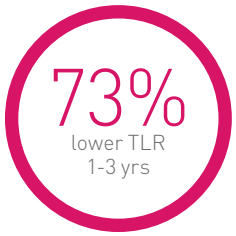
Resolute Integrity



Orsiro

TLR landmark analyses 1 – 3 years[1]





vs. Resolute Integrity

Principal investigator

Prof. Clemens von Birgelen, Enschede, the Netherlands

1. Buiten R et al. Outcomes in patients treated with thin-strut, very thin-strut, or ultrathin-strut drug-eluting stents in small coronary vessels - A prespecified analysis of the randomized BIO-RESORT trial; JAMA Cardiol. Published online May 21, 2019. doi:10.1001/jamacardio.2019.1776; ClinicalTrials.gov: NCT01674803.

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