LEADERS *L*imus *E*luted From *A* *D*urable vs *ER*odable *S*tent Coating

Biolimus-Eluting Stent With Biodegradable Polymer Versus Sirolimus-Eluting Stent With Durable Polymer: A Randomised, Non-Inferiority Trial

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Funded by Biosensors Europe S.A., Switzerland

Biolimus-A9™ Eluting Stent

- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to the abluminal stent surface by a fully automated process.
- Polylactic acid is co-released with biolimus and completely desolves into carbon dioxide and water during a 6-9 months period.
- The stainless steel stent platform has a strut thickness of 112 μm with a quadrature link design.

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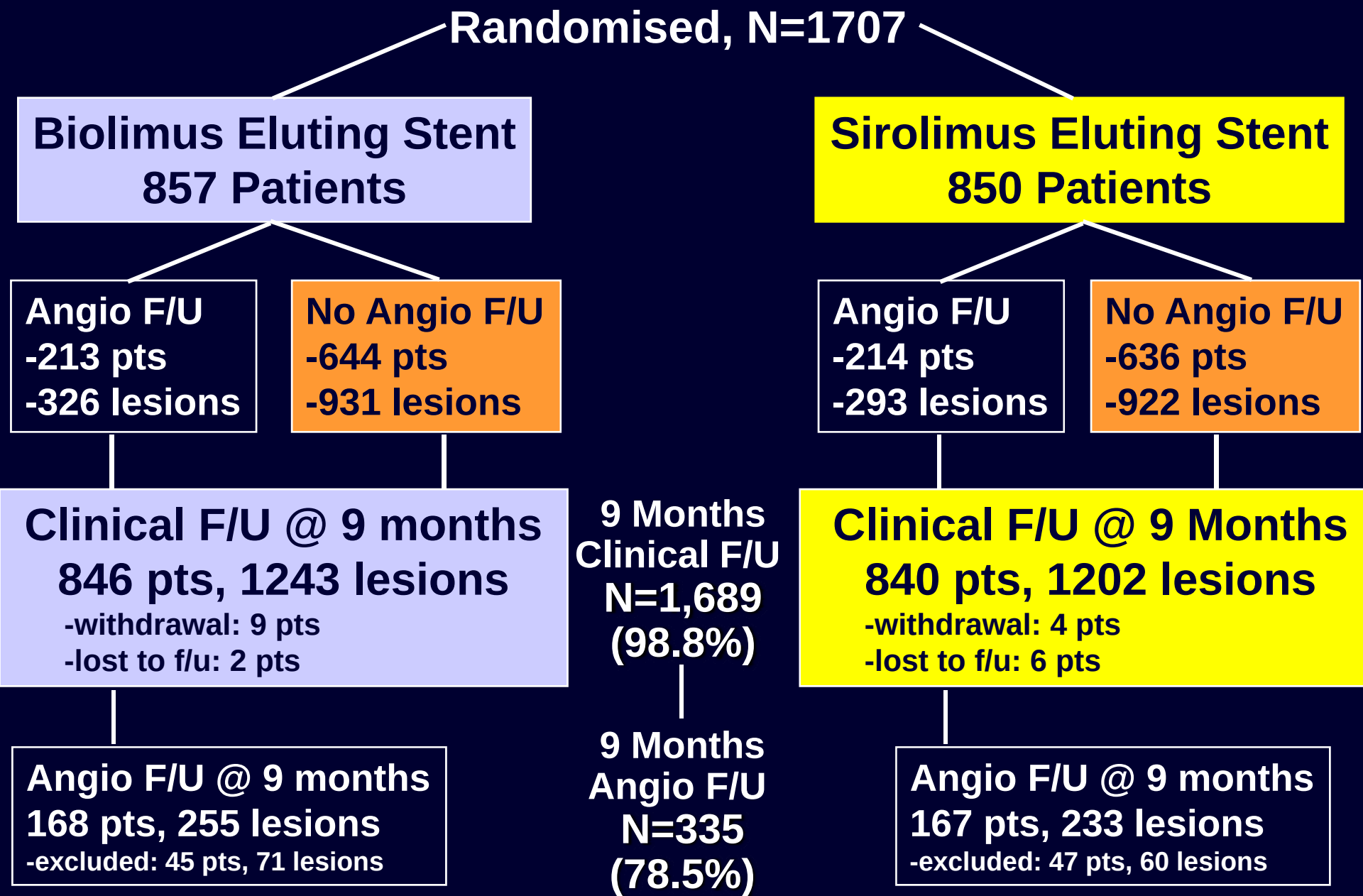
Flow of Patients



Patient Eligibility

Inclusion Criteria

Coronary artery disease

- Stable angina
- Silent ischemia
- Acute coronary syndrome including UA, NSTEMI and STEMI

At least one lesion with

- Diameter stenosis ≥ 50%
- RVD: 2.25-3.5 mm
- Number of lesions: no limitation
- Number of vessels: no limitation
-Vessel length: no limitation

Written informed consent

Exclusion Criteria

Known allergy to

- aspirin, clopidogrel, heparin, stainless steel, sirolimus, biolimus, contrast material

Planned, elective surgery within 6 months of PCI unless

- dual APT could be maintained

Pregnancy

Participation in another trial

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Endpoints

Primary Clinical Endpoint

- Cardiac death, MI, or clinically-indicated TVR @ 9 months
  - Diameter stenosis ≥50% with ischemic signs or symptoms
  - Diameter stenosis ≥70% in the absence of symptoms
- Assumed event rate @ 9 months: 8% in both arms (based on BASKET and SIRTAX)
- Non-inferiority margin = 4%, one sided α = 0.05
- 1700 patients ➡ 90% power

Principal Angiographic Endpoint

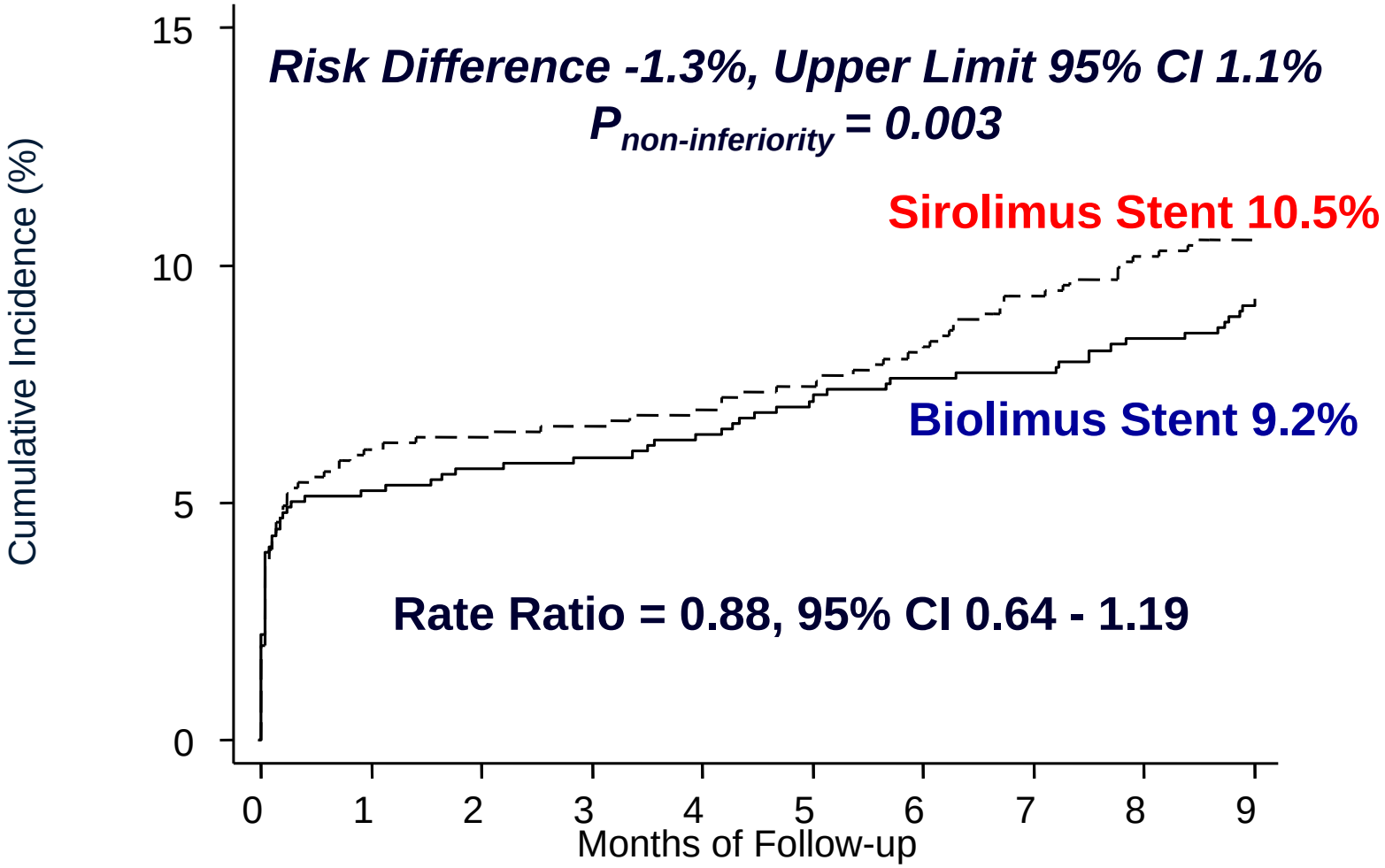
- In-stent percent diameter stenosis @ 9 months
- Assumed % DS = 23 ± 16% in both arms (REALITY trial)
- Non-inferiority margin = 5%, average number of 1.5 lesions, 30% of allocated patients without analysable angiogram, one sided α = 0.05
- 1:3 random sample of 425 patients ➡ 90% power

Patient Characteristics

	Biolimus Stent 857 Patients	Sirolimus Stent 850 Patients
Acute coronary syndrome	55%	56%
- Unstable angina	22%	20%
- Non-ST-elevation MI	18%	19%
- ST-elevation MI	16%	17%
Left ventricular ejection fraction	56 ± 11%	55 ± 12%
Number of lesions per patient	1.5 ± 0.7	1.4 ± 0.7
Lesions per patient		
- 1 lesion	63%	69%
- 2 lesions	29%	22%
- 3 lesions	7%	8%
- > 4 lesions	1%	2%
De novo lesions	92%	91%
Long lesions (>20 mm)	31%	27%
Small vessels (RVD ≤2.75 mm)	68%	69%
Off label use	81%	78%

Primary Endpoint

Cardiac Death, MI, or TVR @ 9 months



No. at risk

BES	857	806	798	796	792	784	779	777	771	761
SES	850	791	786	784	781	777	771	758	751	746

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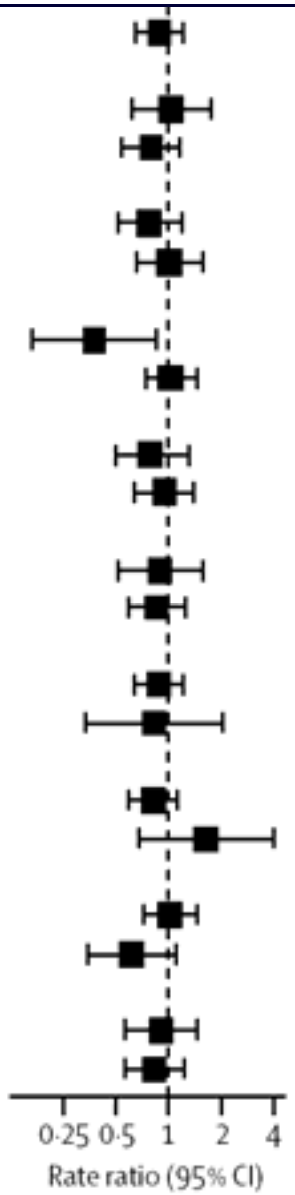
Stratified Analysis of Primary Endpoint

	Biolimus	Sirolimus	Risk Ratio (95% CI)	P Value
Overall	79/857	89/850	0·88 (0·64–1·19)	
Diabetes mellitus				0·40
Yes	31/223	26/191	1·03 (0·61–1·75)	
No	48/634	63/659	0·78 (0·54–1·14)	
Acute coronary syndrome				0·40
Yes	38/470	49/473	0·77(0·50–1·18)	
No	41/387	40/377	1·00 (0·64–1·56)	
ST-elevation MI				0·020
Yes	8/135	21/140	0·37 (0·16–0·84)	
No	71/722	68/710	1·03 (0·74–1·44)	
Left anterior descending				0·52
Yes	34/407	44/417	0·78 (0·50–1·23)	
No	45/449	45/431	0·96 (0·63–1·46)	
Multivessel disease				0·93
Yes	26/209	25/176	0·88 (0·50–1·54)	
No	53/648	64/674	0·85 (0·59–1·23)	
Off-label use				0·91
Yes	71/696	78/665	0·86 (0·62–1·19)	
No	8/160	11/183	0·84 (0·33–2·09)	
De-novo lesions				0·14
Yes	67/788	81/774	0·81 (0·58–1·12)	
No	12/68	8/74	1·64 (0·67–4·01)	
Small-vessel disease				0·15
Yes	61/585	59/568	1·00 (0·70–1·44)	
No	18/271	30/280	0·61 (0·34–1·10)	
Long lesions				0·91
Yes	35/262	34/225	0·89 (0·55–1·44)	
No	44/594	55/623	0·84 (0·56–1·25)	



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Angiographic Follow-up Results

	Biolimus Stent 255 lesions	Sirolimus Stent 233 lesions	P*
MLD			
in-stent (mm)	2.23 ± 0.64	2.11 ± 0.70	0.08
in-segment (mm)	2.01 ± 0.59	1.87 ± 0.64	0.03
Diameter stenosis			
in-stent (%)	20.9 ± 17.5	23.3 ± 19.6	0.26
in-segment (%)	27.1 ± 16.4	29.9 ± 18.5	0.14
Late lumen loss			
in-stent (mm)	0.13 ± 0.46	0.19 ± 0.50	0.34
in-segment (mm)	0.08 ± 0.45	0.15 ± 0.46	0.12
Binary restenosis			
in-stent (%)	5.5	8.7	0.20
in-segment (%)	6.7	10.8	0.15

* P values for superiority

Conclusions

- The biolimus eluting stent with abluminal biodegradable polymer compared against the sirolimus eluting stent with durable polymer resulted in non-inferior safety, efficacy and angiographic outcome at 9 months.
- Since non-inferiority was achieved for the clinical and angiographic outcome measures in a non-restricted patient population with predominant off-label characteristics, the findings of the present study provide a high level of generalisability to routine clinical practice.
- Longer term follow-up will be necessary to determine potential differences in late stent thrombosis related to biodegradable as opposed to durable polymer for drug release.

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