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ANGIOLITE trial two-year follow-up. Non-inferiority randomized clinical trial comparing the efficacy and safety of Angiolite vs Xience

Conflicts of interest

- **Disclosure**
  - Consultant
    - iVascular
    - Abbott
    - Bbraun
    - BMS
    - Boston Scientific
    - Terumo
  - Lecture fees
    - Abbott
    - Boston Scientific
    - Philips – Volcano
  - Research Grants (institutions)
    - iVascular
    - Astra Zeneca
    - Philips – Volcano

Why this study?

- **Angiolite®** (iVascular, Barcelona, *Spain*) is a **new thin-strut cobalt-chromium** sirolimus-eluting stent (SES) with an open-cell design which **has demonstrated in vitro early endothelial cells growth and reduction of smooth muscle cells** proliferation due to the proprietary composition of a biostable fluoro-acrylate polymer.

- Promising preclinical results have shown a **favorable healing process with reduction in injury score** and increase in the percentage of endothelialized surface as compared to EES stent (1).

- These preclinical results were later confirmed in the **Anchor trial** (2) that assessed strut healing after Angiolite® SES implantation. **As early as 3 months after implantation, percentage of strut coverage was 86.3%.**

- For these reasons we considered the **design of a non-inferiority trial** against the DES most often implanted.

(1) Estevez-Loureiro R, Perez de Prado A, Perez-Martinez C, Cuellas-Ramon C, Regueiro-Purrinos M, Gonzalo-Orden JM, Lopez-Benito M, Molina-Crisol M, Duocastella-Codina L, Fernandez-Vazquez F. Safety and efficacy of new sirolimus-eluting stent models in a preclinical study. Rev Esp Cardiol (Engl Ed). 2015;68:1118–1124.

(2) Puri R, Otaegui I, Sabaté M, Serra-Peñaranda A, Puigfel M, Perez de Prado A, Nombela-Franco L, de la Torre Hernandez JM, Ortas Nadal R, Iniguez-Romo A, Jiménez G, Fernandez-Vazquez F, Cuellas-Ramon C, Gonzalo N, Alfonso Jiménez Diaz V, Duocastella L, Molina M, Amoros M, Perez I, Barria Perez A, Pelletier Beaumont E, Nicholls SJ, Garcia Del Blanco B, Rodés-Cabau J. Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite® drug-eluting stent: The ANCHOR study. Catheter Cardiovasc Interv. 2018;91:435-443.

Study design

ANGIOLITE trial is a prospective, randomized, multicenter and controlled trial designed to test the non-inferiority of the Angiolite® SES in comparison with EES in patients with coronary artery disease.

Sample size calculation: Non-inferiority margin LLL 0.2mm, N= 176

Primary endpoints

- **Efficacy**: 6-month intra-stent late lumen loss (QCA analysis, LLL)
- **Safety**: Target Lesion Failure (TLF) at 12 months: cardiac death, target vessel-related MI or clinically-driven TLR

Secondary endpoints

- MACE, a composite of all-cause death, any MI or any revascularization
- Stent thrombosis
- Angiographic results at 6 months: acute gain, in segment LLL, MLD, % diameter stenosis and binary restenosis
- OCT at 6 months: strut level neointimal proliferation, strut coverage measure by % of uncovered stent struts, RUTTS and ISA

Inclusion and exclusion criteria

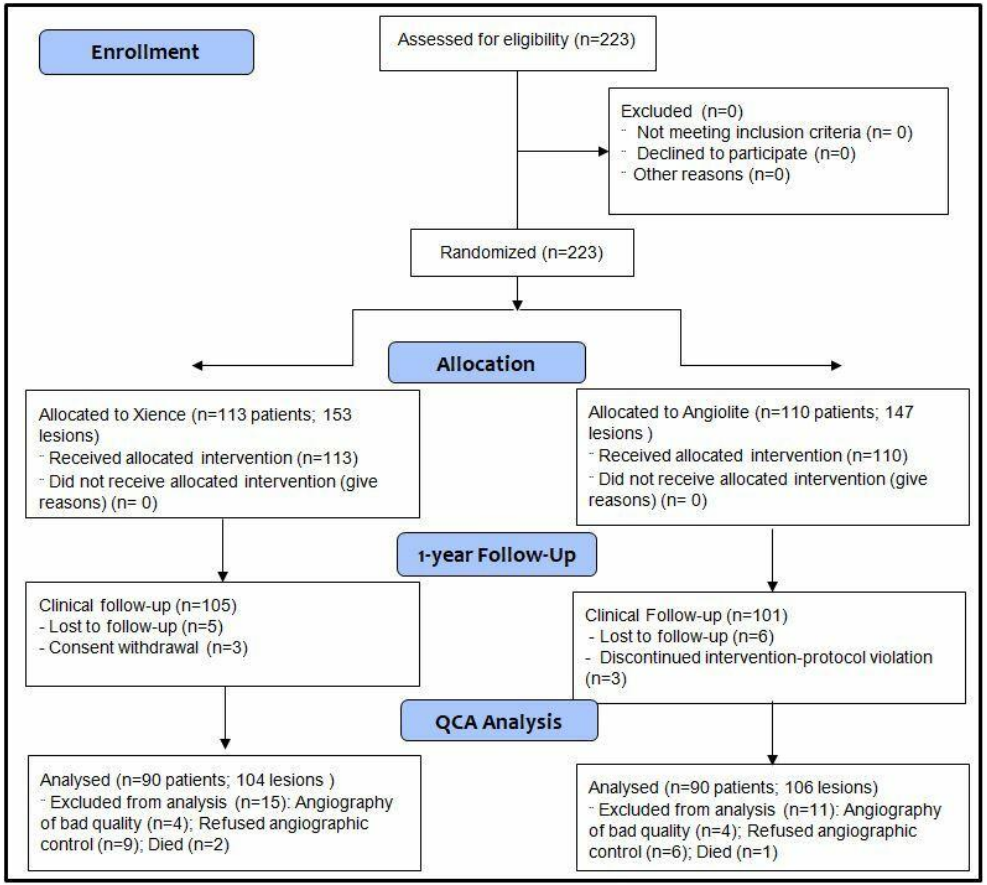
INCLUSION CRITERIA

- Patient age ≥18 years
- Ability to acknowledge verbally the risks, benefits and treatment ramifications in receiving the Angiolite® or Xience Xpedition® stent
- Written informed consent given by legally authorized agent prior to any study-related procedure
- Indication for use of drug-eluting stent based on ACC/AHA/SCAI and ESC/EACTS guidelines and/or clinical judgment of interventional cardiologist
- Target lesion(s) in coronary artery or graft vessel with estimated reference diameter ≥2 mm and ≤4.0 mm
- Target lesion(s) amenable to percutaneous coronary intervention

EXCLUSION CRITERIA

- Known hypersensitivity or contraindication to any of the following agents: heparin, aspirin, clopidogrel, sirolimus, everolimus, cobalt chromium or contrast media
- Inability to tolerate aspirin or clopidogrel for 6-months duration of study
- Females with childbearing potential (unless providing a recent negative pregnancy test) or anticipating pregnancy following study enrollment
- Planned major non-cardiac surgery within designated study period
- Patients with acute myocardial infarction in Killip class III or IV or in cardiogenic shock
- Non-cardiac co-morbid conditions limiting life expectancy (to <1 year) or potentially undermining protocol compliance
- Unwillingness or inability to comply with protocol procedures
- Target lesion located in the Left Main Coronary Artery OR Chronic Total Occlusion as target lesion

Flowchart


Enrollment
Assessed for eligibility (n=223)
Excluded (n=0)
Not meeting inclusion criteria (n= 0)
Declined to participate (n=0)
Other reasons (n=0)
Randomized (n=223)
Allocation
Allocated to Xience (n=113 patients; 153 lesions)
Received allocated intervention (n=113)
Did not receive allocated intervention (give reasons) (n= 0)
Allocated to Angiolite (n=110 patients; 147 lesions)
Received allocated intervention (n=110)
Did not receive allocated intervention (give reasons) (n= 0)
1-year Follow-Up
Clinical follow-up (n=105)
- Lost to follow-up (n=5)
- Consent withdrawal (n=3)
Clinical Follow-up (n=101)
- Lost to follow-up (n=6)
- Discontinued intervention-protocol violation (n=3)
QCA Analysis
Analysed (n=90 patients; 104 lesions)
Excluded from analysis (n=15): Angiography of bad quality (n=4); Refused angiographic control (n=9); Died (n=2)
Analysed (n=90 patients; 106 lesions)
Excluded from analysis (n=11): Angiography of bad quality (n=4); Refused angiographic control (n=6); Died (n=1)

Baseline characteristics

	EES N=113	angiolite N=110	P value
Age, years: mean ± SD	63.6 ± 9.5	62.4 ± 10.5	0.38
Male, n (%)	88 (77.9)	87 (79.1)	0.83
Coronary risk factor			
Diabetes, n (%)	34 (30.4)	28 (25.5)	0.42
Hypertension, n (%)	74 (66.1)	64 (58.2)	0.23
Dyslipidemia, n (%)	57 (50.9)	62 (56.4)	0.41
Never smoker, n (%)	46 (41.1)	40 (36.4)	0.74
Familiar CVD, n (%)	15 (13.4)	16 (14.5)	0.80
CVD history	34 (30.4)	24 (21.8)	0.15
Prior MI, n (%)	18 (16.1)	8 (7.3)	0.04
Prior CABG-PCI, n (%)	21 (18.8)	10 (9.1)	0.04
Prior TIA, n (%)	2 (1.8)	1 (0.9)	1.00
PVD, n (%)	4 (3.6)	5 (4.5)	0.71
AF, n (%)	3 (2.7)	2 (1.8)	1.00
PCI indication			0.25
Silent ischemia, n (%)	9 (8.0)	4 (3.6)	
Stable angina, n (%)	32 (28.3)	29 (26.4)	
Unstable angina, n (%)	29 (25.7)	21 (19.1)	
Non-ST ACS, n (%)	33 (29.2)	44 (40.0)	
ST ACS, n (%)	10 (8.8)	12 (10.9)	

Baseline characteristics

Baseline characteristics	EES (N=113; L=153)	angiolite (N=110; L=147)	P value
Numbers of lesions per patient	1.4±0.6	1.3±0.6	0.46
Number of stents per lesion	1.1±0.3	1.1±0.3	1.00
Culprit artery			0.87
LAD	62(40.5)	67(45.6)	
LCX	40(26.1)	37(25.2)	
RCA	51(33.3)	43(29.3)	
ACC/AHA Classification			0.02
A	33(21.6)	22(15.0)	0.14
B1	68(44.4)	79(53.7)	0.10
B2	47(30.7)	32(21.8)	0.08
C	5(3.3)	14(9.5)	0.03
Pre-PCI TIMI flow grade			0.11
0	6(3.9)	6(4.1)	
1	6(3.9)	0(0.0)	
2	6(3.9)	5(3.4)	
3	135(88.2)	136(92.5)	
Intracoronary thrombus	9(5.9)	15(10.2)	0.17
Severe calcification	17(11.1)	20(13.6)	0.50
Ulcerated lesión	10(6.5)	10(6.8)	0.91
Bifurcation with side branch >2 mm	11(7.2)	15(10.2)	0.35
Lesion length, mm	17.7± 8.1	17.5± 6.7	0.81

Coronary stenting procedure

Coronary stenting procedure	EES (N=113; L=153)	angiolite (N=110; L=147)	P value
Direct stenting	57(37.2)	55(37.4)	0.19
Thrombus aspiration	1(0.7)	2(1.4)	0.62
Lesion debulking	5(3.3)	2(1.4)	0.28
Pre-dilatation	90(58.8)	89(60.5)	0.62
Stent diameter,mm	3.1 ± 0.4	3.0 ± 0.5	0.52
Stent length,mm	20.2 ± 7.0	20.6 ± 5.6	0.57
Post-dilatation	28 18.3)	38(25.9)	0.15
Need for a second stent	14(9.2)	15(10.2)	0.74
Device success	153(100.0)	146(99.3)	0.98
Procedural success	152(99.3)	146(99.3)	0.99

Coronary stenting procedure

	EES (N=90; L=104)	angiolite (N=90; L=106)	P
Baseline			
• MLD,mm	0.98±0.41	0.88±0.38	0.06
• RVD,mm	2.76±0.59	2.81±0.57	0.57
• %DS	64.8±12.8	68.7±11.7	0.02
Post-PCI			
In-stent			
• MLD,mm	2.62±0.45	2.53±0.46	0.16
• RVD,mm	2.93±0.45	2.91±0.48	0.67
• %DS	10.6±6.3	12.9±6.4	0.01
In-segment			
• MLD,mm	2.38±0.46	2.30±0.43	0.17
• RVD,mm	2.93±0.50	2.87±0.51	0.39
• %DS	18.8±6.8	19.9±6.8	0.24
In-stent acute gain, mm	**1.64±0.50**	**1.65±0.48**	**0.84**

QCA at 6 months

	EES (N=90; L=104)	angiolite (N=90; L=106)	P
Follow-up			
In-stent			
• MLD,mm	2.54±0.53	2.49±0.47	0.48
• RVD,mm	2.87±0.46	2.85±0.47	0.72
• %DS	11.8±8.7	12.3±8.6	0.68
In-segment			
• MLD,mm	2.32±0.53	2.29±0.50	0.71
• RVD,mm	2.87±0.52	2.84±0.51	0.73
• %DS	19.3± 10.2	19.3±9.6	0.99
Late Lumen Loss			
• **In-stent LLL,mm**	**0.08±0.38**	**0.04±0.39**	**0.45***
• **In-segment LLL,mm**	**0.06±0.38**	**0.00±0.44**	**0.30***
In-stent binary restenosis	2 (1.9%)	1 (1.0%)	0.58
In-segment binary restenosis	4 (4.4%)	3 (3.3%)	0.70

*P value for non-inferiority: In-stent LLL: 0.002; In-segment LLL: 0.007

OCT at 6 months

OCT outcomes	EES	angiolite	P
Patients analyzed	41(46.6)	47(53.4)	
Stents analyzed	44(45.8)	52(54.2)	
Cross sections analyzed	1411(42.6)	1898(57.4)	
Strut analysis			
Analyzable struts	11660	17348	
Covered struts	10597(90.9)	15547(89.6)	<0.01
Uncovered struts	877(7.5)	1389(8.0)	0.13
Incomplete strut apposition	186(1.6)	412(2.4)	<0.01
Cross section with RUTTS>30%	127(9.0)	187(9.9)	0.41
Stent analisis			
Neo-intimal thickness, µm	86.4±91	72.1±86	<0.01
Luminal area,mm^2	6.6±2.6	6.5±2.5	0.23
Stent area, mm^2	7.3±2.4	6.9±2.3	<0.01
Neo-intimal area obstruction, mm^2	0.7±0.9	0.4±1.0	<0.01

Clinical results at 12 and 24 months

Clinical outcomes	EES (N=105)	angiolite (N=99)	P value	EES (N=105)	angiolite (N=99)	P value
	12 months			24 months		
Target lesion failure	7 (6.7)	4 (4.0)	0.387	8 (7.6)	7 (7.1)	0.881
Cardiac Death	1 (1.0)	0 (0.0)	0.978	1 (1.0)	0 (0.0)	1.000
Myocardial infarction	2 (1.9)	1 (1.0)	0.584	2 (1.9)	2 (2.0)	0.953
Target lesion revascularization	4 (3.8)	3 (3.0)	0.739	5 (4.8)	5 (5.1)	0.924
Major adverse cardiac events	11 (10.5)	11 (10.5)	0.967	12 (11.4)	14 (14.1)	0.561
All-cause death	2(1.9)	1 (1)	0.584	2 (1.9)	1 (1.0)	0.596
Any myocardial infarction	2 (1.9)	1 (1.0)	0.584	2 (1.9)	2 (2.0)	0.953
Any revascularization	7 (6.7)	9 (9.0)	0.958	8 (7.6)	11 (11.1)	0.391
Definite or probable stent thrombosis*	2 (1.9)	1 (1.0)	0.584	2 (1.9)	1 (1.0)	0.596

*ARC definition

Conclusions

- ✓ **Angiographic results demonstrate non inferiority in late lumen loss of Angiolite®** vs the gold standard EES in a broad spectrum of coronary artery disease patients.

- ✓ **The OCT outcomes demonstrate Angiolite® to be comparable with EES** regarding the uncovered struts and the cross section with RUTTS>30% confirming the equivalence in efficacy.

- ✓ From the clinical point of view, the **number of events at 2 years was very low in both groups**, reflecting good clinical performance without the occurrence of late catch-up events after discontinuation of DAPT.

- ✓ The **Angiolite® can be incorporated as a good option** in the armamentarium of the interventional cardiologist.

- ✓ In conclusion, this **first randomized trial** with a novel thin-strut, cobalt-chromium SES with a durable fluoro-acrylate-based biostable polymer **found it to be non-inferior to the gold standard second generation EES** in terms of angiographic parameters of restenosis.