Scuola di Specializzazione in Malattie dell'Apparato Cardiovascolare
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Progetto Formazione Avanzata in Cardiologia nel Web 2014
Scuola di Specializzazione in Malattie dell'Apparato Cardiovascolare

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Is There A LIfe for DES after discontinuation of Clopidogrel (ITALIC) trial

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Background

- I generation DES **VS** BMS
  - ↓ angiographic restenosis and emergency target vessel revascularizaion
  - ↑propensity for late and very late stent thrombosis

- New generation DES **VS** I generation DES or BMS
  - ↑ efficacy and safety
  - ↓ risk of definite or probable stent thrombosis: 50% lower

- Shorter duration of dual antiplatelet therapy (DAPT)?

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Study Design

- Randomized multicenter trial conducted to assess the effect of 6 VS 24 months DAPT on medium-term clinical outcome after coronary intervenction in a real world clinical population receiving new-generation DES.

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Methods: Inclusion Criteria

- ≥ 18 years
- Elegible for PCI
- ≥ 1 Xience V DES (excluded primary PCI for IMA and treatment of the left main artery)
- Pz pre-treated with ASA and Clopidogrel (Prasugrel or Ticagrelor) before PCI

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Methods: Exclusion Criteria

- Prior DES implantation within 1 year
- Platelet level ≤ 100.000 or hemorrhagic diathesis
- TAO or abciximab treatment during hospital stay
- Controindications to ASA or Clopidogrel (Prasugrel or Ticagrelor)
- Major surgery within the preceding 6 weeks
- Evidence of active GI or urogenital bleeding
- Liver failure
- Surgery during the year after enrolment

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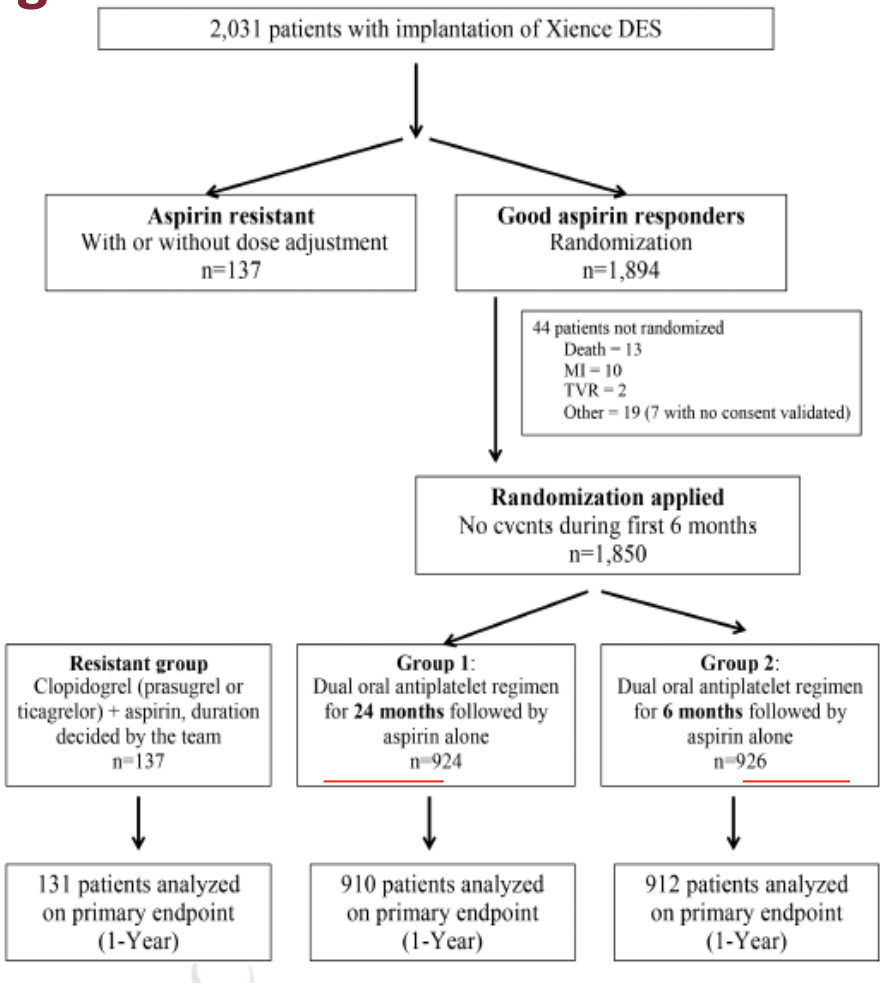
Study Design



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Endpoints

Primary Endpoint

- Composite criterion comprising death, myocardial infarction (MI), repeat emergency target vessel revascularization, stroke or major bleeding → 12 months of stenting

Secondary Endpoints

- Incidence of the same composite endpoint at 24 and 36 months as well as all individual endpoints used in the composite major adverse coronary event score
- Incidence of minor and minimal bleeding complication at 12, 24 and 36 months

SCORE: morte, infarto o ripetizione in emergenza di rivascolarizzazione su vaso bersaglio, o stroke

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Results: Baseline Clinical Characteristics

	Resistant Group n=131	24-month DAPT n=910	6-Month DAPT n=912	P
Age, yrs	62.6 (10.8)	61.5 (11.1)	61.7 (10.9)	0.792
Male gender, n (%)	106 (80.9%)	721 (79.2%)	737 (80.8%)	0.399
Body Mass Index (kg/m^2)	27.5 (4.2)	27.1 (4.7)	27.0 (4.6)	0.549
Type-2 diabetes, n (%)	42 (32.1%)	344 (37.8%)	331 (36.3%)	0.505
Hypertension, n (%)	76 (58.0%)	589 (64.7%)	595 (65.2%)	0.817
Hyperlipidemia, n (%)	84 (64.1%)	611 (67.1%)	612 (67.1%)	0.986
Smoker, n (%)	69 (52.7%)	480 (52.7%)	464 (50.9%)	0.424
Family history, n (%)	50 (38.2%)	325 (35.7%)	322 (35.3%)	0.856
Previous MI, n (%)	36 (27.5%)	134 (14.7%)	142 (15.6%)	0.615
Previous PCI, n (%)	39 (29.8%)	205 (22.5%)	220 (24.1%)	0.421
Previous CABG, n (%)	6 (4.6%)	45 (4.9%)	61 (6.7%)	0.111
Previous stroke, n (%)	6 (4.6%)	26 (2.9%)	25 (2.7%)	0.881
Renal insufficiency	4 (3.1%)	25 (2.7%)	28 (3.1%)	0.682
Ejection fraction				0.321
< 31%	1 (0.8%)	20 (2.2%)	29 (3.2%)	
31 to 50%	21 (16.0%)	151 (16.6%)	162 (17.8%)	
> 50%	65 (49.6%)	514 (56.5%)	482 (52.9%)	
Unknown	44 (33.6%)	225 (24.7%)	239 (26.2%)	
Clinical presentation, n (%)				0.911
Stable angina	53 (40.5%)	378 (41.5%)	375 (41.1%)	
Silent ischemia	18 (13.7%)	183 (20.1%)	185 (20.3%)	
Unstable angina	23 (17.6%)	149 (16.4%)	143 (15.7%)	
NSTEMI	9 (6.9%)	65 (7.1%)	67 (7.3%)	
STEMI	0	3 (0.3%)	1 (0.1%)	
Antiplatelet therapy associated				
Clopidogrel	129 (98.5%)	895 (98.4%)	902 (98.9%)	
Prasugrel	2 (1.5%)	16 (1.8%)	15 (1.6%)	
Ticagrelor	0	0	1 (0.1%)	

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Results: Baseline Procedural Characteristics

Characteristic	Resistant Group n=131	24-Month DAPT n=910	6-Month DAPT n=912	p
Procedural success, n (%)	130 (99.2%)	901 (99.0%)	895 (98.1%)	0.112
Target lesion coronary artery, n (%)				
Left main	4 (3.1%)	8 (0.9%)	14 (1.5%)	0.197
Left anterior descending	96 (73.3%)	658 (72.3%)	669 (73.4%)	0.615
Left circumflex	59 (45.0%)	436 (47.9%)	456 (50.0%)	0.373
Right coronary artery	62 (47.3%)	474 (52.1%)	489 (53.6%)	0.513
Bypass graft	5 (3.8%)	39 (4.3%)	59 (6.5%)	0.038
Total no. of lesion treated/patient, n (%)				0.239
1 lesion treated	77 (58.8%)	494 (54.3%)	459 (50.3%)	
2 lesions treated	38 (29.0%)	252 (27.7%)	275 (30.2%)	
3 of more lesions treated	16 (12.2%)	164 (18.0%)	178 (19.5%)	
Number of XienceV stent per patient,n(%)	1.6 (0.8)	1.7 (1.0)	1.7 (1.0)	0.497
Total stent length, mean ± SD	33.2 (22.7)	37.8 (26.1)	38.6 (25.6)	0.533
Stent diameter, mean ± SD	3.0 (0.2)	3.1 (0.3)	3.1 (0.3)	0.113
Rotablator, n (%)	4 (2.9%)	12 (1.3%)	15 (1.6%)	0.553
At least 1 restenotic lesion, n (%)	5 (3.8%)	51 (5.6%)	54 (5.9%)	0.772

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Results: Incidence of the Endpoints in the Overall Population

	Resistant Group n=131	24-month DAPT n=910	6-Month DAPT n=912	Hazard Ratio [95% CI]	p
Primary end point, n (%)					
Death from any cause, MI*, stroke, TVR†, major bleeding	2 (1.5%)	14 (1.5%)	15 (1.6%)	1.072 [0.517 ; 2.221]	0.85
Secondary end point, n (%)					
Minor bleeding	0	4 (0.4%)	5 (0.5%)	1.247 [0.335 ; 4.643]	0.74
Minimal bleeding	1 (0.8%)	6 (0.7%)	6 (0.7%)	0.997 [0.321 ; 3.090]	0.99
Death, n (%)					
All deaths	1 (0.8%)	7 (0.8%)	8 (0.9%)	1.143 [0.414 ; 3.152]	0.80
Cardiac death	0	3 (0.3%)	5 (0.5%)	1.667 [0.398 ; 6.974]	0.48
Myocardial infarction, n (%)	0	4 (0.4%)	6 (0.7%)	1.500 [0.423 ; 5.317)	0.53
Stroke, n (%)	0	4 (0.4%)	0	N/A	
TVR, n (%)	1 (0.8%)	2 (0.2%)	5 (0.5%)	2.499 [0.485 ; 12.882]	0.27
Stent thrombosis	0	0	3 (0.3%)	N/A	
Major bleeding, n (%)	0	3 (0.3%)	0	N/A	

*MI: myocardial infarction; †TVR: urgent target vessel revascularization

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Results: Incidence of the Endpoints in High Risk Patient: ACS 44% (792 pz)

	Resistant Group n=50	24-month DAPT n=397	6-Month DAPT n=395	Hazard Ratio [95% CI]	p
Primary end point, n (%)					
Death from any cause, MI*, stroke, TVR†, major bleeding	0	4 (1.0%)	7 (1.8%)	1.773 [0.519 ; 6.057]	0.361
Secondary end point, n (%)					
Minor bleeding	0	3 (0.8%)	1 (0.3%)	0.334 [0.035 ; 3.211]	0.34
Minimal bleeding	0	3 (0.8%)	2 (0.5%)	0.669 [0.112 ; 4.002]	0.66
Death, n (%)					
All deaths	0	1 (0.3%)	4 (1.0%)	4.041 [0.452 ; 36.151]	0.21
Cardiac death	0	0	3 (0.8%)	N/A	
Myocardial infarction, n (%)	0	2 (0.5%)	2 (0.5%)	1.006 [0.142 ; 7.144]	0.99
Stroke, n (%)	0	1 (0.3%)	0	N/A	
TVR, n (%)	0	0	3 (0.8%)	N/A	0
Stent thrombosis	0	0	2 (0.5%)	N/A	
Major bleeding, n (%)	0	1 (0.3%)	0	N/A	

*MI: myocardial infarction; †TVR: urgent target vessel revascularization

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Conclusions

- **Non-inferiority** was established for 6-month VS 24-month DAPT eith an absolute risk difference of 0.11% (95% CI: -1.04 to 1.26; **p** for non-inferiority = 0,0002)

- The significance of the test was confirmed by the lower limit of the 1-tailed 97.5% CI (-1.04%) being grater than the non-inferiority margin (-2%)

- Modifications in current guidelines:
  - DAPT for **6** month after new-generation DES in stable angina
  - DAPT for **12** month after new-generation DES in ACS

- **Non increase** in bleeding in the long DAPT arm

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Grazie per la Vostra Attenzione!

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