ARCTIC-INTERRUPTION

2-year- Versus 1year Duration of Dual-Antiplatelet Therapy After DES implantation
The randomized ARCTIC-Interruption Study

JP Collet and G Montalescot
for the ARCTIC
investigators

www.action-coeur.org

ARCTIC: **A**ssessment by a double **R**andomization of a **C**onventional antiplatelet strategy versus a monitoring-guided strategy for drug-eluting stent implantation and,of **T**reatment **I**nterruption versus **C**ontinuation one year after stenting – ARCTIC-INTERRUPTION (NCT 00827411)

Affiliation/Financial Relationship:

Pr Montalescot reports: research grants to the institution or consulting/lecture fees from Bayer, BMS, Boehringer-Ingelheim, Duke Institute, Europa, GSK, Iroko, Lead-Up, Novartis, Springer, TIMI group, WebMD, Wolters, AstraZeneca, Biotronik, Eli Lilly, The Medicines Company, Medtronic, Menarini, Roche, Sanofi-Aventis, Pfizer, Accumetrics, Abbott Vascular, Daiichi-Sankyo, Eli Lilly, Fédération Française de Cardiologie, Fondation de France, INSERM, Institut de France, Nanosphere, ReCor Medical, Stentys, Société Française de Cardiologie.

Background and Design

Trial conduct

ACTION Study Group (Academic Research Organization, Paris):

- Academic Coordinating Center: ACTION - Institute of Cardiology - Pitié-Salpêtrière Hospital, Paris
- Academic Sponsor: ACTION -APHP- DRC - St-Louis Hospital - Paris
- Academic Global Trial Operations: ACTION - URC – Lariboisière Hospital, Paris

- Funding: ACTION, Fondation de France, Fondation SGAM, Sanofi-Aventis Group, Cordis, Boston-Scientific, Medtronic
- Steering Committee: G. Montalescot, JP Collet, G. Cayla, T. Cuisset, S. Elhadad, G. Rangé, E. Vicaut
- Investigation sites : 38 French Intervention Centers

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Hôpital Pontchaillou, Rennes, **Dr Le Breton**

CH Dijon, **Dr Cottin**

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

BMS in stable patients — **1 month**

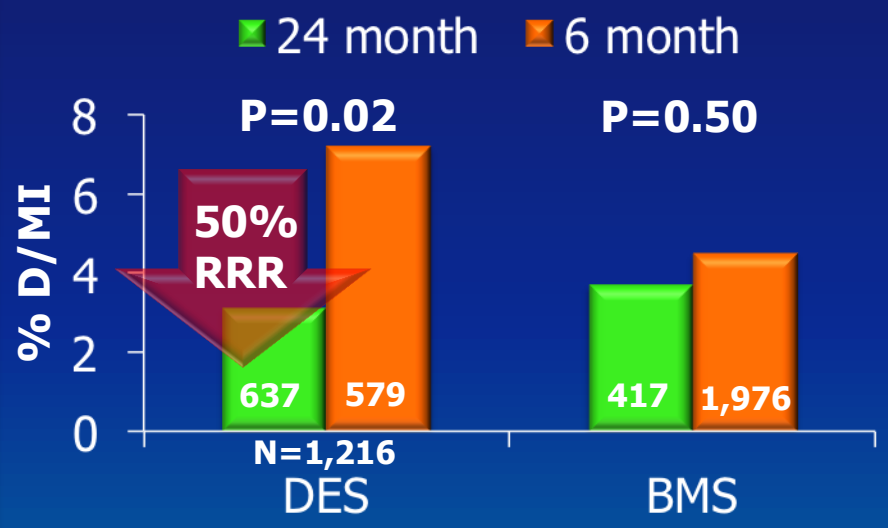
DES in all patients — **6-12 months**

ACS patients — **1 year**

Data suggest that certain patient populations (e.g. high risk for thromboembolic events, patients after SES or PES implantation), may benefit from prolonged DAPT beyond 1 year. The downside of this strategy is the increased rate of severe bleeding complications over time. Recent data suggest that DAPT for 6 months might be sufficient because late and very late stent thrombosis correlate poorly with discontinuation of DAPT.

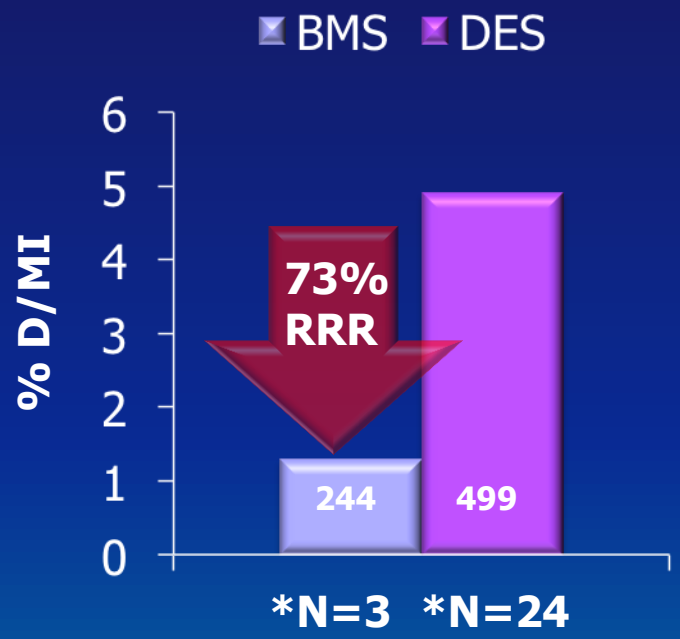
Registries quoted by guidelines
In favor of prolonged DAPT after DES

24 Month Events in Patients who Discontinued or did not Discontinue Clopidogrel at 6 Months Stratified by Stent



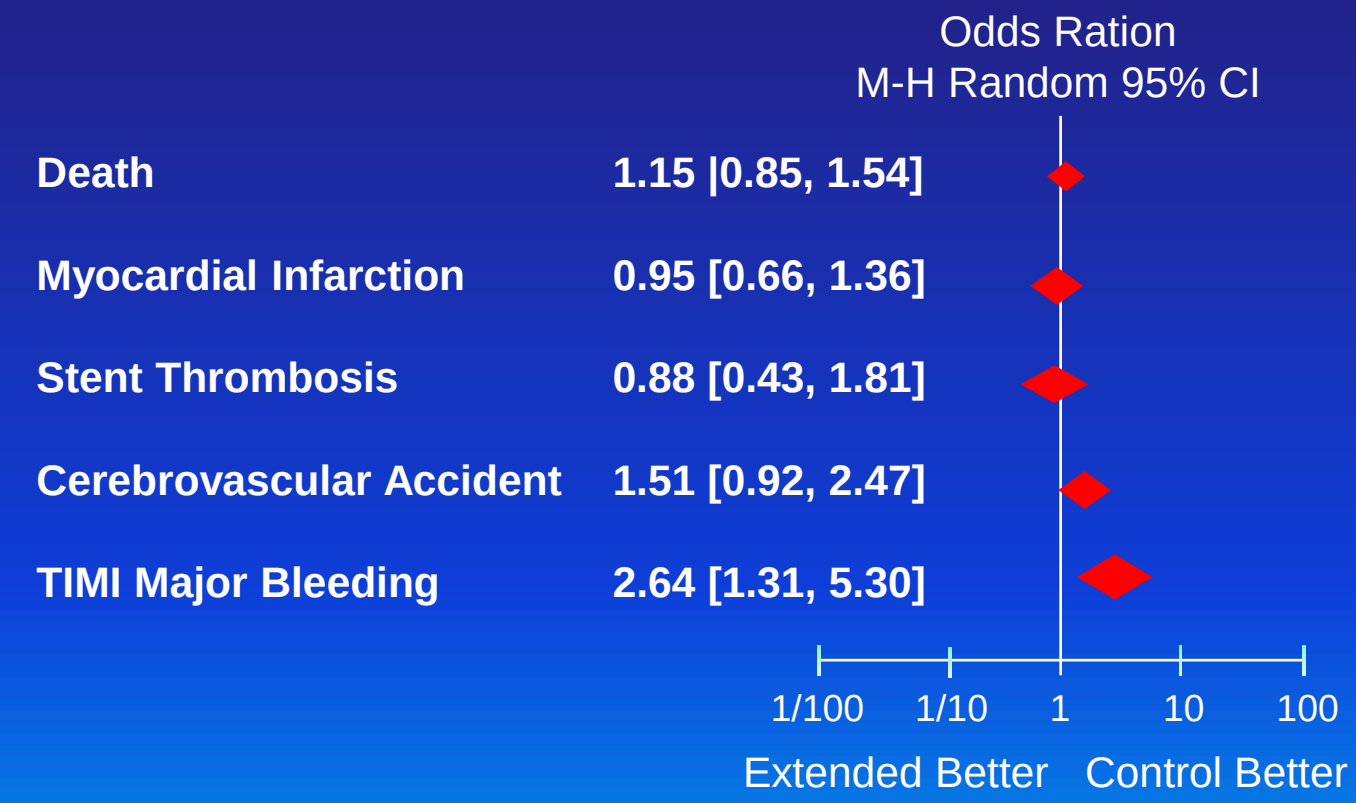
Eisenstein EL et al, JAMA 2007

18 Month Events After Clopidogrel Discontinuation at 6 Months Stratified by Stent Type*



Pfisterer M et al, J Am Coll Cardiol 2006

Clinical Impact of Extended DAPT after PCI
A metanalysis of Randomized trials (n=8231)

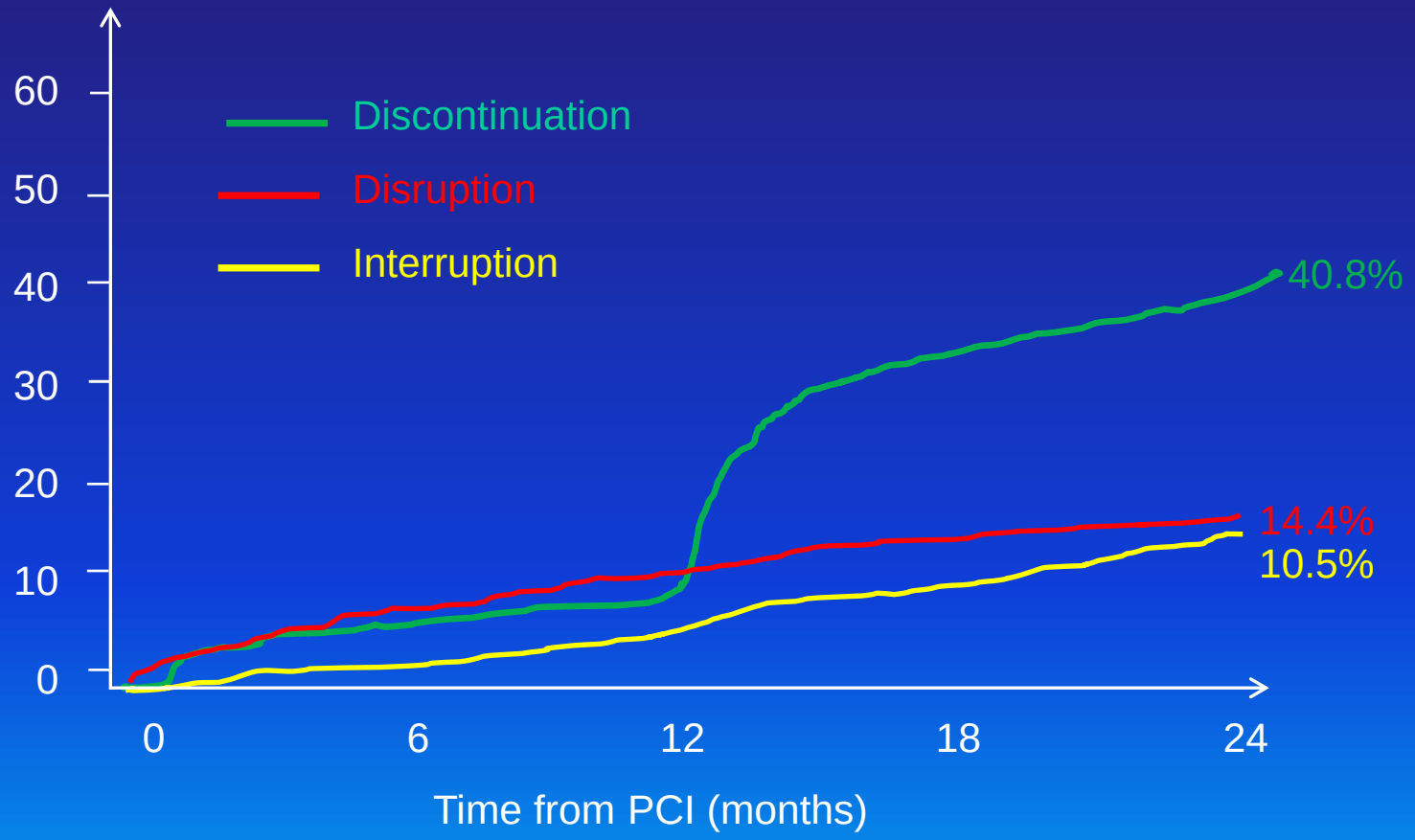


N Engl J Med 2010;362:1374–1382
Circulation 2012;125:2015–2026
Circulation 2012;125:505–513.
J Am Coll Cardiol. 2012 Oct 9;60(15):1340-8.

European Heart Journal 2012; 33: 3078-3087

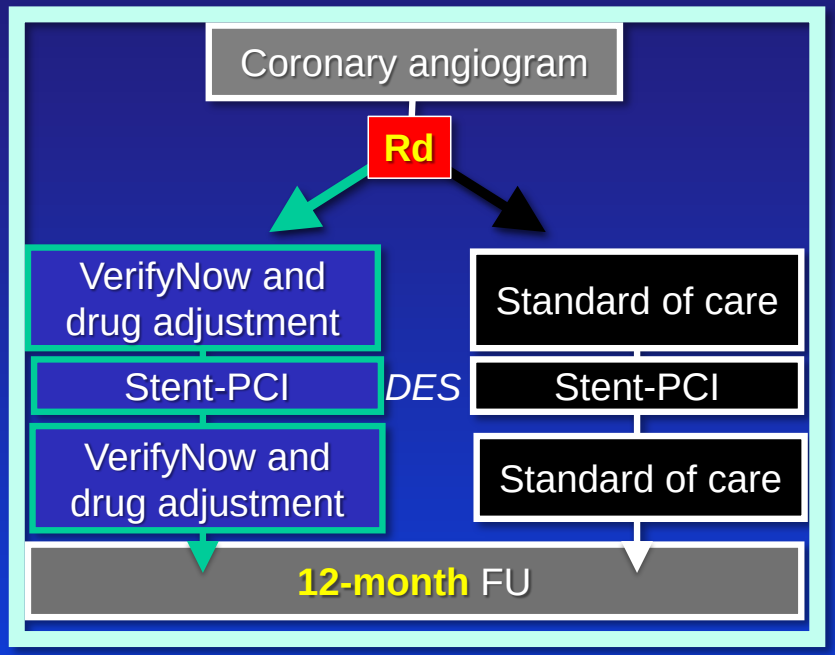
2-year KM Plots of Any Discontinuation, Interruption and Disruption

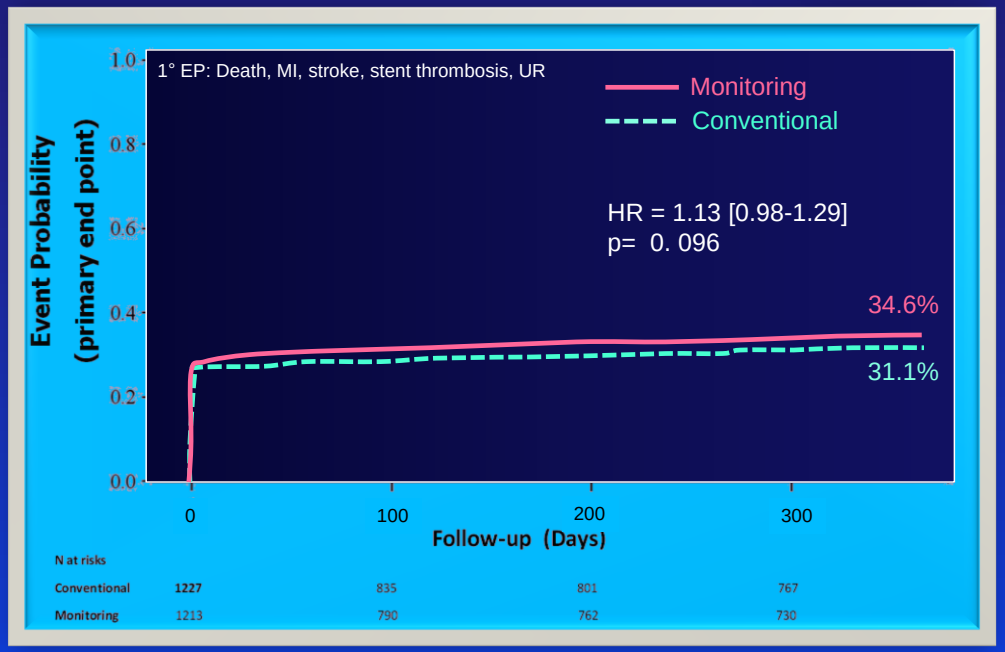
(From the Paris-Registry)

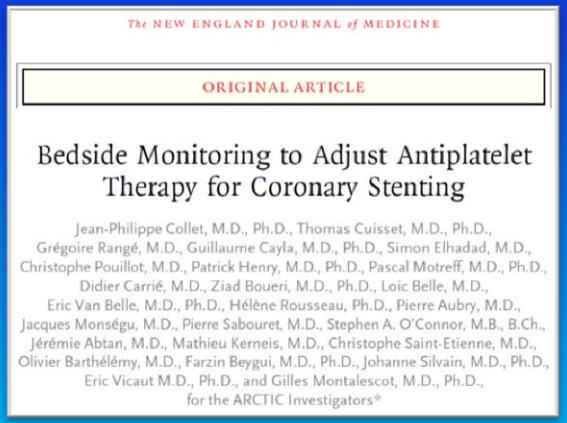


Mehran R. et al Lancet 2013

ARCTIC trial design






The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting

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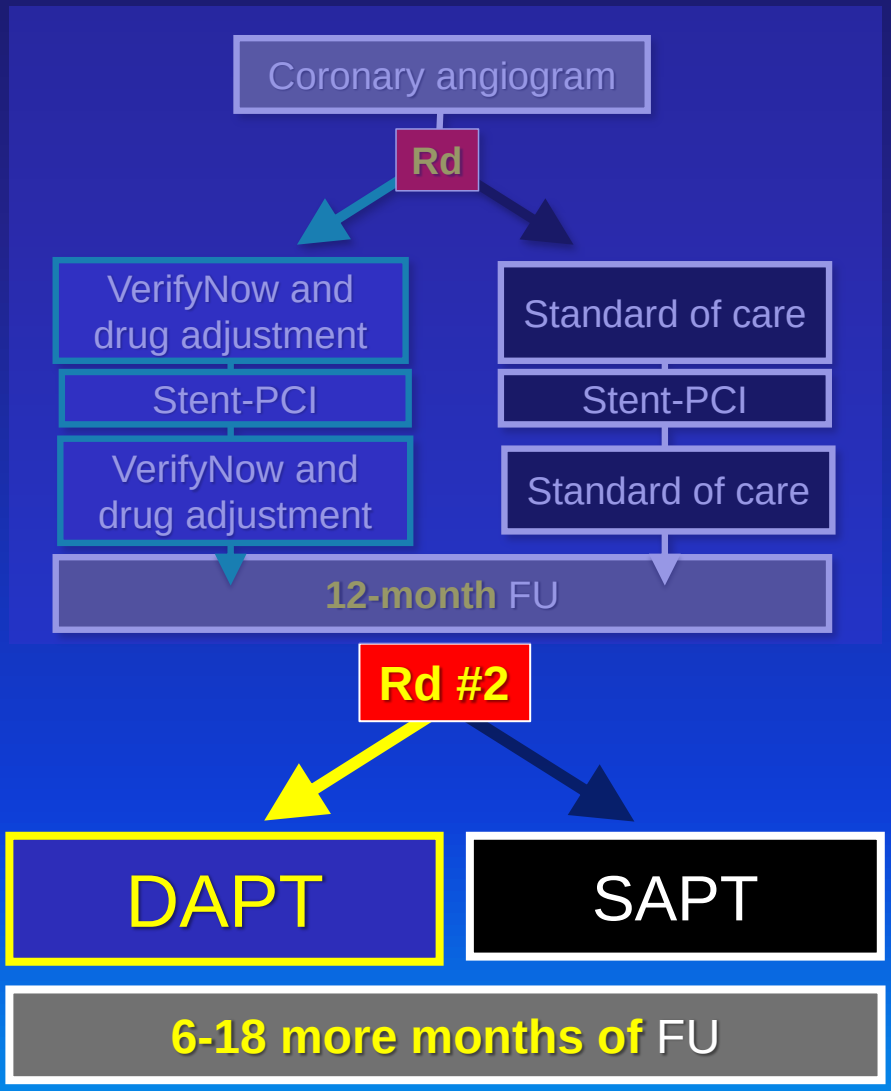
ARCTIC-INTERRUPTION design



1° EP: Death, MI, stroke, stent thrombosis, urg. revasc.

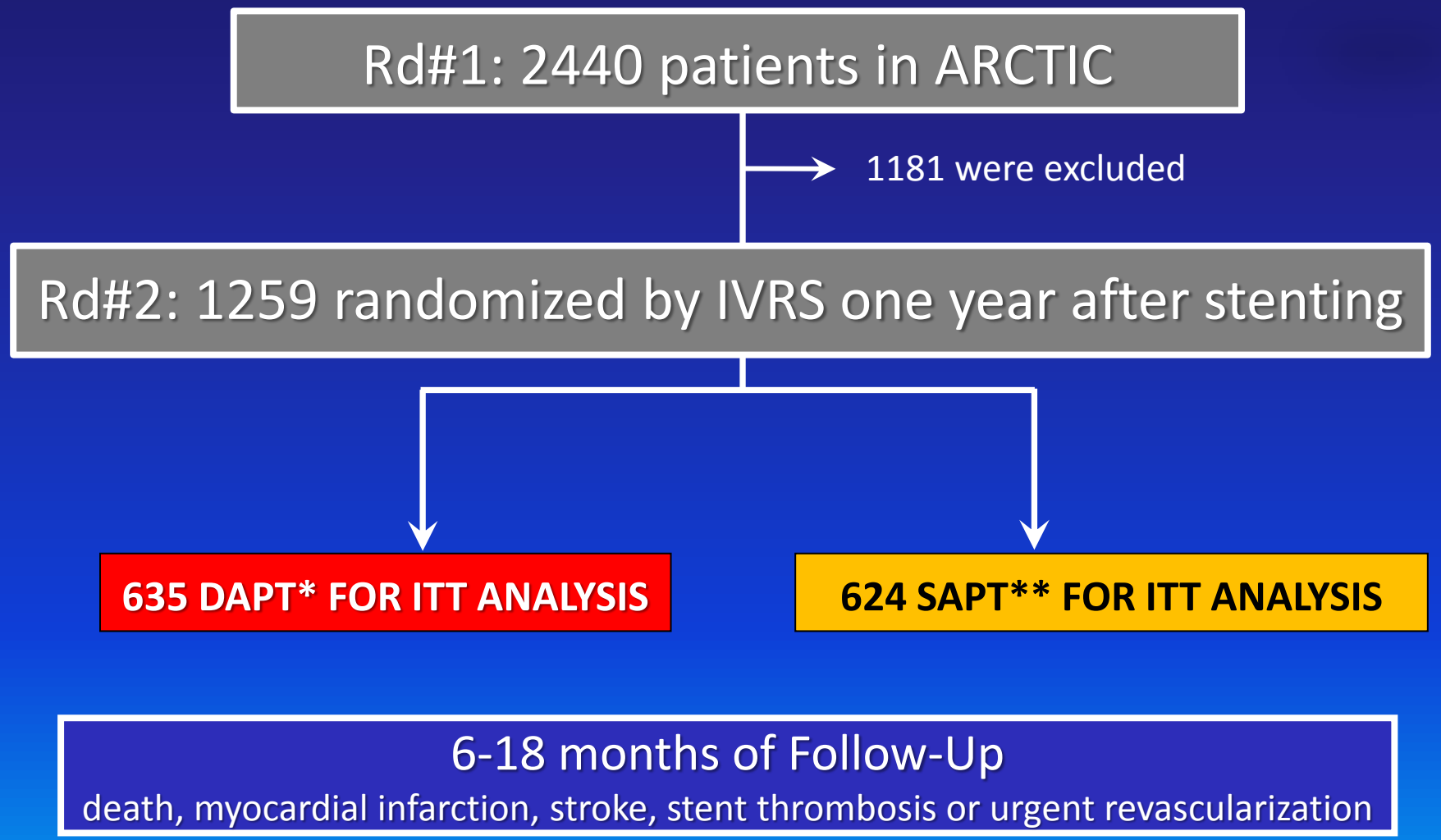
Exclusion for Rd#2

- Any ichemic event of the primary endpoint during the first year of FU
- Any event of the primary safety endpoint during the first year of FU
- Any new revascularisation needing DAPT prolongation
- Contraindication to aspirin withdrawal:

  e.g. Haemorragic GI ulcer, aspirin resistance

- Physician's (or patient's) decision

Flow Chart



*Dual Antiplatelet Therapy; **Single antiplatelet therapy

Results

Randomized *vs.* Non-Randomized

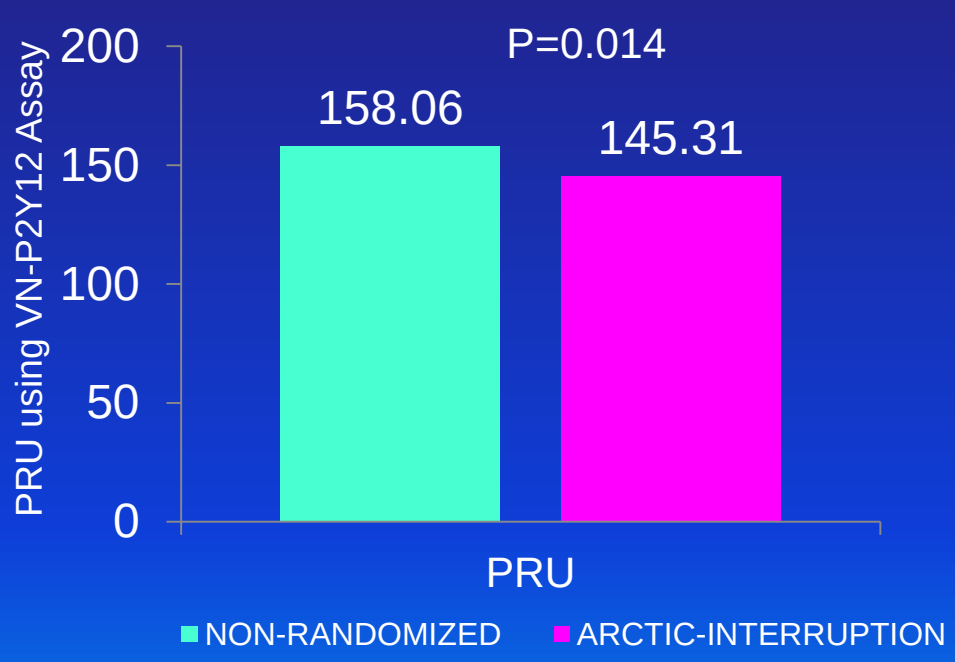
	Randomized (n=1259)	Non-Randomized (n=1181)
Age - median	63	64
Diabetes - %	33	40*
Prior PAD- %	10	14*
Prior PCI - %	41	45
Prior CABG - %	7	7
Proton pump inhibitors - %	31	33
Drug-eluting stent implanted - %	99	95*

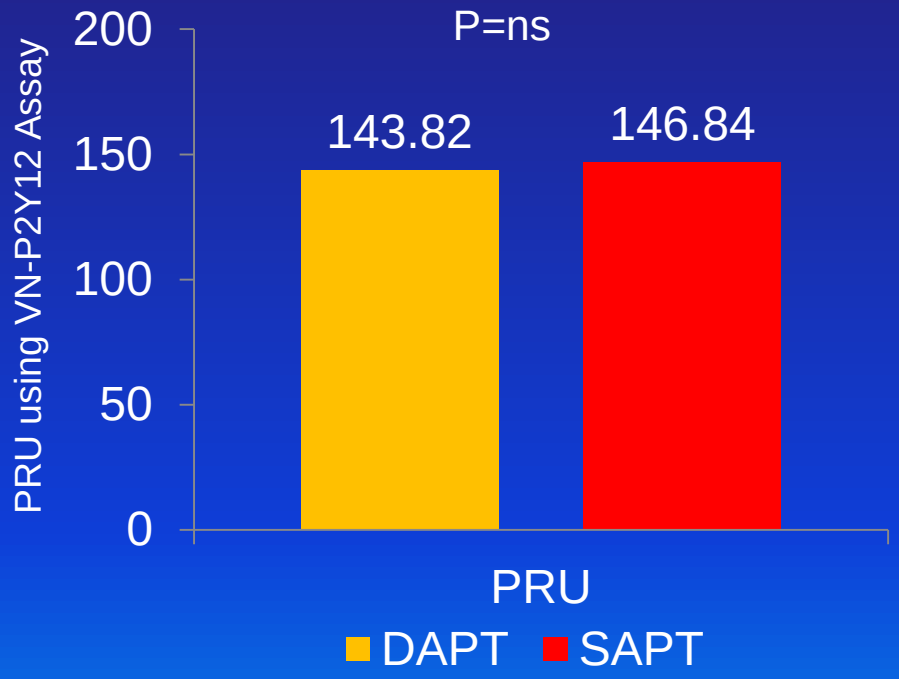
* $p<0.05$

DAPT *vs.* SAPT: Baseline characteristics

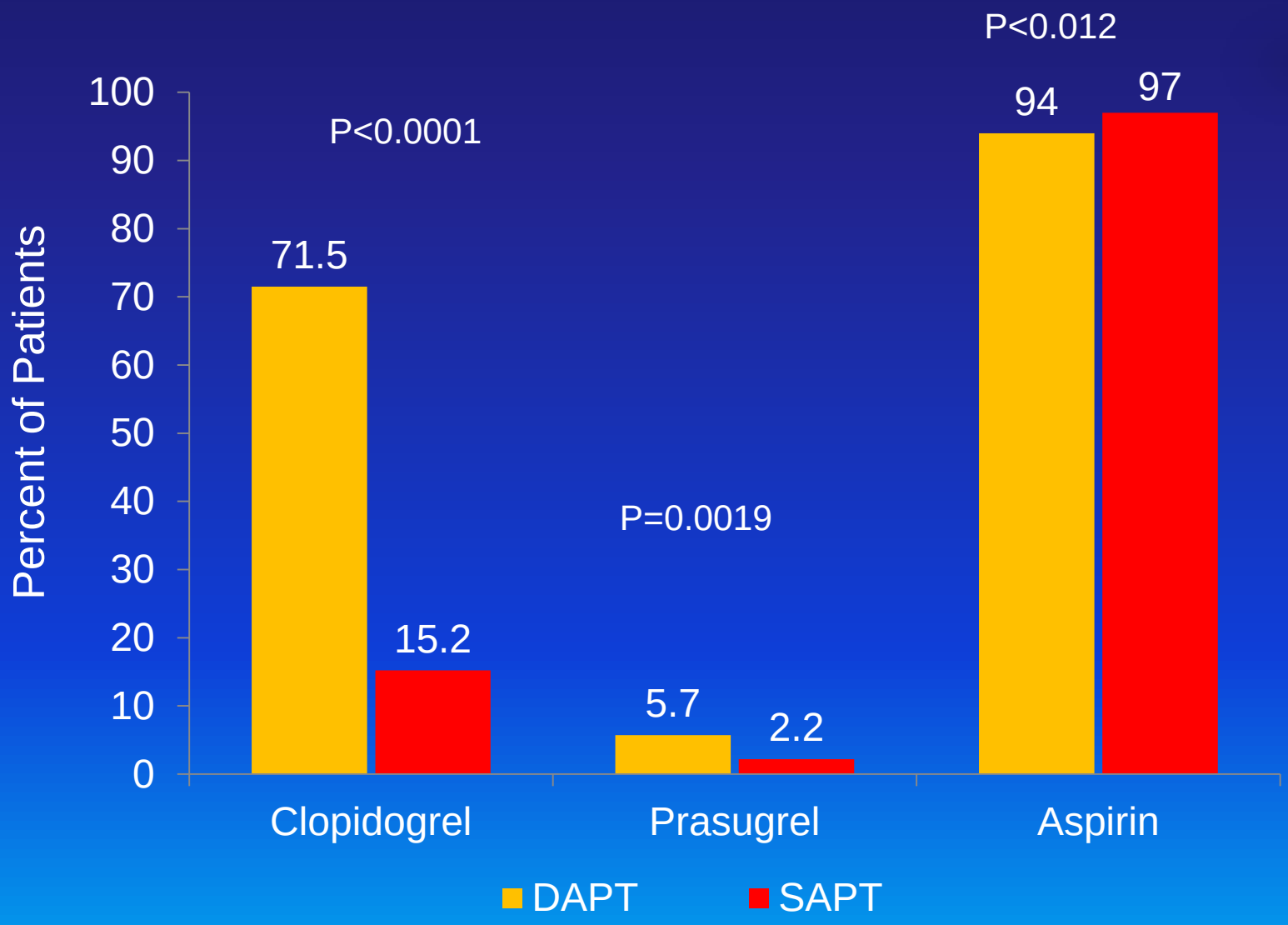
	DAPT (n=635)	SAPT (n=624)
Age - median	64	64
Diabetes - %	36	37
Prior MI - %	31	30
Prior PCI - %	43	40
Prior CABG - %	7	6
Clopidogrel - %	90	90
Clopidogrel 150 mg - %	10	14
Prasugrel - %	8.5	8.5
Proton pump inhibitors - %	33	29
Drug-eluting stent implanted - %	98	99

PRU Assessment on maintenance therapy before Rd#2



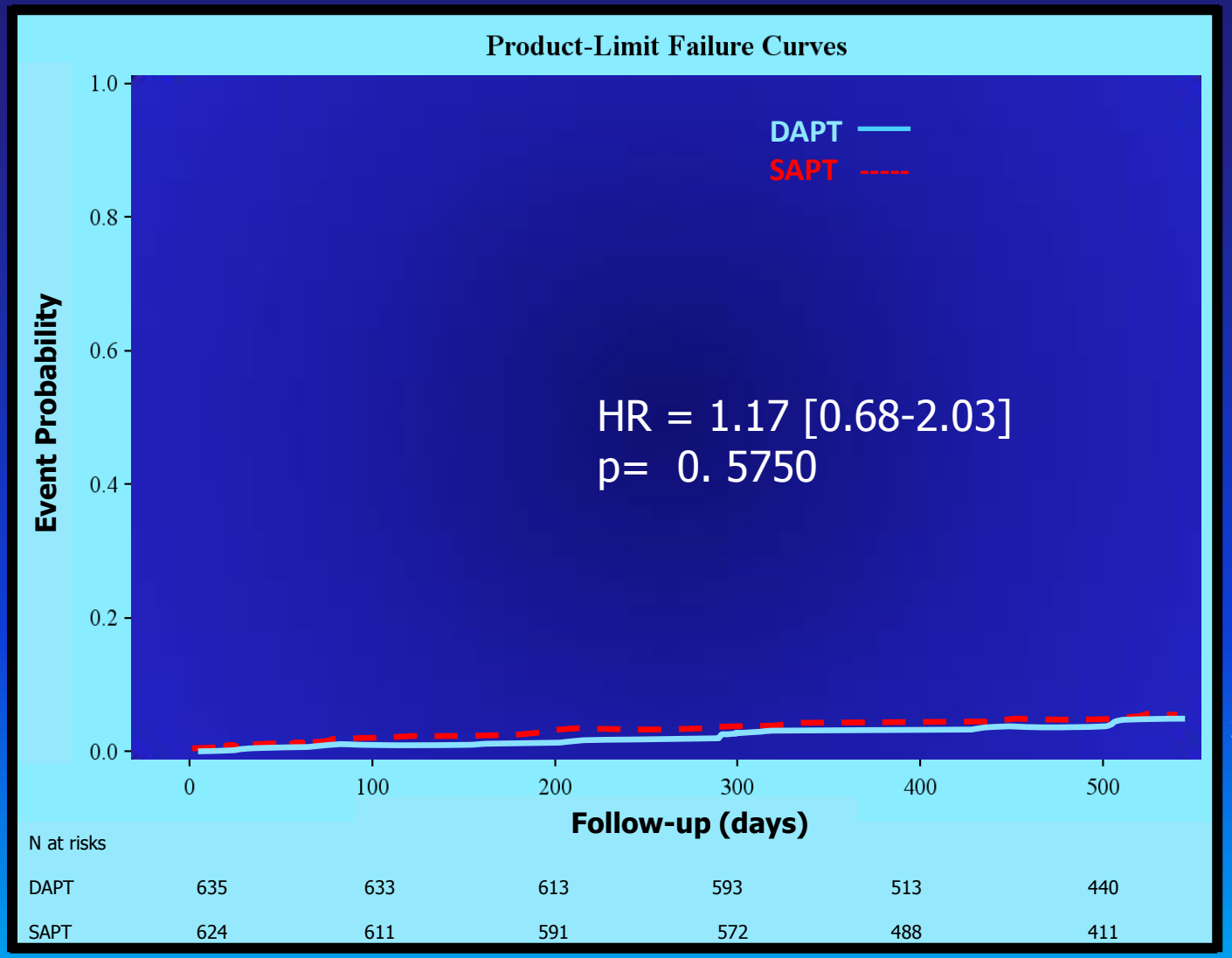


Treatment at last F.U. visit



Primary Endpoint up to 18 months

Death, MI, stroke, stent thrombosis, urgent revascularization



All ischemic Endpoints

	DAPT	SAPT	HR [95%CI]	P
Primary End Point*	3.8	4.3	1.17 [0.68; 2.03]	0.57
Stent thrombosis or Urgent Revasc	1.3	1.6	1.30 [0.51;3.30]	0.58
Death *or* myocardial Infarction - %	2.2	2.7	1.26 [0.62 ;2.55]	0.52
Any death - %	1.1	1.4	1.32 [0.49 ;3.55]	0.58
Myocardial infarction - %	1.4	1.4	1.04 [0.41 ;2.62]	0.94
Stent thrombosis - %	0	0.5		
Stroke *or* TIA- %	0.9	0.6	0.69 [0.19;2.44]	0.56
Urgent revascularization - %	1.3	1.4	1.17 [0.45 ;3.04]	0.74

*Any death, Myocardial infarction, stent thrombosis, stroke or transient ischemic attack, urgent revascularization

Key Safety Outcome

Whole population

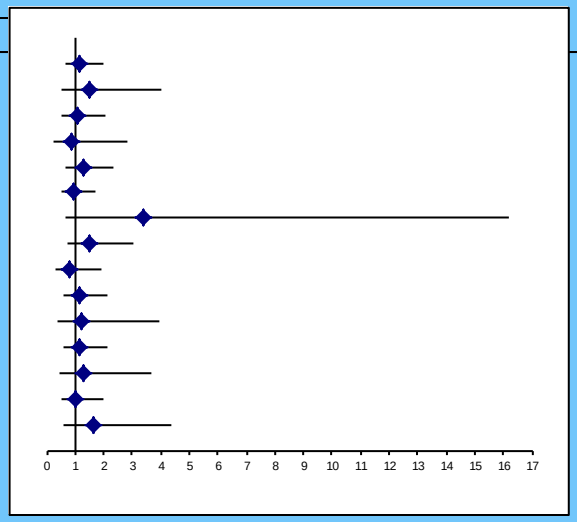
	DAPT	SAPT	HR [95%CI]	P
Major bleeding - %	1.1	0.2	0.15 [0.02; 1.20]	0.073
Minor bleeding - %	0.8	0.3	0.41 [0.08 ;2.13]	0.29
Major *or* minor bleeding - %	1.9	0.5	0.26 [0.07 ;0.91]	0.035
BARC III and V	1.1	0.2	0.15 [0.02 ;1.20]	0.073

STEEPLE definitions - Montalescot G, et al. N Engl J Med 2006; 355:1006–17

Pre-specified subgroups

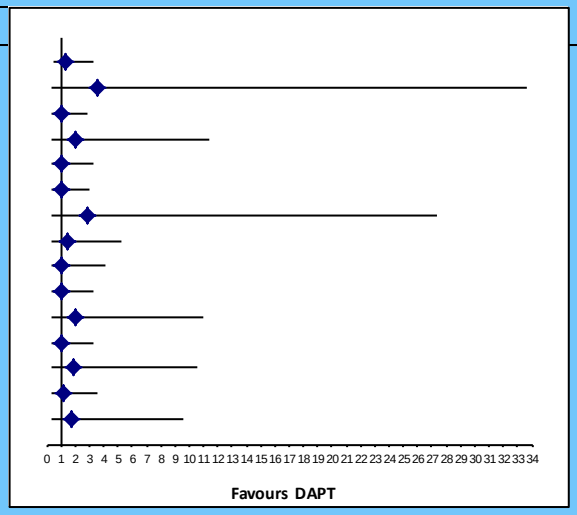
PRIMARY ENDPOINT

	DAPT		SAPT		Relative risk (95%CI)	P Interaction
	n	%	n	%		
Full population	635	3.8%	624	4.3%	1.17 (0.68;2.03)	0.58
Age > 75	117	6.0%	103	8.7%	1.50 (0.56; 4.02)	
Age ≤ 75	518	3.3%	521	3.5%	1.08 (0.56; 2.09)	0.59
Women	127	4.7%	121	4.1%	0.86 (0.26; 2.83)	
Men	508	3.5%	503	4.4%	1.27 (0.68; 2.37)	0.57
BMI ≤ 30	470	4.7%	465	4.3%	0.95 (0.52; 1.74)	
BMI > 30	139	1.4%	144	4.9%	3.36 (0.70; 16.20)	0.14
No diabetes	437	3.0%	402	4.2%	1.48 (0.72; 3.04)	
Diabetes	198	5.6%	222	4.5%	0.80 (0.34; 1.89)	0.29
No Tabac	488	3.9%	472	4.4%	1.16 (0.63; 2.16)	
Tabac	147	3.4%	152	3.9%	1.20 (0.37; 3.94)	0.96
No ACS	479	3.8%	457	4.2%	1.13 (0.59; 2.15)	
ACS	156	3.8%	167	4.8%	1.28 (0.44; 3.68)	0.85
Number of stent=1	410	4.4%	372	4.3%	1.01 (0.51; 1.97)	
Number stent ≥2	213	2.8%	246	4.5%	1.62 (0.60; 4.37)	0.44



SECONDARY ENDPOINT

	DAPT		SAPT		Relative risk (95%CI)	P Interaction
	n	%	n	%		
Full population	635	1,3%	624	1,6%	1.30 (0.51; 3.30)	0.58
Age > 75	117	0.9%	103	2.9%	3.50 (0.36; 33.64)	
Age ≤ 75	518	1.4%	521	1.3%	1.02 (0.36; 2.90)	0.33
Women	127	1.6%	121	3.3%	2.08 (0.38; 11.34)	
Men	508	1.2%	503	1.2%	1.04 (0.34; 3.23)	0.51
BMI ≤ 30	470	1.5%	465	1.5%	1.05 (0.37; 2.99)	
BMI > 30	139	0.7%	144	2.1%	2.85 (0.30; 27.39)	0.43
No diabete	437	0.9%	402	1.2%	1.42 (0.38; 5.28)	
Diabete	198	2.0%	222	2.3%	1.11 (0.30; 4.12)	0.79
No Tabac	488	1.2%	472	1.3%	1.05 (0.34; 3.27)	
Tabac	147	1.4%	152	2.6%	2.01 (0.37; 10.96)	0.54
No ACS	479	1.3%	457	1.3%	1.07 (0.35; 3.32)	
ACS	156	1.3%	167	2.4%	1.92 (0.35; 10.50)	0.57
Number of stent=1	410	1.5%	372	1.6%	1.14 (0.37; 3.53)	
Number stent ≥2	213	0.9%	246	1.6%	1.75 (0.32; 9.56)	0.68



Conclusions

ARCTIC-INTERRUPTION

1. Half of the patients **could not be randomized** 1 year after stenting
2. The **randomized patients were at lower risk**
3. **No ischemic benefit** of DAPT continuation beyond one year
4. Significant **more major or minor bleedings** with DAPT continuation
5. Findings **consistent** across pre-specified subgroups and with prior studies