GRCI 2017
France

TOPIC study

6 AU 8 DÉCEMBRE 2017
Novotel Paris Tour Eiffel

Passion Communication Education

Benefit of switching dual antiplatelet therapy after acute coronary syndrome:

The TOPIC (Timing Of Platelet Inhibition after acute Coronary Syndrome) randomized study

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AP HM
Assistance Publique
Hôpitaux de Marseille

Aix*Marseille
université

Why this study?

DAPT after ACS in guidelines

Recommendations	Class[a]	LoE[b]
DAPT with use of potent $P2Y_{12}$ inhibitors (prasugrel or ticagrelor) is recommended over clopidogrel.	I	C

A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.	I	A

Newer P2Y12 blockers and 1 year DAPT as default strategy after ACS

But one Year with newer P2Y12 blockers ?

ESC guidelines, Eur Heart J 2015

Why this study?

Newer P2Y12 blockers and Stent Thrombosis

Stent thrombosis in TRITON

Thrombotic Benefit greater during early Phase

TRITON PCI study, Lancet 2008

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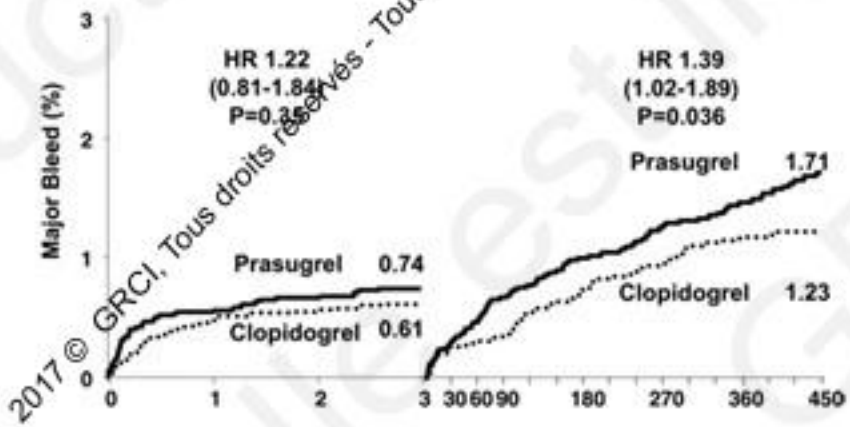
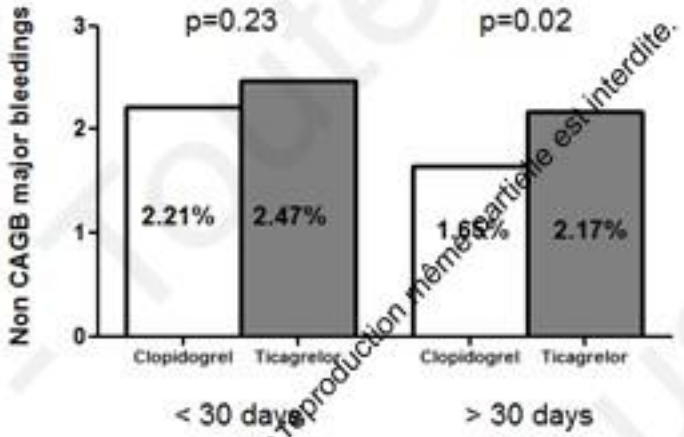
Why this study?

Newer P2Y12 blockers and Bleeding

Bleeding risk in TRITON



Bleeding risk in PLATO



Bleeding Risk mainly on chronic phase

Wallentin et al, N Engl J Med 2010
Wiviott SD et al. N Engl J Med 2007

Why this study?

Newer P2Y12 blockers in ACS

Ischemic benefit greater in early phase

Bleeding hazard mainly on chronic phase

Hypothesis of the TOPIC study:

To assess efficacy and safety of « *evolutive* DAPT » in ACS with 1 Mo 'Potent DAPT' (ASA + Newer P2Y12) followed by ASA + Clopidogrel up to 1 year

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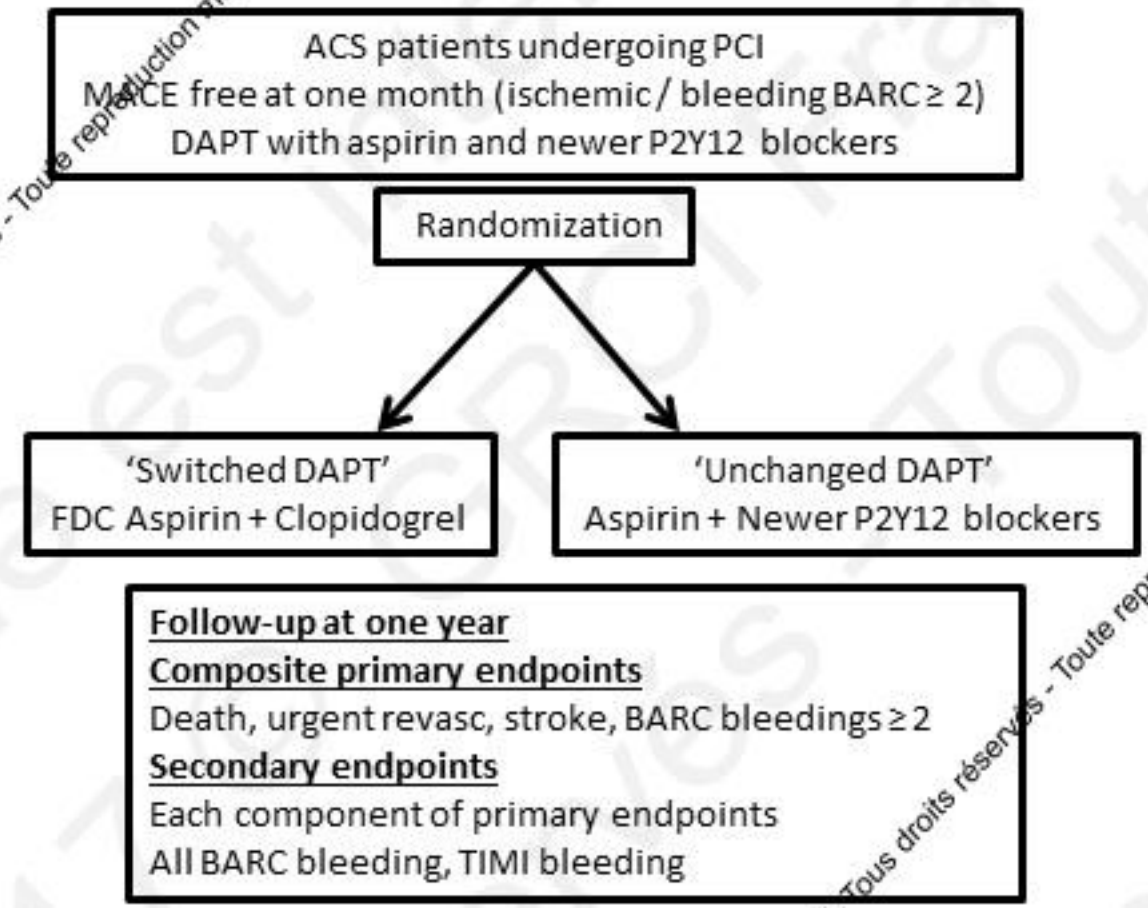
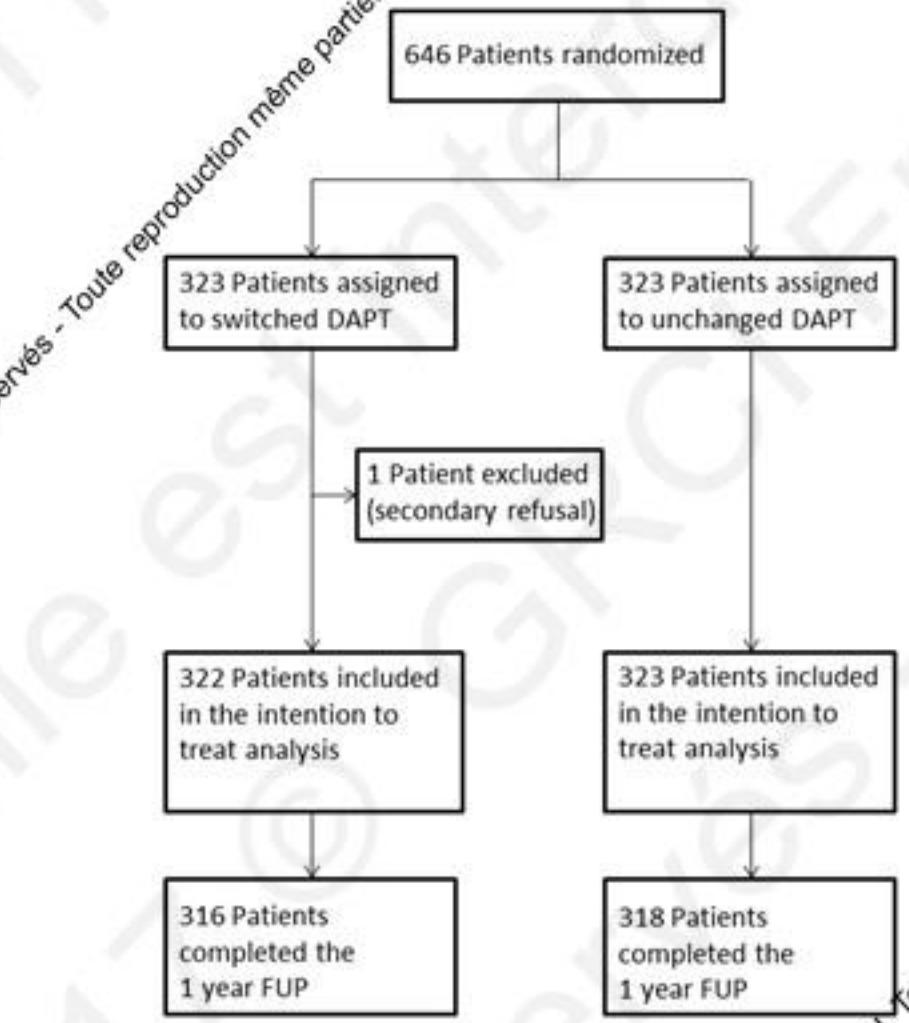
What did we study?

Study Design



Cuisset T, Deharo P et al, Eur Heart J 2017

How was the study conducted?



Flow chart

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How was the study conducted?

Statistics

Trial powered to assess whether switched DAPT was better than unchanged DAPT in the prevention of the primary composite endpoint

We assumed a 10% occurrence rate of PEP at 1Y in the switched DAPT group and 18% in the unchanged DAPT group based on prior studies

Calculation of a minimum sample size of 319 patients in each group to achieve an α level of 0.05 and statistical power of 0.80

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How was the study conducted?

Statistics

Monocentric trial

ACS randomized 1:1 between switched and unchanged DAPT

Cox model (Kaplan Meyer curves)

Time to 1st event analysis

Modified ITT analysis

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What are the essential results?

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Baseline characteristics

BASELINE CHARACTERISTICS	All Patients (n=646)	Switched DAPT (n=323)	Unchanged DAPT (n=323)	P-value
Male gender (n, %)	532 (82%)	261 (81%)	271 (84%)	0.30
Age (years; m ± SD)	60.0 ± 10.2	60.6 ± 10.2	59.6 ± 10.3	0.21
BMI (kg/m2; m ± SD)	27.2 ± 4.5	27.1 ± 4.4	27.3 ± 4.5	0.55
Medical history, (n, %)				
Hypertension	313 (48%)	151 (47%)	162(50%)	0.39
Type 2 diabetes	177 (27%)	84 (26%)	93 (29%)	0.43
Dyslipidemia	283 (44%)	136 (42%)	147 (46%)	0.38
Current smoker	286 (44%)	145 (45%)	141 (44%)	0.75
Previous CAD	197 (30%)	100 (31%)	97 (30%)	0.80
Treatment, (n, %)				
Beta blocker	445 (69%)	213 (66%)	232 (72%)	0.11
RAS-inhibitors	486 (75%)	236 (73%)	250 (77%)	0.20
Statin	614 (95%)	302 (93%)	312 (97%)	0.07
PPI	639 (99%)	316 (98%)	323 (100%)	0.01
Antiplatelet agent, (n, %)				0.53
Ticagrelor (n, %)	276 (43%)	142(44%)	134(42%)	
Prasugrel (n, %)	370 (57%)	181(56%)	189(59%)	
Presentation				0.06
STEMI (n, %)	257 (40%)	117 (36%)	140 (43%)	
UA or NSTEMI (n, %)	389 (60%)	206 (64%)	183 (57%)	
EF (%; m ± SD)	56.4 ± 7.7	57.2 ± 7.1	55.8 ± 8.2	0.04

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Procedure characteristics

PROCEDURAL CHARACTERISTICS	All Patients (n=646)	Switched DAPT (n=323)	Unchanged DAPT (n=323)	P-value
Access site, n (%)				0.11
Femoral	28 (4%)	17 (5%)	11 (3%)	
Radial	628 (96%)	306 (95%)	312 (97%)	
Culprit lesion, n (%)				0.15
LMS	24 (4%)	7 (2%)	17 (5%)	
LAD	299 (46%)	155 (48%)	144 (45%)	
LCX	118 (18%)	65 (20%)	53 (16%)	
RCA	202 (31%)	95 (29%)	107 (33%)	
Venous graft	3 (1%)	1 (0%)	2 (1%)	
Number of vessel treated, n (%)				0.19
1	548 (85%)	266 (82%)	282 (87%)	
2	84 (13%)	48 (15%)	36 (11%)	
3	14 (2%)	9 (3%)	5 (2%)	
Stent type, n (%)				0.10
DES	585 (91%)	297 (92%)	288 (89%)	
BVS	21 (3%)	13 (4%)	8 (3%)	
BMS	24 (4%)	8 (3%)	16 (5%)	
None	16 (3%)	5 (2%)	11 (3%)	
Number of stent (m ± SD)	1.4 ± 0.7	1.4 ± 0.7	1.4 ± 0.7	0.39
Stent diameter, mm (m ± SD)	2.8 ± 0.6	2.8 ± 0.6	2.8 ± 0.5	0.43
Stent length, mm (m ± SD)	26.4 ± 16.4	26.9 ± 16.9	26.4 ± 15.8	0.64

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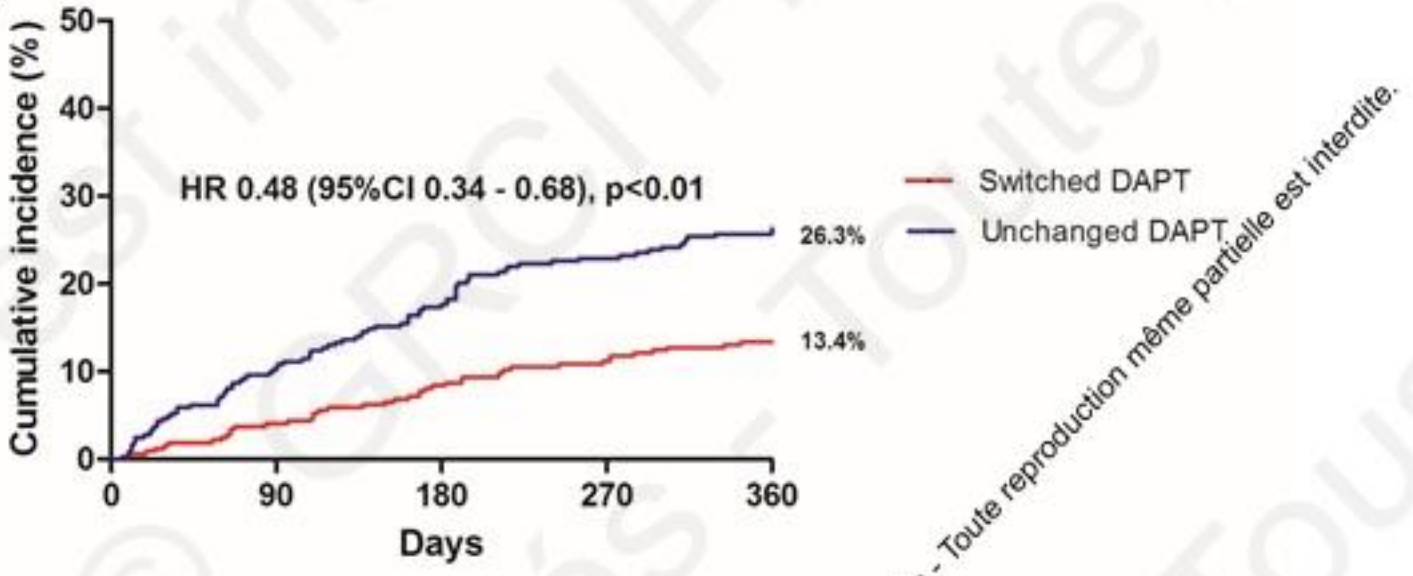
Primary Endpoint

Death, Urgent revasc., Stroke, BARC ≥ 2



Better Prognosis with switched DAPT

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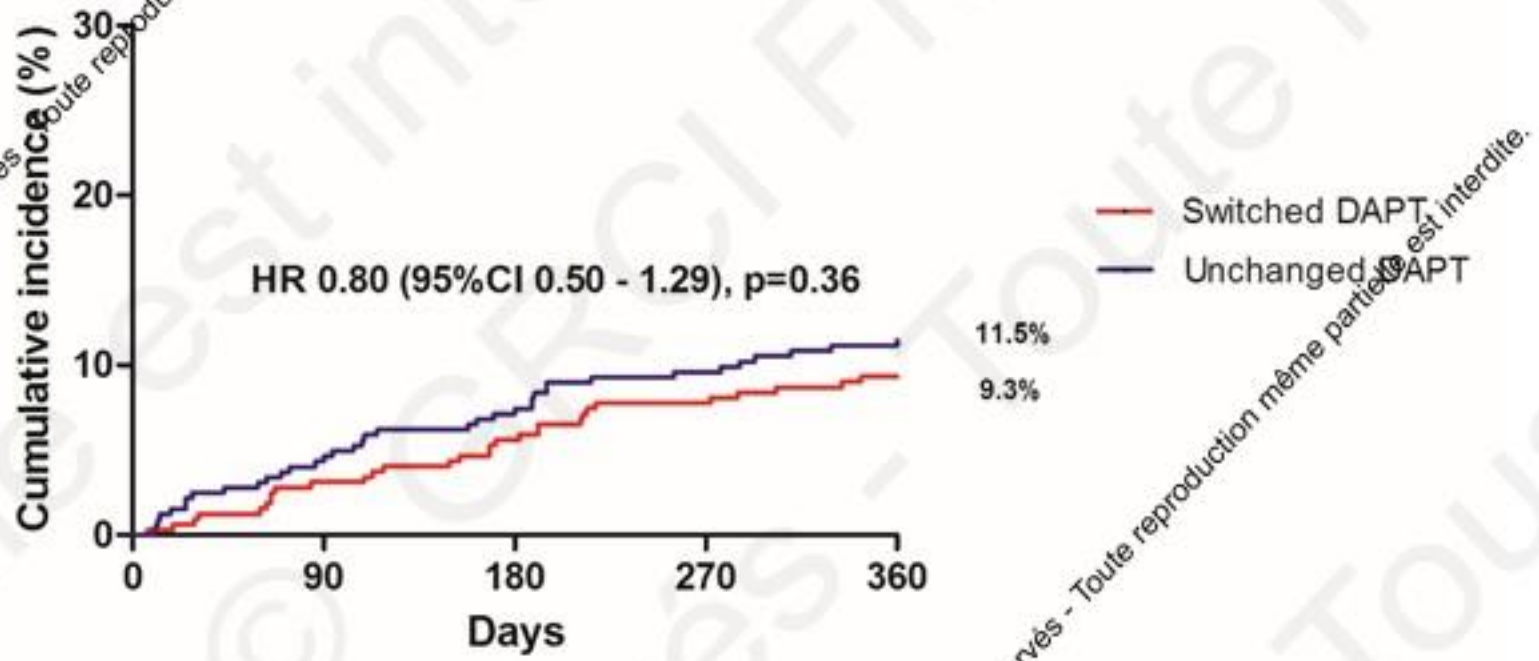
Any ischemic endpoint



No difference for ischemic events

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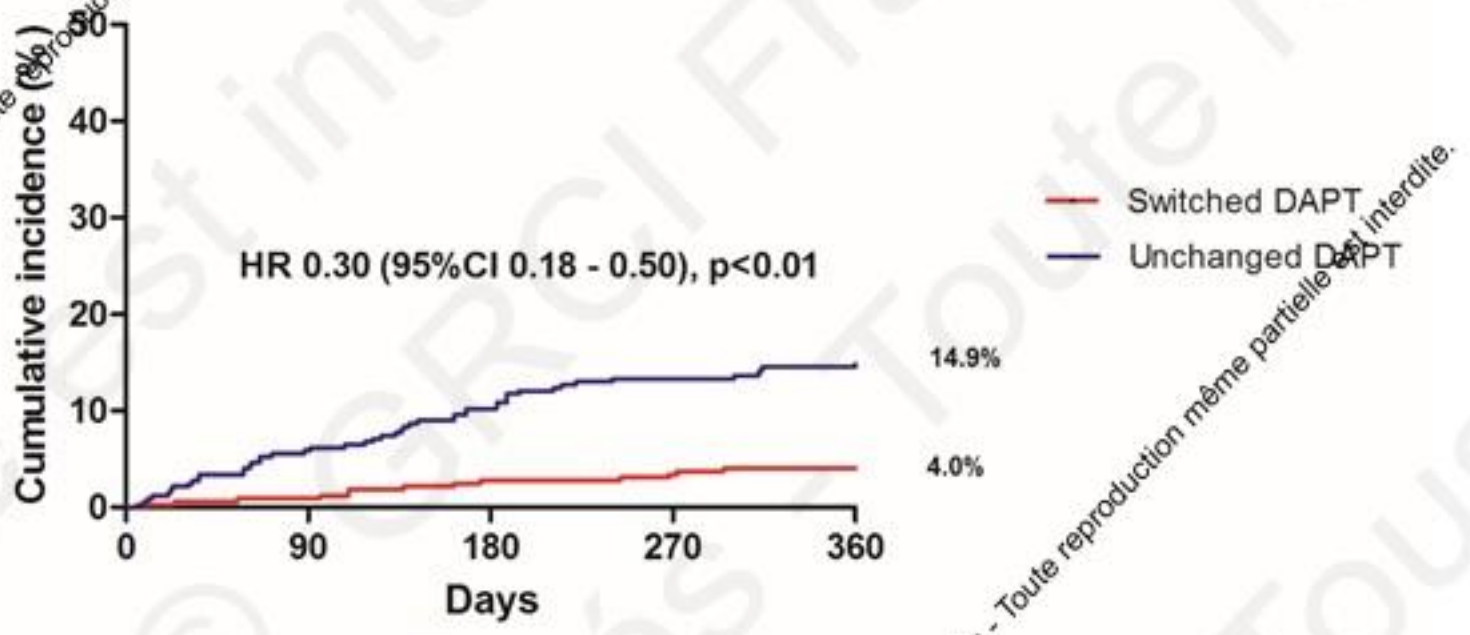
BARC bleedings ≥ 2



Higher Rate of BARC bleeding ≥ 2 with Unchanged DAPT

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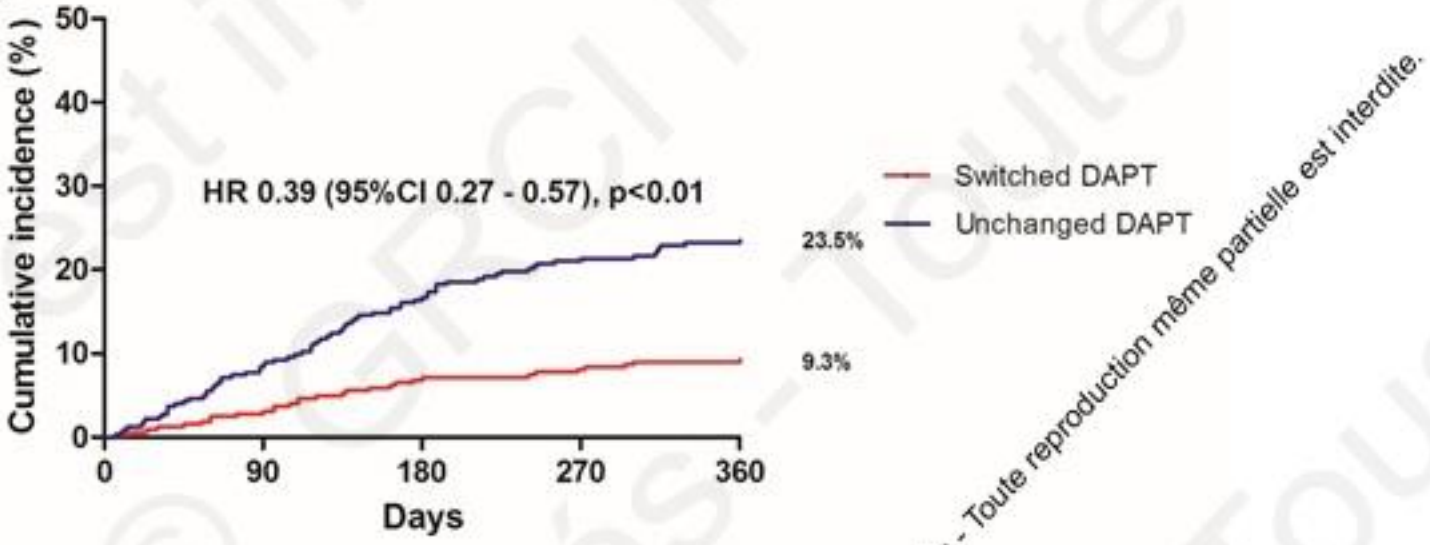
Bleedings all BARC



Higher Rate of BARC bleeding with Unchanged DAPT

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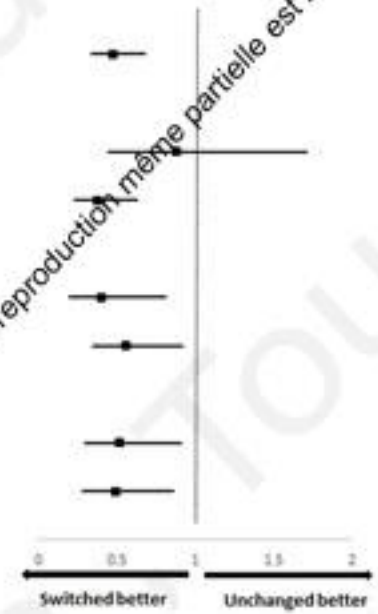
Subgroup analysis

Subgroup	Switched (n=322)		Unchanged (n=323)		Odd ratio (95%CI)	p value for interaction
	Event/total patient (no)	Event rate (%)	Event/total patient (no)	Event rate (%)		
All patient	43/322	13.4	85/323	26.3	0.48 (0.34 - 0.68)	
Diabetes						0.96
Yes	19/84	22.6	24/93	25.8	0.88 (0.45 - 1.71)	
No	24/238	10.1	61/230	26.5	0.38 (0.23 - 0.63)	
ACS presentation						0.85
STEMI	12/116	10.3	36/140	25.7	0.40 (0.20 - 0.81)	
NON STEMI	31/206	15.1	49/183	26.8	0.56 (0.35 - 0.92)	
P2Y12 blocker						0.95
Ticagrelor	23/141	16.3	42/134	31.3	0.52 (0.30 - 0.91)	
Prasugrel	20/181	11.1	43/189	22.7	0.49 (0.28 - 0.86)	



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Limitations

Study not sized for hard endpoints (ST or mortality)

Benefit Driven by safety (as WOEST or ISAR Triple)

Single Center and Open label

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Conclusion

In patients without adverse event 1 month after stented ACS, a switched DAPT is superior to an unchanged DAPT strategy to prevent bleeding complications without increased risk of ischemic events following ACS.

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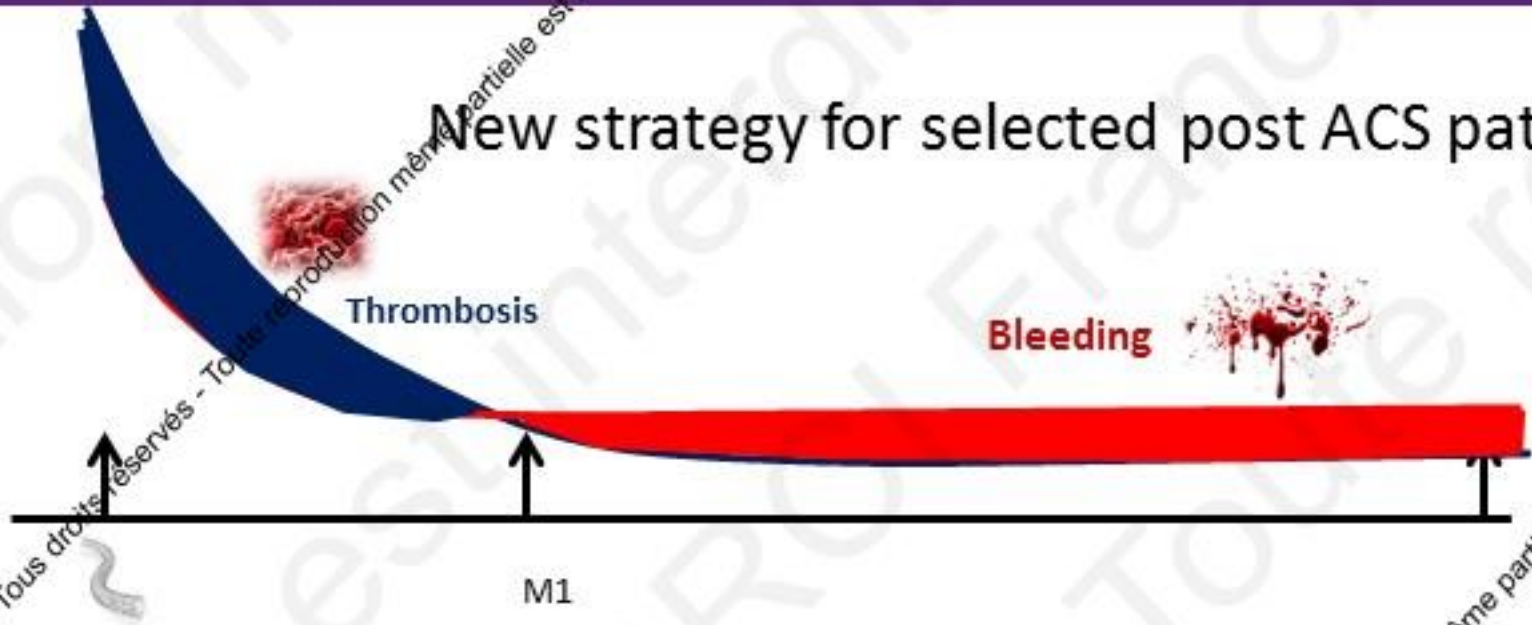
Why this is important?

New strategy for selected post ACS patients



Thrombotic risk > Bleeding Risk

Bleeding Risk >Thrombotic risk

Integration of dynamic risk post ACS

t0 PCI for ACS

M1 Switch

M12

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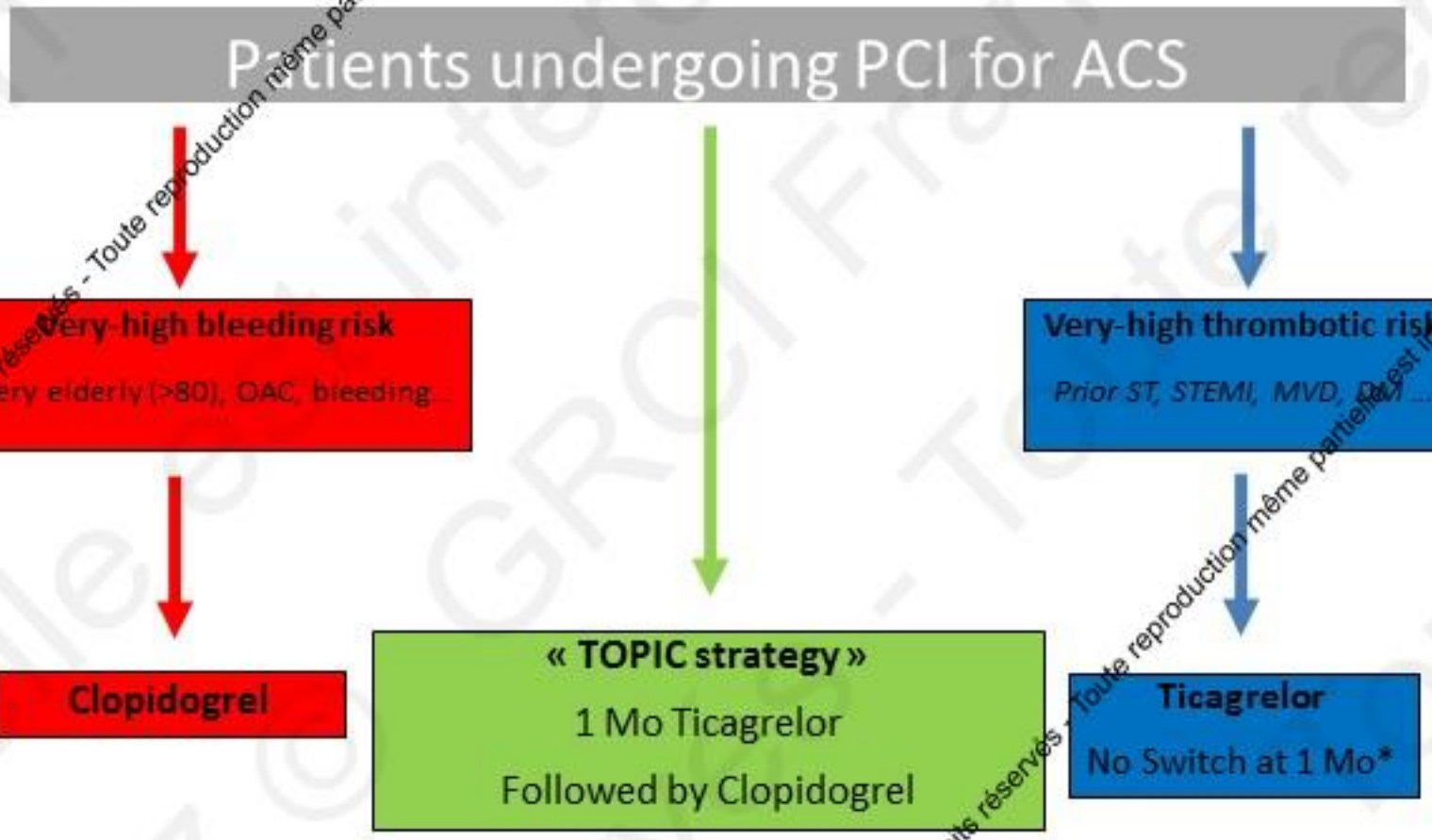
P2Y12 blockers after ACS/PCI



* Timing of switch could be tailored according to patient's risk profile

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