Double antiagrégation plaquettaire 12 mois ? Plus ? Moins ? Un peu de clarté ...

Pr Gilles LEMESLE
USIC et Centre Hémodynamique, CHRU de Lille
Institut Pasteur de Lille, UMR 1011

Déclaration de liens d'intérêts

- Honoraires : Amgen, Astra Zeneca, Bayer, Biopharma, Bristol Myers Squibb, Boehringer Ingelheim, Daiichi Sankyo, Lilly, MSD, Novartis, Pfizer, Sanofi Aventis, Servier, The medicine company

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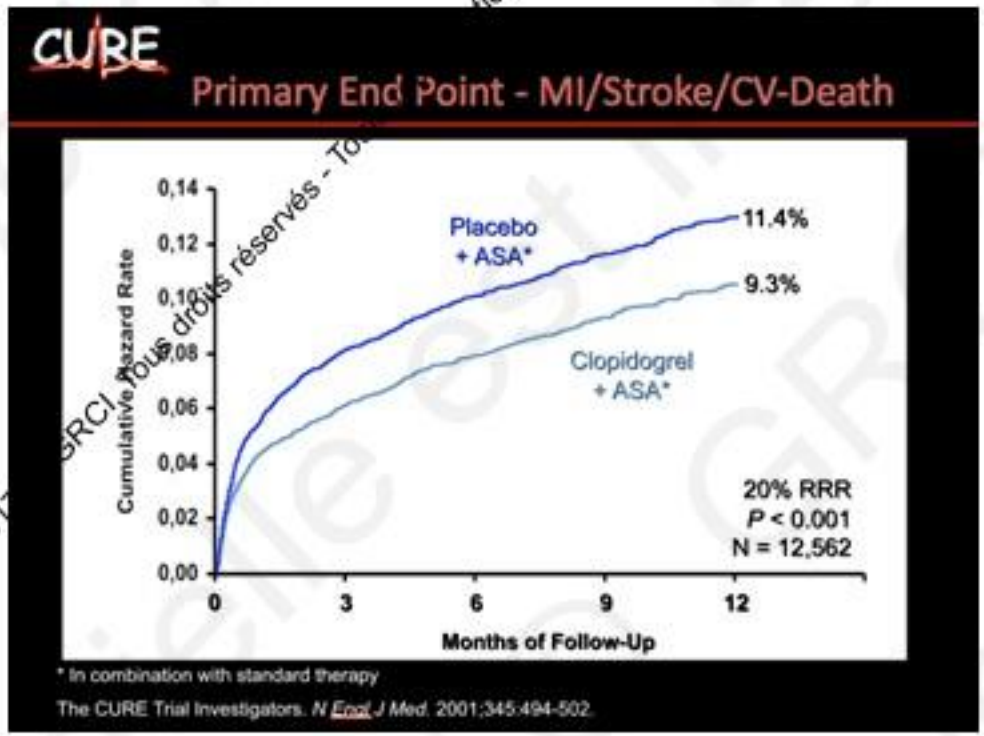
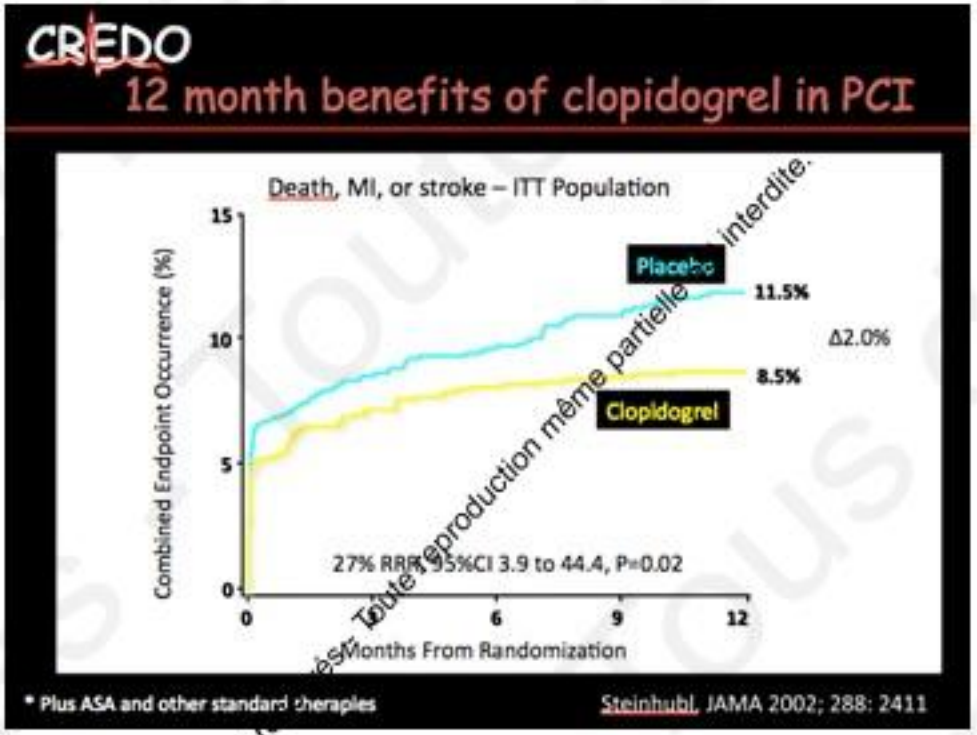
Ce que l'on savait …

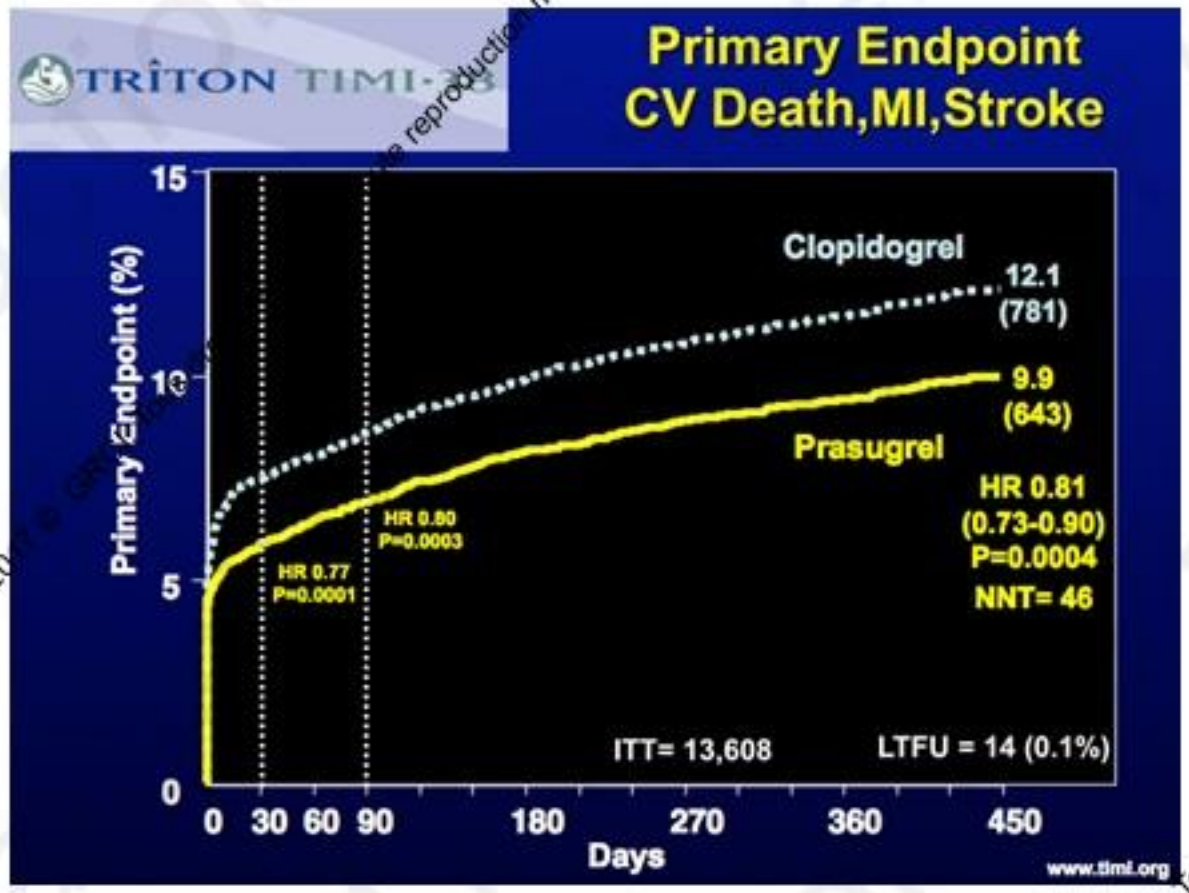
- At least 12 months in ACS patients …
- And 12 months in stable patients with first generation DES implantation (delay of endothelialization) …

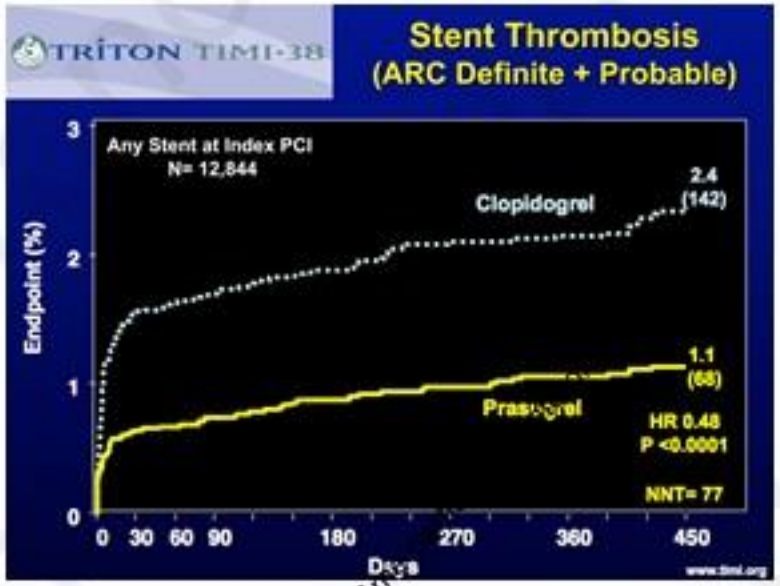
Du temps du clopidogrel ...

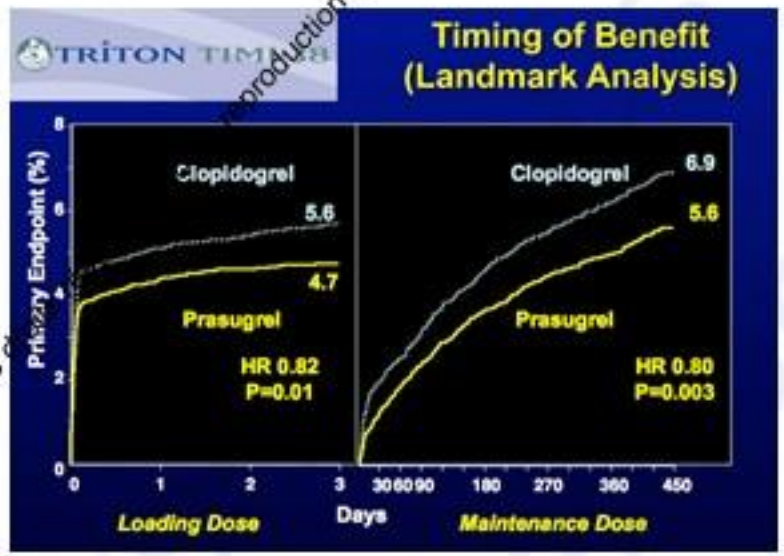




TRITON



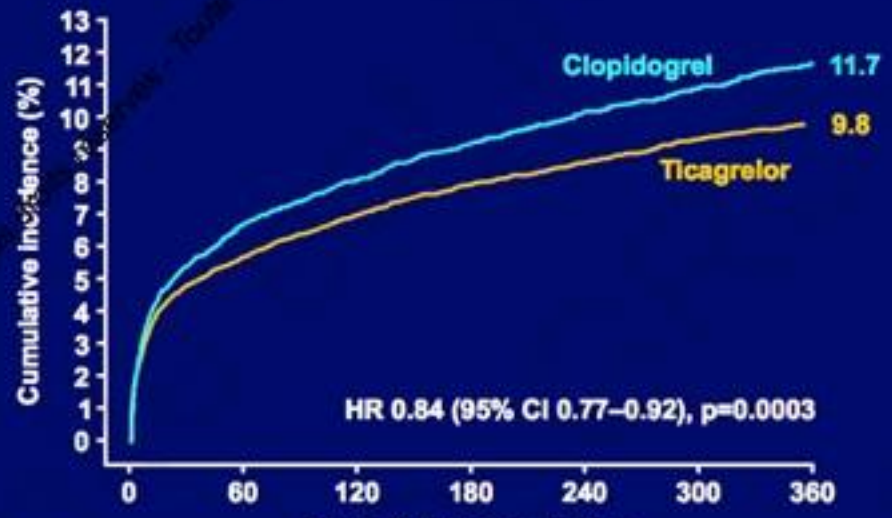




PLATO

K-M estimate of time to first primary efficacy event (composite of CV death, MI or stroke)

PLATO



No. at risk							
Ticagrelor	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,743	5,096	4,047

K-M = Kaplan-Meier; HR = hazard ratio; CI = confidence interval

UCR

Duke Clinical Research Institute

Stent thrombosis

(evaluated in patients with any stent during the study)

PLATO

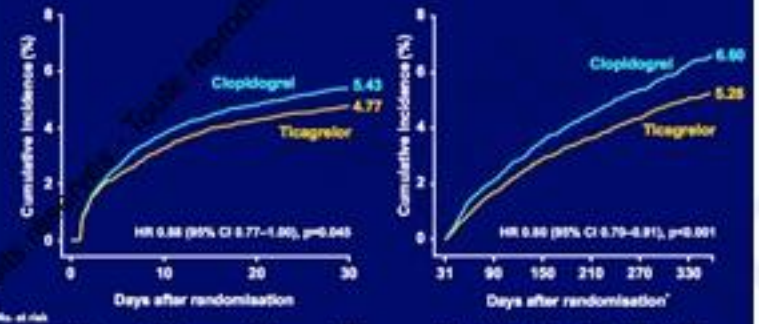
	Ticagrelor (n=5,640)	Clopidogrel (n=5,649)	HR (95% CI)	p value
Stent thrombosis, n (%)				
Definite	71 (1.3)	106 (1.9)	0.67 (0.50–0.91)	0.009
Probable or definite	118 (2.1)	158 (2.8)	0.75 (0.59–0.95)	0.02
Possible, probable, definite	155 (2.8)	202 (3.6)	0.77 (0.62–0.95)	0.01

*Time-at-risk is calculated from first stent insertion in the study or date of randomisation

UCR

Primary efficacy endpoint over time (composite of CV death, MI or stroke)

PLATO



*Excludes patients with any primary event during the first 30 days

UCR

Les guidelines …

NSTEMI 2013

…tions for platelet inhibition in non-ST-… acute coronary syndromes

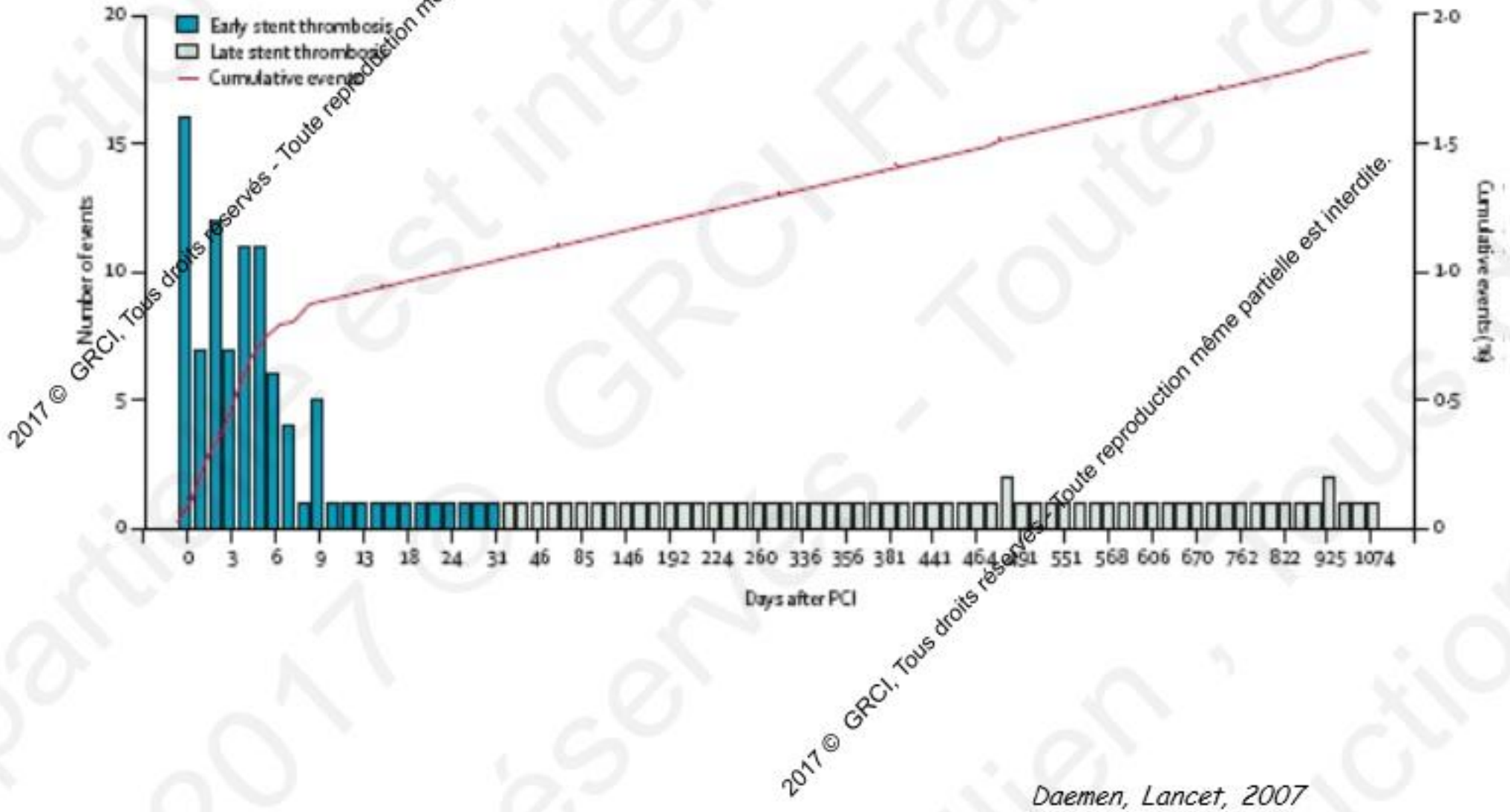
Recommendations	Class[a]	Level[b]	Ref[c]
Oral antiplatelet therapy			
Aspirin is recommended for all patients without contraindications at an initial oral loading dose[d] of 150–300 mg (in aspirin-naive patients) and a maintenance dose of 75–100 mg/day long-term, regardless of treatment strategy.	I	C	129–132
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	137, 148, 153
• Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications,[e] for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started).	I	B	153
• Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.[e]	I	B	148, 164
• Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation.	I	B	137
$P2Y_{12}$ inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.	IIb	A	187–189, 192

STEMI 2017

…nance antithrombotic strategy after ST-elevation myocardial infarction

Recommendations	Class[a]	Level[b]
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.[329]	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel are not available or are contraindicated), is recommended for 12 months after PCI, unless there are contraindications such as excessive risk of bleeding.[186,187]	I	A
A PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.[330–337]	I	B
In patients with an indication for oral anticoagulation, oral anticoagulants are indicated in addition to antiplatelet therapy.[5]	I	C
In patients who are at high risk of severe bleeding complications, discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.[332,338,340]	IIa	B
In STEMI patients with stent implantation and an indication for oral anticoagulation, triple therapy[d] should be considered for 1–6 months (according to a balance between the estimated risk of recurrent coronary events and bleeding).[5]	IIa	C
DAPT for 12 months in patients who did not undergo PCI should be considered unless there are contraindications such as excessive risk of bleeding.	IIa	C
In patients with LV thrombus, anticoagulation should be administered for up to 6 months guided by repeated imaging.[341–343]	IIa	C
In high ischaemic-risk patients[e] who have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg twice a day on top of aspirin for longer than 12 months may be considered for up to 3 years.[333]	IIb	B
In low bleeding-risk patients who receive aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered.[338]	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and oral anticoagulation.	III	C

Stable CAD setting ...



Daemen, Lancet, 2007

PLUS de 12 mois ?

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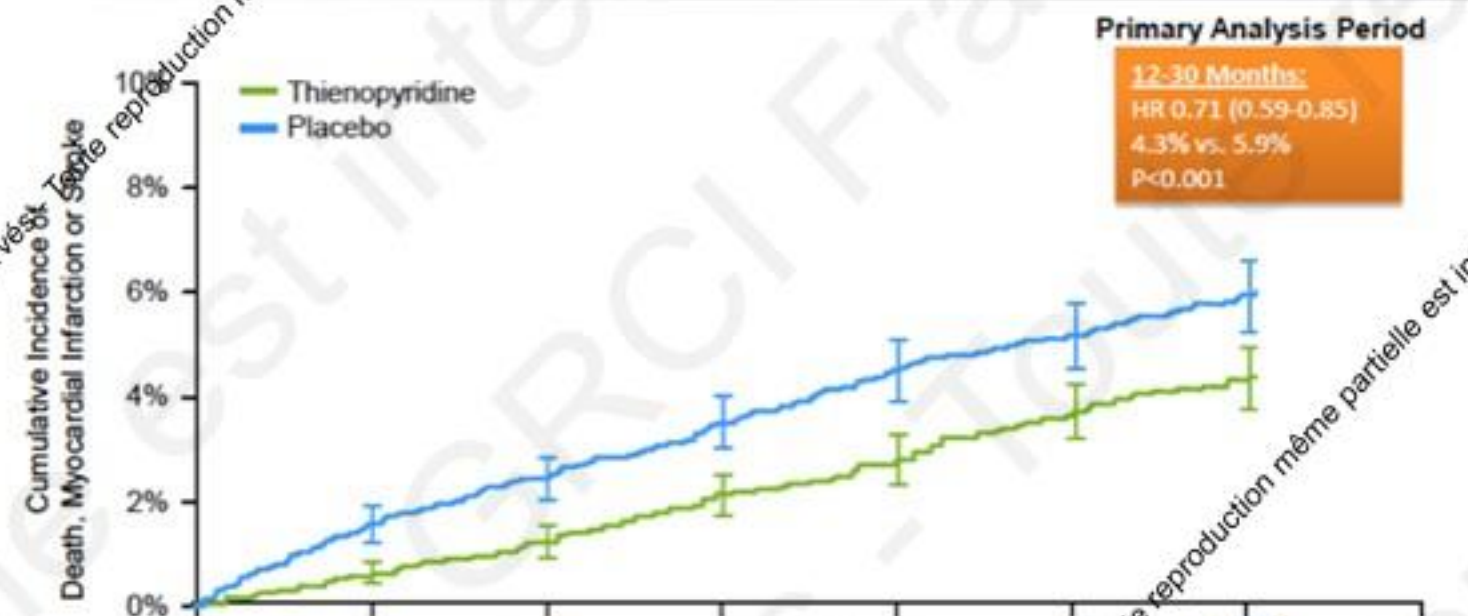
The DAPT trial



# At Risk								
Thienopyridine	5020	4917	4840	4778	4702	4611	4554	3029
Placebo	4941	4799	4715	4635	4542	4476	4412	2997

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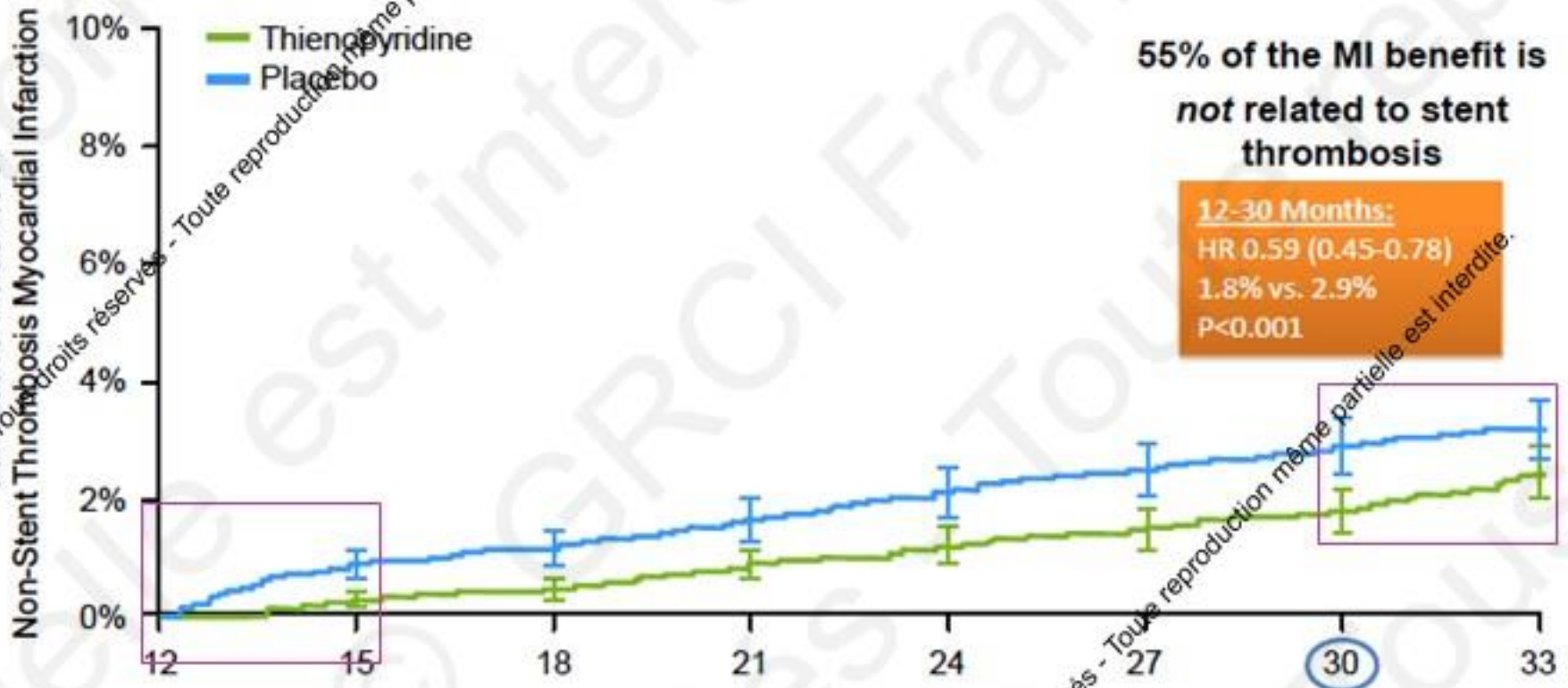
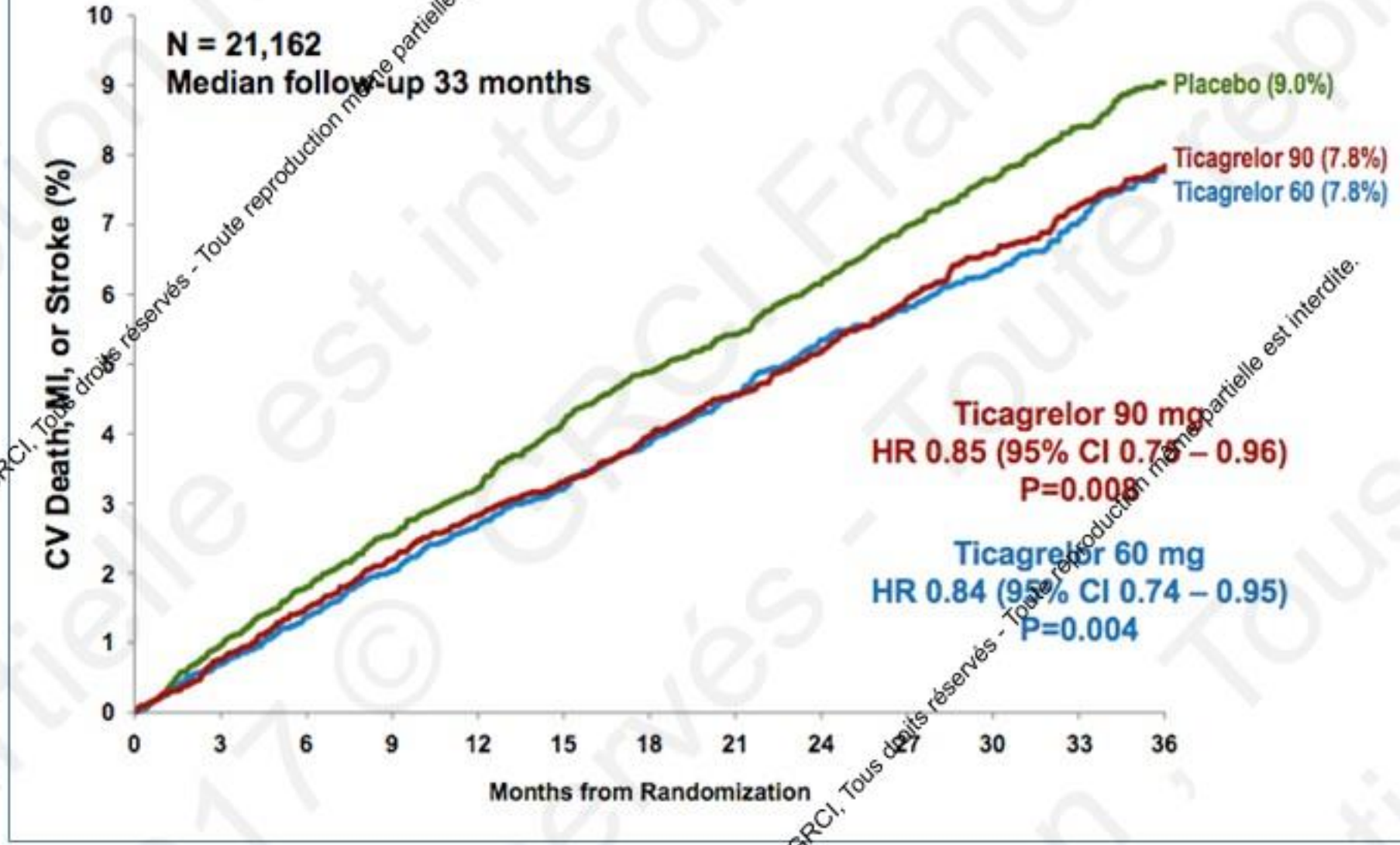
What happened after clopidogrel cessation ?

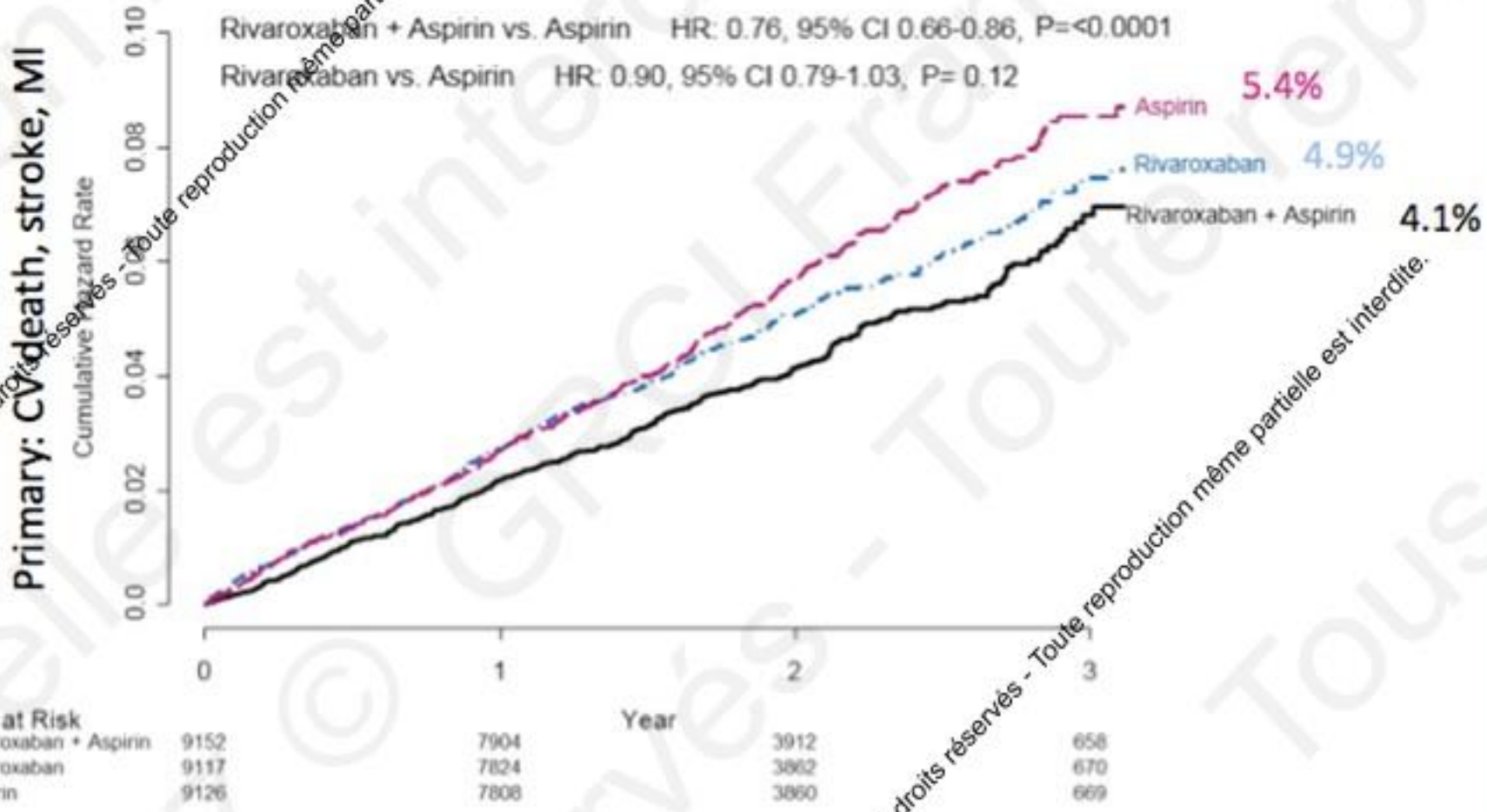


# At Risk								
Thienopyridine	5020	4920	4851	4792	4721	4641	4588	3066
Placebo	4941	4820	4751	4686	4607	4547	4491	3052

The PEGASUS trial

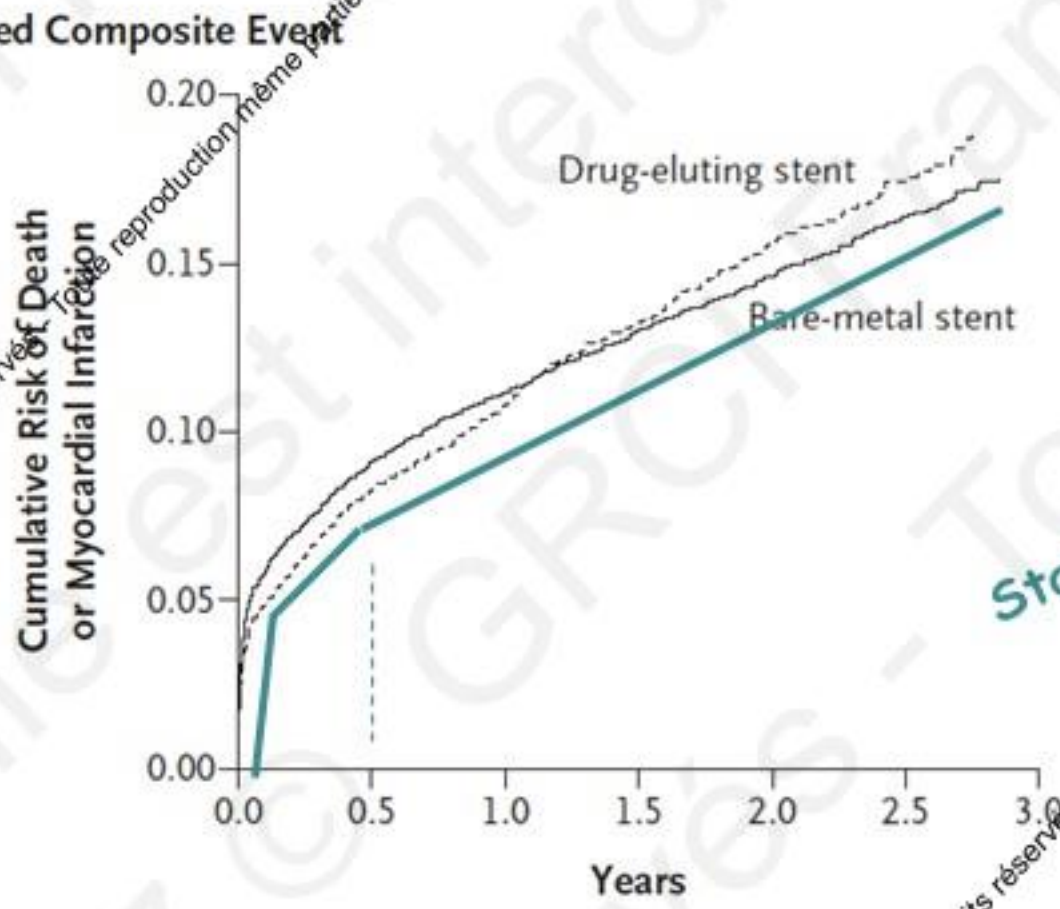


The COMPASS trial



MOINS de 12 mois ?

Natural history after an acute coronary event



Stability at 6 months !!!

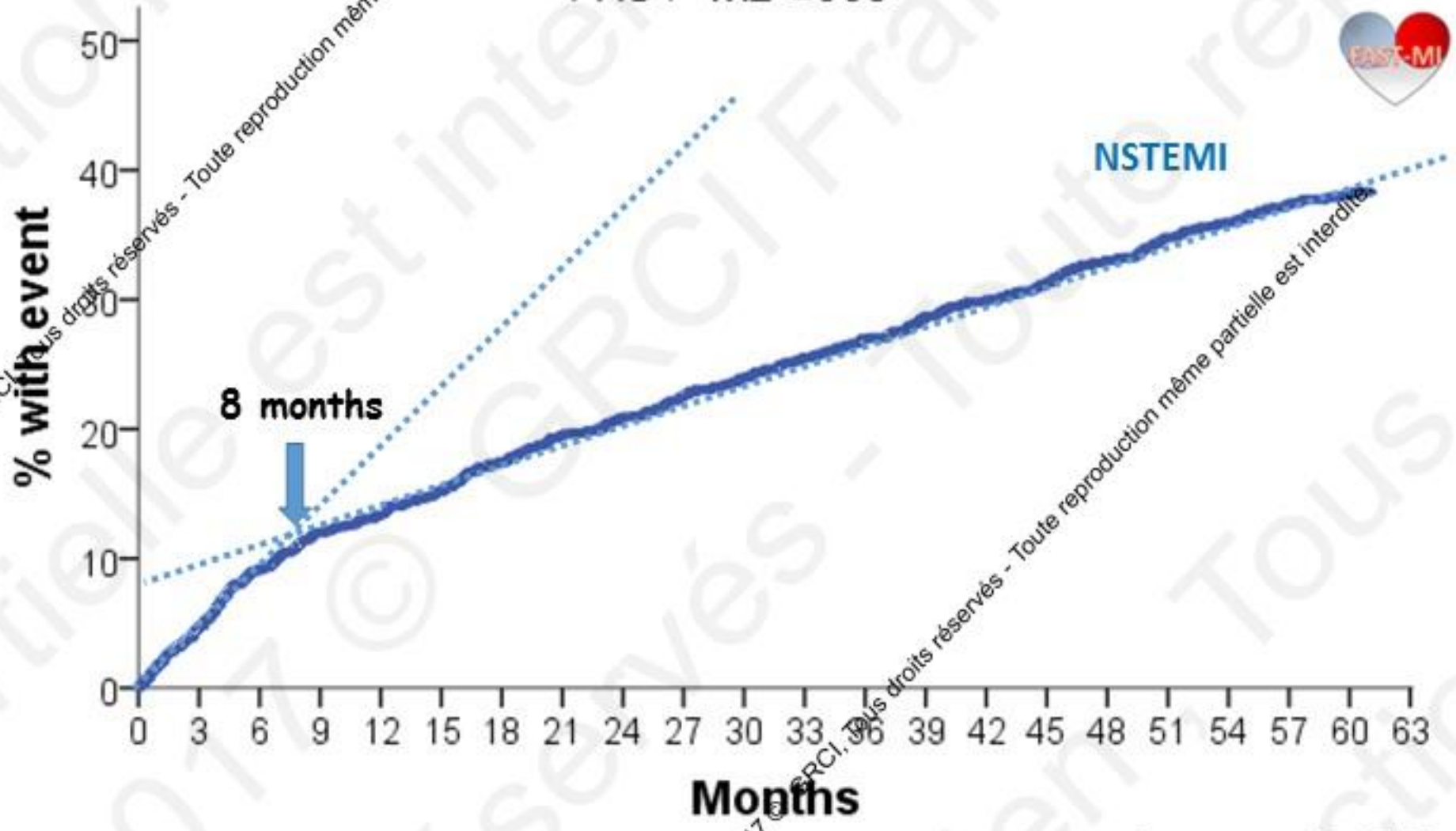
No. at Risk

Bare-metal stent	12,880	11,706	11,432	8665	5520	2963	7
Drug-eluting stent	5,770	5,307	5,158	3216	1608	580	0

Lagerqvist et al. NEJM 2007 SCAAR Registry

Survenue des évènements CV après un infarctus

Décès, re-infarctus, ou AVC à 5 ans après un infarctus.
FAST-MI 2005



Puymirat E. ESC 2015

Survenue des évènements CV après un infarctus

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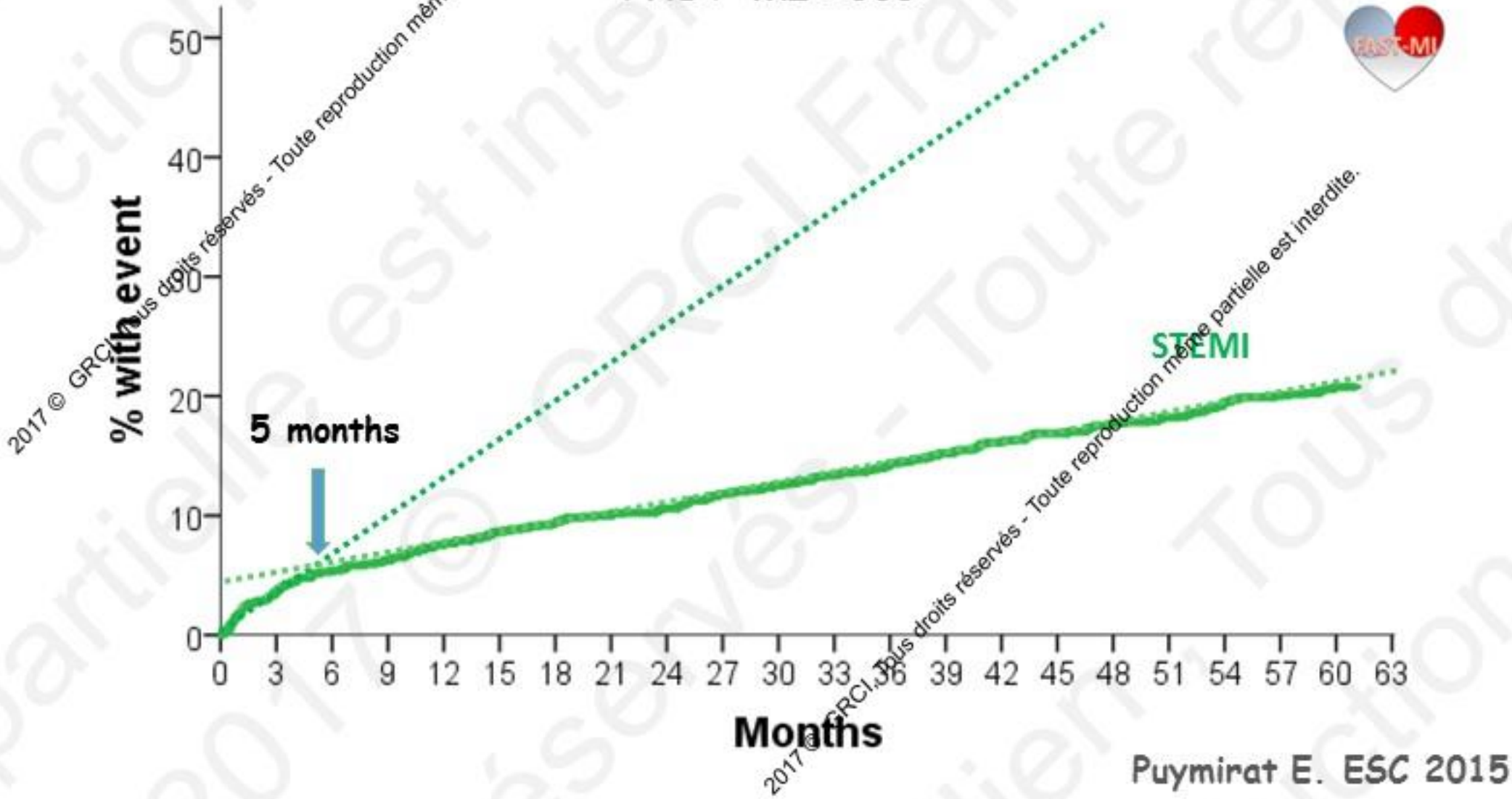
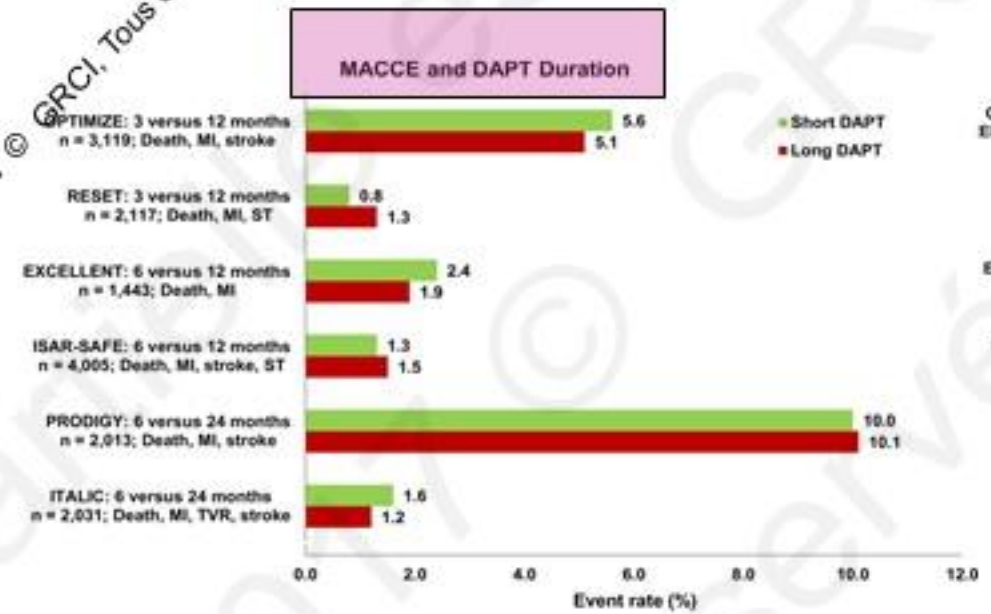
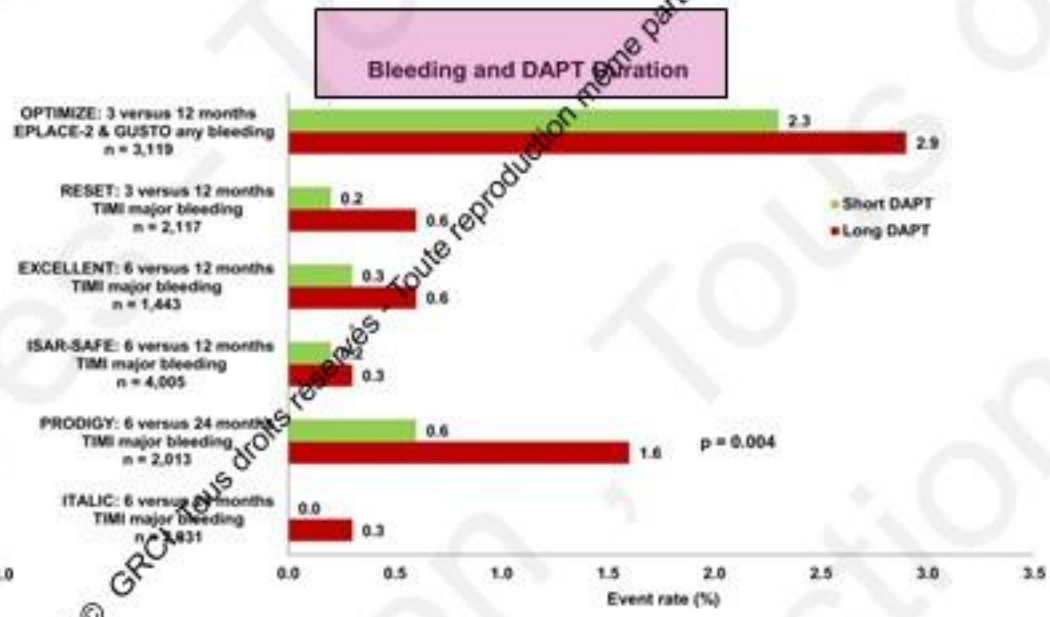


Puymirat E. ESC 2015

Randomized studies

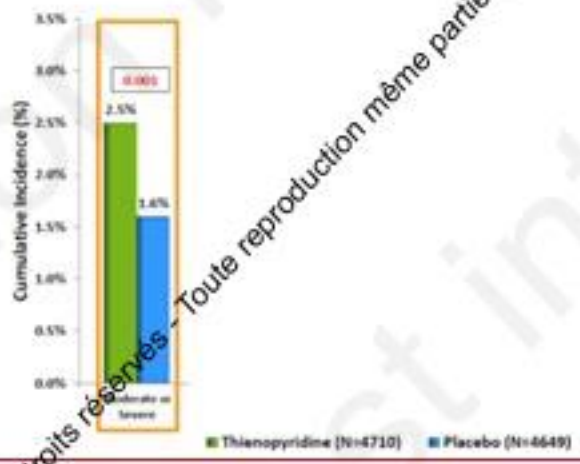
- EXCELLENT (1443 patients – 6 mois vs 12 mois) ≈50% IDM
- OPTIMIZE (3119 patients – 3 mois vs 12 mois) ≈ 5% IDM
- SECURITY (1404 patients – 6 mois vs 12 mois) => Aucun IDM
- RESET (2148 patients – 3 mois vs 12 mois) ≈15% IDM
- PRODIGY (2013 patients – 6 vs 24 mois) ≈50% IDM
- ISAR-SAFE (4005 patients – 6 mois vs $9_{/12}$ mois) ≈20% IDM
- ITALIC (2031 patients – 6 mois vs $12_{/24}$ mois) ≈7% IDM
- I-LOVE-IT-2 (1829 patients – 6 mois vs 12 mois) ≈25% IDM
- IVUS-XPL (1400 patients – 6 mois vs 12 mois) ≈15% IDM
- NIPPON (3773 patients – 6 mois vs 18 mois) ≈15% IDM



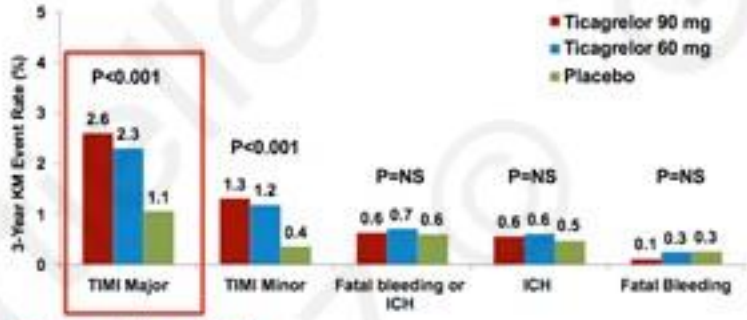


Binder et al. Eur Heart J 2015;36:1207-1211

The DAPT trial



The PEGASUS trial



Primary safety endpoint

Ticag 90: HR 2.69 (1.96-3.70)

Ticag 60: HR 2.32 (1.68-3.21)

The COMPASS trial

Outcome	R + A N=9,152	R N=9,117	A N=9,126	Rivaroxaban + Aspirin vs. Aspirin		Rivaroxaban vs. Aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	P	HR (95% CI)	P
Major bleeding	288 (3.1%)	255 (2.8%)	170 (1.9%)	1.70 (1.40-2.05)	<0.0001	1.51 (1.25-1.84)	<0.0001
Fatal	15 (0.2%)	14 (0.2%)	10 (0.1%)	1.49 (0.67-3.33)	0.32	1.40 (0.62-3.15)	0.41
Non fatal ICH*	21 (0.2%)	32 (0.4%)	19 (0.2%)	1.10 (0.59-2.04)	0.77	1.69 (0.96-2.98)	0.07
Non-fatal other critical organ*	42 (0.5%)	45 (0.5%)	29 (0.3%)	1.45 (0.88-2.29)	0.14	1.57 (0.98-2.50)	0.06

* symptomatic

COMMENT DECIDER ?

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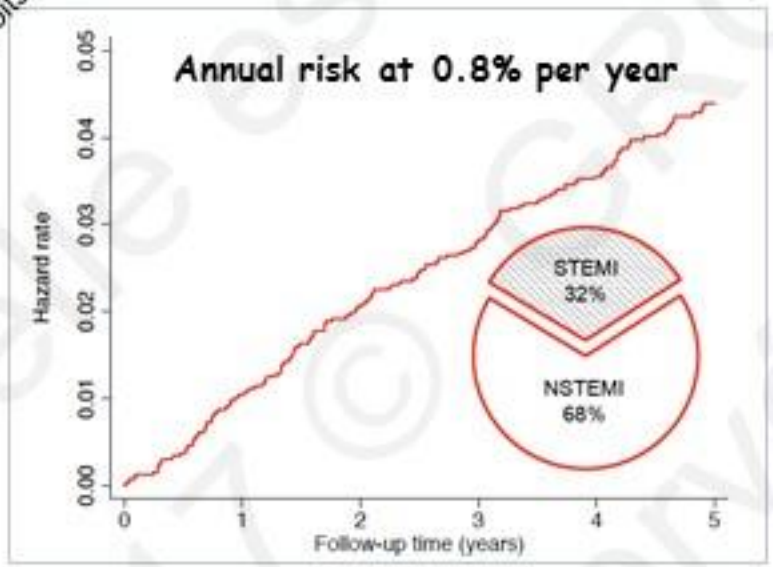
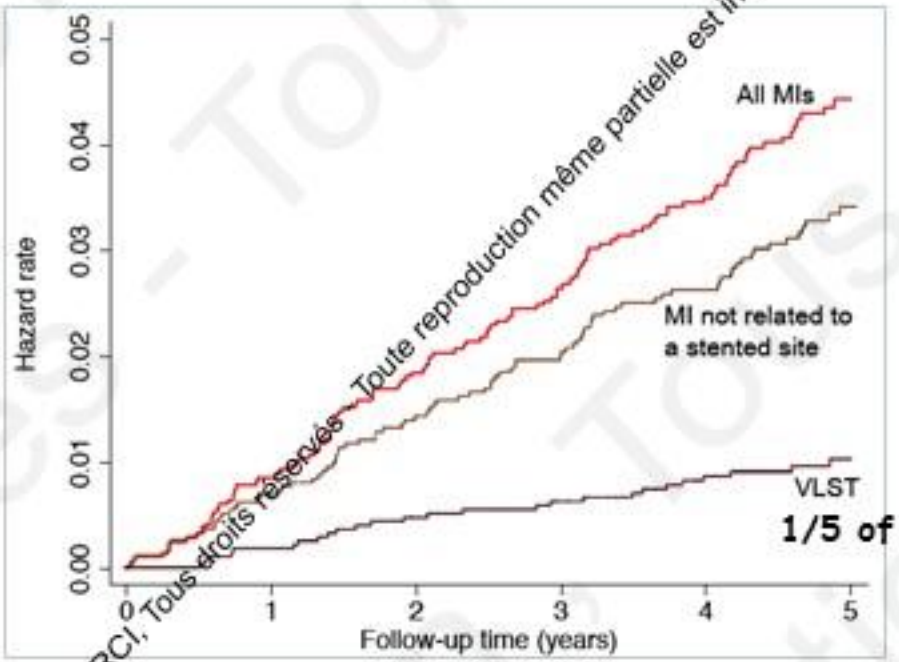
Sur quels critères décider ?

- La notion de risque résiduel du coronarien stable ... Le stent ou la maladie

Registre CORONOR

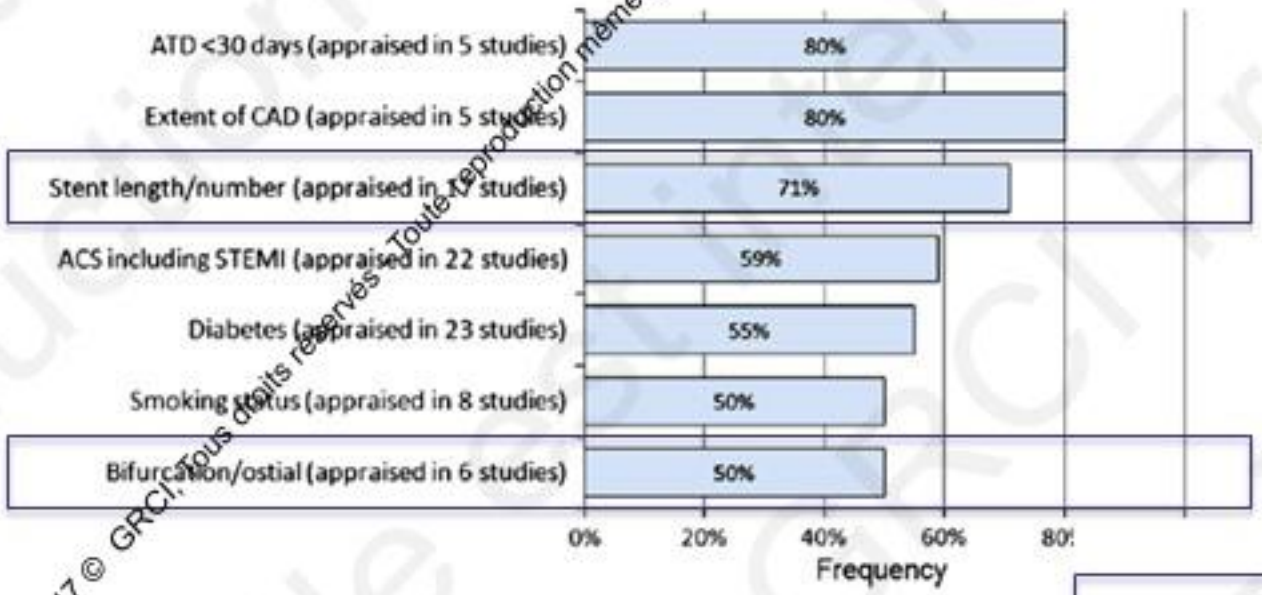




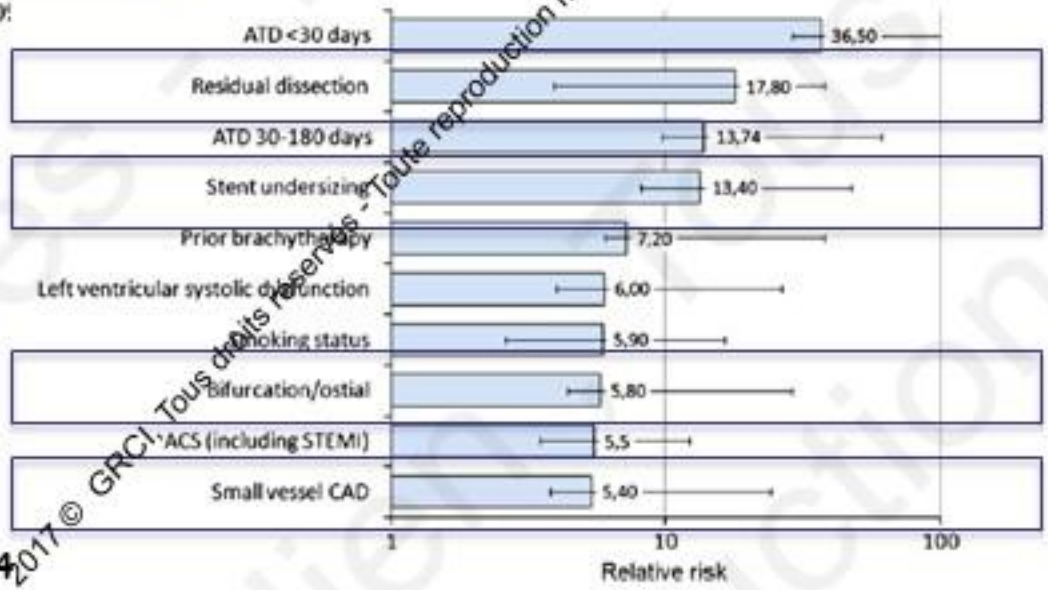
Lemesle et al. JACC 2017 in press

Evaluer le risque de TS très tardive

Les plus fréquents

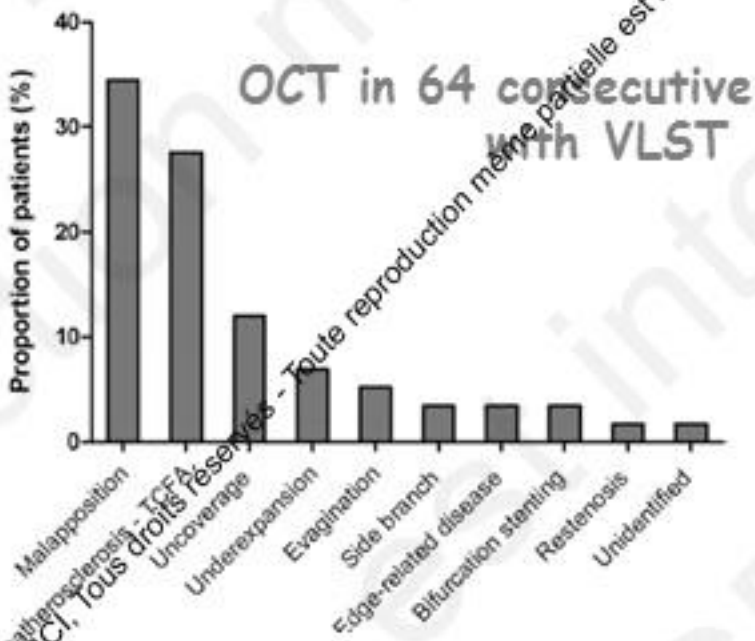


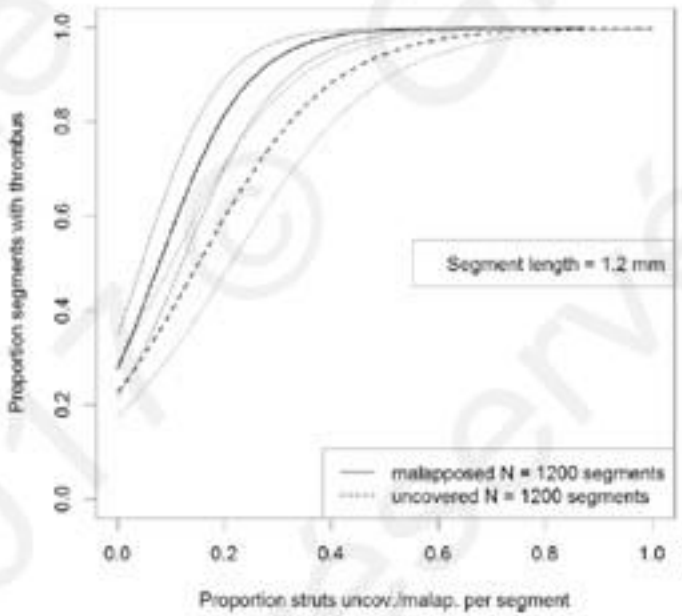
Les plus puissants

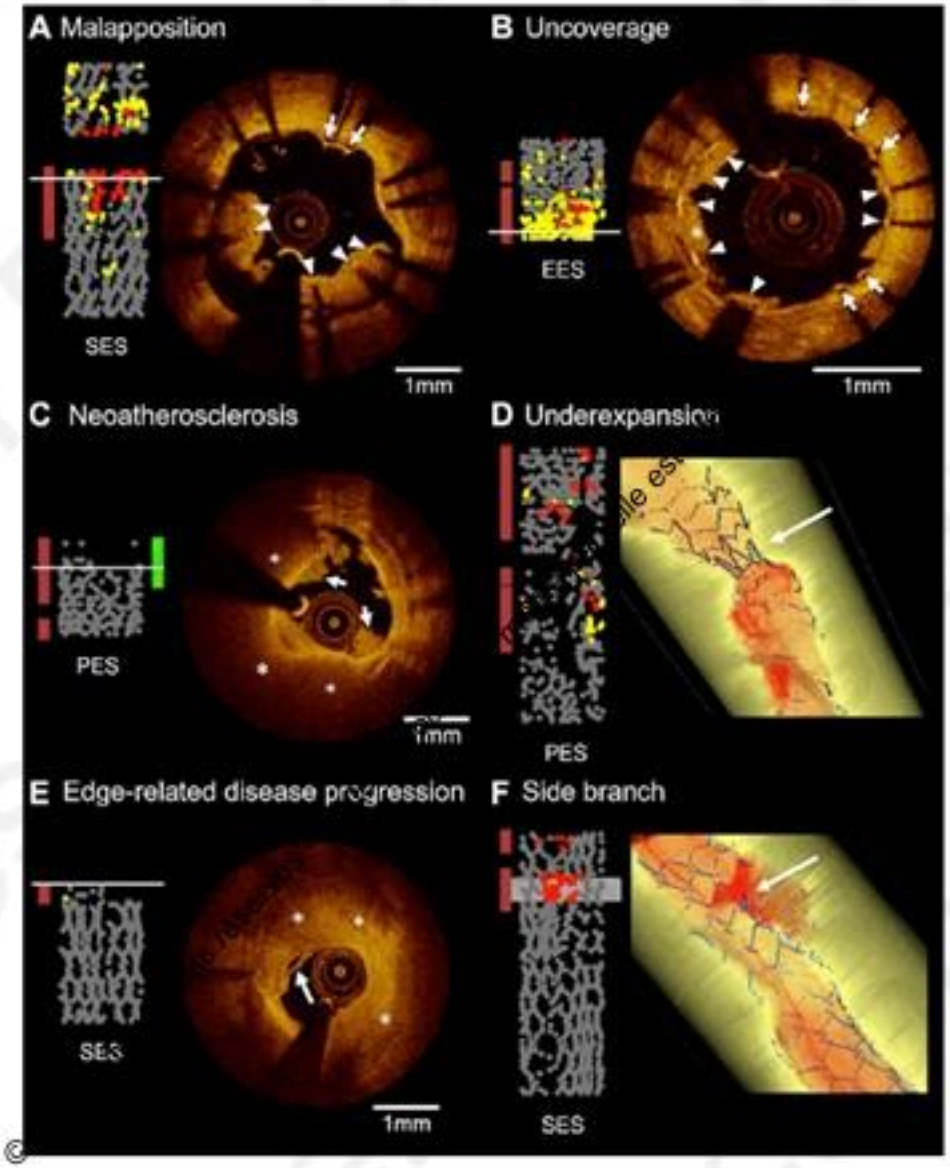


D'Ascenzo et al. IJC 2013 Jul 31;167(2):575-84

La mal-apposition dans 1/3 des cas





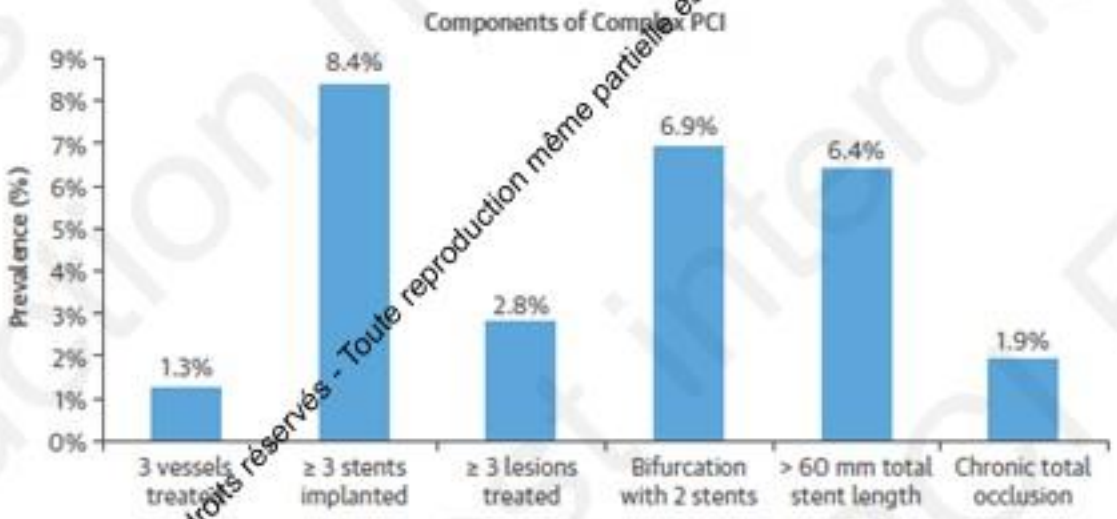


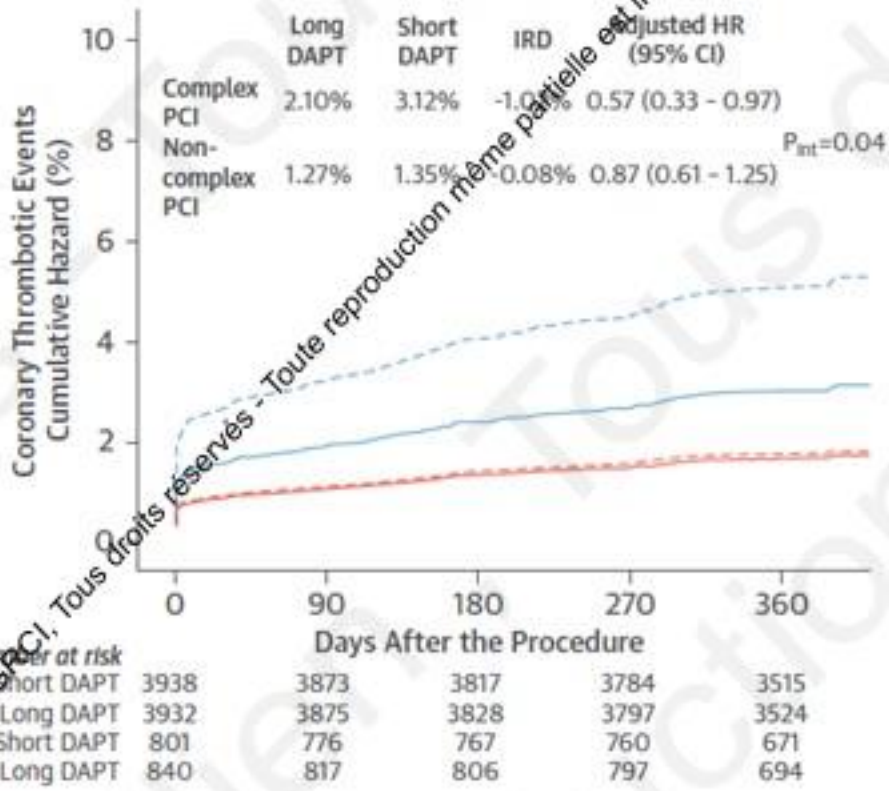
Taniwaki et al. Circulation. 2016;133:650-660

Une meta-analyse

6 Studies

- SECURITY
- PRODIGY
- ITALIC
- EXCELLENT
- OPTIMIZE
- RESET





Giustino et al. J Am Coll Cardiol 2016;68:1851-64

Sur quels critères décider ?

- La notion de risque résiduel du coronarien stable …

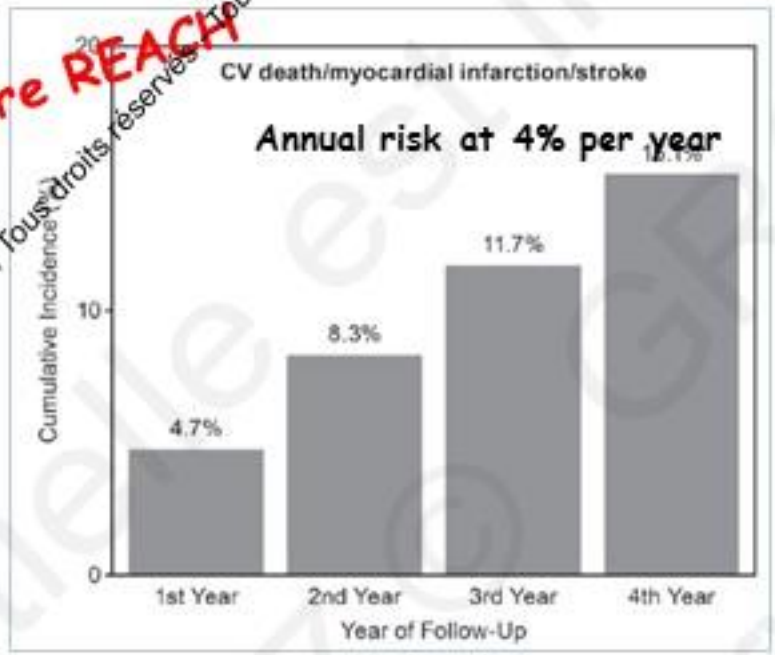
Registre CORONOR

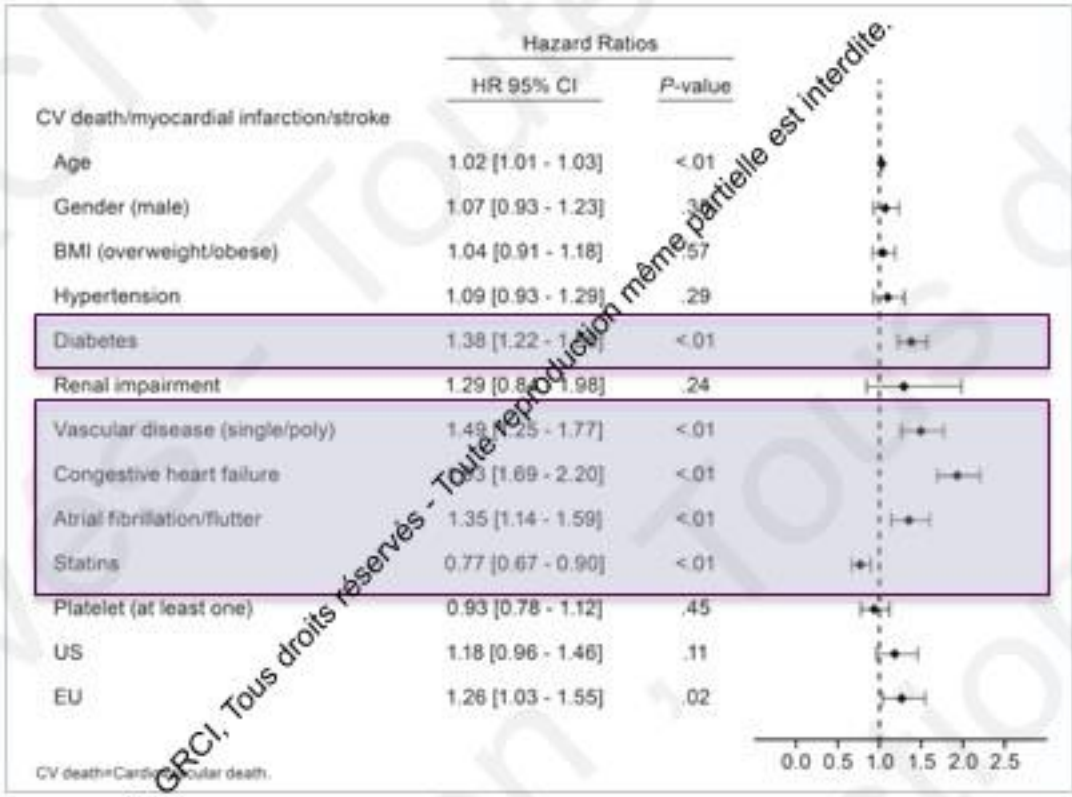
Variable	SHR	95% CI	p value
Current smoker	1.87	1.27 – 2.77	0.002
LDL-cholesterol (per 10 mg/dL)	1.06	1.02 – 1.11	0.007
Prior coronary bypass	0.53	0.32 – 0.86	0.011
Multi-vessel CAD	1.53	1.08 – 2.15	0.015
Diabetes mellitus with HbA1c > 7%	1.62	1.09 – 2.40	0.016
Persistent angina at inclusion	1.70	1.06 – 2.73	0.028

Lemesle et al. JACC 2017 in press

Sur quels critères décider ?

- La notion de risque résiduel du coronarien stable ...





Abran et al. Clinical Cardiology 2016; 39(11):670-677

Sur quels critères décider ?

- Evaluer le risque hémorragique du coronarien stable

Registre REACH

Table 1 Bleeding risk score sheet

Factor	Points			
Age, years	45–54 0	55–64 2	65–74 4	75 + 6
Peripheral arterial disease	No 0	Yes 1		
Congestive heart failure	No 0	Yes 2		
Diabetes	No 0	Yes 1		
Hypercholesterolaemia	No 1	Yes 0		
Hypertension	No 0	Yes 2		
Smoking	Never 0	Former 1	Current 2	
Antiplatelet agents	None 0	ASA 1	Other 2	Both 4
Oral anticoagulants	No 0	Yes 4		

ASA, acetylsalicylic acid

Registre CORONOR

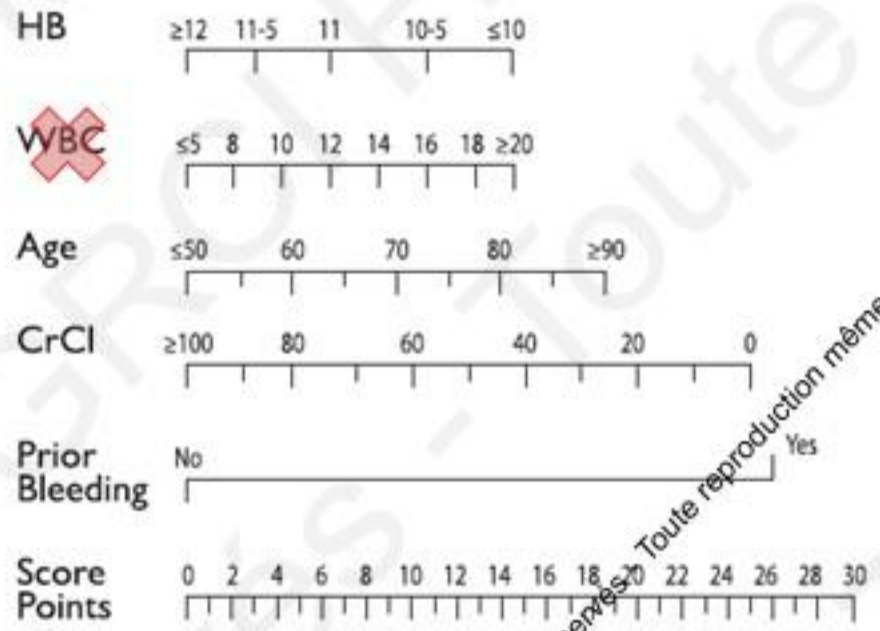
TABLE 3 Multivariate Predictors of Major Bleeding

	Hazard Ratio	95% CI	p Value
Vitamin K antagonists	4.69	2.60-8.44	<0.0001
Diabetes mellitus	2.76	1.54-4.96	0.005
Age (per yr)	1.04	1.01-1.08	0.001
eGFR (per ml/min/1.73 m^2)	0.98	0.97-0.99	0.008

Ducrocq et al. Eur Heart J. 2010;31:1257-65

Hanon M, Lemesle G et al., JACC, 2014;64(14):1430-1436

Le score PRECISE-DAPT

Time of use	At the time of coronary stenting
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)
Score calculation[a]	
Score range	0 to 100 points
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT
Calculator	www.precisedaptscore.com

Le score DAPT

Prediction of CV Death, MI, stroke

	Characteristics	Impact on Net Treatment Effect	% of Variation Explained
Bleeding Predictors	Age ≥ 75	-1.2%	6.0%
	Age 65 - < 75	-0.5%	2.1%
	Age < 65 (reference)	-	-
Ischemia Predictors	Prior PCI or MI	1.1%	14.6%
	Stent Diameter < 3 mm	0.9%	10.1%
	CHF or LVEF < 30%	1.9%	9.9%
	MI at Presentation	1.0%	9.6%
	Paclitaxel-Eluting Stent	1.0%	8.8%
	Cigarette Smoker	0.7%	4.3%
	Diabetes	0.6%	4.3%
	Vein Graft PCI	1.6%	3.7%
Bleeding and Ischemia Predictors	Hypertension	0.2%	0.4%
	Renal Insufficiency	0.4%	0.3%
	PAD	-0.1%	0.04%

Conclusion

- Le courrier doit mentionner la durée de 12 mois = stratégie de base selon les recommandations

- Si raccourcissement cela doit être mentionné dans le courrier avec les arguments (ACS vs stable)
- Si nécessité d'une anticoagulation au long cours, la conduite à tenir des premiers mois doit être clairement indiquée

- La décision de prolonger ou pas le traitement ne peut à mon sens n'être prise qu'au delà de 6-12 mois en raison des variables qui affectent cette décision
- Elle doit être réévaluée à chaque consultation