

EXCELSIOR **LOAD**

**Randomized comparison of periinterventional platelet inhibition
of different thienopyridine loading strategies in patients
undergoing elective coronary intervention**

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Objective

...to test to what extent loading with prasugrel can provide a more rapid peri-interventional antiplatelet effect than clopidogrel 600mg.

Study design

- Three-armed, controlled PROBE (Prospective, Randomized, Open, Blinded End-points) Phase IIIb trial with register arm for patients already pretreated with clopidogrel.
- Randomization to loading with clopidogrel 600mg, prasugrel 30mg or prasugrel 60mg in a 1:1:1 fashion
- 100 patients per randomized group.
- Primary endpoint: proportion of patients with high on-treatment platelet reactivity (≥ 468 AU x min; Multiplate Test, Roche Diagnostics)
- Clinical safety endpoints: ischemic events (mortality, myocardial infarction, urgent revasc., stroke) and bleeding events (BARC 2-5).

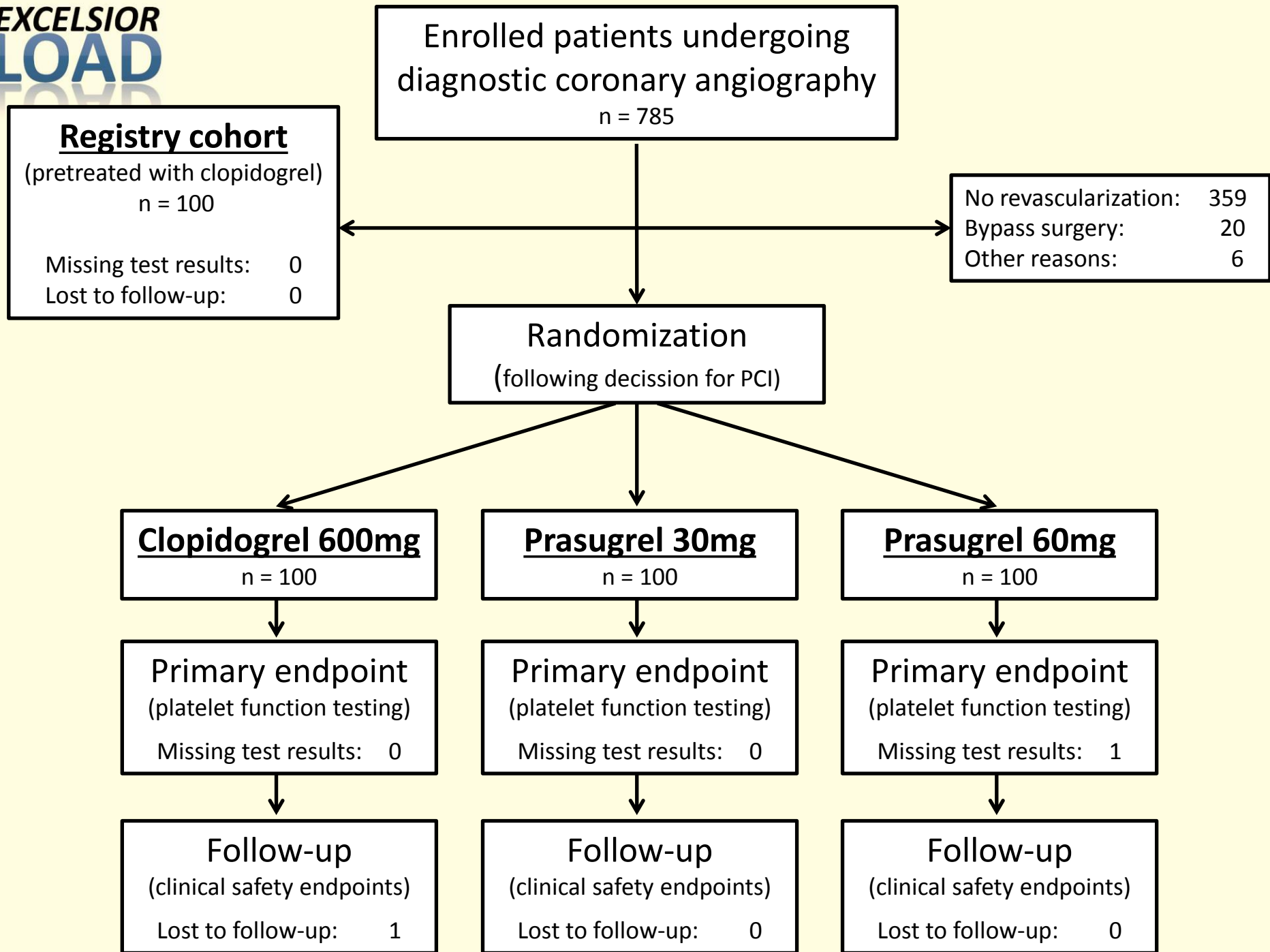
Key inclusion/exclusion criteria

Inclusion criteria:

- Stable patients with obstructive coronary heart disease and planned coronary stent implantation.
- Pretreatment with aspirin .
- Age \geq 18 years.

Exclusion criteria:

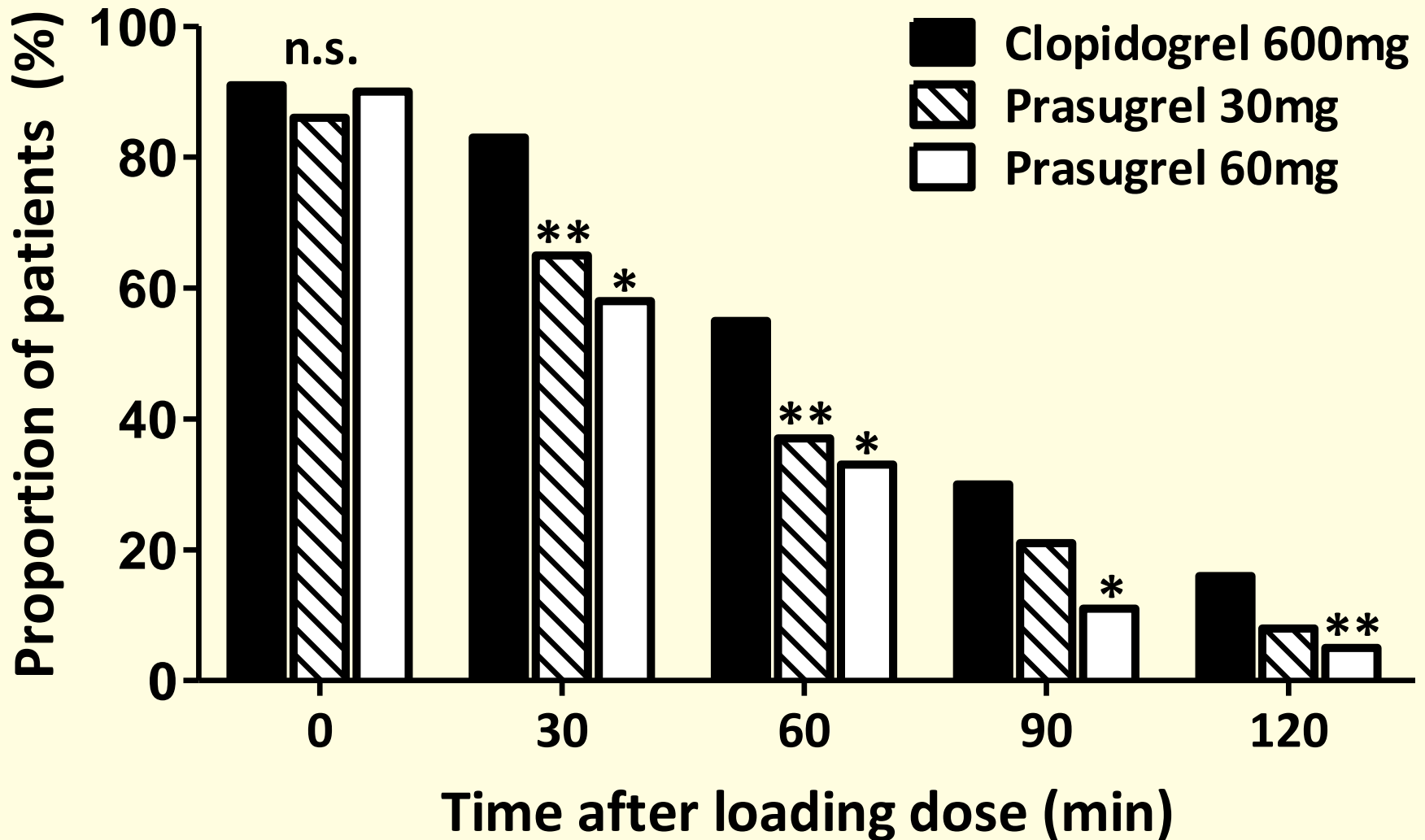
- Acute myocardial infarction
- Treatment with ticagrelor, prasugrel, fibrinolysis, or GP IIb/IIIa inhibitor within 7 days before enrollment.
- Contraindication for treatment with aspirin, clopidogrel, or prasugrel.
- Current oral anticoagulation.
- Severe thrombocytopenia ($< 50.000/\mu\text{l}$).
- Known severe disorder of the coagulation system.



Baseline Characteristics

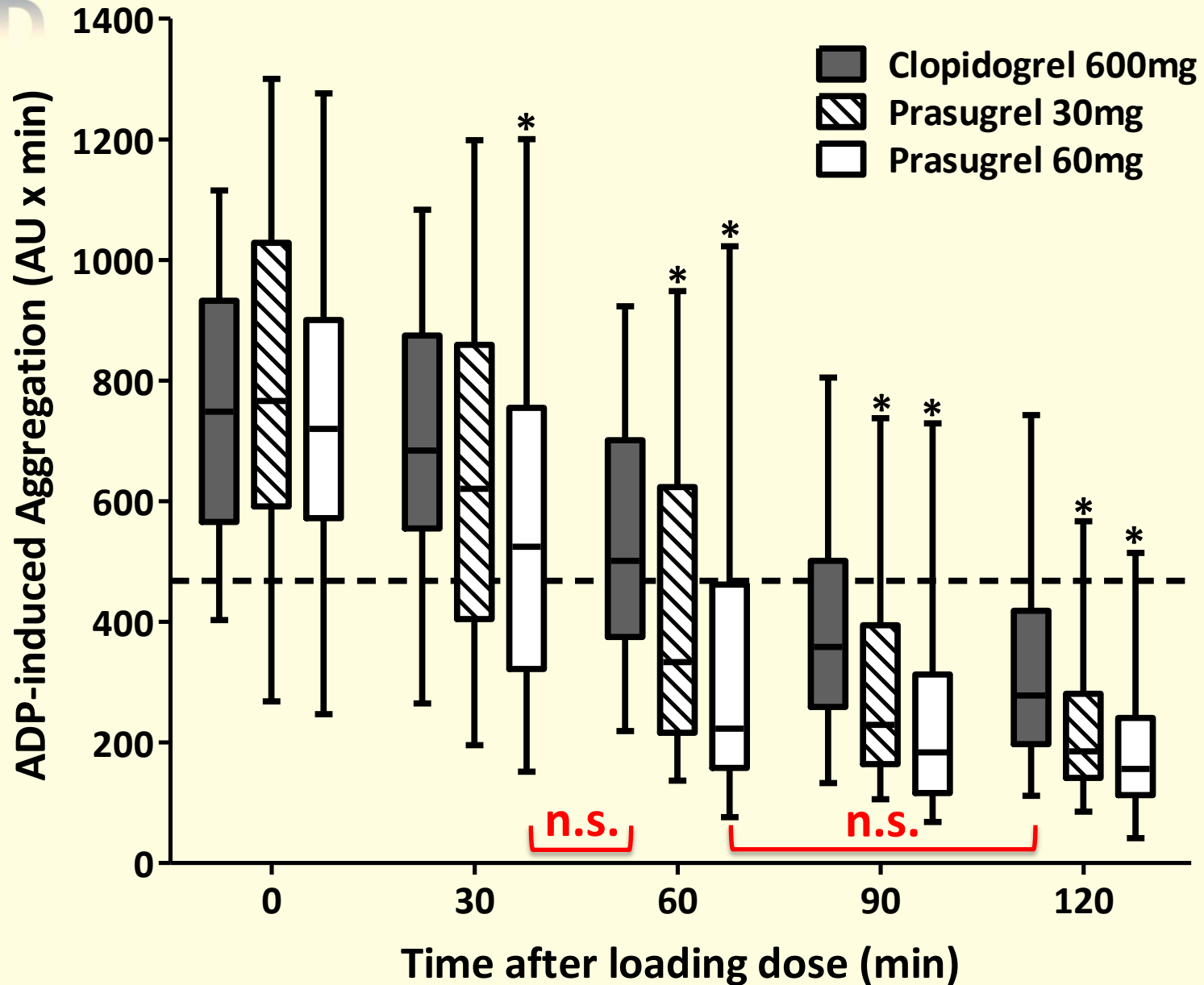
	Clopidogrel 600mg	Prasugrel 30mg	Prasugrel 60mg
	n = 100	n = 100	n = 100
Age (years)	68 (60-74)	70 (64-76)	68 (59-75)
Male	78	79	85
Active smoker	6	6	6
Arterial hypertension	83	76	81
Hypercholesterolemia	84	76	82
Diabetes mellitus	27	25	26
Body mass index (kg/m ²)	27.7 (25.6-30.2)	27.4 (25.3-30.4)	27.7 (25.2-30.1)
Previous balloon angioplasty	33	43	51
Previous CABG	14	7	18
Previous myocardial infarction	14	18	19
Reduced LV ejection fraction	17	28	21
Coronary angiography result			
1-vessel disease	20	21	14
2-vessel disease	32	28	26
3-vessel disease	48	51	60
Radial access	54	55	55
Vascular closure system used	4	3	2

Proportion of patients with HTPR



*P <0.001; **P <0.025 as compared to Clopidogrel 600mg.

ADP-induced platelet reactivity



*P <0.001 as compared to Clopidogrel 600mg.

Clinical safety parameters

	Clopidogrel 600mg	Prasugrel 30mg	Prasugrel 60mg
Death	0	0	1
Myocardial infarction	4	4	3
Target vessel revascularization	1	0	1
Ischemic stroke	1	1	0
BARC 2-5 bleeding	5	11	5
BARC 2	5	9	4
BARC 3	0	2	1
Location of bleeding			
Vascular access site	5	8	3
Epistaxis	0	0	1
Hematuria	0	2	0
Gastrointestinal	0	1	0
Pericardial	0	0	1

Conclusions

In stable patients undergoing PCI, loading with 60mg of prasugrel is already after 30min significantly more effective than loading with clopidogrel 600mg.

This strategy achieves a similar effect as the full final effect of loading with clopidogrel within 1 hour.

Thus, it might be considered as an option for ad-hoc PCI particularly in high-risk settings.