



Randomized comparison of oral P2Y₁₂-receptor inhibitor loading strategies for transitioning from cangrelor

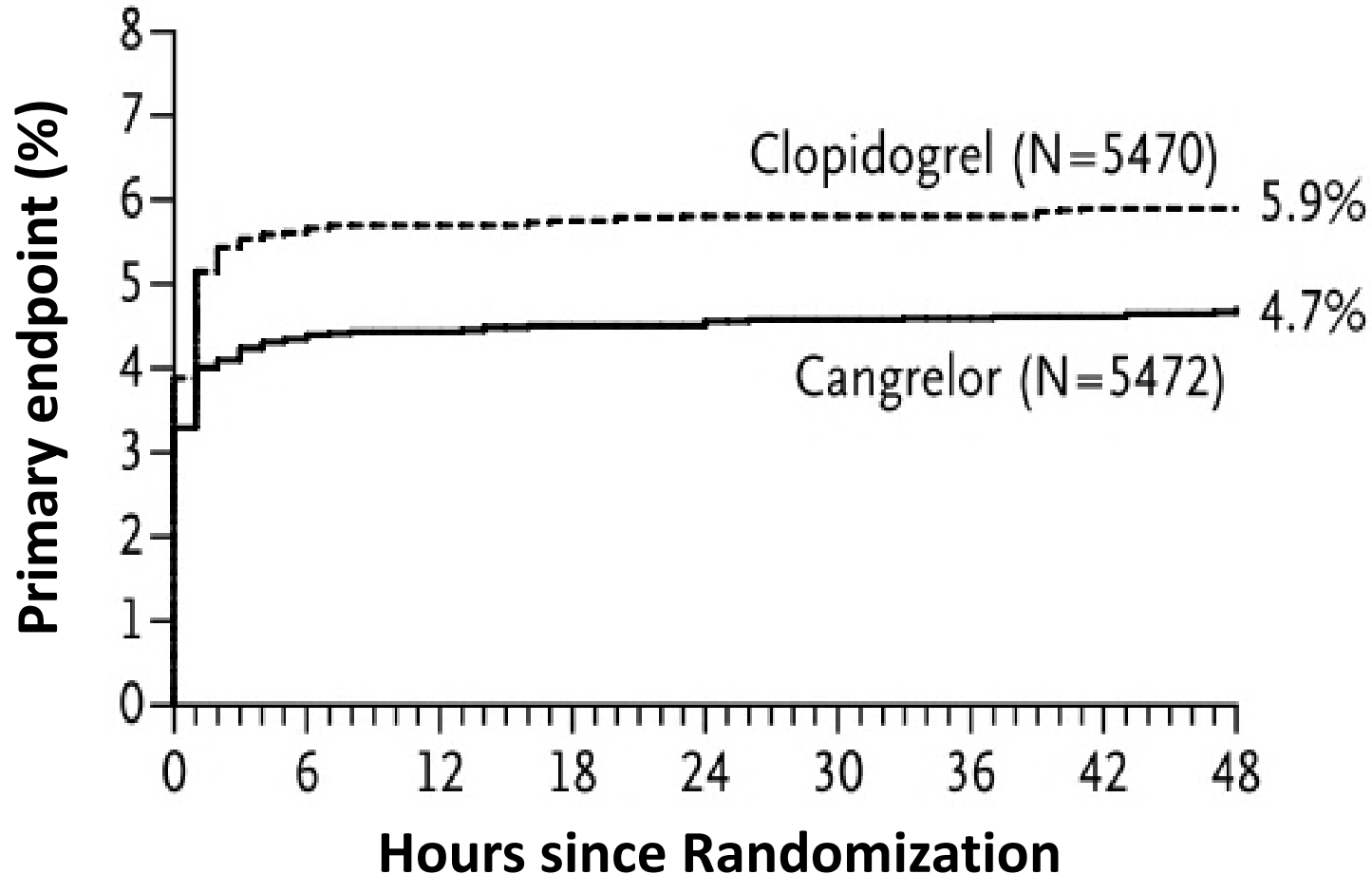
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German Clinical Trial Register ([drks.de](https://www.drks.de), identifier: DRKS00009739)



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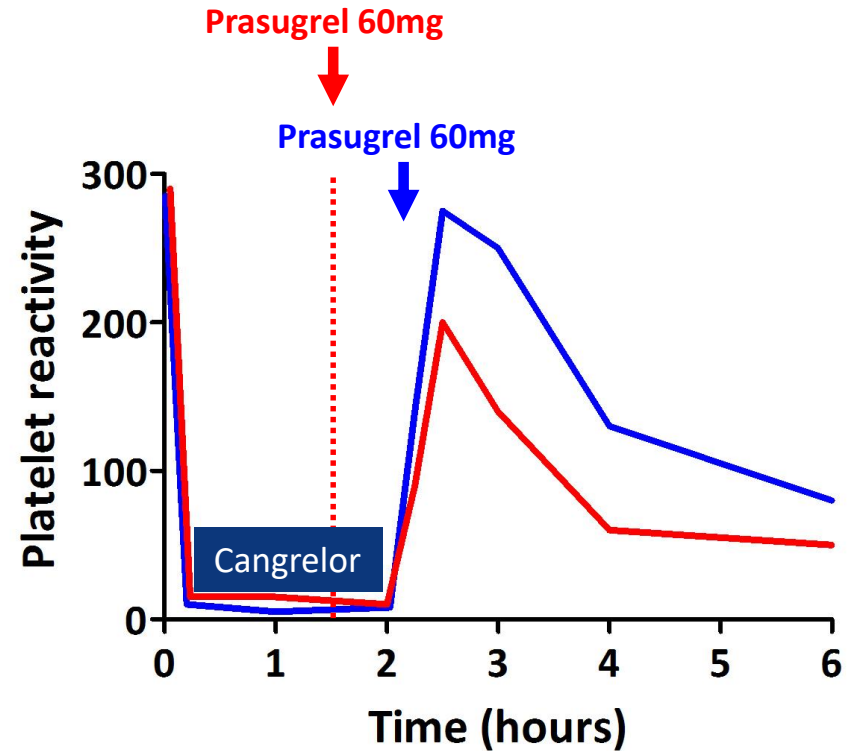
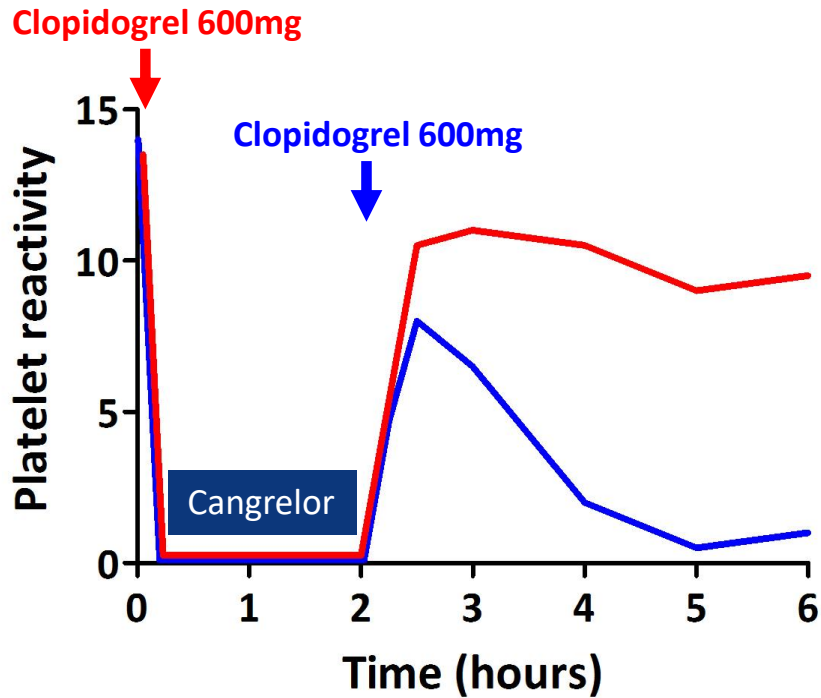
Cangrelor reduces periinterventional events



Primary endpoint (%):

death from any cause, myocardial infarction, ischemia-driven revasc., stent thrombosis

Cangrelor interacts with thienopyridines

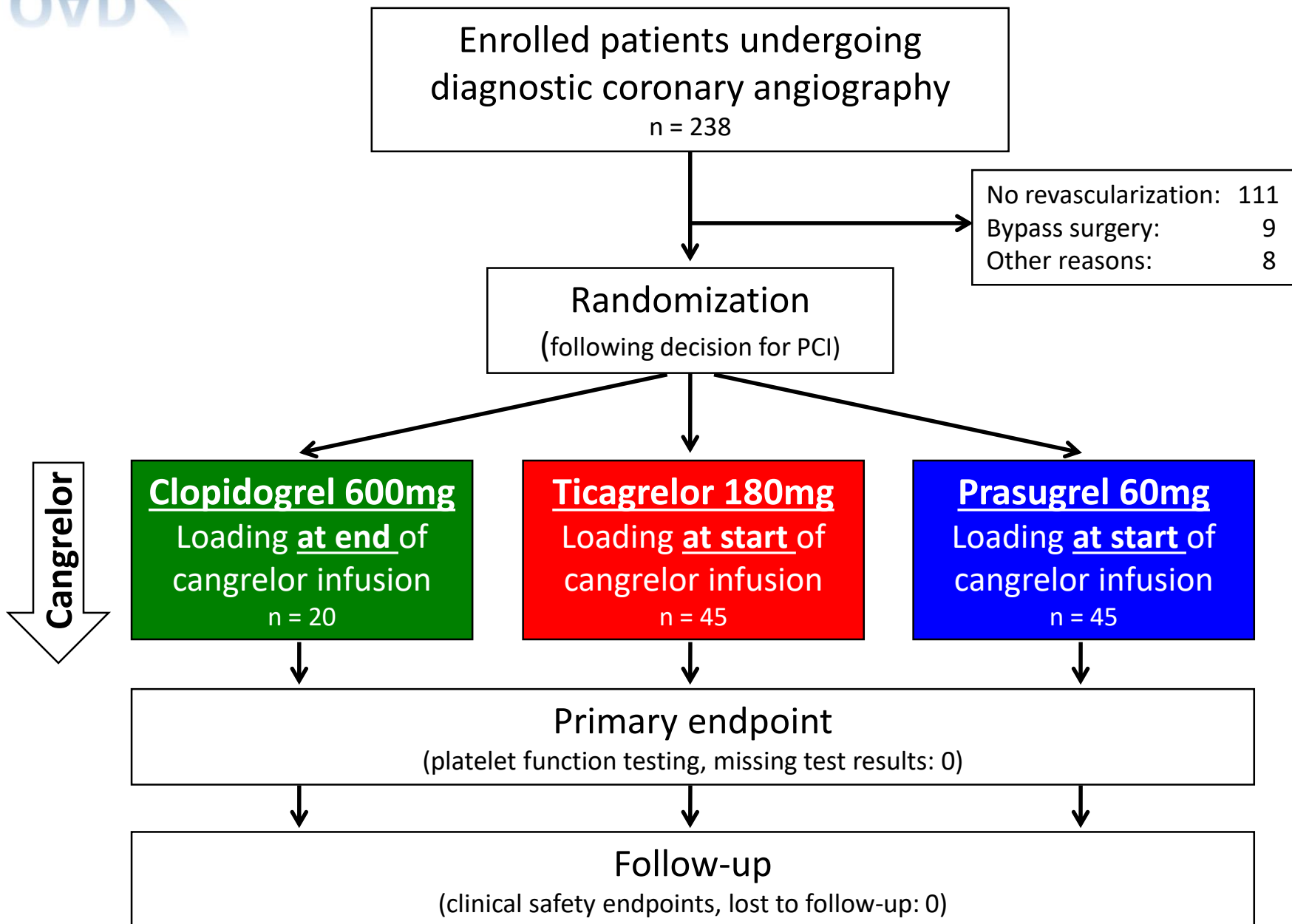


Half-life of active metabolite of prasugrel is supposed to be longer than average infusion time of cangrelor...

...to test if early loading with prasugrel can provide sufficient platelet inhibition even when given at the start of a 2-hour infusion of cangrelor.

- Three-armed, controlled PROBE (Prospective, Randomized, Open, Blinded End-points) Phase IIIb trial.
- P2Y₁₂-receptor blocker naive patients undergoing PCI with use of cangrelor
- Randomization to loading with prasugrel 60 mg or ticagrelor 180mg at start of cangrelor (n=45 each) or loading with clopidogrel 600mg after discontinuation of cangrelor (n=20).
- Primary endpoint: proportion of patients with high on-treatment platelet reactivity 1 hour after stop of cangrelor (≥468 AU x min; Multiplate Test, Roche Diagnostics)
- Clinical safety endpoints: ischemic events (mortality, myocardial infarction, urgent revasc., stroke) and bleeding events (BARC 3-5).

Trial design



Key inclusion criteria:

- Hemodynamically stable patients with planned coronary stent implantation and use of cangrelor.
- Pretreatment with aspirin.

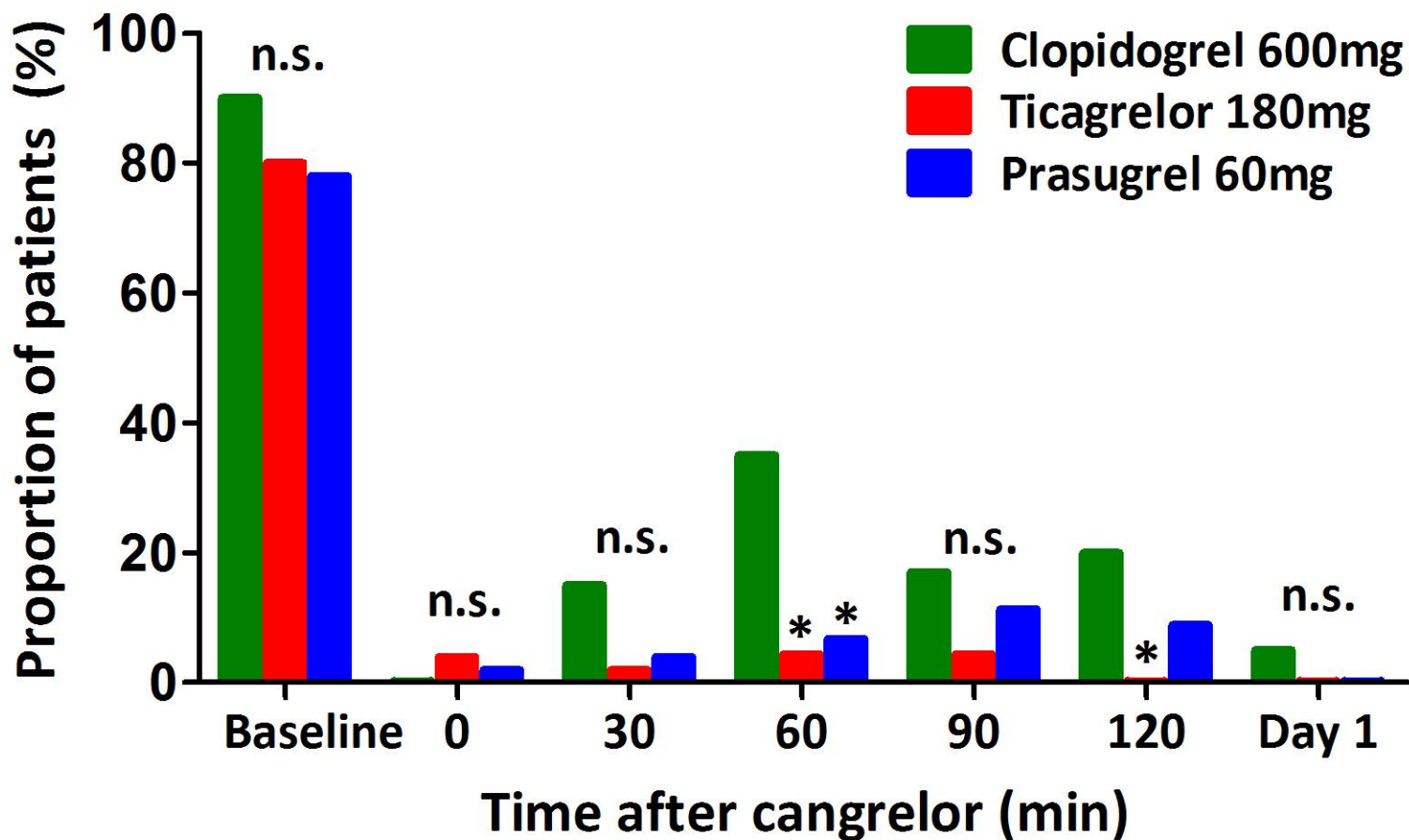
Key exclusion criteria:

- Acute myocardial infarction.
- P2Y12-receptor inhibitor, fibrinolysis, or GP IIb/IIIa inhibitor within 7 days before enrollment.
- Contraindication for treatment with aspirin, cangrelor, clopidogrel, ticagrelor or prasugrel according to EMEA label.
- Known severe disorder of the coagulation system.

Baseline characteristics

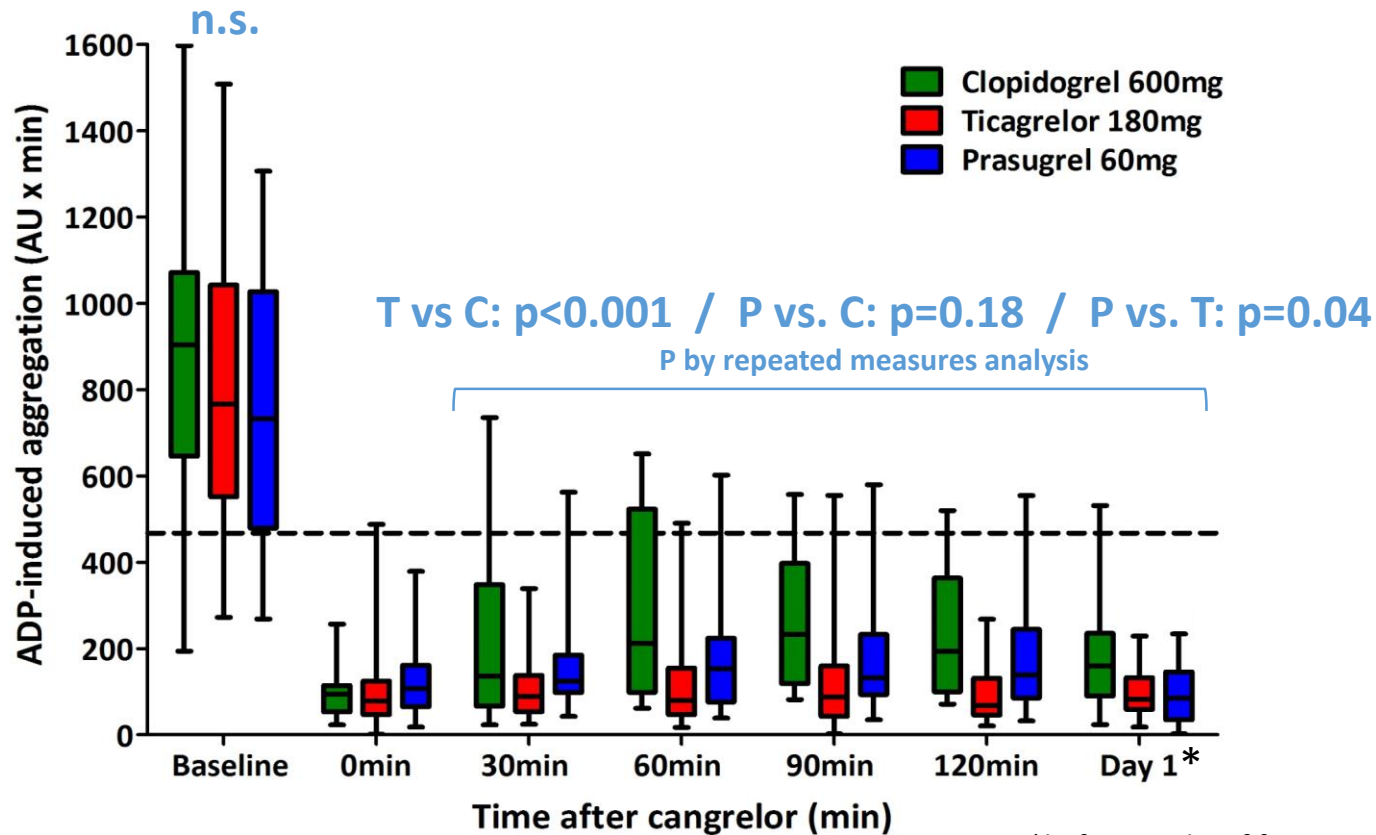
	Clopidogrel 600mg	Ticagrelor 180mg	Prasugrel 60mg
	n = 20	n = 45	n = 45
Age (years)	69 (62-76)	69 (63-75)	70 (61-75)
Female	7 (35%)	10 (22%)	8 (18%)
Active smoker	4 (20%)	5 (11%)	7 (16%)
Arterial hypertension	16 (80%)	36 (80%)	38 (84%)
Hypercholesterolemia	17 (85%)	43 (96%)	38 (84%)
Diabetes mellitus	5 (25%)	10 (22%)	9 (20%)
Body mass index (kg/m ²)	28.4 (25.3-32.8)	27.8 (24.8-30.3)	28.0 (25.5-31.0)
Previous balloon angioplasty	5 (25%)	17 (38%)	13 (29%)
Previous CABG	3 (15%)	6 (13%)	8 (18%)
Previous myocardial infarction	2 (10%)	5 (11%)	4 (9%)
Reduced LV ejection fraction	3 (15%)	10 (22%)	7 (16%)
Coronary angiography result			
1-vessel disease	6 (30%)	10 (22%)	12 (27%)
2-vessel disease	6 (30%)	12 (27%)	11 (24%)
3-vessel disease	8 (40%)	23 (51%)	22 (49%)
Radial access	12 (60%)	35 (78%)	34 (76%)
Sheath size >6 French	1 (5%)	2 (4%)	2 (4%)

Less patients with HTPR



*P < 0.01 as compared to clopidogrel 600 mg.

Stronger platelet inhibition



*before intake of first maintenance dose

*P < 0.01 as compared to clopidogrel 600 mg.

Clinical safety parameters

	Clopidogrel 600mg	Ticagrelor 180mg	Prasugrel 60mg
	n = 20	n = 45	n = 45
Death	0	1 (2.2%)	0
Myocardial infarction	0	2 (4.4%)	5 (11.1%)
BARC 3-5 bleeding			
BARC 3a	1 (5.0%)	1 (2.2%)	1 (2.2%)
BARC 5	0	1 (2.2%)	0
Location of bleeding			
Vascular access site	1 (5.0%)	1 (2.2%)	1 (2.2%)
Hematuria	0	1 (2.2%)	0
Pericardial	0	1 (2.2%)	0

Conclusions

- Loading with prasugrel 60 mg given at the start of a 2-hour infusion of cangrelor can provide a sufficient platelet inhibition post cangrelor despite the known interaction.
- This approach prevents the transient gap in platelet inhibition seen with oral loading with clopidogrel or prasugrel after discontinuation of cangrelor.
- This regimen might be considered as an option for transitioning from cangrelor to oral therapy as an alternate to ticagrelor particularly in high-risk settings.

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The ExcelsiorLOAD2 Trial

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