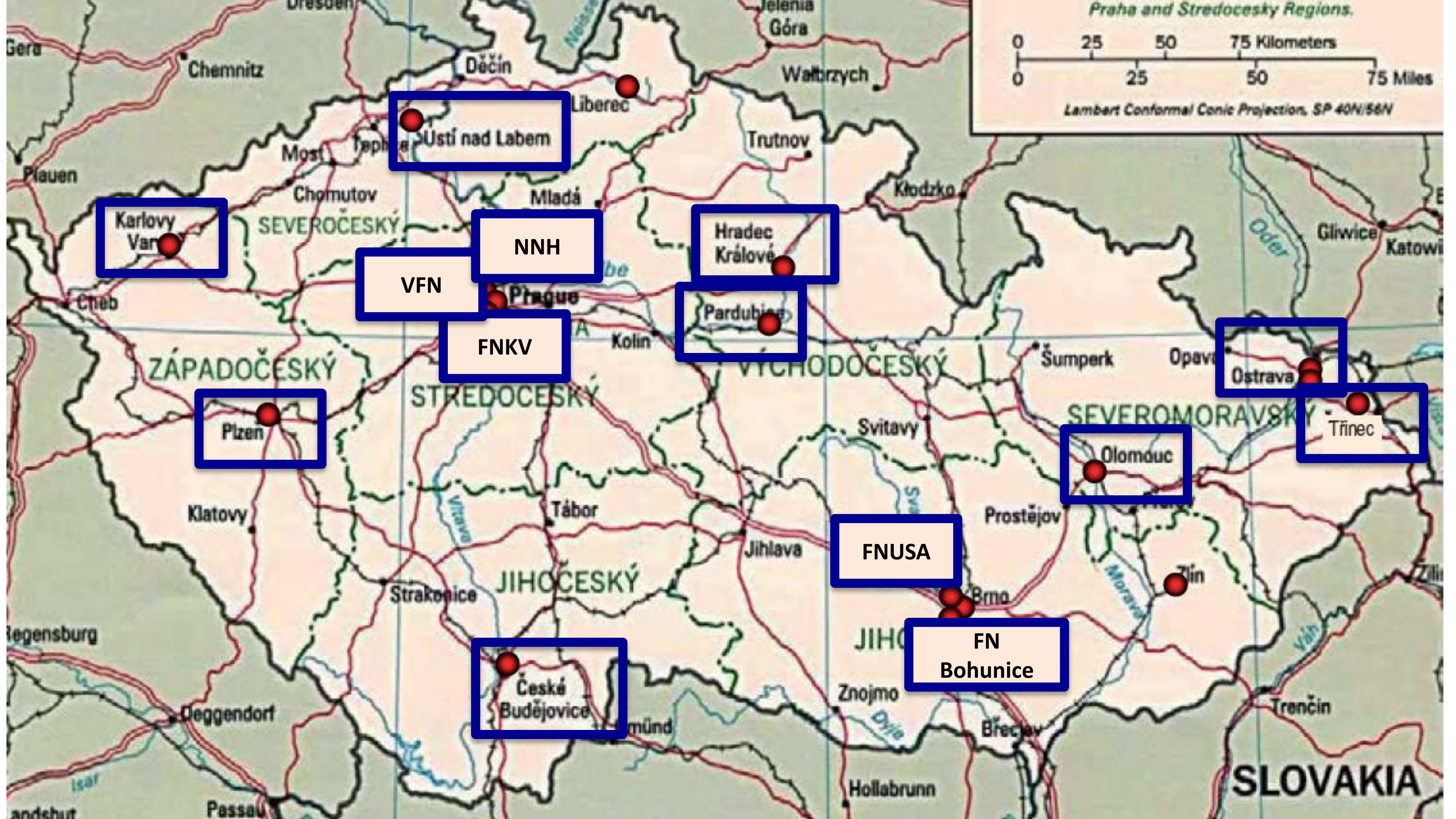
PRAGUE-18 Study: Randomized comparison of ticagrelor versus prasugrel in STEMI

Outcomes during the first month



Praha and Stredocesky Regions
0 25 50 75 Kilometers
0 25 50 75 Miles
Lambert Conformal Conic Projection, SP 40N/56N
Ústí nad Labem
Liberec
Děčín
Chemnitz
Jelenia Góra
Wałbrzych
Trutnov
Most
Chomutov
Mladá
Plauen
Karlovy Vary
SEVEROČESKÝ
NNH
VFN
Prague
FNKV
Hradec Králové
Pardubice
Kolín
Cheb
ZÁPADOČESKÝ
STREDOČESKÝ
VÝCHODOČESKÝ
Šumperk
Opava
Ostrava
Třinec
Kłodzko
Gliwice
Oder
SEVEROMORAVSKÝ
Olomouc
Plzen
Svitavy
Prostějov
Klatovy
Tábor
Jihlava
FNUSA
Zlín
Strakonice
JIHOČESKÝ
Brno
Regensburg
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Study aims

1. „Head-to-head“ comparison of prasugrel vs. ticagrelor in STEMI treated by p-PCI strategy
2. Safety of (economically motivated) post-discharge switch from prasu/tica to clopidogrel.

Entry criteria

Inclusion

- STEMI (or non-STEMI with ongoing ischemia)
- Emergent CAG / pPCI
- Signed informed consent.

Exclusion criteria

- History of stroke
- Serious bleeding during previous 6 months
- Indication for OAC
- Prerandomization clopidogrel ≥300 mg
- Body weight <60 kg in a patient >75 years
- Moderate-to-severe liver disease
- Concomitant treatment with potent CYP3A4 inhibitors
- Known hypersensitivity to prasugrel or ticagrelor.

End-points

Primary end-point:

Combined end-point at 7 days (or at discharge if earlier):

- Death
- Re-infarction
- Stroke
- Major bleeding
- Urgent IRA revascularization

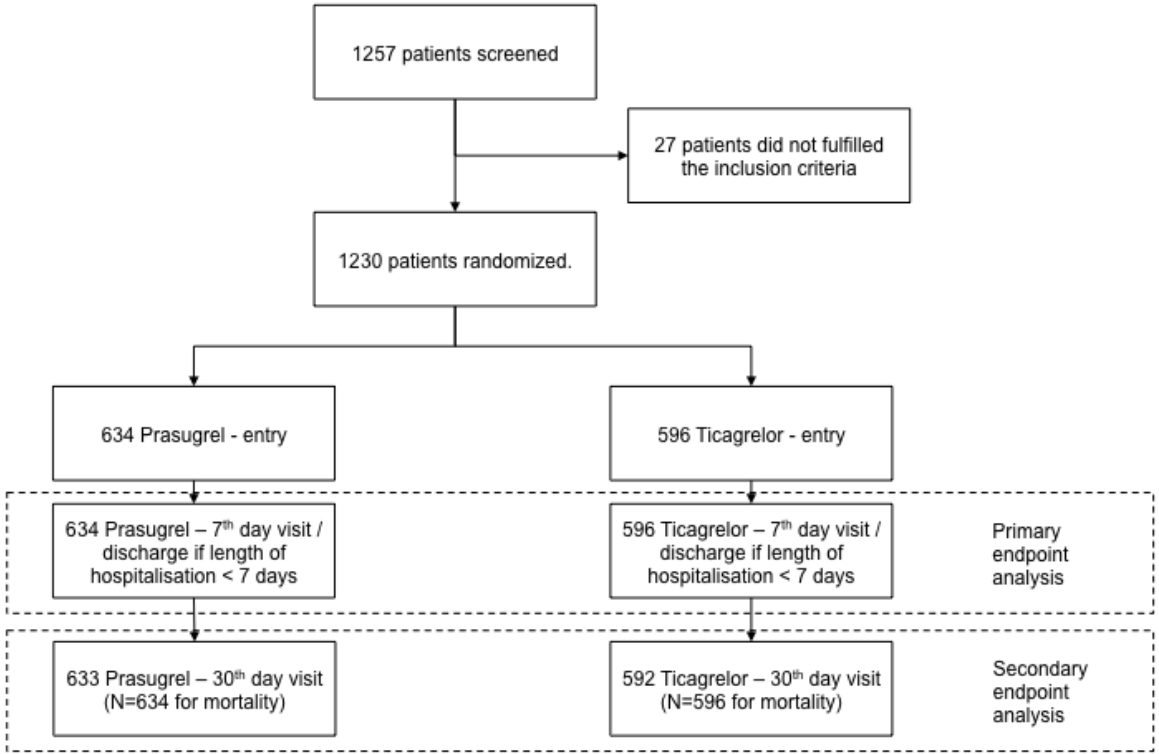
Secondary EP

- CV death/nonfatal MI/stroke at 30 days
- CV death / nonfatal MI / stroke / any revascularization / re-hospitalization.
- Individual components of primary end-point.
- Stent thrombosis.
- Bleeding according to modified TIMI and BARC criteria.
- TIMI flow at the end of primary PCI.
- LV function on day 7 (echocardiography).

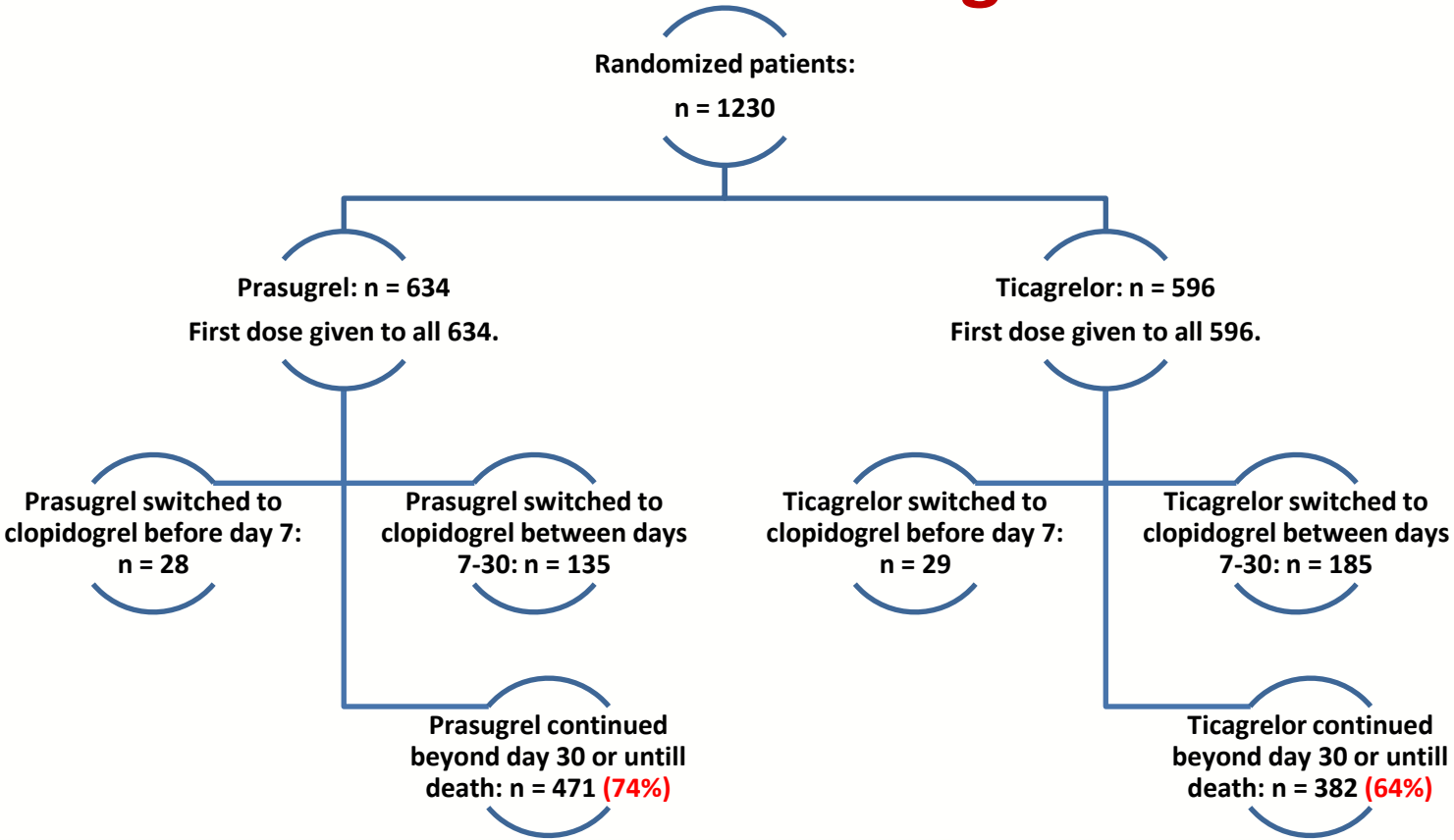
Methods

- Randomization immediately after arrival to PCI center: (A) prasugrel 60 mg orally followed by 10 mg / day (5mg / day if > 75 years or < 60 kg) for 1 year or (B) ticagrelor 180 mg orally followed by 90 mg b.i.d. for 1 year.
- Purely academic study, no industrial support
- Patients had to cover the costs of ticagrelor or prasugrel after hospital discharge as per local health care regulations.
- Thus, some patients decided to switch after discharge to clopidogrel (fully covered by local health care).
- The planned number of patients in the study was 2500 (total). Interrupted preliminarily for futility.

Study flow chart



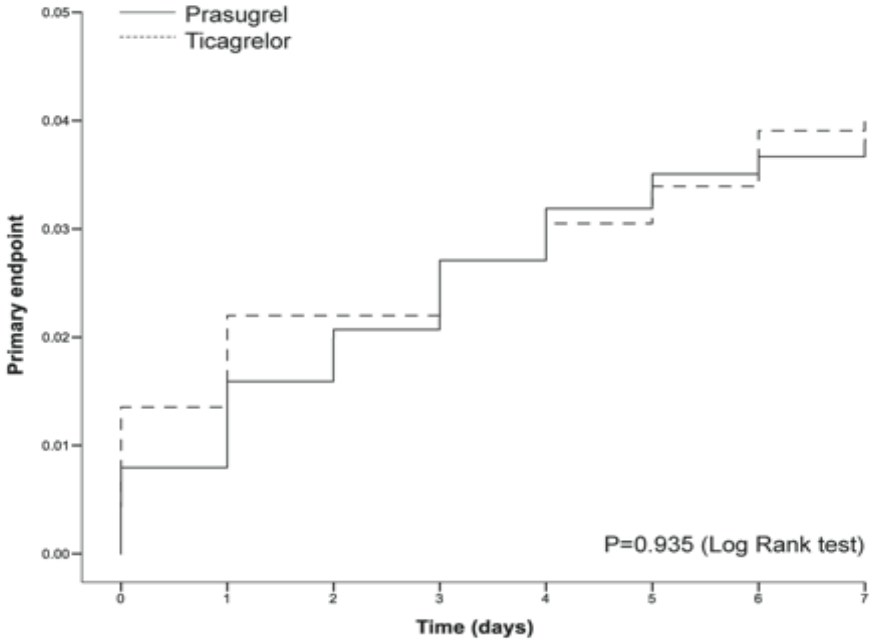
The use of P2Y12 inhibitors during the initial 30 days



Baseline and procedural characteristics

	Prasugrel (n=634)	Ticagrelor (n=596)	P value
Females	22.9%	26.3%	0.157
Mean age	61.8 (42.7; 78.7)	61.8 (44.6; 79.8)	0.755
Killip III-IV class on admission	5.4%	4.8%	0.696
Known diabetes mellitus	20.0%	20.8%	0.736
Prior MI	7.4%	9.2%	0.249
Known chronic kidney disease	1.3%	1.3%	0.901
History of old serious bleeding (>6 mo)	0.8%	0.2%	0.219
GP IIb/IIIa inhibitors during PCI	19.4%	20.5%	0.639
Radial access	66.7%	66.1%	0.820
DES used	65.9%	64.4%	0.553

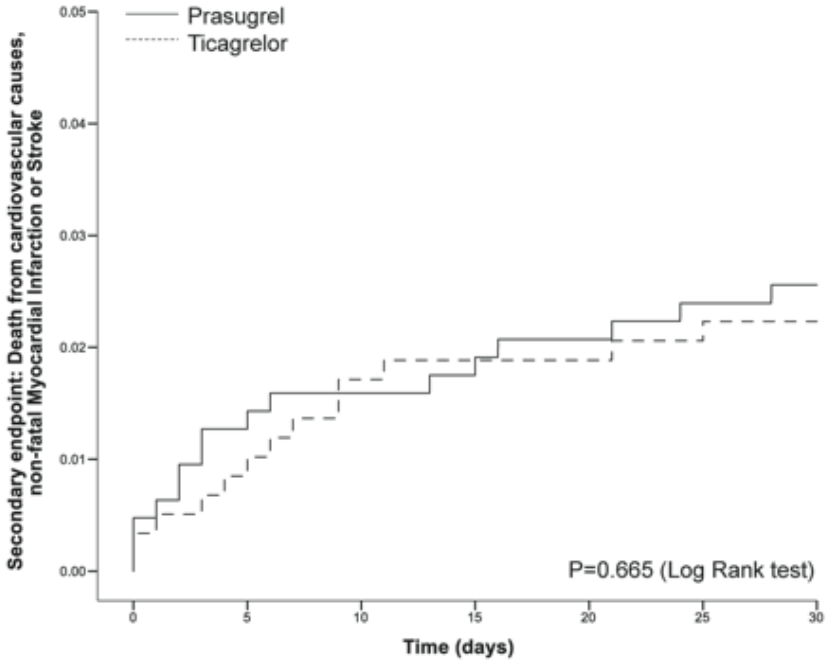
Primary end-point (7 days)



No at risk

Time (day)	1	2	3	4	5	6	7
Prasugrel (N=634)	629	624	621	617	614	612	611
Ticarelor (N=596)	588	583	583	580	578	576	573

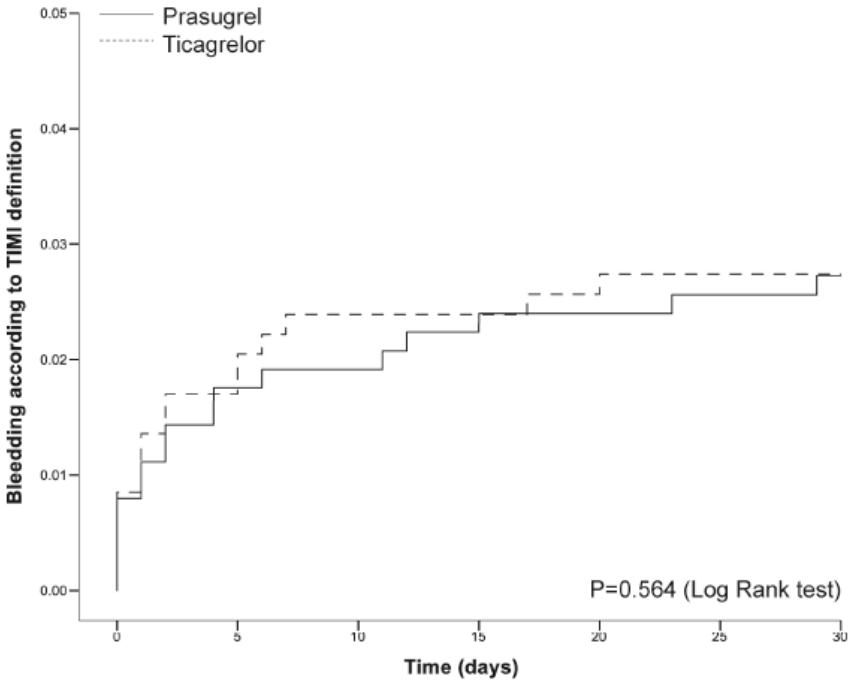
Key secondary end point (30 days)



No at risk

Time (day)	5	10	15	20	25	30
Prasugrel (N=634)	626	623	622	619	617	616
Ticarelor (N=596)	591	585	583	583	582	580

30-DAY BLEEDING



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Prasugrel (N=634)	623	622	618	617	615	614
Ticarelor (N=596)	586	582	581	580	579	578

Other outcomes

	Prasugrel (n=634)	Ticagrelor (n=596)	P value
All-cause mortality (30 days)	N=14 (2.2%)	N=16 (2.7%)	0.589
Re-infarction (30 days)	N=8 (1.3%)	N=7 (1.2%)	0.895
Stroke / TIA (30 days)	N=2 (0.3%)	N=1 (0.2%)	0.608
Urgent repeat TVR (7 days)	N=9 (1.4%)	N=7 (1.2%)	0.714
Serious bleeding requiring transfusion or prolonging hospital stay (7 days)	N=8 (1.3%)	N=7 (1.2%)	0.900
Definite stent thrombosis (30 days)	N=3 (0.5%)	N=5 (0.9%)	0.428
TIMI-3 flow after pPCI	N=592 **(94.3%)**	N=556 (94.8%)	0.708

Conclusion

The study did not show any difference between ticagrelor and prasugrel in the early phase of acute myocardial infarction treated by primary PCI.

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Circulation

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Prasugrel Versus Ticagrelor in Patients With Acute Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention: Multicenter Randomized PRAGUE-18 Study

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For the PRAGUE-18 Study Group

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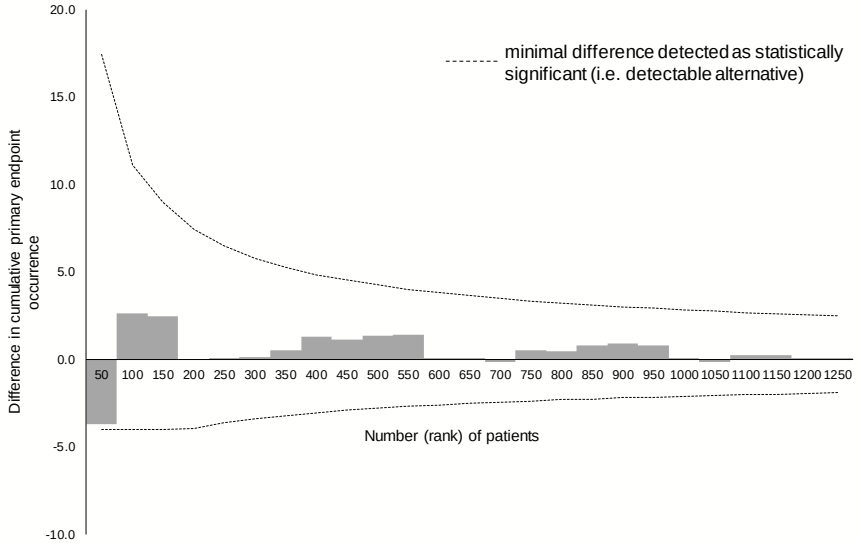
FUTILITY ANALYSIS



Difference in cumulative primary endpoint occurrence (ticagrelor – prasugrel) based on the given rank of patients in registry

50	100	150	200	250	300	350	400	450	500	550	600	650	700	750	800	850	900	950	1000	1050	1100	1150	1200	1230
-3.7%	2.6%	2.5%	0.0%	0.0%	0.1%	0.5%	1.3%	1.1%	1.4%	1.4%	0.1%	0.1%	-0.2%	0.5%	0.5%	0.8%	0.9%	0.8%	0.0%	-0.2%	0.3%	0.3%	0.1%	0.1%

Comparing real differences with a minimal difference detected as statistically significant for given number of patients, it never crosses.

Back-up slides

Low mortality rates: only one center did enroll trully unselected patients (including shock or CPR)

	Other centers (N=902)	Center A (N=328)	
30 day mortality	N=12 (1.3%)	N=18 (5.5%)	<0.001
Proportion of pts. In Killip classes:			
I	N=822 (91.8%)	N=256 (78.3%)	<0.001
II	N=55 (6.1%)	N=27 (8.3%)	
III	N=11 (1.2%)	N=6 (1.8%)	
IV	N=7 (0.8%)	N=38 (11.6%)	
Intubation, ventillation	*N=29 (3.2%)*	*N=35 (10.7%)*	*<0.001*