HIGH TECH MARSEILLE

28-30 JANVIER 2026

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New data on antithrombotic management after ACS:

TARGET-FIRST and NEO-MINDSET

Pr Gilles Lemesle

USIC et Centre Hémodynamique, Institut cœur poumon, CHU de Lille

Faculté de Médecine de l'Université Lille

Institut Pasteur de Lille, UMR 1011

Université de Lille

Institut Pasteur de Lille

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Déclaration de liens d’intérêts

- Honoraria and fees: Alnylam, Astra Zeneca, Bayer, Bristol Myers Squibb, Boehringer Ingelheim, Boston Scientific, Inari, Lilly, MSD, Novartis, Novonordisk, Organon, Penumbra, Pfizer, Sanofi Aventis, Viatris

BACKGROUND

12-month dual antiplatelet therapy (DAPT) with aspirin + P2Y12 inhibitor is standard for patients with acute coronary syndromes (ACS) treated with percutaneous coronary intervention (PCI).

However, DAPT is associated with increased risk of **bleeding**.

Recent evidence supports shorter DAPT strategies, with **withdrawal of aspirin after 1-3 months** followed by monotherapy with P2Y12 inhibitor.

Still, the **early post-PCI period** carries substantial risk of thrombotic and bleeding events.

It is unclear whether an **<u>early</u> aspirin-free** approach is effective and safe.

Byrne et al. Eur Heart J 2023; 44: 3720–3826
Davide Capodanno et al. Circulation 2023;147:1933-1944

TARGET-First STUDY

Early Aspirin Discontinuation Following PCI in Low-Risk Acute MI Patients: Results from the TARGET FIRST Trial

Prof. GIUSEPPE TARANTINI, MD, PhD, FESC
on behalf of the TARGET-FIRST Investigators
Cardiology Clinic, University of Padova, Italy

31 August 2025

STUDY DESIGN

International 40 Eu sites , open-label RCT[1]

TARGET-First STUDY

CRO: *CERC, France*
Sponsor: *Microport, France*

Patients with AMI at low ischemic risk treated with **PCI (N= 2246):**
- ***Contemporary stent platform (Firehawk)***
- ***Early complete revascularization***

Giuseppe Tarantini: P.I.

Pieter C. Smits: Co-P.I.
Guillaume Cayla: Co-P.I.

DAPT (P2Y12-I + ASA)

Not eligible: Termination

Randomization 1:1

1 Month

12 Month

SAPT P2Y12-I

DAPT

Firehawk Liberty DES

- Abluminal biodeg. polymer
- Eluting Low dose Sirolimus

- **Primary Endpoint: NACCE Composite (Non-Inferiority) @ 1 year**
- **Powered Secondary Endpoint: BARC 2, 3 or 5 Bleedings (Superiority) @ 1 year**

1. TARGET-First design. Tarantini G. et al. EuroIntervention 2023

ENDPOINTS & STATISTICAL ASSUMPTIONS

TARGET-First STUDY

Primary Endpoint (NACCE)

Composite of **all-cause death, myocardial infarction, stent thrombosis, stroke, or major bleeding (BARC type 3 or 5)** assessed at 11 months post-randomization

Non-inferiority design (Intention-to-treat - ITT)

- Assumed event rates: **3.5% (control)** vs. **2.5% (intervention)**
- **Non-inferiority margin**: **1.25 percentage points** (absolute difference)

Main Secondary Endpoint (powered)

BARC type 2, 3, or 5 bleeding at 11 months

Superiority (only if non-inferiority was demonstrated). Tested using **hierarchical sequential testing** to preserve type I error

Sample Size and Power

- **1,908 randomized patients** for **80% power** (one-sided $\alpha = 2.5\%$)
- Total **target enrollment: 2,246** (accounts for 15% attrition: non-randomized or lost to follow-up)
- **Sensitivity analyses**: Per-protocol and as-treated

COMPLIANCE TO ASSIGNED TREATMENT

Initial DAPT:

- **37.0 ± 4.6 days** (both groups)

P2Y12 inhibitor at M1 visit	Intervention (%)	Control (%)
Ticagrelor	73.5	74.5
Prasugrel	21.7	20.0
Clopidogrel	4.8	5.4

Compliance at 11 M:

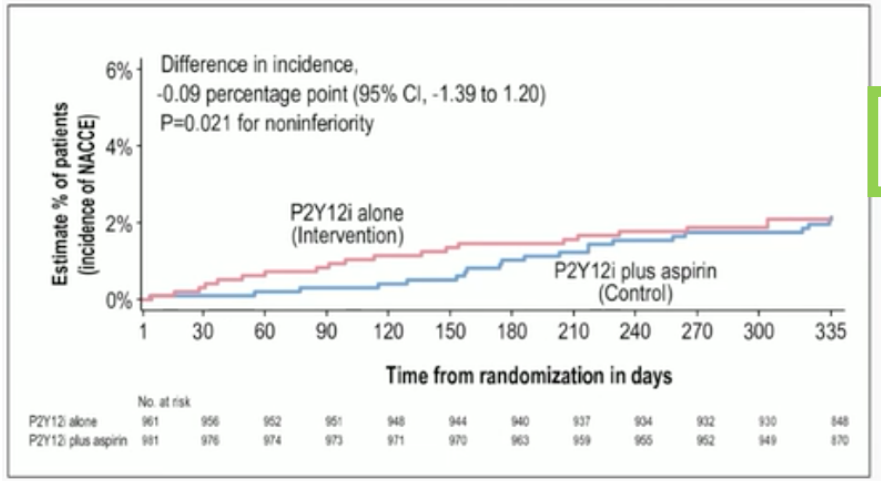
- **87%** (intervention)
- **89%** (control)

Reason for Non-Compliance	Intervention (13%)	Control (11%)
Bleeding, %	4.1	14.4
Adverse Event, % (non-bleeding)	33.5	27.2
Pro-active antiplatelet adjustment, %	60.6	57.6

STUDY RESULTS: PRIMARY ENDPOINT (NACCE)

TARGET-First STUDY

Non-inferiority (Intention-to-treat)



	Intervention (N=961) N (%)	Control (N=981) N (%)
Primary Endpoint: NACCE	**20 (2.1)**	**21 (2.2)**
Death (any cause)	4 (0.4)	2 (0.2)
Myocardial infarction	7 (0.7)	10 (1.1)
Stent thrombosis (definite or probable)	1 (0.1)	0 (0.0)
Any stroke	3 (0.3)	2 (0.2)

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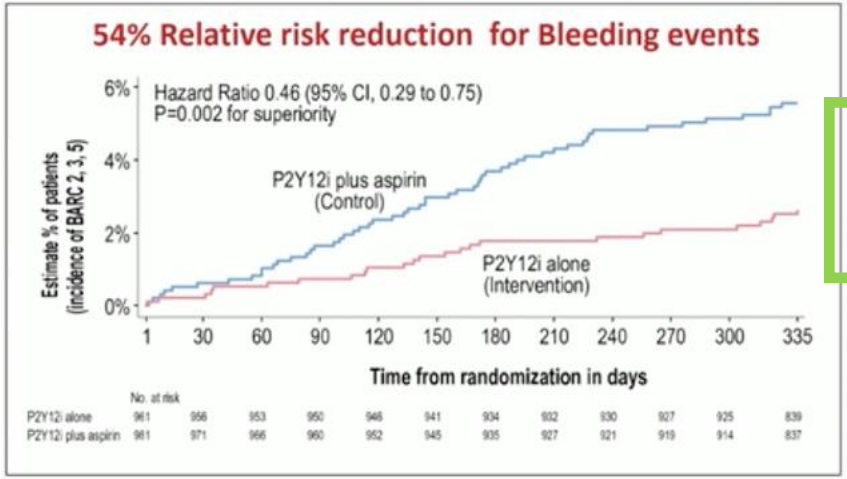
STUDY RESULTS: Main 2nd ENDPOINT (BARC type 2,3 or 5)

TARGET-First STUDY

Non-inferiority I EP achieved (Intention-to-treat)

54% Relative risk reduction for Bleeding events



	Intervention (N=961) N (%)	Control (N=981) N (%)
Main secondary Endpoint: BARC 2, 3 or 5 bleeding	**25 (2.6)**	**54 (5.6)**
BARC Type 2	18 (1.9)	47 (4.8)
BARC Type 3a	1 (0.1)	1 (0.1)
BARC Type 3b	6 (0.6)	3 (0.3)
BARC Type 3c	0 (0.0)	3 (0.3)
BARC Type 5	0 (0.0)	0 (0.0)

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PercutaNEOus Coronary Intervention Followed by Monotherapy INstead of Dual Antiplatelet Therapy in the SETting of Acute Coronary Syndromes

The NEO-MINDSET trial

Pedro A. Lemos MD PhD
Hospital Israelita Albert Einstein, São Paulo, Brazil
@PedroLemosMD

On behalf of the NEO-MINDSET trial Steering Committee and Investigators

ClinicalTrials.gov Number: NCT04360720

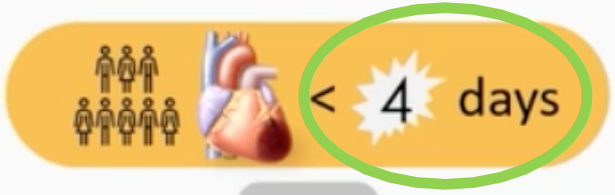
EINSTEIN Hospital Israelita · PROADI SUS · SUS · MINISTÉRIO DA SAÚDE · GOVERNO FEDERAL BRASIL UNIÃO E RECONSTRUÇÃO · NEO-MINDSET

STUDY DESIGN

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

Median 2.3 days



3400 pts with ACS who underwent succesful PCI < 4 days from admission

R 1:1

* ***Prasugrel*** *or* ***ticagrelor*** *were chosen at investigator's discretion before randomization*

MONOTHERAPY
*Potent P2Y12 inhibitor**

DAPT
*ASA + Potent P2Y12 inhibitor**

Unblinded DSMB review
400, 1/3, ½, 3/5, and all patients with 30-day fup

12 months

PRIMARY ISCHEMIC OUTCOME (Noninferiority)
All-cause death, MI, stroke, or urgent target vessel revascularization

Hierarchical

PRIMARY BLEEDING OUTCOME (Superiority)
Major or clinically relevant nonmajor bleeding (BARC 2, 3, or 5)

ANTIPLATELET TREATMENT

NEO-MINDSET

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	Monotherapy (n=1712)	DAPT (n=1698)
Antiplatelet therapy before randomization		
Aspirin	1641 (95.9)	1656 (97.6)
Clopidogrel	1442 (84.3)	1439 (84.8)
Ticagrelor	136 (8.0)	129 (7.6)
Prasugrel	99 (5.8)	98 (5.8)
P2Y12 inhibitor post-randomization		
Prasugrel	1192 (69.6)	1172 (69.0)
Ticagrelor	480 (28.0)	501 (29.5)
Other	40 (2.3)	25 (1.5)

Numbers are count (%)

SAMPLE SIZE CALCULATION

NEO-MINDSET

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PRIMARY ISCHEMIC OUTCOME
NONINFERIORITY

Estimated event rate in both groups: 7%

One side type I error: 0.025

Power: 80%

Noninferiority margin = 2.5% (relative 36%)

Estimated lost to follow-up = 4% (N=136)

SAMPLE SIZE

3400
1700 in each arm

PRIMARY BLEEDING OUTCOME
SUPERIORITY

Estimated event rate in DAPT group = 8%

Two-side type I error: 0.025

Power: 88%

Reduction in events from 8% (DAPT)
to 5% (mono)
(37.5% relative risk reduction)

ISCHEMIC PRIMARY OUTCOME

NEO-MINDSET

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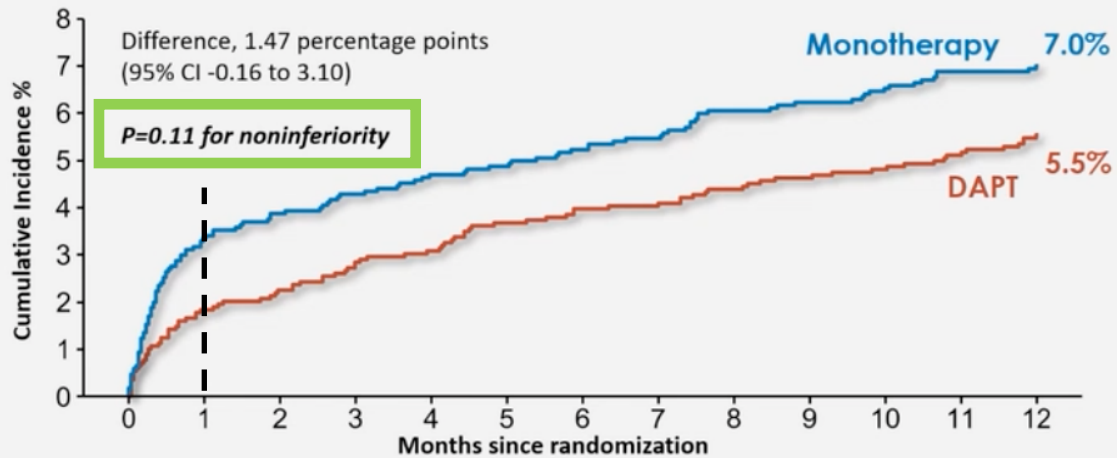
All-cause death, MI, stroke, or urgent target vessel revascularization



No. at risk

DAPT	1698	1659	1652	1640	1631	1621	1616	1613	1608	1590	1577	1571	1546
Monotherapy	1712	1647	1637	1630	1620	1617	1610	1605	1595	1588	1577	1569	1543

BLEEDING PRIMARY OUTCOME

NEO-MINDSET

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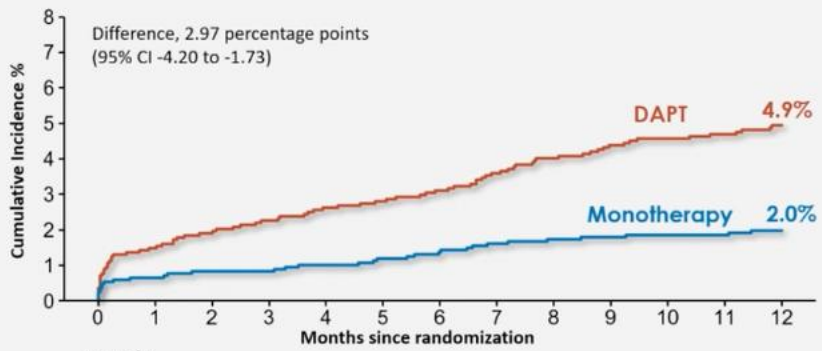
BARC 2, 3, or 5 bleeding



No. at risk

DAPT	1698	1649	1639	1627	1613	1605	1596	1586	1577	1557	1540	1535	1511
Monotherapy	1712	1668	1661	1658	1646	1641	1635	1629	1620	1611	1602	1598	1569

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12-MONTH SECONDARY OUTCOMES

NEO-MINDSET

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	Monotherapy (n=1712)	DAPT (n=1698)	Hazard Ratio (95% CI)
All-cause death	62 (3.6)	50 (3.0)	1.24 (0.85 to 1.79)
Cardiovascular death	42 (2.5)	34 (2.0)	1.23 (0.78 to 1.93)
Stroke	20 (1.2)	15 (0.9)	1.33 (0.68 to 2.60)
Myocardial infarction	45 (2.7)	31 (1.9)	1.45 (0.92 to 2.30)
Definite or probable stent thrombosis	12 (0.7)	4 (0.2)	2.99 (0.97 to 9.28)
Urgent target-vessel revascularization	22 (1.3)	12 (0.7)	1.83 (0.90 to 3.69)
BARC Bleeding			
Type 1 to 5	75 (4.5)	150 (9.0)	0.49 (0.37 to 0.64)
Type 1	45 (2.7)	76 (4.6)	0.58 (0.40 to 0.84)
Type 2	21 (1.3)	50 (3.0)	0.41 (0.25 to 0.69)
Type 3	11 (0.7)	33 (2.0)	0.33 (0.17 to 0.65)
Type 5	1 (0.1)	2 (0.1)	0.50 (0.05 to 5.48)
Net adverse clinical events*	145 (8.5)	166 (9.9)	0.86 (0.69 to 1.08)

*All-cause death, MI, stroke, urgent TVR, BARC 2, 3 or 5

Numbers are count (% KM estimates)

Conclusion

- De plus en plus de données pour P2Y12i puissant en monothérapie après un SCA (TARGET-FIRST, ULTIMATE, 4D-ACS, T-PASS, ….)
  - => revoir les recos

- Après 1 mois c'est oui …
- Dès la phase hospitalière, c'est plutôt non !

- Quid à 12 mois ?
  - Switch vers aspirine
  - Switch vers clopidogrel
  - Maintien du P2Y12 puissant seul

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