NEO-MINDSET

O. Hlinomaz

I. IKAK, ICRC, FN u sv. Anny a Masarykova univerzita, Brno, Česká republika
CINRE s.r.o., Bratislava, Slovenská republika
Univmed s.r.o., Brno, Česká republika

2023 euroPCR

EAPCI
European Society of Cardiology

The NEW ENGLAND JOURNAL of MEDICINE

Full results available online now

ORIGINAL ARTICLE

Early Withdrawal of Aspirin after PCI in Acute Coronary Syndromes

P.O. Guimarães,[1] M. Franken,[1] C.A.M. Tavares,[1,2] M.O. Antunes,[2,3] F.S. Silveira,[4] P.B. Andrade,[5] R.R. Bergo,[6] R.M. Joaquim,[7] J.E. Tinoco de Paula,[8] B.R. Nascimento,[9] F.G. Pitta,[1,2] J.A. Arruda,[10] R.G. Serpa,[11] L.N. Ohe,[12] F.M. Mangione,[13] R.H.M. Furtado,[2,14] E. Ferreira,[15] F.B.A. Sampaio,[16] C. T. do Nascimento,[17] L.O.O. Genelhu,[18] C.G. Bezerra,[19] R. Sarmento-Leite,[20] L.N. Maia,[21] F.R.A. Oliveira,[22] M.V. Wainstein,[23] F.T.C. Dall'Orto,[6] F. Monfardini,[1] S.R.L. Assis,[1] J.C. Nicolau,[7] A.C. Sposito,[24] R.D. Lopes,[25] Y. Onuma,[26] M. Valgimigli,[27] D.J. Angiolillo,[28] P.W.J.C. Serruys,[26] O. Berwanger,[29,30] F. Bacal,[1,2] and P.A. Lemos,[1] for the NEO-MINDSET Trial Investigators*

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

Percuta*NEO*us Coronary Intervention Followed by *M*onotherapy *IN*stead of *D*ual Antiplatelet Therapy in the *SET*ting 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 POPULATION

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

KEY INCLUSION CRITERIA

- Admitted with acute coronary syndrome (STEMI, NSTEMI, UA)
- Successful PCI of all target lesions < 4 days of admission

KEY EXCLUSION CRITERIA

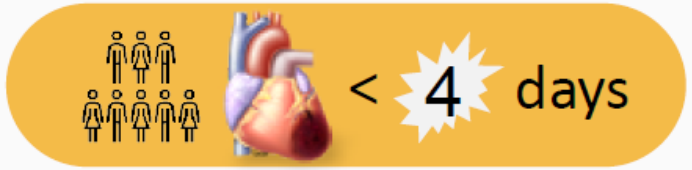
- Prior ischemic stroke < 30 days
- Major active/recent bleeding, or need for oral anticoagulation, or prior intracranial bleeding, or fibrinolytics < 24 h., or bleeding diathesis.

STUDY DESIGN

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

50 center v Brazílii
Funding Brazilian Ministry of Health



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)

SAMPLE SIZE CALCULATION

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

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)

BASELINE & PROCEDURAL CHARACTERISTICS

	Monotherapy (n=1712)	DAPT (n=1698)
Age, y	59.5 (±10.9)	59.8 (±10.7)
Female sex	502 (29.3)	497 (29.3)
Diabetes	459 (26.8)	477 (28.1)
Qualifying index event		
STEMI	1058 (61.8)	1061 (62.5)
NSTEMI	527 (30.8)	512 (30.2)
Unstable Angina	127 (7.4)	125 (7.4)
ARC High bleeding risk	339 (19.8)	335 (19.7)
Multivessel coronary artery disease	777 (45.4)	719 (42.3)
Radial access	1465 (85.6)	1445 (85.2)
Treated vessel LAD	1010 (59.2)	999 (59.1)
At least one bifurcation lesion	219 (12.8)	184 (10.8)
Number of implanted stents	1.6 (1.0)	1.6 (1.0)
Days from admission to first PCI	1.0 (1.3)	0.9 (1.0)
Days from admission to randomization	2.3 (1.3)	2.3 (1.0)

Numbers are mean (±SD) or count (%)

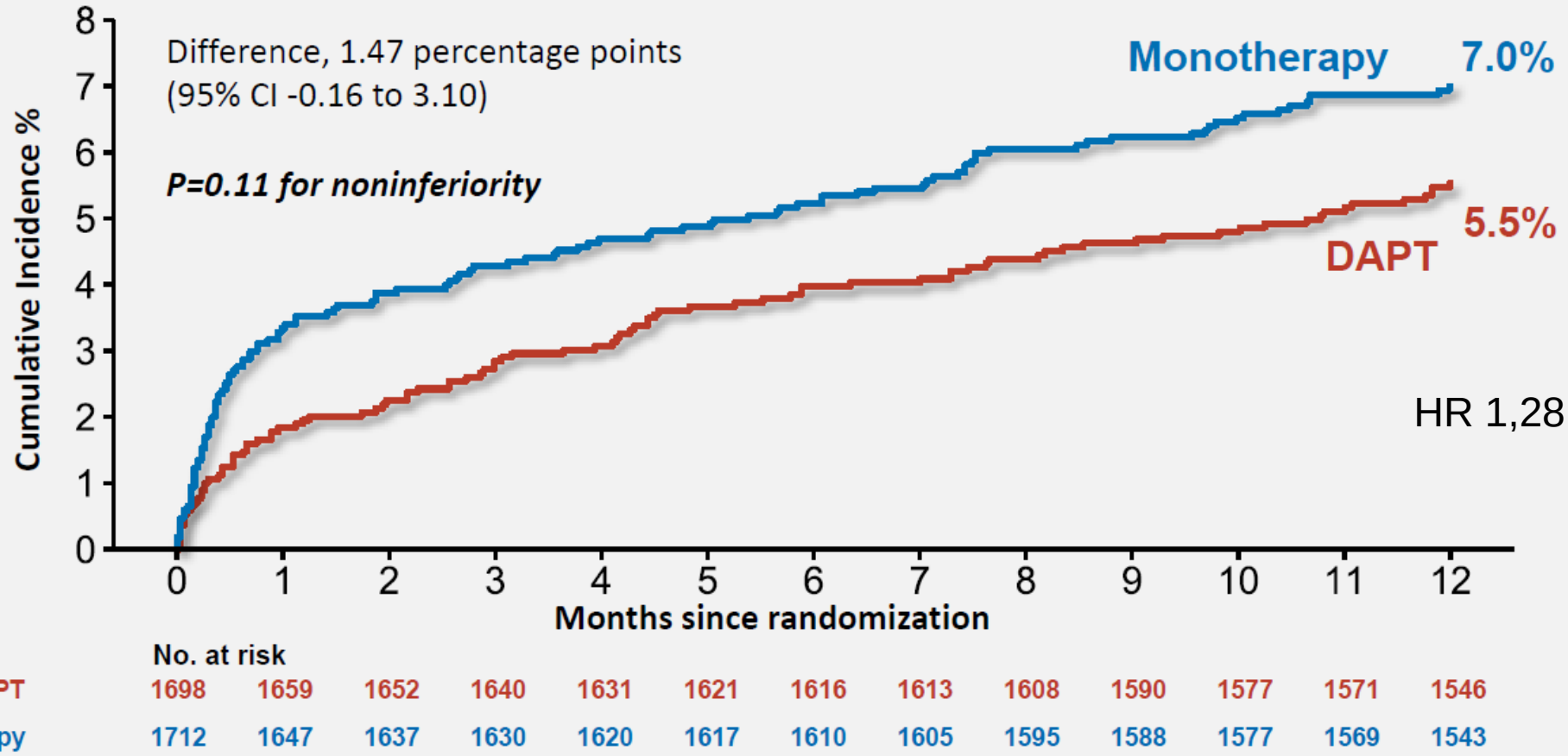
ANTIPLATELET TREATMENT

	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 (%)

ISCHEMIC PRIMARY OUTCOME

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



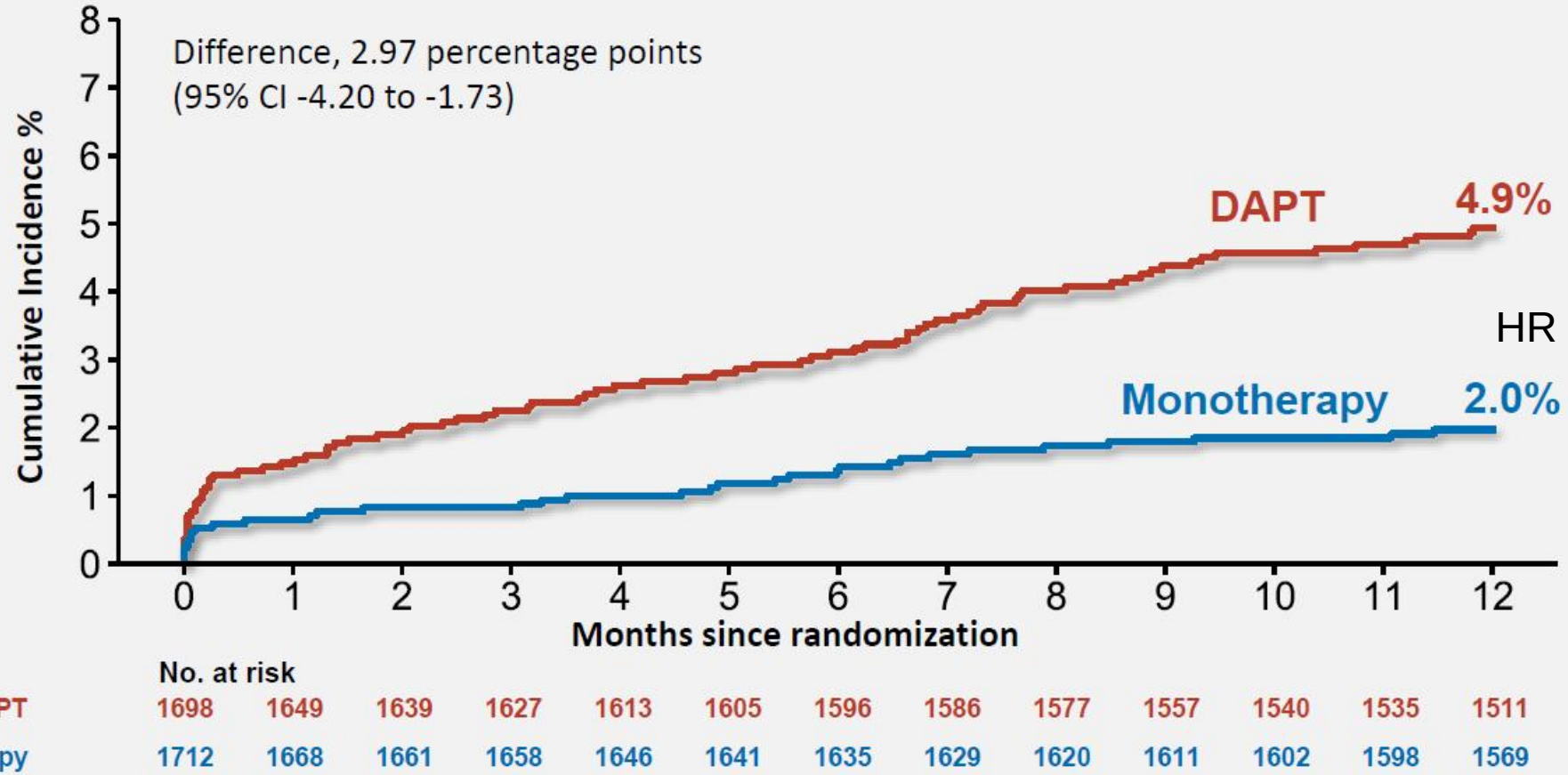
HR 1,28 (0,98-1,68)

BLEEDINGPRIMARY OUTCOME

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

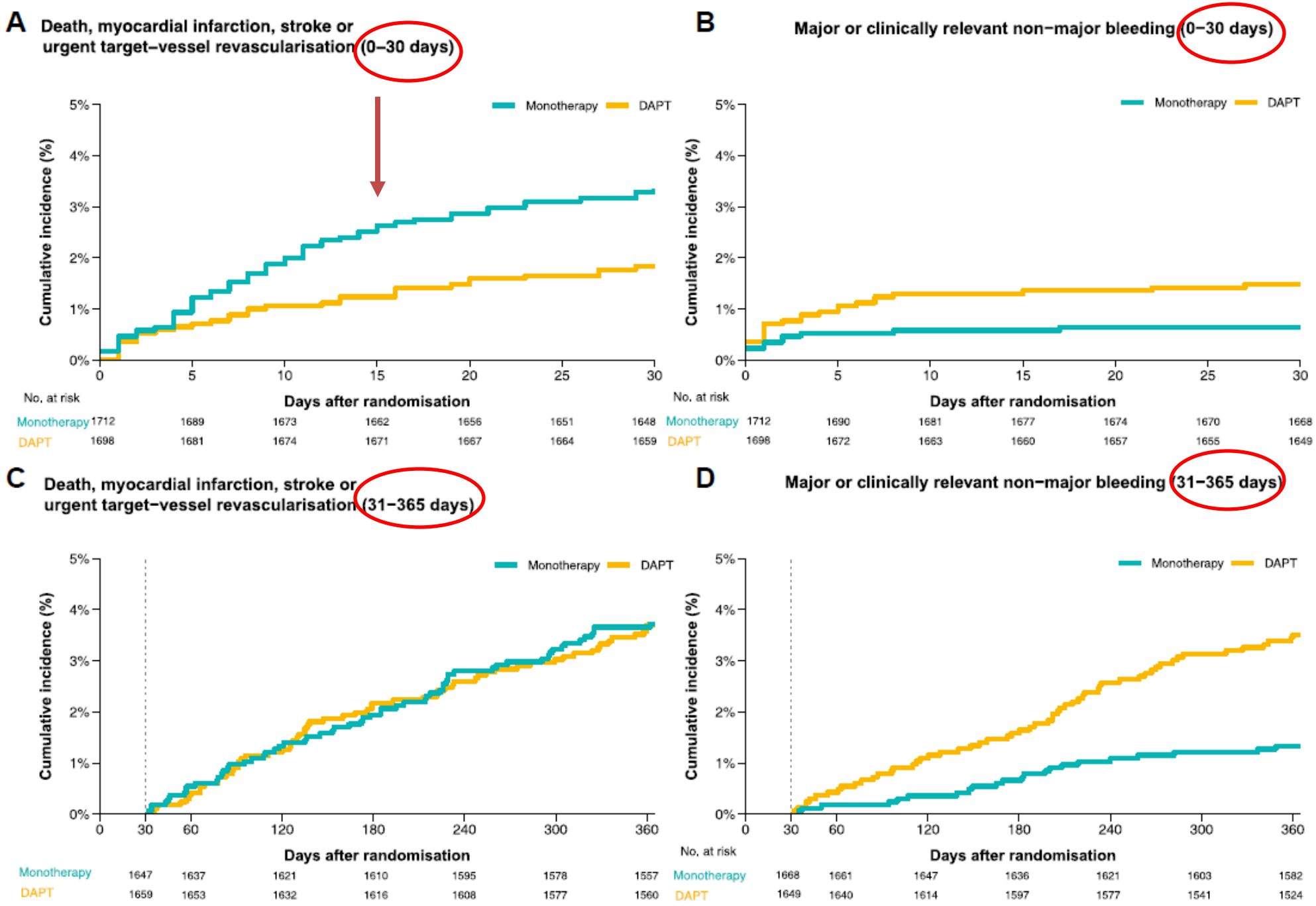
BARC 2, 3, or 5 bleeding



HR 0,40 (0,26-0,59)

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


A
Death, myocardial infarction, stroke or urgent target−vessel revascularisation (0–30 days)
Monotherapy
DAPT
Cumulative incidence (%)
5%
4%
3%
2%
1%
0%
0
5
10
15
20
25
30
Days after randomisation
No. at risk
Monotherapy 1712 1689 1673 1662 1656 1651 1648
DAPT 1698 1681 1674 1671 1667 1664 1659
B
Major or clinically relevant non−major bleeding (0–30 days)
Monotherapy
DAPT
Cumulative incidence (%)
5%
4%
3%
2%
1%
0%
0
5
10
15
20
25
30
Days after randomisation
No. at risk
Monotherapy 1712 1690 1681 1677 1674 1670 1668
DAPT 1698 1672 1663 1660 1657 1655 1649
C
Death, myocardial infarction, stroke or urgent target−vessel revascularisation (31–365 days)
Monotherapy
DAPT
Cumulative incidence (%)
5%
4%
3%
2%
1%
0%
0
30
60
120
180
240
300
360
Days after randomisation
Monotherapy 1647 1637 1621 1610 1595 1578 1557
DAPT 1659 1653 1632 1616 1608 1577 1560
D
Major or clinically relevant non−major bleeding (31–365 days)
Monotherapy
DAPT
Cumulative incidence (%)
5%
4%
3%
2%
1%
0%
0
30
60
120
180
240
300
360
Days after randomisation
No. at risk
Monotherapy 1668 1661 1647 1636 1621 1603 1582
DAPT 1649 1640 1614 1597 1577 1541 1524

12-MONTH SECONDARY OUTCOMES

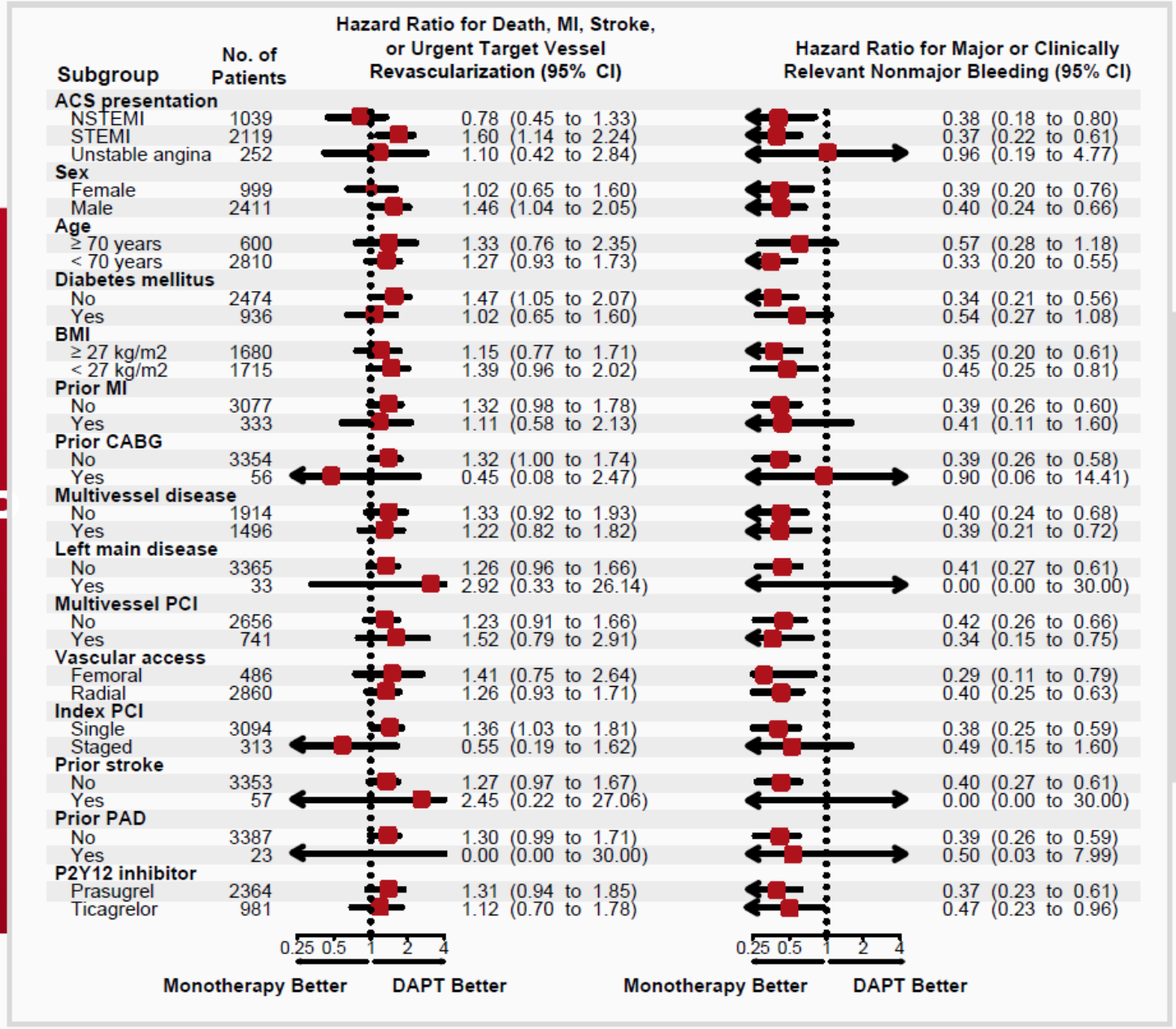
	Monotherapy (n=1712)	DAPT (n=1698)	Hazard Ratio (95% CI)
All-cause death	62 (3.6)	50 (3.0)	1.24 (0.85 to 1.79)
Cardiovascular death	42 (2.5)	34 (2.0)	1.23 (0.78 to 1.93)
Stroke	20 (1.2)	15 (0.9)	1.33 (0.68 to 2.60)
Myocardial infarction	45 (2.7)	31 (1.9)	1.45 (0.92 to 2.30)
Definite or probable stent 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)

ST monoth. 12 pt.: 10 subacute (24hrs-30D), 2 late (30D-1Yr)
ST DAPT 4 pt.: 1 acute, 2 subacute, 1 late

SUBGROUP ANALYSIS



All p-values for interaction terms were non-significant

Deepak L. Bhatt comments at ESC 2025

- NEO-MINDSET is an important, well-conducted trial
- In patients with recent ACS, despite percutaneous revascularization of culprit and non-culprit vessels, early aspirin-free monotherapy with potent P2Y12 inhibition was not non-inferior to DAPT
- Therefore, DAPT after ACS should remain the standard of care
- Duration of that DAPT remains a topic of debate, but an absolute minimum of one month if then de-escalating to a P2Y12 inhibitor (instead of aspirin) and if stent optimization with intravascular imaging had been performed; would default to 3-12 months if ACS
- Bottom line, still need to individualize therapy based on bleeding/ischemic risks, not just of the lesions/stents, but the patient

Závěry

1. DAPT<1M výjimečně při krvácení (BARC ≥3)
2. Po PCI pro AKS DAPT 1-3-12 měsíců, po 1-3M lze ASA ex
3. Léčbu doporučuje interv. kardiolog, modifikuje ošetřující kardiolog dle rizika ischem. příhody/krvácení
4. DCB-POBA? Scaffolds?

De-eskalace

1. TWILIGHT –high risk pac. po PCI (význ. ACS): tica+ASA 3M, poté tica - ↓ krvácení
2. TICO –ACS pac.: 3M tica+ASA, poté tica lepší než 12M tica+ASA
3. T-PASS – ACS+DES: stop ASA po 16 dnech, tica only lepší než tica+ASA 12M
4. GLOBAL-LEADERS: lze 1M tica+ASA, poté 23M tica
5. ULTIMATE-DAPT – PCI+ACS: ASA+tica 1M, poté tica - ↓ krvácení, beze změn ischem. Příhody
6. STOP-DAPT 3 Circ 2024 ACS or high bleeding risk: Pra 3,75mg OD vs DAPT méně krvácení, více ischem. Příhod
7. TARGET-FIRST low risk IM: 1M DAPT followed by monoth. (pra/tica) ↓ bleeding, bez nárůstu ischem. příhod
8. TAILORED-CHIP ESC 2025 complex high risk PCI: 60mg tica+ASA 0-6M, than clopi alone 6-12M vs clopi+ASA 12M- no net clinical benefit

Historie

1. ASA+warfarin 90. léta
2. ASA+ticlopidine/clopidogrel 12M 2000
3. ASA+prasugrel/ticagrelor 2009
4. De-eskalace
    a. DAPT 1-3 M, poté ASA
    b. DAPT 0-1-3 M, poté Pra/Tica

European Society of Cardiology

2024 Guidelines on Chronic Coronary Syndromes

DAPT consisting of aspirin 75–100 mg and clopidogrel 75 mg daily for up to 6 months is recommended as the default antithrombotic strategy after PCI-stenting.

Standard DAPT duration

6 months

CONCLUSIONS

TARGET-First STUDY

In ***low-risk acute MI*** patients undergoing ***early complete revascularization*** with a ***contemporary DES and no*** ischemic or bleeding ***events after 1 month of DAPT***, switching to ***P2Y12 inhibitor monotherapy***:

- Was **non-inferior** to continued DAPT in ***preventing net adverse cardiovascular and cerebrovascular events***
- Was associated with a **54% relative reduction *in clinically relevant bleeding events***

- These findings highlight that **when *complete revascularization meets personalized pharmacotherapy*, *abbreviated DAPT*** emerges as a **safe and effective** strategy for carefully **selected patients.**

Conclusions, after PCI in AMI/ACS

→ 1 month DAPT is mandatory

→ In low-risk patients (and not only in HBR patients), an « *ASA-free* » strategy is possible after 1 month of DAPT

→ There is less evidence for an « *ASA-only* » strategy after 1 month of DAPT

→ The current recommendations on the duration of DAPT are obsolete.

Montalescot G.: Discussant to Target-First study, ESC 2025

BACKGROUND

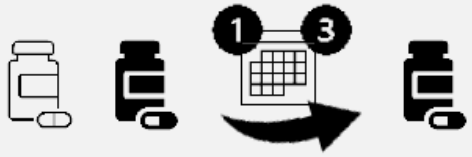
NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

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

OBJECTIVES

NEO-MINDSET

EINSTEIN Hospital Israelita Cardiologia

We therefore designed the ***NEO-MINDSET,*** a large-scale, academic-led, multicenter, randomized, open-label trial including ACS patients treated with PCI to determine whether:

Early aspirin-free monotherapy with potent P2Y12i *versus* DAPT would be:

Noninferior — **Ischemic Events**

↓ **Hierarchical**

Superior — **Bleeding events**

STUDY ORGANIZATION

Steering Committee

Pedro A. Lemos (Chair)
Marcelo Franken (Co-Chair)
Patricia O. Guimarães
Andrei C. Sposito
Dominick J. Angiolillo
Fernando Bacal
José Carlos Nicolau
Marco Valgimigli
Otavio Berwanger
Patrick W. J. C. Serruys
Renato D. Lopes
Yoshinobu Onuma

Trial Leadership

Pedro A. Lemos (Chair)
Marcelo Franken (Co-Chair)
Patricia O. Guimarães, Project Coord.
Caio A. M. Tavares, trialist
Frederico Monfardini, Statistician
Silvia R. L. Assis, Statistician

Data Safety Monitoring Board (DSMB)

Christopher B. Granger (Chair)
Roberto R. Giraldez
Tiago Mendonça (Statistician)

Funding

Brazilian Ministry of Health
Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde
PROADI-SUS

Coordinating Center

ARO Hospital Israelita Albert Einstein

Patrícia O. Guimarães
Caio A. M. Tavares
Ronaldo V. P. Soares
Diogo D. F. Moia
Camila S. N. Alburquerque
Luciana Pereira Almeida de Piano
Lailah C. C. Abrao
Bruna dos Santos Sampaio
Rosana C. Rocha
Gabriela Souza Murizine
Roberta G. R. A. P. Momesso
Elaine de Jesus Santos
Cintia Selles Santos
Silvia R. L. Assis
Frederico Monfardini
Graziele Pereira Lunas
Sanarelly Adonias Borges de Queiroz
Fabiana Teixeira Fabrete
Larissa Emidio de Franca Silva
Jaqueline Amalia de Paulo
Bruna Ladeira Moreno

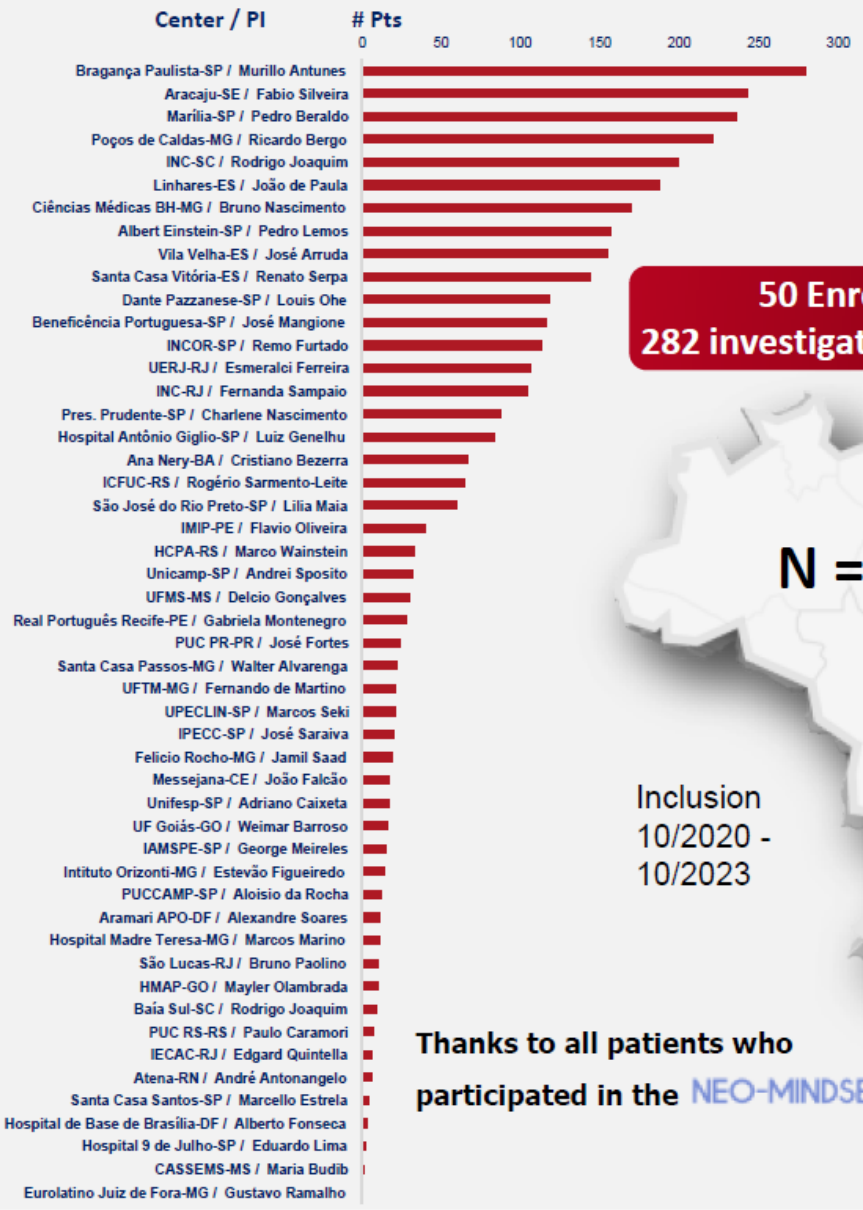
Data Analysis

ARO Hospital Israelita Albert Einstein

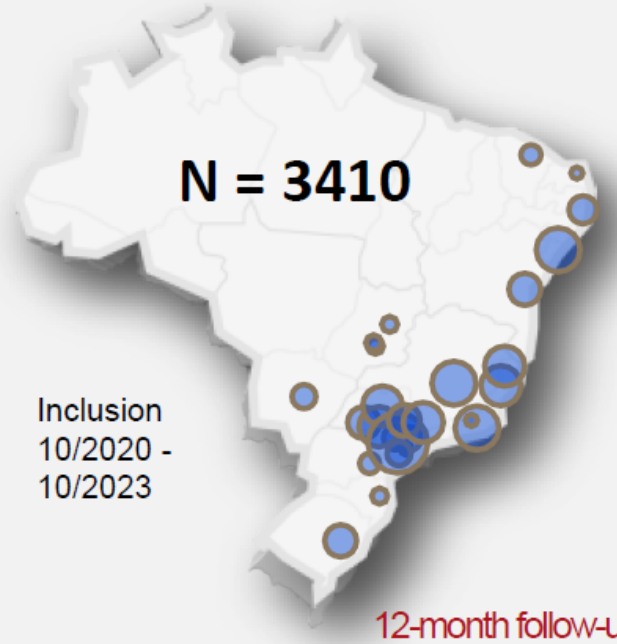
Frederico Monfardini
Silvia R. L. Assis
Gustavo P. Santos

Clinical Events Classification (CEC) Committee

Hélio Penna Guimarães (Chair)
Antonio Aurélio Fagundes Júnior
Adriano Truffa
Izabela Chaves Pedro



50 Enrolling Centers
282 investigators and study coord.



Inclusion
10/2020 -
10/2023

12-month follow-up
(99.2%)

Thanks to all patients who participated in the NEO-MINDSET

ESC Congress 2025 Madrid
TOGETHER WITH World Congress of Cardiology

NEO-MINDSET

ASA 81-100mg
Loading 180mg tica, 60mg pra u pac. na clopi. Když již byli na pra/tica, tak no loading
Maintanance pra 5/10mg OD, tica 90mg BID