

PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA

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di Confindustria

**Auditorium
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IL PAZIENTE AD ALTO RISCHIO DI SANGUINAMENTO

**QUANDO LO STENT FA LA DIFFERENZA: I
TRIAL CLINICI SULLA SOSPENSIONE
DELLA DAPT**

Pasceri Vincenzo

Criteria per definizione HBR e Rischio trombotico

Bleeding (ARC-HBR)

Major	Minor
	Age \geq 75 years
Anticipated use of long-term oral anticoagulation*	
Severe or end-stage CKD (eGFR $<$ 30 mL/min)	Moderate CKD (eGFR 30-59 mL/min)
Hemoglobin $<$ 11 g/dL	Hemoglobin 11-12.9 g/dL for men and 11-11.9 g/dL for women
Spontaneous bleeding requiring hospitalization or transfusion in the past 6 months, or any time, if recurrent	Spontaneous bleeding requiring hospitalization or transfusion within the past 12 months not meeting the major criterion
Moderate or severe baseline thrombocytopenia (platelet count $<$ 100x10 ⁹ /L)	
Chronic bleeding diathesis	
Liver cirrhosis with portal hypertension	
	Long term use of oral NSAIDs or steroids
Active malignancy (excluding nonmelanoma skin cancer) within the past 12 months	
Previous spontaneous intracranial hemorrhage	
Previous traumatic intracranial hemorrhage within the past 12 months	
Presence of brain AVM	
Moderate or severe ischemic stroke (NIHSS score \geq 5) within the past 6 months	Any ischemic stroke at any time not meeting the major criterion
Nondeferrable major surgery on DAPT	
Recent major surgery or major trauma within 30 days before PCI	

Urban et al. Circ 2019

Thrombotic

High thrombotic risk (early events)	High ischemic risk (long-term events)
Acute coronary syndrome	Previous myocardial infarction
Previous stent thrombosis while on antiplatelet treatment	Multivessel coronary artery disease
PCI complexity	Polyvascular disease
3 vessels treated	Diabetes mellitus
\geq 3 stents implanted	Chronic kidney disease
\geq 3 lesions treated	Heart failure
Bifurcation with 2 stents implanted	
Total stent length $>$ 60 mm	
Surgical bypass graft PCI	
Chronic total occlusion PCI	
Atherectomy device use	
Left main PCI	

Angiolillo et al. 2021



Recenti trials Short DAPT

- GLOBAL LEADERS: 1 vs 12 mesi DAPT (ticagrelor vs DAPT) Biomatrix stent
- SMART CHOICE 3 vs 12 mesi DAPT (Xience, Promus/Synergy, Orsiro stent)
- STOP DAPT 2 1 mese vs 12 mesi DAPT (asa+clop vs solo clop) stent Xience
- REDUCE 3 mesi vs 12 mesi DAPT post ACS (COMBO stent)
- TWILIGHT 3 mesi vs 12 mesi (Ticagrelor vs asa+ticagrelor)
- MASTER DAPT 1 mese vs standard (6 mesi) DAPT in HBR (stent Ultimaster)
- One month trial (1 mese con Biofreedom vs 12 mesi con BMX/Ultimaster)

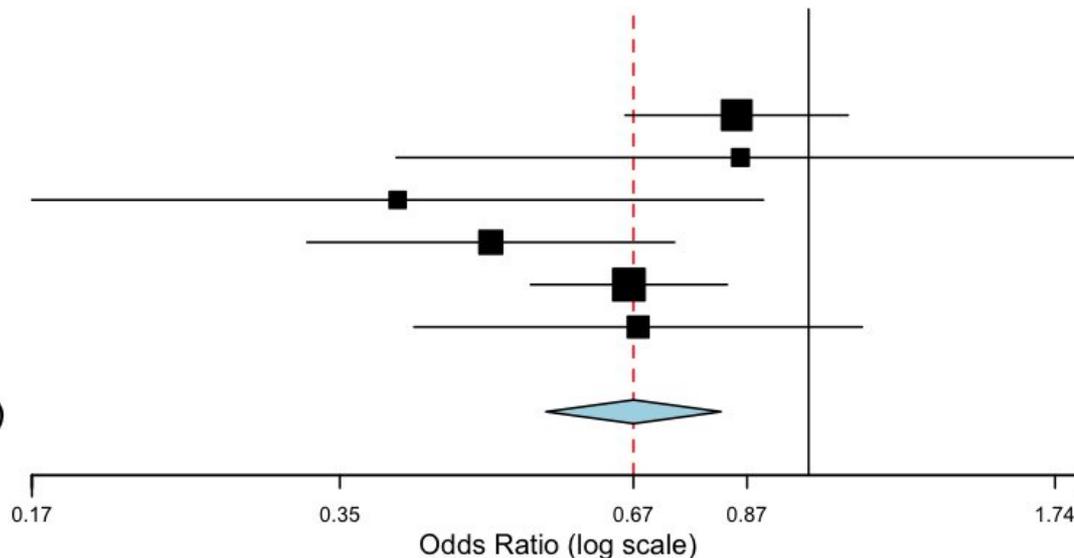


Rischio di Sanguinamenti (BARC 3-5) e short DAPT (1-3 mesi vs. 6-12 mesi)

Studies

- Global Leaders 2018
- Smart Choice 2019
- STOP DAPT 2 2019
- Twilight 2019
- MASTER DAPT 2021
- One month 2021

Overall ($I^2=3305\%$, $P=0.188$)



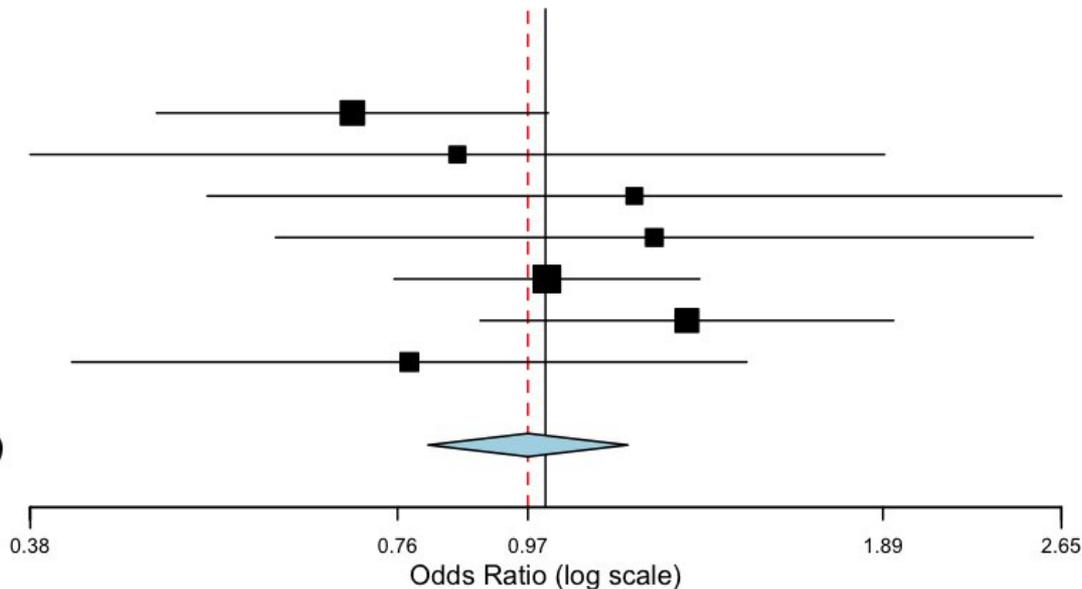


Infarto Miocardico e short DAPT (1-3 mesi vs. 6-12 mesi)

Studies

- Global Leaders 2018
- Smart Choice 2019
- STOP DAPT 2 2019
- Reduce 2019
- Twilight 2019
- MASTER DAPT 2021
- One month 2021

Overall (I²=998 % , P=0.353)



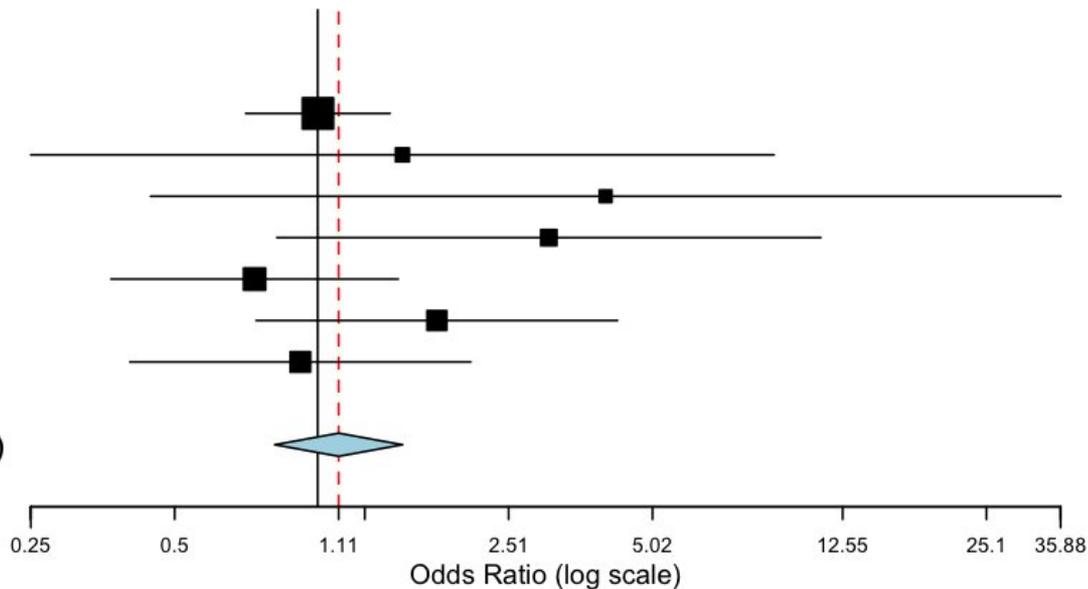


Trombosi Stent (Def+Prob) e short DAPT (1-3 mesi vs. 6-12 mesi)

Studies

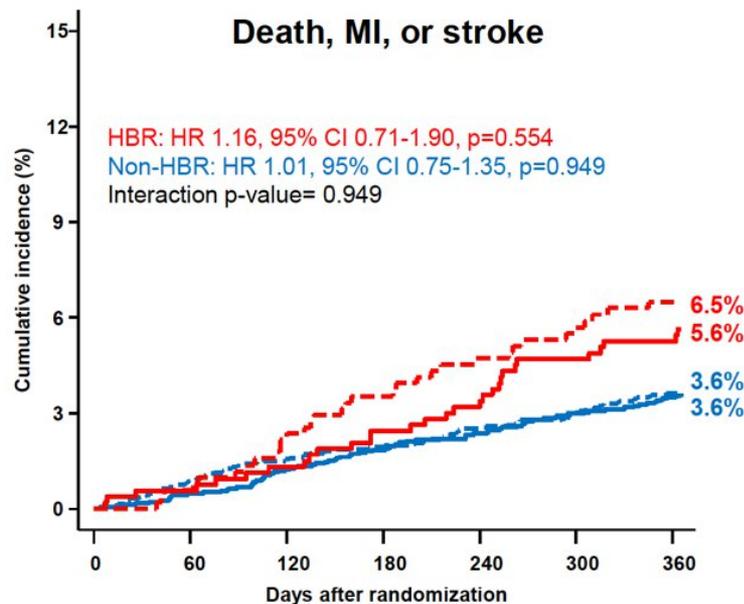
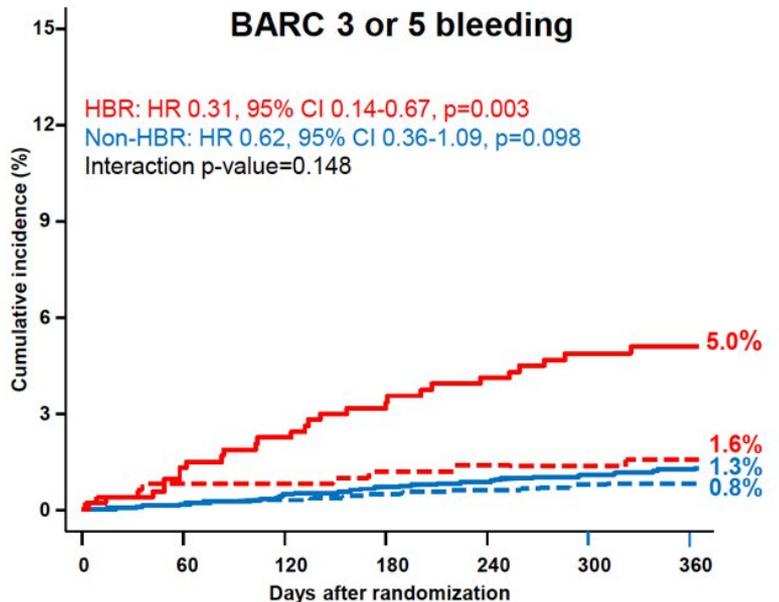
- Global Leaders 2018
- Smart Choice 2019
- STOP DAPT 2 2019
- Reduce 2019
- Twilight 2019
- MASTER DAPT 2021
- One month trial 2021

Overall (I²=986 % , P=0.354)





TTWILIGHT: Analisi Pazienti alto rischio sanguinamenti (HBR)



— HBR: Tica+Aspirin — Non-HBR: Tica+Aspirin
- - - HBR: Tica+Placebo - - - Non-HBR: Tica+Placebo



Trials DAPT 1 mese in HBR con stent specifici

ZEUS	828 pz	Endeavor vs BMS
SENIOR	1200 pz	Synergy vs BMS in >75aa
LEADERS FREE	2466 pz	Biofreedom vs BMS
ONYX ONE	1996 pz	Onyx vs Biofreedom

LEADERS FREE

- Double blinded, 2466 pazienti con HBR
- 1 mese DAPT
- DES Biofreedom vs BMS (Gazelle)
- Anticoagulante 37%
- NSTEMI 22%, STEMI 4%
- 1.9 stent/pt, PCI multivaso 22%

ZEUS

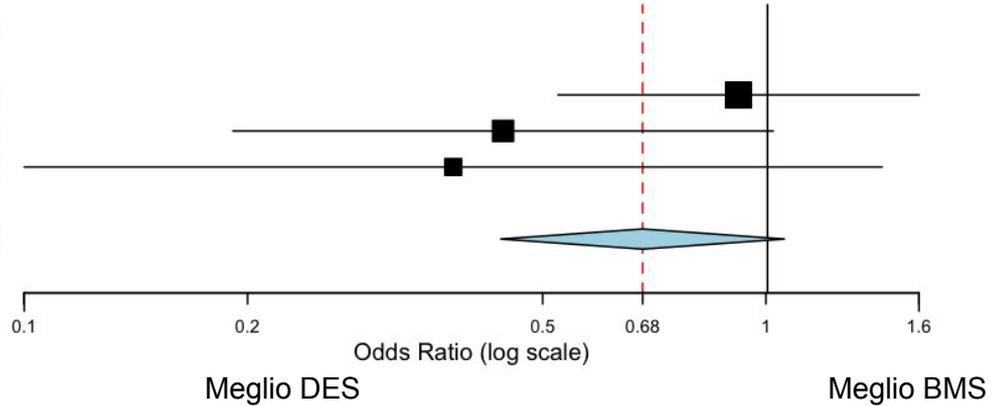
- Single blinded, 1606 pazienti
- 1 mese DAPT con DES con polimero stabile (Endeavor) vs BMS
- High Bleeding Risk 50%
- NSTEMI 27%, STEMI 19%
- Anticoagulante 13%
- 1.7 stent/pt, PCI multivaso 27%

SENIOR

- Single blinded, 1200 pazienti >75 anni
- 1 mese DAPT o 6 mesi se ACS
- Synergy (DES polimero riassorbibile) vs BMS
- NSTEMI, STEMI 11%
- Anticoagulante 18%
- 1.7 stent/pt, PCI multivaso 27%

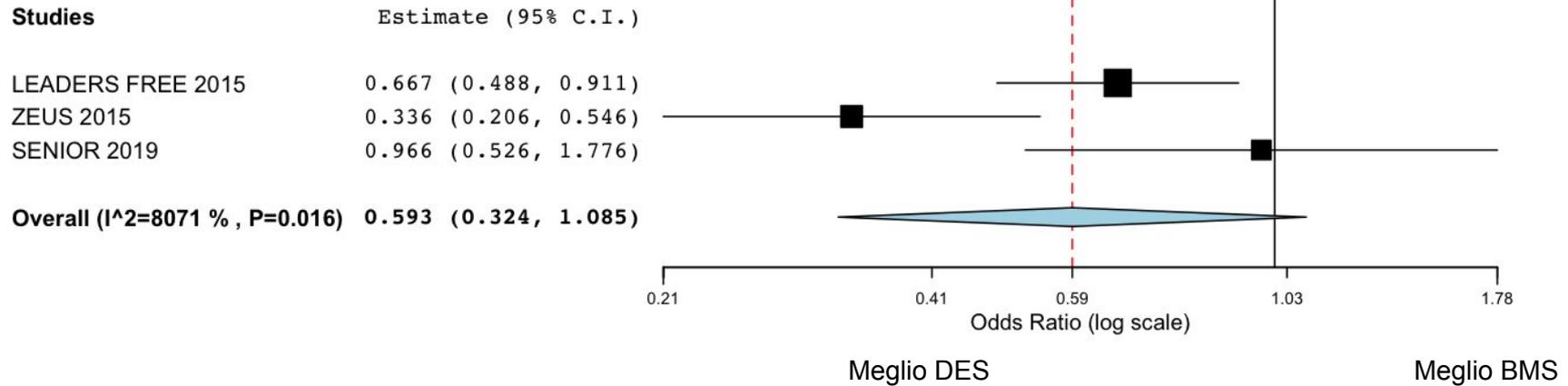
Trombosi Stent DES vs BMS con short DAPT

Studies	Estimate (95% C.I.)
LEADERS FREE 2015	0.914 (0.522, 1.601)
ZEUS 2015	0.440 (0.190, 1.018)
SENIOR 2018	0.377 (0.100, 1.428)
Overall (I²=0 % , P=0.240)	0.679 (0.437, 1.053)



Infarto Miocardico

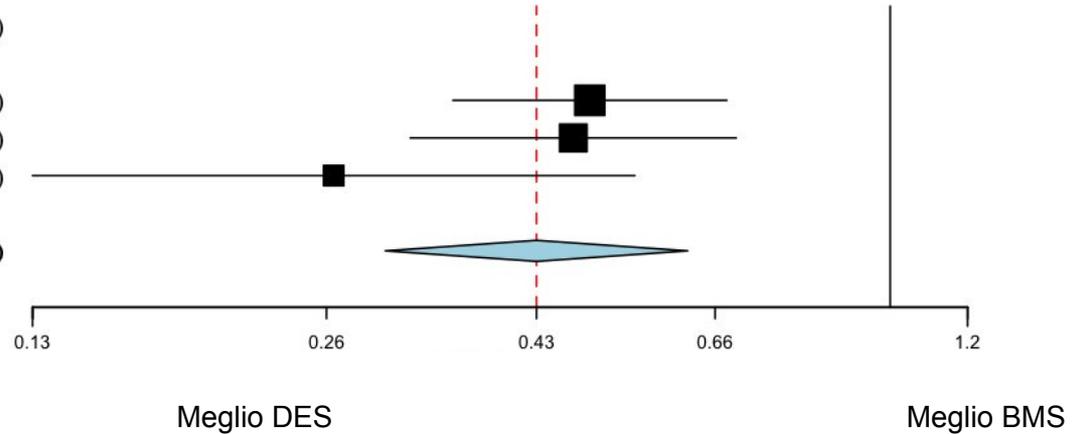
DES vs BMS con short DAPT



Target Lesion Revascularization DES vs BMS con short DAPT

Studies

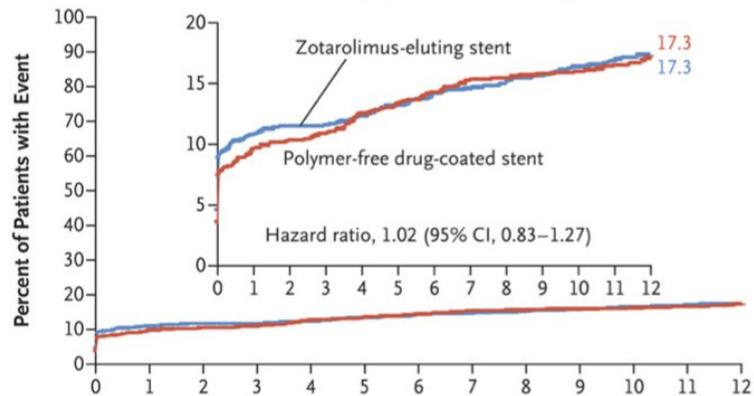
	Estimate (95% C.I.)
LEADERS FREE 2015	0.493 (0.357, 0.680)
ZEUS 2015	0.474 (0.323, 0.696)
SENIOR 2018	0.269 (0.132, 0.548)
Overall (I²=4980 % , P=0.306)	0.434 (0.304, 0.620)



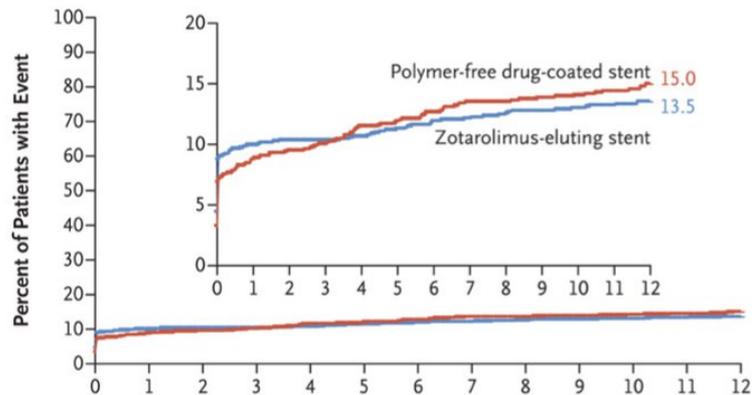
ONYX ONE

- Single blinded, 1996 pazienti tutti con HBR
- 1 mese DAPT
- DES ONYX (polimero stabile) vs Biofreedom (senza polimero)
- Anticoagul 39%
- NSTEMI 27%, STEMI 6%
- 1.8 stent/pt, PCI multivaso 18%

A Primary Outcome of Death from Cardiac Causes, Myocardial Infarction, or Stent Thrombosis



C Myocardial Infarction



One month DAPT trial

- Open Label, 3020 pazienti
- 1 mese DAPT con stent senza polimero (Biofreedom) vs 12 mesi DAPT con stent con polimero riassorbibile (Biomatrix o Ultimaster)
- NSTEMI 3%, nessuno STEMI
- Anticoagul 3%
- 1.3 stent/pt, PCI multivaso 13%



Trial in corso con DAPT 1 mese

BIOFLOW DAPT Orsiro vs Onyx in HBR

COMPARE 60/80 Supraflex Cruz vs Ultimaster in HBR



Sommario

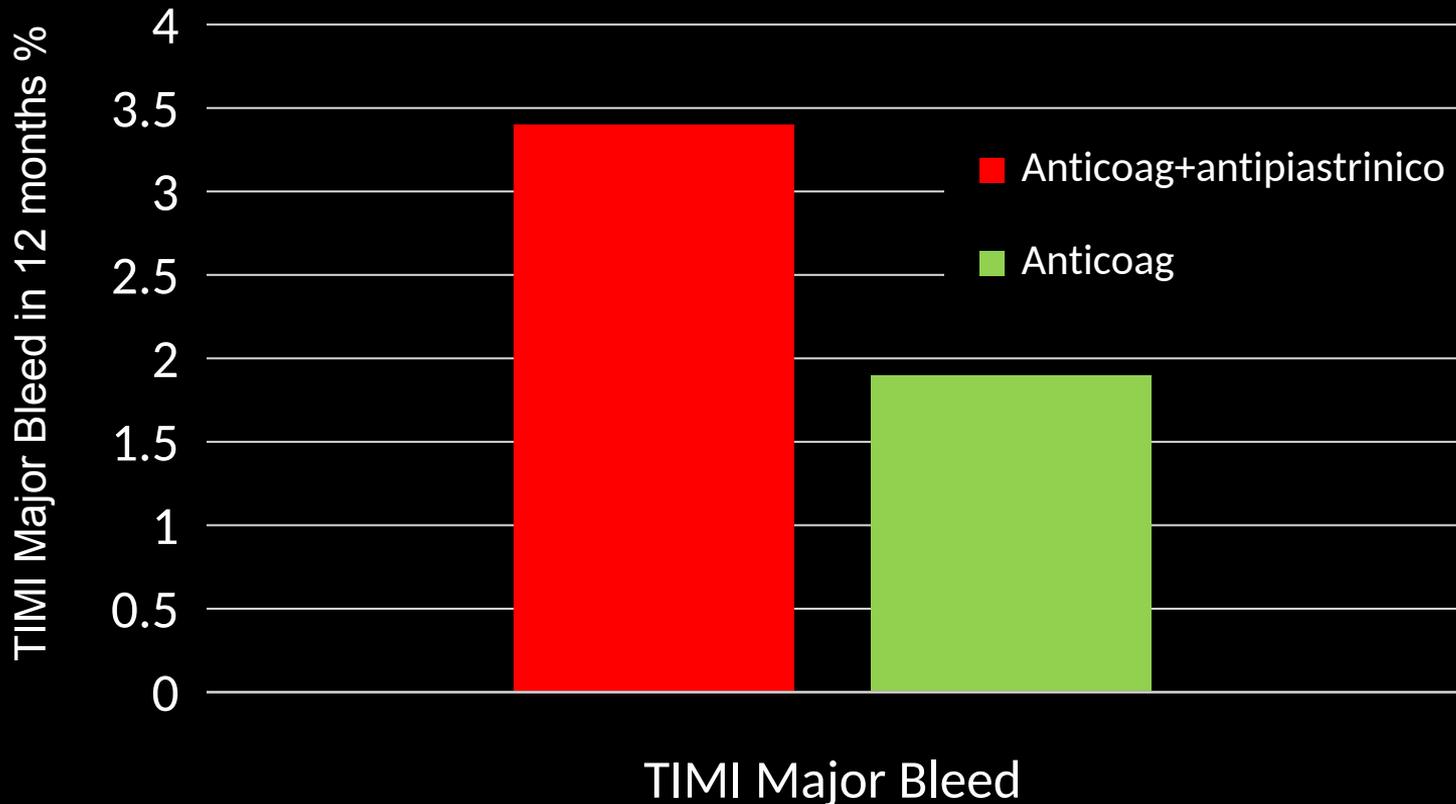
- HBR: short DAPT (0-3 mesi) riduce sanguinamenti - teniamo però conto che gli studi includono pochi pazienti molto complessi (>3 stent, doppio stent su biforcazione, CTO, ecc)
- I dati non mostrano differenze tra tipi di stent attualmente in commercio, ma la qualità delle evidenze è diversa
 - Trial vs BMS: Biofreedom, Synergy
 - Trial di equivalenza tra DES: Onyx/Biofreedom
 - Trial di confronto tra diversa durata Tx: Ultimaster, Xience, BMX
 - Registri (Coroflex, Cre8)



Conclusioni

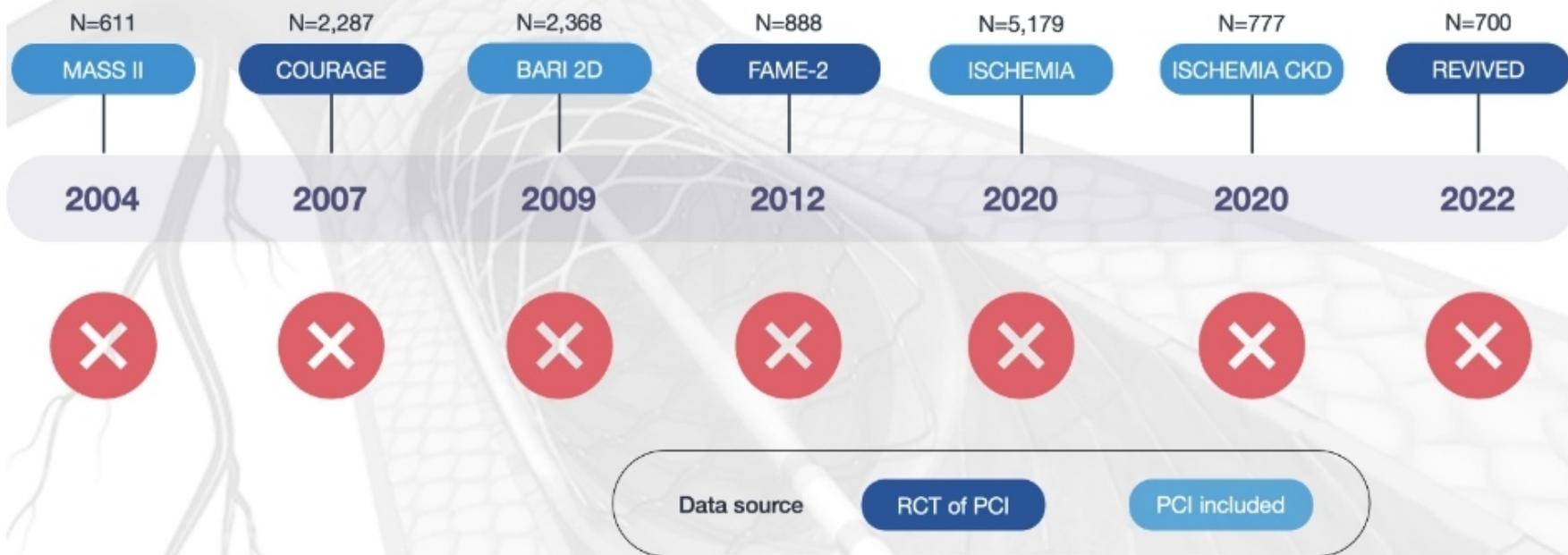
Forse gli stent sono tutti uguali,
sicuramente i pazienti sono molto diversi

Rischio di Sanguinamenti gravi quando si aggiunge un antiplastrinico a Tx anticoagulante per un anno



PCI or medical therapy for SIHD

Any significant reduction in hard clinical outcomes (i.e., all-cause death, cardiac death)?

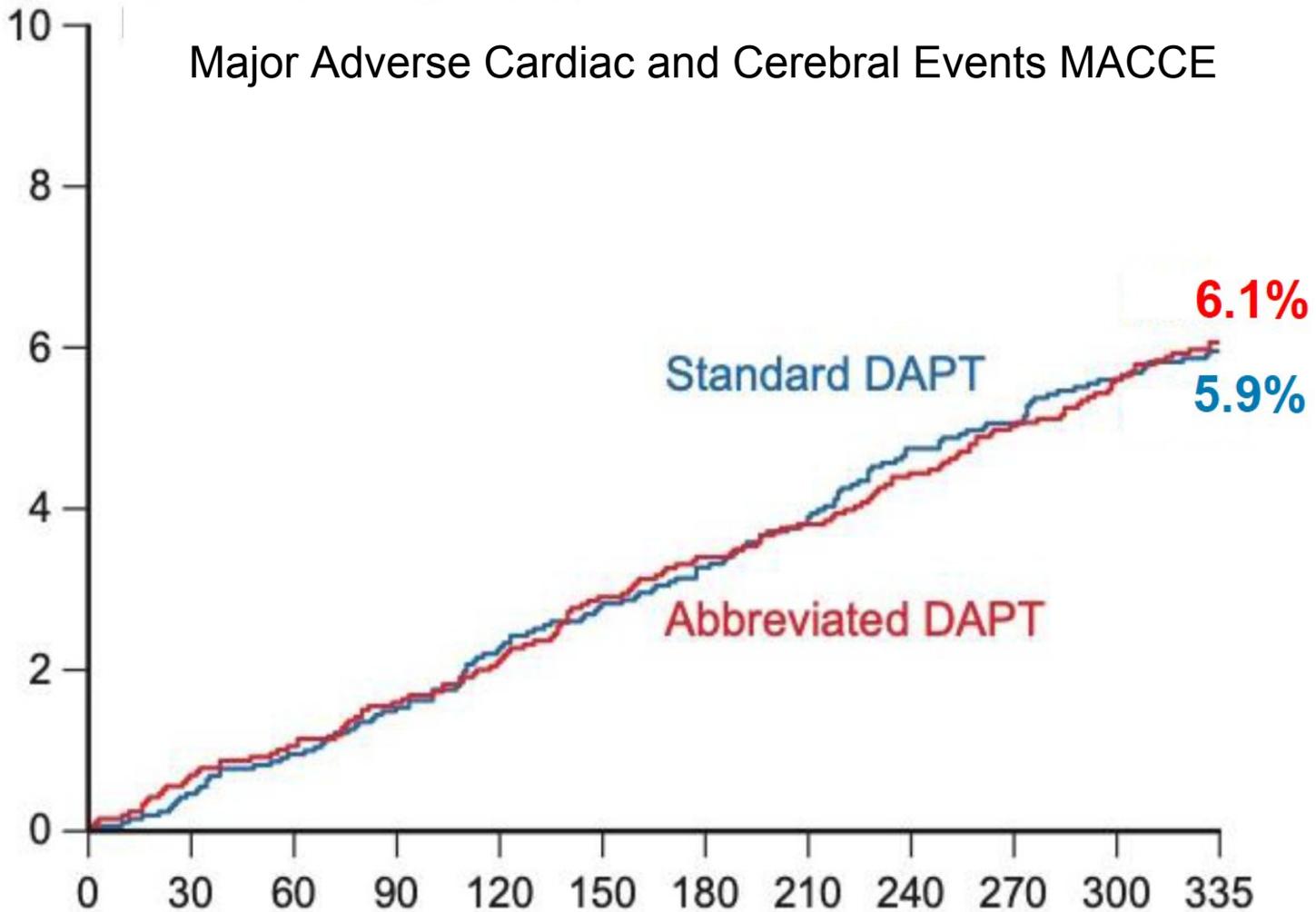


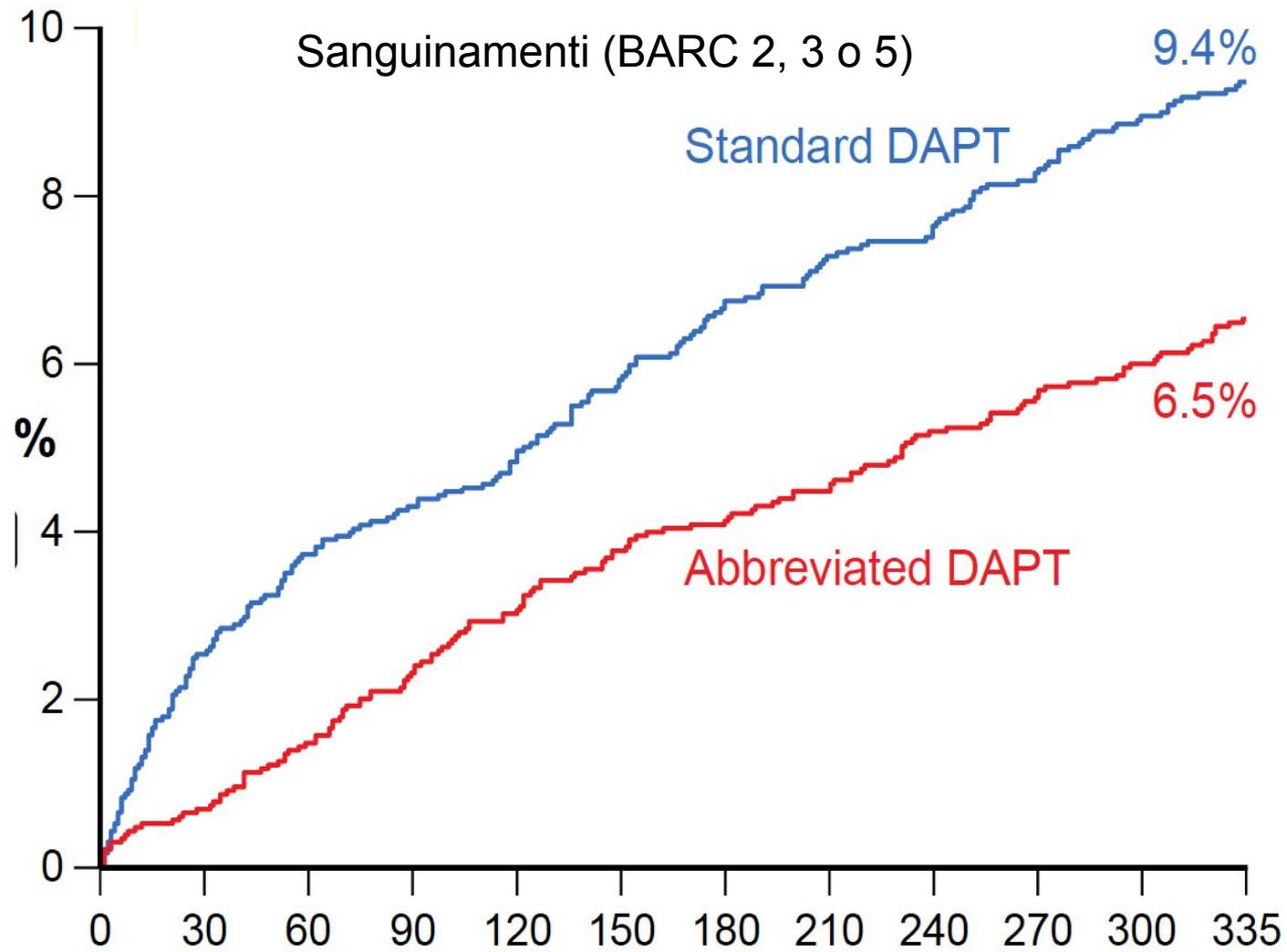


MASTER DAPT

- Open Label
- "Short" vs Standard DAPT in HBR (34 vs 193 gg)
- Stent Ultimaster (80 μ , polimero riassorbibile in 3 mesi)
- NSTEMI 36%, STEMI 12%
- Anticoagul 37%
- 1.7 stent/pt, 26% PCI multivaso, biforcazione doppio stent
3%

Major Adverse Cardiac and Cerebral Events MACCE







Strategie per ridurre il sanguinamento

- Ridurre Intensita' DAPT nelle SCA (TOPIC, TALOS AMI, TROPICAL ACS,)
- Ridurre durata P2Y12 (DAPT-STEMI, SMART DATE, REDUCE ACS)
- Ridurre durata ASA (GLOBAL LEADERS, SMART CHOICE, STOP DAPT 2, TWILIGHT, TICO)
- Ridurre durata DAPT (MASTER DAPT)
- Clopidogrel+Anticoag (WOEST, ENTRUST, PIONEER AF PCI, ENTRUST AF PCI, RE DUAL PCI)

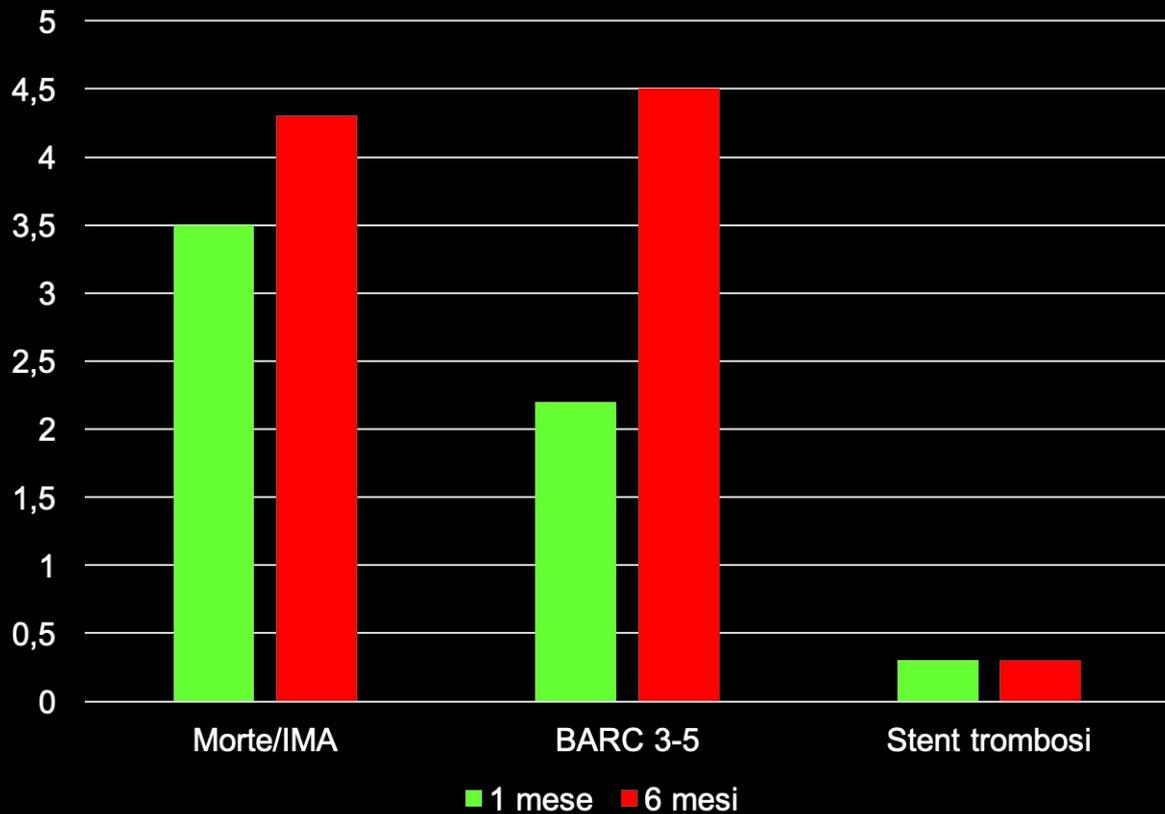
Registro POEM (Synergy)

- Registro con confronto con una performance standard
- 443 pz con 1 mese DAPT
- High Bleeding Risk
- NSTEMI 18%, STEMI 7%
- Anticoagul 36%
- 1.7 stent/pt
- A un anno morte/IMA/trombosi 4.8%
- Trombosi stent a un anno 0.94%
- Sanguinamenti gravi (BARC 3-5) 2.1%

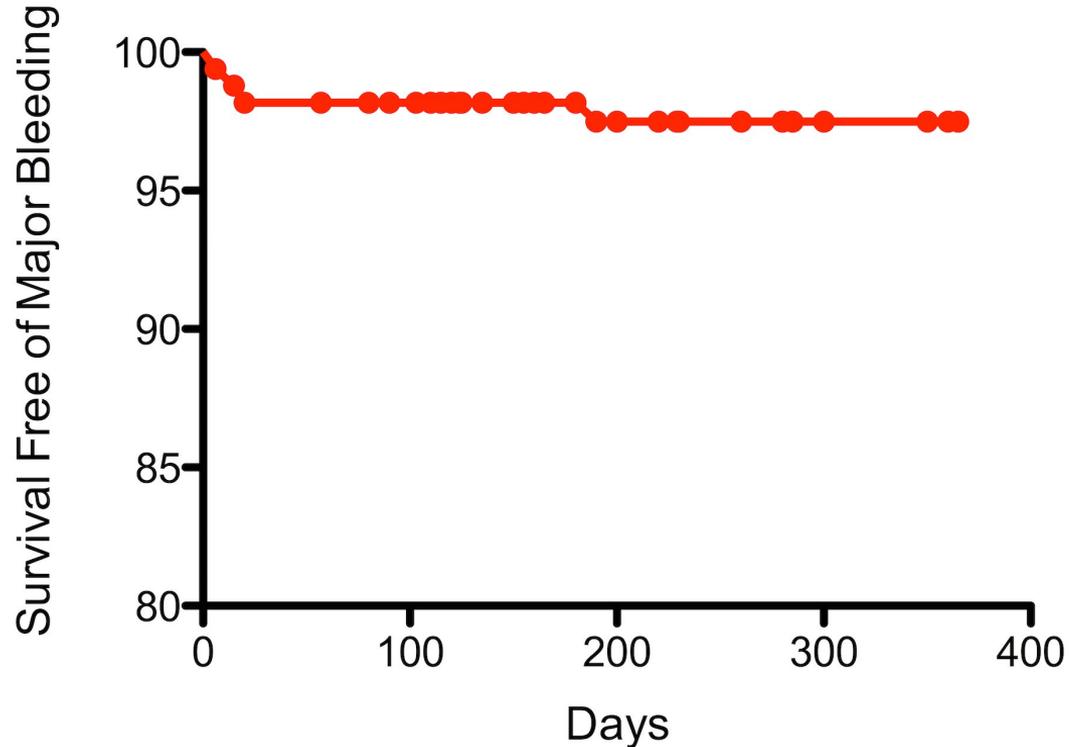
XIENCE 28

- Registro con controlli storici
- 1 mese DAPT
- High Bleeding Risk
- NSTEMI 18%
- Anticoagulante 44%
- 1.0 stent/pt, PCI multivaso 0%
- Riportata a 6 mesi trombosi stent 0.4%, sanguinamenti BARC 3-5 2.2%

XIENCE 28



Sicurezza dei DES in Pazienti con FA con Solo un Mese di DAPT+TAO seguito da solo Clopidogrel+TAO Sanguinamenti Maggiori



Efficacia dei DES in Pazienti con FA con Solo un Mese di Tripla Terapia, poi TAO+clopidogrel

