



**Start  
Antiplatelet**

## **THE START-ANTIPLATELET REGISTER**

# **A MULTICENTER OBSERVATIONAL PROSPECTIVE STUDY TO ASSESS THE RISK-BENEFITS OF ANTITHROMBOTIC THERAPY IN ACS PATIENTS**



**START-Register**  
SURVEY ON ANTICOAGULATED PATIENTS - REGISTER

Registro computerizzato per la raccolta dei dati di pazienti trattati cronicamente con anticoagulanti



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## **IL SETTING CLINICO**

**Perché un registro sugli antiaggreganti?**

**ANTICOAGULAZIONE:**

**attualità cliniche, di laboratorio e aspetti sociali**

BOLOGNA, 21-22 GENNAIO 2016

# ACUTE CORONARY SYNDROME PATIENTS

## DUAL ANTIPLATELET THERAPY



12 months

### Recommendations for oral antiplatelet agents (1) NSTEMI 2011

Recommendations	Class	Level
Aspirin should be given to all patients without contraindications at an initial loading dose of 150-300 mg, and at a maintenance dose of 75-100 mg daily long-term regardless of treatment strategy.	I	A
A P2Y <sub>12</sub> inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A
A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors ( <i>H. elicobacter pylori</i> infection, age ≥ 65 years, concurrent use of anticoagulants or steroids).	I	A
Prolonged or permanent withdrawal of P2Y <sub>12</sub> inhibitors within 12 months after the index event is discouraged unless clinically indicated.	I	C
Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended for all patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins), regardless of initial treatment strategy and including those pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced).	I	B
Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended for P2Y <sub>12</sub> -inhibitor-naïve patients (especially diabetics) in whom coronary anatomy is known and who are proceeding to PCI unless there is a high risk of life-threatening bleeding or other contraindications.	I	B

[www.escardio.org/guidelines](http://www.escardio.org/guidelines)

European Heart Journal (2011) 32:2999-3054  
doi:10.1093/eurheartj/ehr236



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## Recommendations for oral antiplatelet agents (2) **NSTEMI 2011**

Recommendations	Class	Level
Clopidogrel (300 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.	I	A
A 600 mg loading dose of clopidogrel (or a supplementary 300 mg dose at PCI following an initial 300 mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I	B
A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding.	IIa	B
Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases.	IIb	B
Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used.	IIb	B
In patients pre-treated with P2Y <sub>12</sub> inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered.	IIa	C
Ticagrelor or clopidogrel should be considered to be (re-)started after CABG surgery as soon as considered safe.	IIa	B
The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended.	III	C

[www.escardio.org/guidelines](http://www.escardio.org/guidelines)

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## ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

**2012**

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
<b>Antiplatelet therapy</b>			
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B	133, 134
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A	135, 136
• Prasugrel in clopidogrel-naïve patients, if no history of prior stroke/TIA, age <75 years.	I	B	109
• Ticagrelor.	I	B	110
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C	-
GP IIb/IIIa inhibitors should be considered for bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication.	IIa	C	-
Routine use of a GP IIb/IIIa inhibitor as an adjunct to primary PCI performed with unfractionated heparin may be considered in patients without contraindications.	IIb	B	137–141
Upstream use of a GP IIb/IIIa inhibitor (vs. in-lab use) may be considered in high-risk patients undergoing transfer for primary PCI.	IIb	B	127, 128, 137, 142
Options for GP IIb/IIIa inhibitors are (with LoE for each agent):			
• Abciximab		A	137
• Eptifibatid (with double bolus)		B	138, 139
• Tirofiban (with a high bolus dose)		B	140, 141
<b>Anticoagulants</b>			
An injectable anticoagulant must be used in primary PCI.	I	C	-
Bivalirudin (with use of GP IIb/IIIa blocker restricted to bailout) is recommended over unfractionated heparin and a GP IIb/IIIa blocker.	I	B	124
Enoxaparin (with or without routine GP IIb/IIIa blocker) may be preferred over unfractionated heparin.	IIb	B	122
Unfractionated heparin with or without routine GP IIb/IIIa blocker must be used in patients not receiving bivalirudin or enoxaparin.	I	C	I
Fondaparinux is not recommended for primary PCI.	III	B	118
The use of fibrinolysis before planned primary PCI is not recommended.	III	A	127, 143

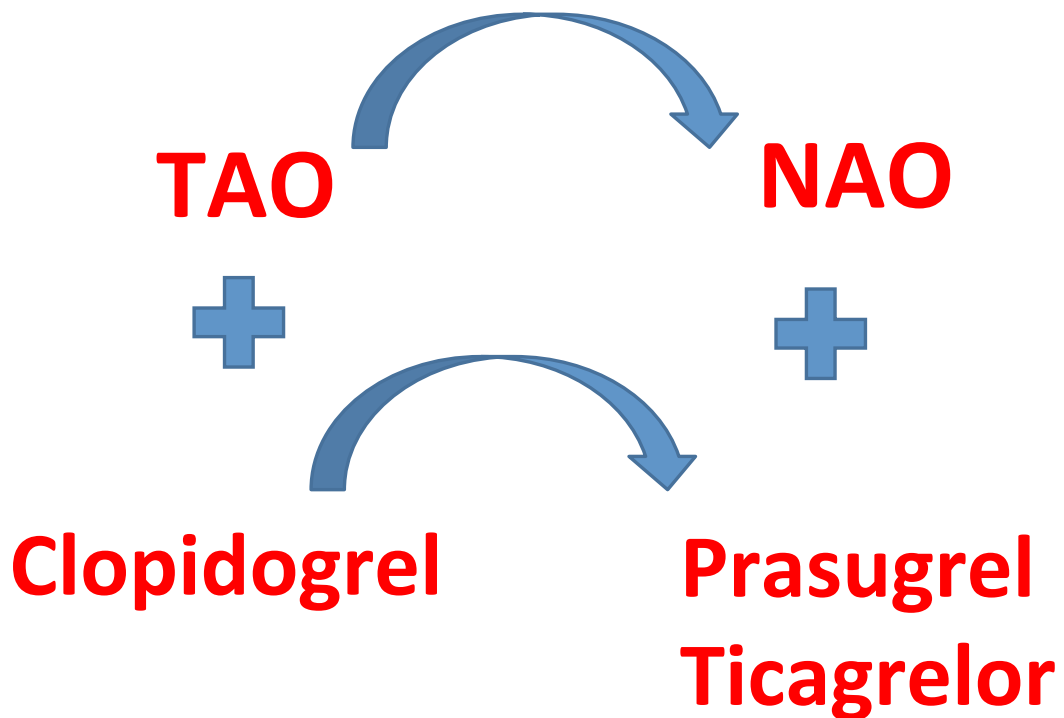
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## Un problema clinico emergente

- La **TRIPLICE** terapia antitrombotica  
**DOPPIA** antiaggregazione + **ANTICOAGULANTE**
- La **DOPPIA** terapia antitrombotica  
con i **NUOVI** antiaggreganti e/o anticoagulanti



## Emergency Hospitalizations for Adverse Drug Events in Older Americans

DS Budnitz, *n engl j med*, 2011

Medication	Annual National Estimate of Hospitalizations (N=99,628)		Proportion of Emergency Department Visits Resulting in Hospitalization
	no.	% (95% CI)	%
<b>Most commonly implicated medications†</b>			
Warfarin	33,171	33.3 (28.0–38.5)	46.2
Insulins	13,854	13.9 (9.8–18.0)	40.6
Oral antiplatelet agents	13,263‡	13.3 (7.5–19.1)	41.5
Oral hypoglycemic agents	10,656	10.7 (8.1–13.3)	51.8
Opioid analgesics	4,778	4.8 (3.5–6.1)	32.4
Antibiotics	4,205	4.2 (2.9–5.5)	18.3
Digoxin	3,465	3.5 (1.9–5.0)	80.5
Antineoplastic agents	3,329‡	3.3 (0.9–5.8)‡	51.5
Antiadrenergic agents	2,899	2.9 (2.1–3.7)	35.7
Renin–angiotensin inhibitors	2,870	2.9 (1.7–4.1)	32.6
Sedative or hypnotic agents	2,469	2.5 (1.6–3.3)	35.2
Anticonvulsants	1,653	1.7 (0.9–2.4)	40.0
Diuretics	1,071‡	1.1 (0.4–1.8)‡	42.4
<b>High-risk or potentially inappropriate medications§</b>			
HEDIS high-risk medications	1,207	1.2 (0.7–1.7)	20.7
Beers-criteria potentially inappropriate medications	6,607	6.6 (4.4–8.9)	42.0
Beers-criteria potentially inappropriate medications, excluding digoxin	3,170	3.2 (2.3–4.1)	27.6



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### Gruppi attualmente attivi nel registro:

**Rossella MARCUCCI, Serafina VALENTE; Firenze**  
**Vittorio PENGO; Padova**  
**Giuseppe PATTI; Roma**  
**Paolo GRESELE; Perugia**  
**Paolo CALABRO'; Napoli**  
**Plinio CIRILLO; Napoli**

### Prossimo ingresso:

**Raffaele DE CATERINA; Chieti**  
**Pasquale PIGNATELLI, Francesco VIOLI; Roma**



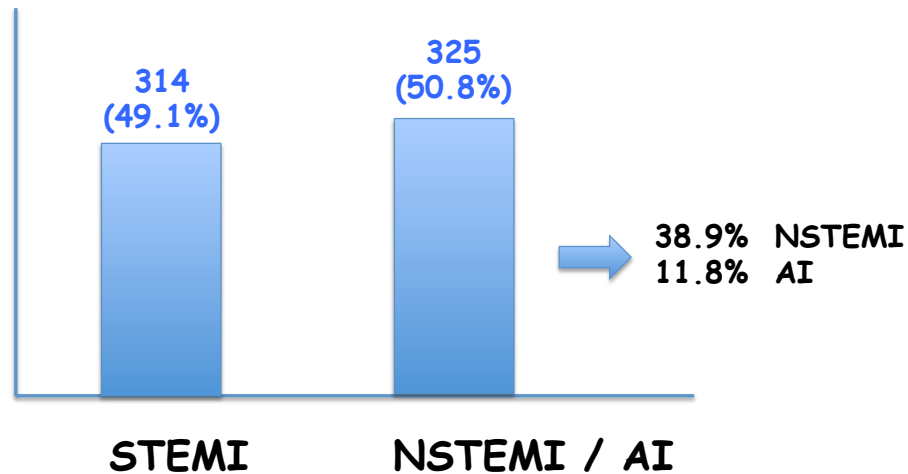
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**N = 639** pazienti con SCA

**478 M/ 161 F**

**Età: 66,7± 12,6**

Analisi a dicembre 2014



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**n=639**

## ANAMNESI....

Analisi a dicembre 2014

Pregresso IMA 132/639 (20,7%)

Pregressa PCI 128/639 (20%)

Pregresso TIA 26/639 (4,1%)

Pregresso stroke 18/639 (2,8%)

PAD 53/639 (8,3%)

Pregressa emorragia maggiore 9/639 (1,4%)  
3 cerebrale  
4 gastrointestinale  
1 metrorragia

Pregressa emorragia minore 3/639 (0,4%)

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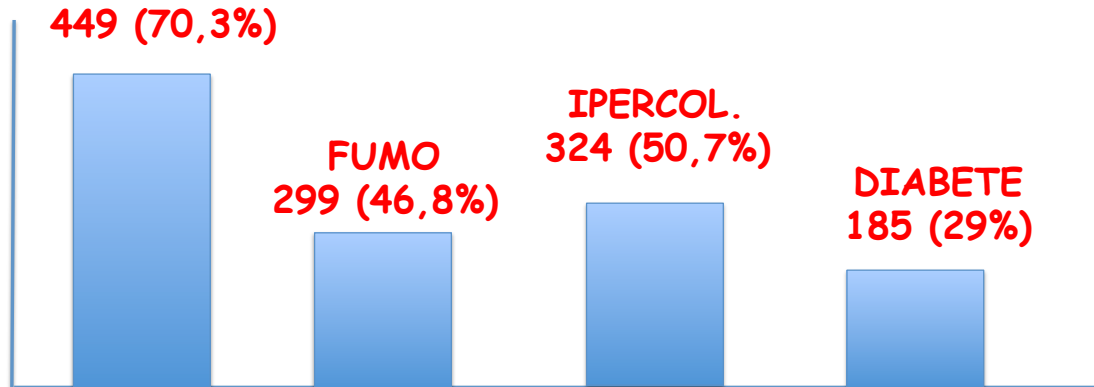
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n=639

Analisi a dicembre 2014

FANV	35/ 639	(5,5%)
FAV	11/639	(1,7%)
Protesi Valvolari Meccaniche	4/639	(0,6%)
TEV	6/639	(0,9%)

### IPERTENSIONE



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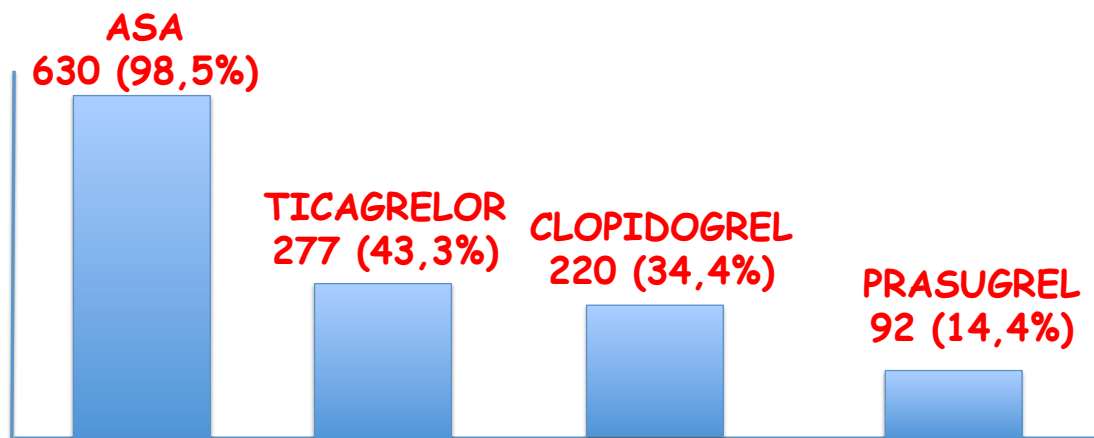
639

Analisi a dicembre 2014

PCI  
n= 515

Bypass AoC  
n= 20

Terapia Medica  
n= 104



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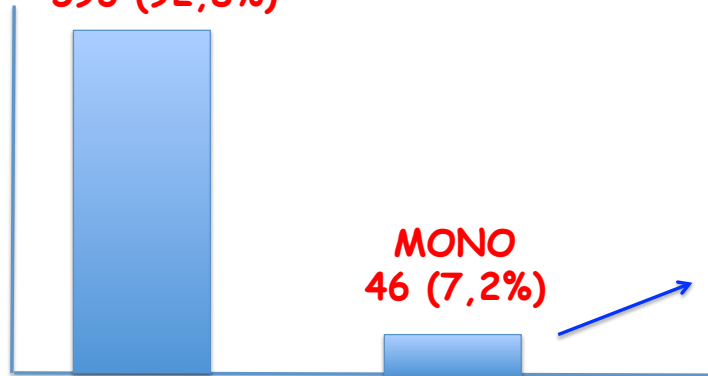


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Analisi a dicembre 2014

## TERAPIA ANTIAGGREGANTE

**DOPPIA**  
**ASA + tienopiridina**  
**593 (92,8%)**



6 solo ASA  
40 solo tienopiridina



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## TERAPIA ANTIAGGREGANTE

### TRIPLICE TERAPIA ANTITROMBOTICA

46/639 7.2%

35: WARFARIN + ASA + CLOPIDOGREL

10: DABIGATRAN + ASA + CLOPIDOGREL

1: APIXABAN + ASA + CLOPIDOGREL

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## FATTORI PREDITTIVI SOMMINISTRAZIONE CLOPIDOGREL

		Variabili nell'equazione					95% CI per EXP(B)		
		B	E.S.	Wald	df	Sig.	Exp(B)	Inferiore	Superiore
Passo 1 <sup>a</sup>	Sesso	,104	,261	,159	1	,690	1,110	,665	1,852
	età	,048	,011	20,292	1	,000	1,049	1,027	1,071
	nstemistemiVAR00001	-,879	,223	15,485	1	,000	,415	,268	,643
	tiastroke	,894	,458	3,812	1	,051	2,444	,997	5,996
	Arteriopatiaobliteranteperiferica	-,342	,434	,622	1	,430	,710	,304	1,662
	BMI	-,004	,008	,175	1	,675	,997	,980	1,013
	Stent	-,432	,391	1,218	1	,270	,649	,302	1,398
	Iperensione	-,656	,262	6,289	1	,012	,519	,311	,866
	Fumo	-,278	,237	1,373	1	,241	,757	,475	1,206
	Ipercolesterolemia	,212	,227	,871	1	,351	1,236	,792	1,930
	Diabete	,271	,244	1,234	1	,267	1,311	,813	2,113
	anticoagulante	3,127	,629	24,682	1	,000	22,809	6,642	78,324
	Costante	-2,921	,859	11,568	1	,001	,054		

a. Variabili immesse al passo 1: Sesso, età, nstemistemiVAR00001, tiastroke, Arteriopatiaobliteranteperiferica, BMI, Stent, Iperensione, Fumo, Ipercolesterolemia, Diabete, anticoagulante.



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## FATTORI PREDITTIVI SOMMINISTRAZIONE PRASUGREL

		Variabili nell'equazione					95% CI per EXP(B)		
		B	E.S.	Wald	df	Sig.	Exp(B)	Inferiore	Superiore
Passo 1 <sup>a</sup>	Sesso	-,523	,361	2,100	1	,147	,593	,292	1,202
	età	-,048	,012	16,426	1	,000	,953	,932	,976
	nstemistemiVAR00001	1,603	,320	25,124	1	,000	4,968	2,654	9,297
	tiastroke	-1,115	,788	2,004	1	,157	,328	,070	1,535
	Arteriopatiaobliteranteperiferica	-,550	,658	,697	1	,404	,577	,159	2,097
	BMI	,013	,008	2,550	1	,110	1,013	,997	1,030
	Stent	1,658	1,039	2,547	1	,110	5,248	,685	40,203
	Iperensione	,626	,303	4,278	1	,039	1,870	1,033	3,385
	Fumo	-,051	,280	,034	1	,854	,950	,549	1,644
	Ipercolesterolemia	-,016	,264	,003	1	,953	,985	,587	1,651
	Diabete	,225	,302	,557	1	,455	1,253	,693	2,262
	anticoagulante	-1,510	1,045	2,091	1	,148	,221	,029	1,710
	Costante	-1,878	1,320	2,026	1	,155	,153		

a. Variabili immesse al passo 1: Sesso, età, nstemistemiVAR00001, tiastroke, Arteriopatiaobliteranteperiferica, BMI, Stent, Iperensione, Fumo, Ipercolesterolemia, Diabete, anticoagulante.



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## FATTORI PREDITTIVI SOMMINISTRAZIONE TICAGRELOR

	Variabili nell'equazione						95% CI per EXP(B)	
	B	E.S.	Wald	df	Sig.	Exp(B)	Inferiore	Superiore
Sesso	-,054	,228	,055	1	,814	,948	,606	1,482
età	-,010	,008	1,456	1	,228	,990	,974	1,006
nstemistemiVAR00001	-,168	,189	,783	1	,376	,846	,584	1,226
tiastroke	-,081	,412	,039	1	,844	,922	,411	2,067
Arteriopatiaobliteranteperiferica	,128	,370	,119	1	,730	1,136	,550	2,348
BMI	-,009	,010	,842	1	,359	,991	,972	1,010
Stent	,246	,363	,462	1	,497	1,279	,629	2,604
Iperensione	,090	,216	,173	1	,677	1,094	,717	1,670
Fumo	,179	,201	,790	1	,374	1,195	,806	1,772
Ipercolesterolemia	-,076	,190	,158	1	,691	,927	,639	1,345
Diabete	-,187	,213	,772	1	,380	,829	,547	1,259
anticoagulante	-2,814	,740	14,473	1	,000	,060	,014	,256
Costante	,831	,734	1,280	1	,258	2,295		

a. Variabili immesse al passo 1: Sesso, età, nstemistemiVAR00001, tiastroke, Arteriopatiaobliteranteperiferica, BMI, Stent, Iperensione, Fumo, Ipercolesterolemia, Diabete, anticoagulante.



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Analisi a dicembre 2014

## FOLLOW-UP 12 MESI

**n= 202**

<b>MORTE</b>	<b>11 (5,4%)</b>
<b>MORTE CARDIOVASCOLARE</b>	<b>10 (5%)</b>
<b>TVR</b>	<b>9 (4,5%)</b>
<b>IMA</b>	<b>5 (2,4%)</b>
<b>SANGUINAMENTI</b>	
<b>TIMI maggiori</b>	<b>2 (0.9%)</b>
<b>TIMI minori</b>	<b>10 (5%)</b>
<b>ISTH maggiori</b>	<b>2 (0.9%)</b>
<b>ISTH minori</b>	<b>10 (5%)</b>

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**FOLLOW-UP 12 MESI**

Analisi a dicembre 2014

**n= 202**

### **COMPLICANZA EMORRAGICA**

6/10 (60%) pazienti in **TRIPLICE TERAPIA** (13% dei pz in triplice ha fatto sanguinamento)

4/10 (40%) pazienti in **DOPPIA TERAPIA** (2.5% dei pazienti in doppia antiaggregazione)

### **COMPLICANZA ISCHEMICA**

6	Clopidogrel	(10% dei pazienti in clopidogrel)
3	Ticagrelor	(5% dei pazienti in ticagrelor)
1	Prasugrel	(5% dei pazienti in prasugrel)