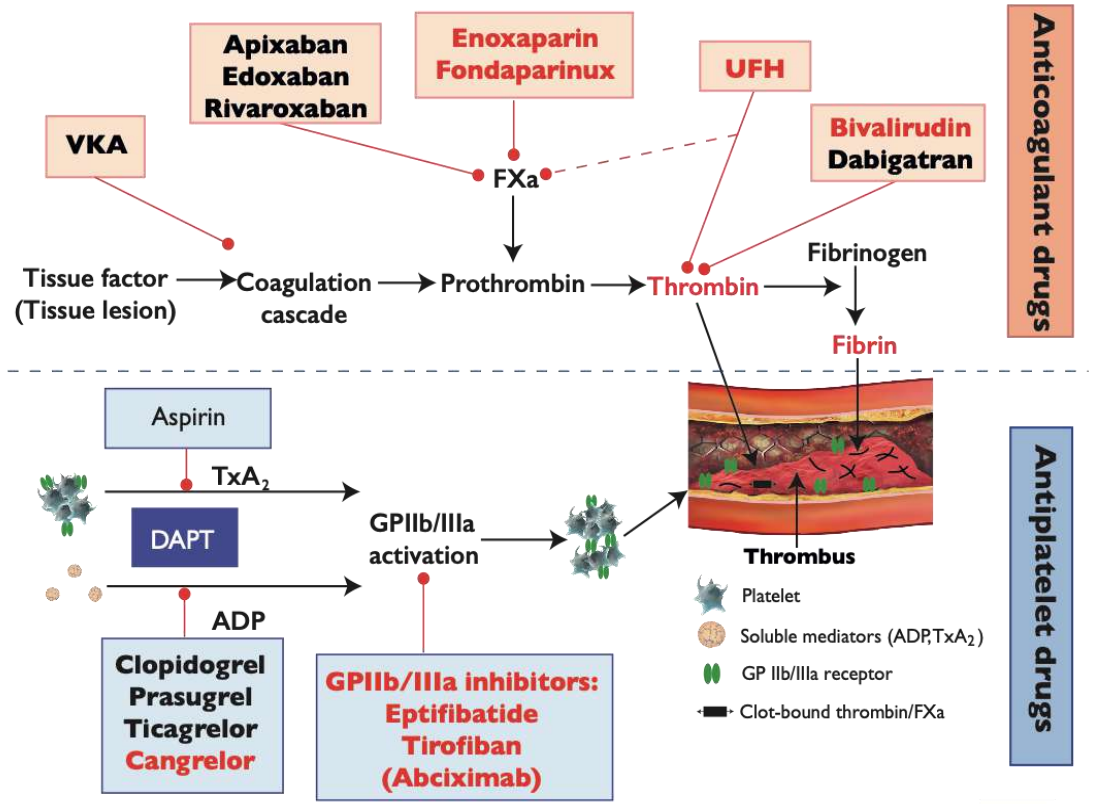
Առանց ST սեգմենտի բարձրացման սուր կորոնար համախտանիշի սուր և քրոնիկական փուլերում ըստ 2020 ESC ուղեցույցի



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Antithrombotic treatments in non-ST-segment elevation acute coronary syndrome patients: pharmacological targets. Drugs with oral administration are shown in black letters and drugs with preferred parenteral administration in red. Abciximab (in brackets) is not supplied anymore.

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Antithrombotic treatments in NSTE-ACS: pharmacological targets

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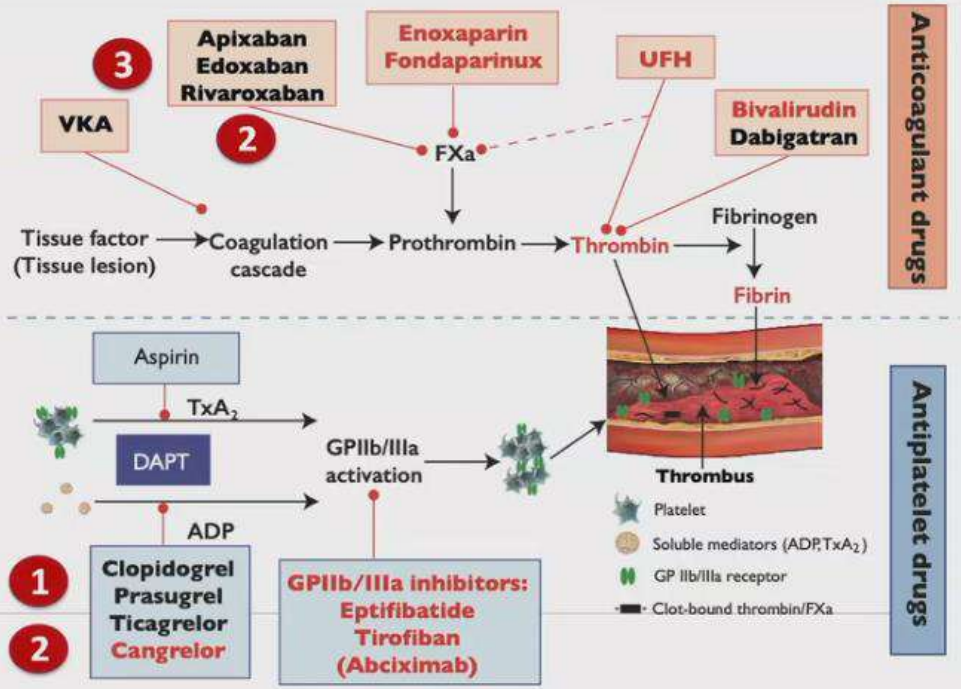
Focus on:

1. *$P2Y_{12}$ inhibition*
2. *Extended Tx*
3. *Triple vs. Dual Tx*



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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Determinants of antithrombotic treatment in coronary artery disease patients

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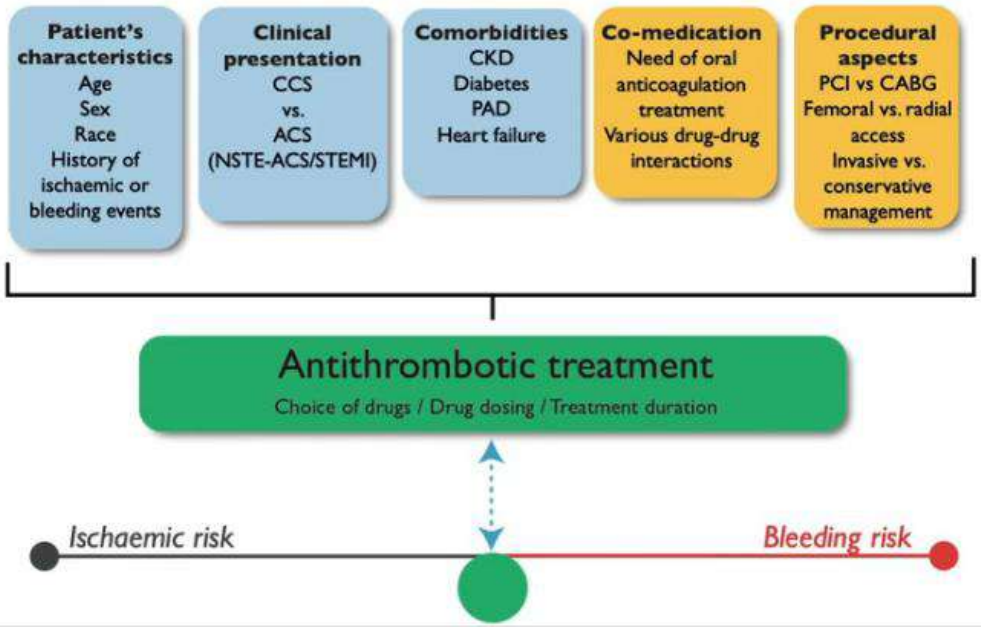

Intrinsic (in blue: patient's characteristics, clinical presentation & comorbidities) and extrinsic (in yellow: co-medication & procedural aspects) variables influencing the choice, dosing, and duration of antithrombotic treatment.

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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

1

Novel aspects on $P2Y_{12}$ receptor inhibition in NSTE-ACS (1) – Choice of treatment

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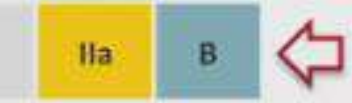
Recommendations	Class	Level
Antiplatelet treatment		
A $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, and maintained over 12 months unless there are contraindications or an excessive risk of bleeding. Options are:	I	A
• Prasugrel in $P2Y_{12}$ receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg/d as standard dose, 5 mg/d for patients aged ≥75 years or with a body weight <60 kg).	I	B
• Ticagrelor irrespective of the planned treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d.).	I	B
• Clopidogrel (300–600 mg LD, 75 mg daily dose), only when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.	I	C
Prasugrel should be preferred over ticagrelor for NSTE-ACS patients who proceed to PCI.	IIa	B



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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

1 Novel aspects on $P2Y_{12}$ receptor inhibition in NSTE-ACS (1) – Choice of treatment

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor or Prasugrel in Patients with Acute Coronary Syndromes

- ISAR-REACT 5: 4018 ACS patients with planned invasive management
- 2365/4018 with unstable angina or NSTEMI (PCI in 84%)

Prasugrel superior over ticagrelor for ischemic outcomes / similar bleeding risk

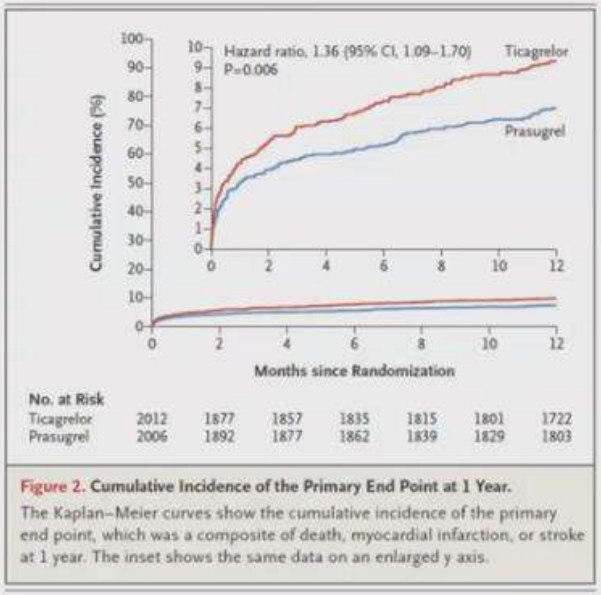


Figure 2. Cumulative Incidence of the Primary End Point at 1 Year.
The Kaplan–Meier curves show the cumulative incidence of the primary end point, which was a composite of death, myocardial infarction, or stroke at 1 year. The inset shows the same data on an enlarged y axis.

Schüpke et al., N Engl J Med. 2019

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

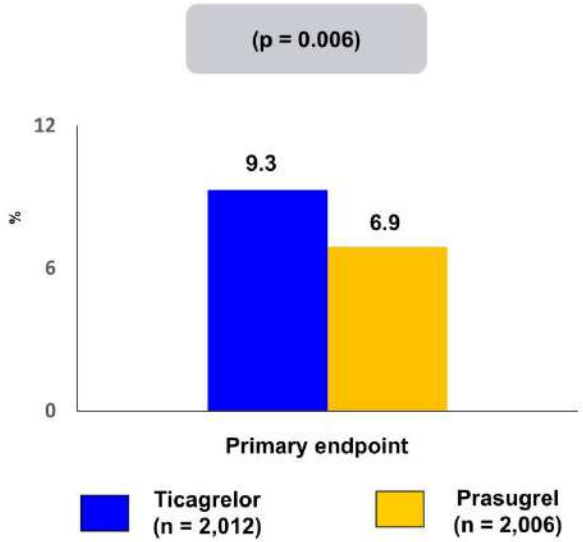
1

ISAR-REACT 5

#ESCCongress

AMERICAN COLLEGE of CARDIOLOGY

Trial Description: Patients with an acute coronary syndrome undergoing planned early invasive therapy were randomized to ticagrelor versus prasugrel.



RESULTS

- Primary efficacy endpoint: death, myocardial infarction, or stroke at 1 year occurred in 9.3% of the ticagrelor group compared with 6.9% of the prasugrel group (p = 0.006)
- BARC major bleeding (types 3, 4, or 5): 5.4% in the ticagrelor group vs. 4.8% in the prasugrel group (p = NS)

CONCLUSIONS

- In patients across the acute coronary syndrome spectrum undergoing planned coronary angiography, prasugrel was superior to ticagrelor at preventing major adverse ischemic events
- Benefit from prasugrel was accomplished without an increase in major bleeding

Schüpke S, et al. N Engl J Med 2019;Sep 1:[Epub]

1 Novel aspects on $P2Y_{12}$ receptor inhibition in NSTE-ACS (2) - Pretreatment

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Recommendations	Class	Level
Antiplatelet treatment		
Pre-treatment with a $P2Y_{12}$ receptor inhibitor may be considered in patients with NSTE-ACS who are not planned to undergo an early invasive strategy and do not have an HBR.	IIb	C
It is not recommended to administer routine pre-treatment with a $P2Y_{12}$ receptor inhibitor in patients in whom coronary anatomy is not known and an early invasive management is planned.	III	A

(1) Lack of evidence for a pre-treatment benefit (*ACCOAST, #SCAAR registry, §ISAR-REACT 5)
(2) Potent P2Y12 inhibition = fast onset of action => LD administration directly before PCI
(3) Pre-treatment strategy risky for some patients: e.g. aortic dissection or undiscovered bleeding complications
(4) Increased bleeding risk & delay in conjunction with CABG

*Montalescot et al., N Engl J Med. 2013, #Dworeck et al., in press 2020, §Schüpke et al., N Engl J Med. 2019

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Conclusions

- In NSTE-ACS patients managed invasively within 48 hours of admission, pre-treatment with prasugrel does not reduce major ischemic events through 30 days but increases major bleeding complications.
- The results are consistent among patients undergoing PCI supporting treatment with prasugrel once the coronary anatomy has been defined.
- No subgroup appears to have a favorable risk/benefit ratio of pre-treatment.
- Reappraisal of routine pre-treatment strategies in NSTE-ACS is needed.

Algorithm for antithrombotic therapy in NSTE-ACS patients without AF undergoing PCI

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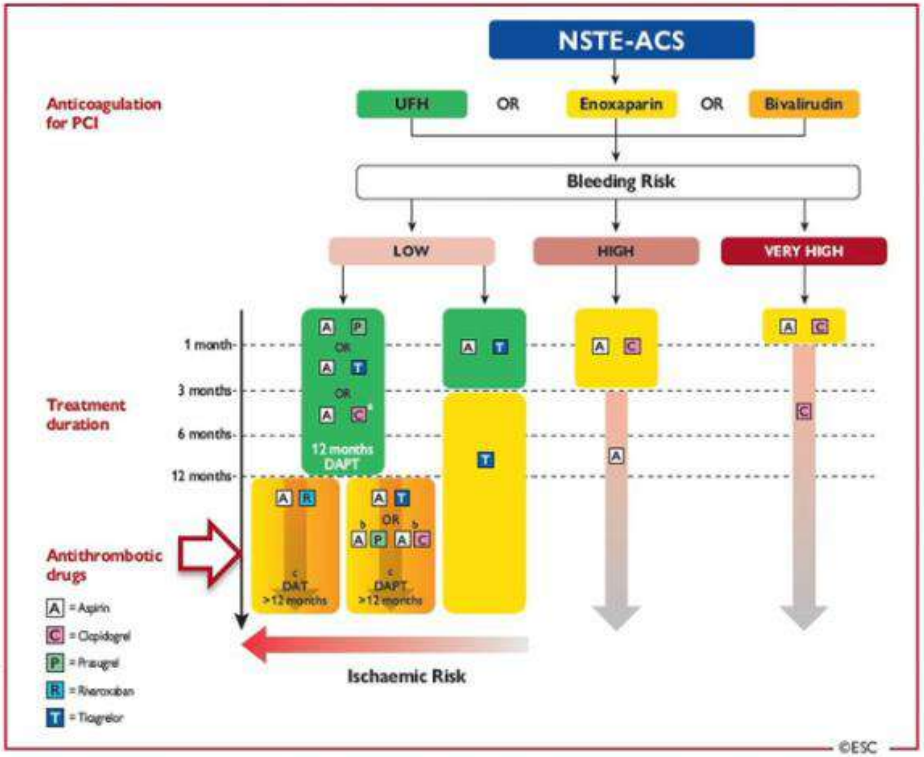

(1) **Bleeding risk determines recommendations for choice, duration and extended Tx**

(2) **Different options for extended Tx > 12 months**

Very HBR is defined as recent bleeding in the past month and/or not deferrable planned surgery.

= Class I = Class IIa = Class IIb

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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2

Recommendations for extended long-term secondary prevention antithrombotic treatment

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2015	2020
Pharmacological treatments	
$P2Y_{12}$ inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient.	Adding a second antithrombotic agent to aspirin for extended long-term secondary prevention should be considered in patients at high risk of ischaemic events and without increased risk of major or life-threatening bleeding.

Class I	Class IIa	Class IIb

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2

Risk criteria for extended treatment with a second antithrombotic agent

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High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Risk enhancers	
Diabetes mellitus requiring medication	Diabetes mellitus requiring medication
History of recurrent MI	History of recurrent MI
Any multivessel CAD	Polyvascular disease (CAD plus PAD)
Polyvascular disease (CAD plus PAD)	CKD with eGFR 15–59 mL/min/1.73 m
Premature (<45 years) or accelerated (new lesion within a 2-year time frame) CAD	
Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis)	
CKD with eGFR 15–59 mL/min/1.73 m^2	
Technical aspects	
At least 3 stents implanted	
At least 3 lesions treated	
Total stent length >60 mm	
History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel)	
History of stent thrombosis on antiplatelet treatment	

(1) Stratification for complex vs. non-complex CAD: individual clinical judgement & cardiovascular history and/or coronary anatomy.

(2) Risk-enhancing factors are based on evidence from RCTs and large-scale registries (see GL document)

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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2

Risk criteria for extended treatment with a second antithrombotic agent (1)

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High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Risk enhancers	
Diabetes mellitus requiring medication	Diabetes mellitus requiring medication
History of recurrent MI	History of recurrent MI
Any multivessel CAD	Polyvascular disease (CAD plus PAD)
Polyvascular disease (CAD plus PAD)	CKD with eGFR 15–59 mL/min/1.73 m^2
Premature (<45 years) or accelerated (new lesion within a 2-year time frame) CAD	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries.

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2

Risk criteria for extended treatment with a second antithrombotic agent (2)

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High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Risk enhancers (continued)	
Concomitant systemic inflammatory disease (e.g. human immunodeficiency virus, systemic lupus erythematosus, chronic arthritis)	
CKD with eGFR 15–59 mL/min/1.73 m^2	
Technical aspects	
At least 3 stents implanted	
At least 3 lesions treated	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries

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2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2

Risk criteria for extended treatment with a second antithrombotic agent (3)

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High thrombotic risk (Class IIa)	Moderately increased thrombotic risk (Class IIb)
Complex CAD and at least 1 criterion	Non-complex CAD and at least 1 criterion
Technical aspects (continued)	
Total stent length >60 mm	
History of complex revascularization (left main, bifurcation stenting with ≥2 stents implanted, chronic total occlusion, stenting of last patent vessel)	
History of stent thrombosis on antiplatelet treatment	

In line with guideline recommendations, CAD patients are stratified into two different risk groups (high vs. moderately increased thrombotic or ischaemic risk). Stratification of patients towards complex vs. non-complex CAD is based on individual clinical judgement with knowledge of patients' cardiovascular history and/or coronary anatomy. Selection and composition of risk-enhancing factors are based on the combined evidence of clinical trials on extended antithrombotic treatment in CAD patients and on data from related registries.

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

2 Treatment options for extended long-term secondary prevention treatment

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Drug	Dose	Indication	NNT (ischaemic outcomes)	NNH (bleeding Outcomes)
DAT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Rivaroxaban (COMPASS trial)	2.5 mg b.i.d.	Patients with CAD or symptomatic PAD at high risk of ischaemic events	77	84
DAPT regimens for extended treatment (including aspirin 75–100 mg o.d.)				
Clopidogrel (DAPT trial)	75 mg/d	Post MI in patients who have tolerated DAPT for 1 year	63	105
Prasugrel (DAPT trial)	10 mg/d (5 mg/d if body weight <60 kg or age >75 years)	Post PCI for MI in patients who have tolerated DAPT for 1 year	63	105
Ticagrelor (PEGASUS-TIMI 54)	60/90 mg b.i.d.	Post MI in patients who have tolerated DAPT for 1 year	84	81

Drugs (in addition to aspirin 75–100 mg/d) for extended DAPT treatment options are in alphabetical order. For indications and definitions for high/moderately increased risk and bleeding risk see *published ESC guideline*. NNT refers to the primary ischaemic endpoints of the respective trials and NNH refers to the key safety (bleeding) endpoints. NNT and NNH numbers from the DAPT trial are pooled numbers for clopidogrel and prasugrel.

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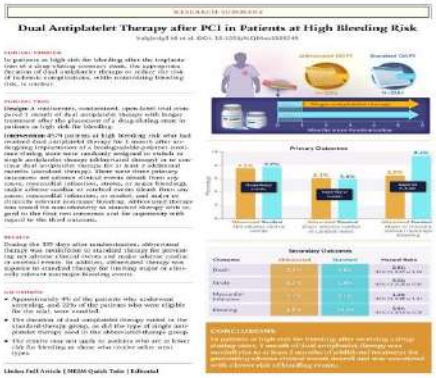
2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

COMPASS PCI

Conclusions

- DPI compared with aspirin alone:
  - Produced consistent reductions in CV death, MI, stroke as well as all-cause death with or without prior PCI
  - Increased major bleeding without a significant increase in fatal bleeding or intracranial hemorrhage
- In patients with prior PCI:
  - Consistent reductions in CV death, MI, stroke as well as all-cause death were demonstrated with DPI irrespective of the timing of prior PCI (as far back as 10-years)



PEGASUS TIMI 54

Conclusion

Long-term dual antiplatelet therapy with low-dose aspirin and ticagrelor should be considered in appropriate patients with a myocardial infarction.

3 Recommendations for combining antiplatelet agents and anticoagulants in non-ST-segment elevation acute coronary syndrome patients requiring chronic oral anticoagulation

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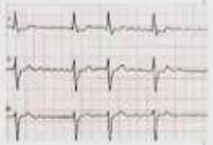

A ISTH MAJOR OR CLINICALLY RELEVANT NONMAJOR BLEEDING

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	204	2279	367	2277	26.8%	0.56 [0.47, 0.65]
ENTRUST AF-PCI	128	751	152	755	22.3%	0.85 [0.68, 1.05]
PIONEER AF-PCI	117	696	178	697	22.7%	0.66 [0.53, 0.81]
RE-DUAL PCI	305	1744	264	981	28.2%	0.65 [0.56, 0.75]
Total (95% CI)		**5470**		**4710**	**100.0%**	**0.66 [0.56, 0.78]**
Total events	754		961			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 9.65$, df = 3 (P = 0.02); $I^2 = 69\%$
Test for overall effect: Z = 5.03 (P < 0.00001)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

C TRIAL-DEFINED MACE

Study or Subgroup	DAT Events	DAT Total	TAT Events	TAT Total	Weight	Risk Ratio M-H, Random, 95% CI
AUGUSTUS	168	2307	149	2307	37.1%	1.13 [0.91, 1.40]
ENTRUST AF-PCI	49	751	46	755	11.1%	1.07 [0.73, 1.58]
PIONEER AF-PCI	41	694	36	695	8.9%	1.14 [0.74, 1.76]
RE-DUAL PCI	239	1744	131	981	42.9%	1.03 [0.84, 1.25]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.08 [0.95, 1.23]**
Total events	497		362			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.47$, df = 3 (P = 0.92); $I^2 = 0\%$
Test for overall effect: Z = 1.13 (P = 0.26)

Risk Ratio M-H, Random, 95% CI
0.01 0.1 1 10 100
Favours DAT Favours TAT

Gargiulo et al., EHJ 2019

DAT vs. TAT

PIONEER AF-PCI

RE-DUAL PCI
Study in NVAF patients undergoing PCI

Augustus

Engage-AF

2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

3 Recommendations for combining antiplatelet agents and anticoagulants in non-ST-segment elevation acute coronary syndrome patients requiring chronic oral anticoagulation

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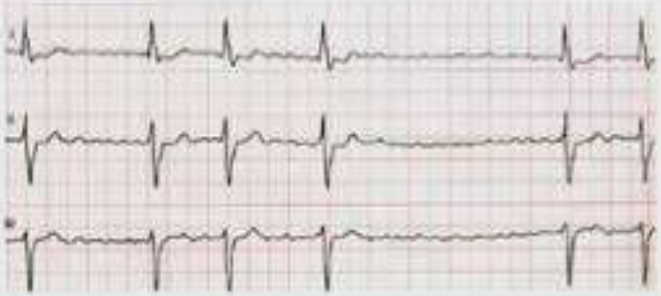

NOAC + clopidogrel preferred

Antithrombotic treatment
In patients with AF (CHA_2DS_2-VASc score ≥1 in men and ≥2 in women), after a short period of TAT (up to 1 week from the acute event), DAT is recommended as the default strategy using a NOAC at the recommended dose for stroke prevention and single oral antiplatelet agent (preferably clopidogrel).
Discontinuation of antiplatelet treatment in patients treated with OACs is recommended after 12 months.
DAT with an OAC and either ticagrelor or prasugrel may be considered as an alternative to TAT with an OAC, aspirin, and clopidogrel in patients with a moderate or high risk of stent thrombosis, irrespective of the type of stent used.

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3 Algorithm for antithrombotic therapy in NSTE-ACS patients with AF undergoing PCI or medical management

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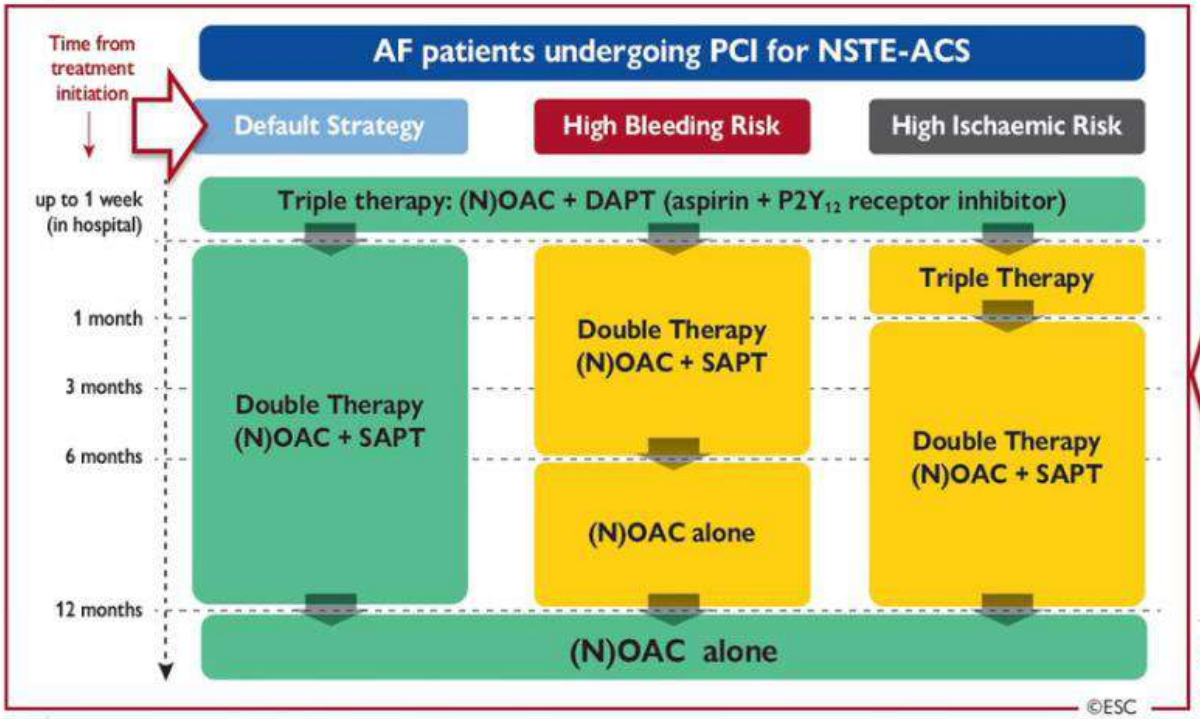

PIONEER AF-PCI

RE-DUAL PCI Study in NVAF patients undergoing PCI

Augustus

Engage-AF

Green (Class I)

yellow (Class IIa)

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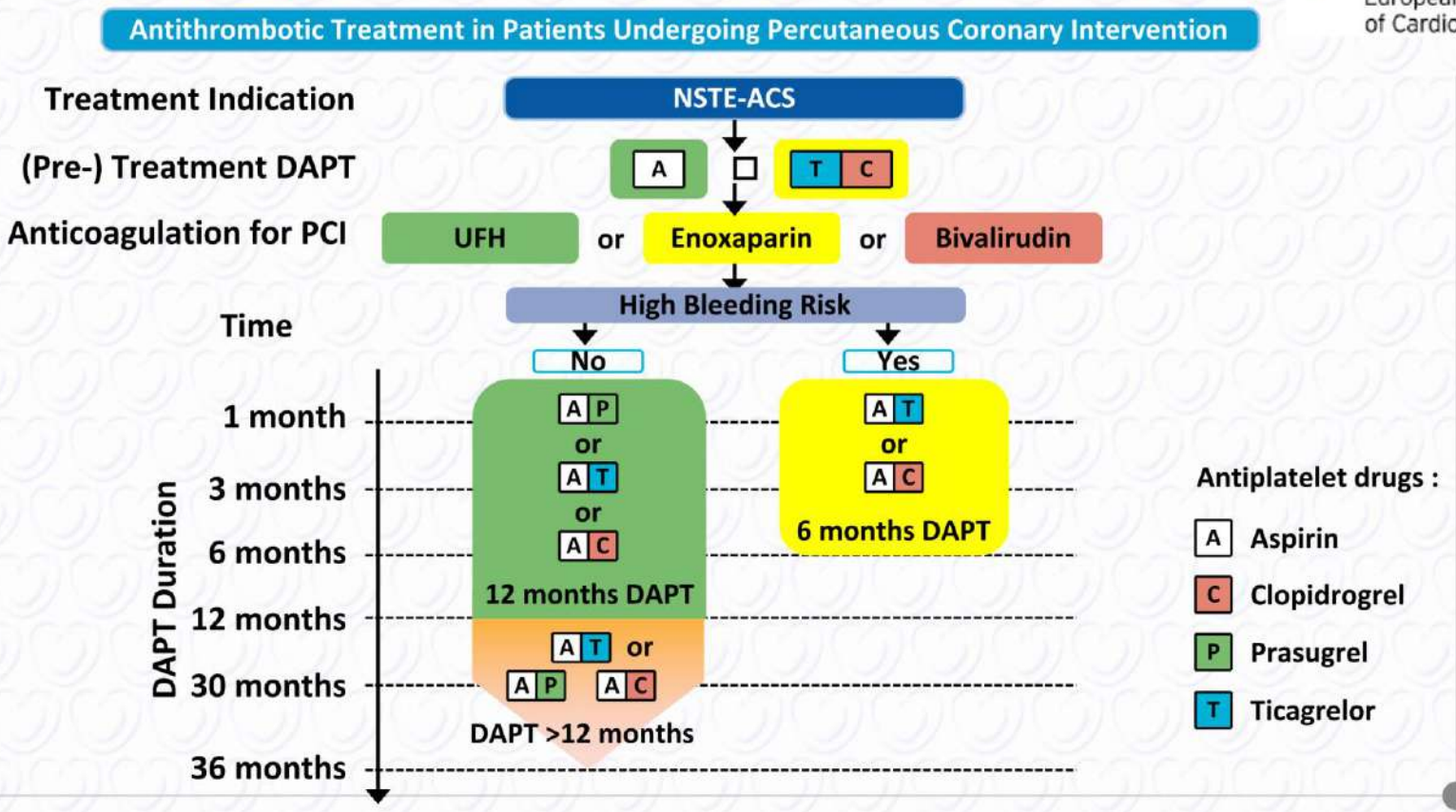
2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (European Heart Journal 2020 - doi/10.1093/eurheartj/ehaa575)

Algorithm for the use of antithrombotic drugs in patients undergoing percutaneous coronary intervention (3)



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2018 ESC/EACTS Guidelines on myocardial revascularisation
European Heart Journal (2018) 00, 1-96 - doi:10.1093/eurheartj/ehy394

Algorithm for the use of antithrombotic drugs in patients undergoing percutaneous coronary intervention (4)

EACTS

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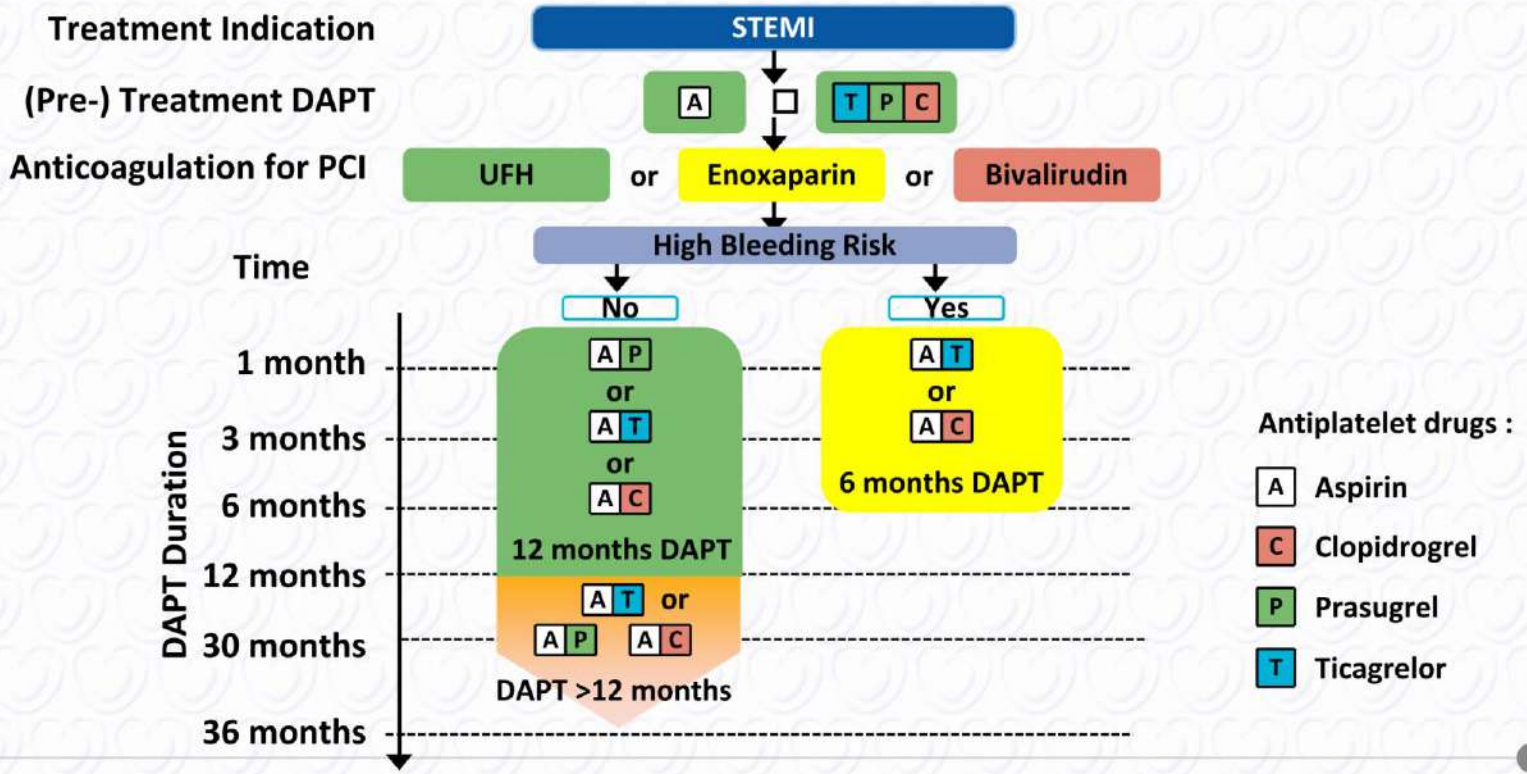
Antithrombotic Treatment in Patients Undergoing Percutaneous Coronary Intervention



2018 ESC/EACTS Guidelines on myocardial revascularisation
European Heart Journal (2018) 00, 1-96 - doi:10.1093/eurheartj/ehy394