ESC NSTEMI Guidelines

An Update

Christian W. Hamm
Medical Clinic I
University Hospital Giessen

& Kerckhoff Heart and Thorax Center
Bad Nauheim, Germany
ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation

The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC)

Authors/Task Force Members: Christian W. Hamm (Chairperson) (Germany)*, Jean-Pierre Bassand (Co-Chairperson) (France), Stefan Agewall (Norway), Dean B. Zanstra (The Netherlands), Eric Boersma (The Netherlands), Hector Bueno Caso (Italy), Dariusz Dudek (Poland), Stephan Gielen (Germany), Richard A. O. A. Folts (Austria), Magnus Ohman (USA), Mark C. Petrie (UK), Frank Sonntag (Germany), Miguel Sousa Uva (Portugal), Robert F. Storey (UK), William Wijns (Belgium), Irun Zahger (Israel).

For Practice Guidelines: Jeroen J. Bax (Chairperson) (The Netherlands), Angelo Auricchio (Italy), Monika Baumgartner (Germany), Claudio Ceconi (Italy), Veronica Dean (France), Christi Deaton (South Africa), David Dejaegere (Belgium), Christian Funck-Brentano (France), David Hasdai (Israel), Arno Hoes (The Netherlands), Philippe Kolh (Belgium), Theresa McDonagh (UK), Cyril Moulin (France), Halldor Adalsteinsson (Iceland), T. Alexander Baccarelli (Italy), Richard A. O. A. Folts (Austria), Zdenko Reiner (Croatia), Udo Sechtem (Germany), Bob Sharp (USA), John Sutton (UK), Robert F. Storey (UK), William Wijns (Belgium), Irun Zahger (Israel).
What was new?

- **Diagnostic**
  - High-sensitive troponin introduced
  - Echocardiography standard
  - Coronary CT for rule-out in low/intermediate risk patients

- **Risk Stratification**
  - 3-hour fast rule-out protocol
  - Bleeding risk score (CRUSADE)

- **Medical Treatment**
  - Ticagrelor and prasugrel introduced

- **Revascularization**
  - Timing of revascularization
What is new 2013?

- hs-Troponin: more data
- CT: new studies
- Invasive strategy: new metaanalysis
- Prasugrel new study: TRILOGY
- Vorapaxar: new antiplatelet drug
- Rivaroxaban: new anticoagulation
## Recommendations for diagnosis and risk stratification

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood has to be drawn promptly for troponin (cardiac troponin T or I) measurement. The result should be available within 60 min. The test should be repeated 6-9 h after initial assessment if the first measurement is not conclusive. Repeat testing after 12-24 h is advised if the clinical condition is still suggestive.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>A rapid rule-out protocol (0 and 3 h) is recommended when highly sensitive troponin tests are available.</td>
<td></td>
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<tr>
<td>An echocardiogram is recommended for all patients to evaluate regional and global LV function and to rule in or rule out differential diagnoses.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Coronary angiography is indicated in patients in whom the extent of CAD or the culprit lesion has to be determined.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Coronary CT angiography should be considered as an alternative to invasive angiography to exclude ACS when there is a low to intermediate likelihood of CAD and when troponin and ECG are inconclusive.</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>In patients without recurrence of pain, normal ECG findings, negative troponins tests, and a low risk score, a non-invasive stress test for inducible ischaemia is recommended before deciding on an invasive strategy.</td>
<td>I</td>
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</tr>
</tbody>
</table>

European Heart Journal (2011) 32:2999–3054
doi:10.1093/eurheartj/ehr236
Rapid rule-out of ACS with high-sensitivity troponin.

Acute Chest Pain

hsTn < ULN
- Pain >6h
  - hsTn no change
    - Painfree, GRACE <140, differential diagnoses excluded
      - Discharge/Stress testing
  - Pain <6h

hsTn > ULN
- Re-test hsTn: 3h
  - Δ change
    1 value > ULN
      - Highly abnormal Tn + clinical presentation
      - Work-up differential diagnoses
    - hsTn no change
      - Invasive management
Evolution of the cardiac troponin (cTn) assays

Mahajan V S, Jarolim P Circulation 2011;124:2350-2354
Hs-Troponin Elevation on Admission

Prevalence of AMI in Chest Pain Patients, %

Baseline hs-cTnT, ng/L

- ≥200
- 100-199
- 50-99
- 14-49
- <14

T. Reichlin, Arch Intern Med. 2012
How to use high-sensitivity cardiac troponins in acute cardiac care†

Kristian Thygesen*, Johannes Mair, Evangelos Giannitsis, Christian Mueller, Bertil Lindahl, Stefan Blankenberg, Kurt Huber, Mario Plebani, Luigi M. Biasucci, Marco Tubaro, Paul Collinson, Per Venge, Yonathan Hasin, Marcello Galvani, Wolfgang Koenig, Christian Hamm, Joseph S. Alpert, Hugo Katus, and Allan S. Jaffe, the Study Group on Biomarkers in Cardiology of the ESC Working Group on Acute Cardiac Care

Department of Cardiology, Aarhus University Hospital, Tage-Hansens Gade 2, DK-8000 Aarhus C, Denmark

Received 19 February 2012; revised 13 April 2012; accepted 7 May 2012; online publish-ahead-of-print 21 June 2012
Algorithm for Rapid Rule-in

Rapid early rule-in of AMI with high-sensitivity cardiac troponin

1. Acute chest pain
   - Initial hs-cTn value ≤ URL
   - Initial hs-cTn value > URL

2. Measurement at admission
   - Initial hs-cTn value ≤ URL
     - hs-cTn value at 3 h > URL + increase > 50% of URL
     - Myocardial necrosis
       - hs-cTn value at 6 h > URL + increase > 50% of URL
       - Evidence of ischaemia*
       - Myocardial infarction
   - Initial hs-cTn value > URL
     - hs-cTn value at 3 h > URL + increase > 20% of initial value
     - Myocardial infarction
### Recommendations for diagnosis and risk stratification (2)

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Coronary CT Angiography versus Standard Evaluation in Acute Chest Pain

Length of Stay in the Hospital and Proportion of Patients Discharged.

### Criteria for high risk with indication for invasive management

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<td>• Relevant rise or fall in troponin.</td>
</tr>
<tr>
<td>• Dynamic ST- or T-wave changes (symptomatic or silent).</td>
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</table>

<table>
<thead>
<tr>
<th>Secondary</th>
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<td>• Diabetes mellitus.</td>
</tr>
<tr>
<td>• Renal insufficiency (eGFR &lt; 60 mL/min/1.73 m²).</td>
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<tr>
<td>• Reduced LV function (ejection fraction &lt; 40%).</td>
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<tr>
<td>• Early post infarction angina.</td>
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<tr>
<td>• Recent PCI.</td>
</tr>
<tr>
<td>• Prior CABG.</td>
</tr>
<tr>
<td>• Intermediate to high GRACE risk score.</td>
</tr>
</tbody>
</table>
Meta-analysis in Diabetes

Invasive vs conservative Management

- RR 0.89 (0.68-1.16)
  ARR 2.2% (-3.4% to 7.9%)

- RR 0.75 (0.59-0.95)
  ARR 3.0% (0.1% to 5.8%)

- RR 0.93 (0.69-1.24)
  ARR 0.9% (-3.3 to 5.1%)

- RR 1.04 (0.79-1.37)
  ARR 0.1% (-3.0% to 2.8%)

- RR 1.03 (0.82-1.31)
  ARR -0.2% (-1.9% to 1.5%)

- RR 1.03 (0.81-1.31)
  ARR -0.2% (-2.6% to 2.2%)

Death or MI at 12 months (%)
## Recommendations for oral antiplatelet agents

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<td>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.</td>
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<td>A P2Y$_{12}$ 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.</td>
<td>I</td>
<td>A</td>
</tr>
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<td>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 (H. elicobacter)</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended for P2Y$_{12}$-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.
Prasugrel vs. Clopidogrel for Acute Coronary Syndromes Patients Managed without Revascularization — the TRILOGY ACS trial

On behalf of the TRILOGY ACS Investigators

www.clinicaltrials.gov Identifier: NCT00699998
TRILOGY ACS Study Design

Medically Managed UA/NSTEMI Patients

Randomization Stratified by:
Age, Country, Prior Clopidogrel Treatment
(Primary analysis cohort — Age < 75 years)

- Medical Management Decision ≤ 72 hrs
  (No prior clopidogrel given) — 4% of total
  - Clopidogrel\(^1\)
    300 mg LD +
    75 mg MD

- Medical Management Decision ≤ 10 days
  (Clopidogrel started ≤ 72 hrs in-hospital OR on chronic clopidogrel) — 96% of total
  - Prasugrel\(^1\)
    30 mg LD +
    5 or 10 mg MD
  - Clopidogrel\(^1\)
    75 mg MD
  - Prasugrel\(^1\)
    5 or 10 mg MD

Minimum Rx Duration: 6 months; Maximum Rx Duration: 30 months

Primary Efficacy Endpoint: CV Death, MI, Stroke

1. All patients were on aspirin and low-dose aspirin (< 100 mg) was strongly recommended. For patients <60 kg or ≥75 years, 5 mg MD of prasugrel was given. Adapted from Chin CT et al. Am Heart J 2010;160:16-22.e1.
Primary Efficacy Endpoint to 30 Months (Age < 75 years)

HR (95% CI) ≤ 1 Year: 0.99 (0.84, 1.16)
HR (95% CI) > 1 Year: 0.72 (0.54, 0.97)
HR (95% CI): 0.91 (0.79, 1.05)  P = 0.21
Interaction P = 0.07

No. at risk:
Prasugrel: 3620 3248 2359 1611 953 389
Clopidogrel: 3623 3244 2390 1596 946 399
TIMI Major Bleeding to 30 Months
(Age < 75 years)

HR (95% CI):
1.31 (0.81, 2.11)
P = 0.27

No. at risk:
Prasugrel: 3590 3072 2244 1499 885 427
Clopidogrel: 3590 3116 2303 1552 925 425
Vorapaxar:
- First-in-class
- Oral PAR-1 inhibitor

Metabolism:
- Primarily hepatic via CYP 3A4
- Terminal half-life: ~126–269 hrs

Prior trials:
- No increase in bleeding and fewer MIs

Chackalamannil S, J Med Chem, 2006
**Trial Design**

**NSTE Acute Coronary Syndromes**

- **1:1 Randomized Double-blind**
  - Placebo
  - Vorapaxar
  - Loading: 40 mg
  - Maintenance: 2.5 mg daily

**Key inclusion criteria**
- Within 24 hrs of symptoms
- ↑ biomarkers or ECG changes
- 1 other high-risk feature

**Follow-up:** 1, 4, 8, 12 months, then every 6 months

Standard of care based on practice guidelines

**Efficacy Endpoints**
- **Primary:** CV death, MI, stroke, hospitalization for ischemia, urgent revascularization
- **Key Secondary:** CV death, MI, stroke

**Bleeding Endpoints:** GUSTO moderate or severe and clinically significant TIMI bleeding
Primary Endpoint
CV Death, MI, Stroke, Hospitalization for Ischemia, Urgent Revascularization

No. at risk
Placebo  6471  5844  5468  5121  3894  2291  795
Vorapaxar  6473  5897  5570  5199  3881  2318  832

2-year KM rate
Placebo  19.9%
Vorapaxar  18.5%

HR (95% CI): 0.92 (0.85, 1.01)
P-value= 0.072
### Key Secondary Endpoint
CV Death, MI, Stroke

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Vorapaxar</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2-year KM rate</strong></td>
<td>16.4%</td>
<td>14.7%</td>
</tr>
</tbody>
</table>

**HR (95% CI): 0.89 (0.81, 0.98)**

**P-value: 0.018**

<table>
<thead>
<tr>
<th>Months from Randomization</th>
<th>Placebo</th>
<th>Vorapaxar</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6471</td>
<td>6473</td>
</tr>
<tr>
<td>1</td>
<td>5895</td>
<td>5949</td>
</tr>
<tr>
<td>2</td>
<td>5575</td>
<td>5684</td>
</tr>
<tr>
<td>3</td>
<td>5263</td>
<td>5356</td>
</tr>
<tr>
<td>4</td>
<td>3922</td>
<td>4023</td>
</tr>
<tr>
<td>5</td>
<td>2383</td>
<td>2427</td>
</tr>
<tr>
<td>6</td>
<td>830</td>
<td>868</td>
</tr>
</tbody>
</table>

**No. at risk**

- **Placebo**: 6471, 5895, 5575, 5263, 3922, 2383, 830
- **Vorapaxar**: 6473, 5949, 5684, 5356, 4023, 2427, 868

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[Image: Duke Clinical Research Institute]
Bleeding Outcomes

**GUSTO Moderate/Severe**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Vorapaxar</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-year KM rate</td>
<td>5.2%</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

HR (95% CI): 1.35 (1.16, 1.58)
P-value <0.001

No. at risk:

- Placebo: 6441, 5536, 5137, 4674, 3393, 1972, 650
- Vorapaxar: 6446, 5529, 5108, 4598, 3278, 1883, 625

**ICH**

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Vorapaxar</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-year KM rate</td>
<td>0.24%</td>
<td>1.07%</td>
</tr>
</tbody>
</table>

HR (95% CI): 3.39 (1.78, 6.45)
P-value <0.001

No. at risk:

- Placebo: 6441, 5673, 5281, 4823, 3511, 2038, 678
- Vorapaxar: 6446, 5694, 5272, 4760, 3411, 1965, 657
## Recommendations for anticoagulants

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation is recommended for all patients in addition to antiplatelet therapy.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The anticoagulation should be selected according to both ischaemic and bleeding risks, and according to the efficacy-safety profile of the chosen agent.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favourable efficacy-safety profile with respect to anticoagulation.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>If the initial anticoagulant is fondaparinux, a single bolus of UFH (85 IU/kg adapted to ACT, or 60 IU in the case of concomitant use of GPIIb/IIIa receptor inhibitors) should be added at the time of PCI.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Enoxaparin (1 mg/kg twice daily) is recommended when fondaparinux is not available.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>If fondaparinux or enoxaparin are not available, UFH with a target aPTT of 50-70 s or other LMWHs at the specific recommended doses are indicated.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Bivalirudin plus provisional GPIIb/IIIa receptor inhibitors are recommended as an alternative to UFH plus GPIIb/IIIa receptor inhibitors in patients with an intended urgent or early invasive strategy, particularly in patients with a high risk of bleeding.</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>

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European Heart Journal (2011) 32:2999–3054
doi:10.1093/eurheartj/ehr236
Anti-Xa Therapy to Lower Cardiovascular Events in Addition to Standard Therapy in Subjects with Acute Coronary Syndrome – Thrombolysis in Myocardial Infarction 51 Trial (ATLAS-ACS 2 TIMI 51):
A Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of Rivaroxaban in Subjects with Acute Coronary Syndrome

Funded by a Research Grant from Johnson and Johnson and Bayer to Brigham & Women’s Hospital. Dr. Gibson has received honoraria & consulting fees from J&J and Bayer.
Recent ACS: STEMI, NSTEMI, UA
No increased bleeding risk, No warfarin, No ICH, No prior stroke if on ASA + Thienopyridine
Stabilized 1-7 Days Post-Index Event

Stratified by Thienopyridine use at MD Discretion

Placebo
N=5,176
ASA + Thieno, n=4,821
ASA, n=355

RIVAROXABAN
2.5 mg BID
n=5,174
ASA + Thieno, n=4,825
ASA, n=349

RIVAROXABAN
5.0 mg BID
N=5,176
ASA + Thieno, n=4,827
ASA, n=349

PRIMARY ENDPOINT:
Efficacy: CV Death, MI, Stroke* (Ischemic + Hemg.)
Safety: TIMI major bleeding not associated with CABG
Event driven trial of 1,002 events in 15,342 patients**

* Stroke includes ischemic stroke, hemorrhagic stroke, and uncertain stroke
** 184 subjects were excluded from the efficacy analyses prior to unblinding
**PRIMARY EFFICACY ENDPOINT:**

CV Death / MI / Stroke* (Ischemic + Hemg.)

- **Rivaroxaban (both doses):**
  - HR 0.84 (0.74-0.96)
  - ARR 1.7%
  - mITT p = 0.008
  - ITT p = 0.002
  - NNT = 59

---

* First occurrence of cardiovascular death, MI, stroke (ischemic, hemorrhagic, and uncertain) as adjudicated by the CEC across thienopyridine use strata

Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine use are provided per mITT approach; Stratified log-rank p-values are provided for both mITT and ITT approaches; ARR=Absolute Relative Reduction; NNT=Number needed to treat; Rivaroxaban=Pooled Rivaroxaban 2.5 mg BID and 5 mg BID.
STENT THROMBOSIS*
ARC Definite, Probable, Possible

Rivaroxaban (both doses)

**Placebo**

**Rivaroxaban**

Estimated Cumulative incidence (%)

2 Yr KM Estimate

- Placebo: 2.9%
- Rivaroxaban: 2.3%

2.9%

HR 0.69
(0.51- 0.93)

mITT p = 0.016

ITT p = 0.008

ARC Definite/probable: HR=0.65, mITT p=0.017, ITT p=0.012

* End point events are as adjudicated by the CEC across thienopyridine use strata

Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine use are provided per mITT approach; Stratified log-rank p-values are provided for both mITT and ITT approaches; Rivaroxaban=Pooled Rivaroxaban 2.5 mg BID and 5 mg BID.
PRIMARY EFFICACY ENDPOINTS: 2.5 mg PO BID
In Patients Treated with ASA + Thienopyridine

**CV Death / MI / Stroke**

- **Placebo**
  - HR 0.85
  - mITT p=0.039
  - ITT p=0.011

- **Rivaroxaban 2.5 mg BID**
  - Estimated Cumulative incidence (%)
  - 0 months: 2.5%
  - 12 months: 10.4%
  - 24 months: 12%

- **NNT = 71**

**Cardiovascular Death**

- **Placebo**
  - HR 0.62
  - mITT p<0.001
  - ITT p<0.001

- **Rivaroxaban 2.5 mg BID**
  - Estimated Cumulative incidence (%)
  - 0 months: 2.5%
  - 12 months: 4.2%
  - 24 months: 5%

- **NNT = 59**

**All Cause Death**

- **Placebo**
  - HR 0.64
  - mITT p<0.001
  - ITT p<0.001

- **Rivaroxaban 2.5 mg BID**
  - Estimated Cumulative incidence (%)
  - 0 months: 2.7%
  - 12 months: 4.5%
  - 24 months: 5%

- **NNT = 56**

*: First occurrence of cardiovascular death, MI, stroke (ischemic, hemorrhagic, and uncertain) as adjudicated by the CEC

Two year Kaplan-Meier estimates, HR and 95% confidence interval estimates from Cox model stratified by thienopyridine use are provided per mITT approach; Stratified log-rank p-values are provided for both mITT and ITT approaches; NNT=Number needed to treat.
TREATMENT-EMERGENT FATAL BLEEDS AND ICH

*Among patients treated with aspirin + thienopyridine, there was an increase in fatal bleeding among patients treated with 5.0 mg of Rivaroxaban (15/5110) vs 2.5 mg of Rivaroxaban (5/5115) (p=0.02)
Conclusion

- Many interesting new data
- Nothing to change our current strategy
Thank you!
## P2Y<sub>12</sub> Inhibitors

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
<th>Ticagrelor</th>
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<tbody>
<tr>
<td><strong>Class</strong></td>
<td>Thienopyridine</td>
<td>Thienopyridine</td>
<td>Triazolopyrimidin e</td>
</tr>
<tr>
<td><strong>Reversibility</strong></td>
<td>Irreversible</td>
<td>Irreversible</td>
<td>Reversible</td>
</tr>
<tr>
<td><strong>Activation</strong></td>
<td>Prodrug, limited by metabolism</td>
<td>Prodrug, not limited by metabolism</td>
<td>Active drug</td>
</tr>
<tr>
<td><strong>Onset of effect</strong></td>
<td>2-4 h</td>
<td>30 min</td>
<td>30 min</td>
</tr>
<tr>
<td><strong>Duration of effect</strong></td>
<td>3-10 days</td>
<td>5-10 days</td>
<td>3-4 days</td>
</tr>
<tr>
<td><strong>Withdrawal before major surgery</strong></td>
<td>5 days</td>
<td>7 days</td>
<td>5 days</td>
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Recommendations for oral antiplatelet agents (1)

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<td>Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended for all</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>patients at moderate-to-high risk of ischaemic events (e.g. elevated troponins),</td>
<td></td>
<td></td>
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<tr>
<td>regardless of initial treatment strategy and including those pre-treated with</td>
<td></td>
<td></td>
</tr>
<tr>
<td>clopidogrel (which should be discontinued when ticagrelor is commenced).</td>
<td></td>
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</tr>
<tr>
<td>P2Y₁₂-inhibitor-naïve patients (especially diabetics) in whom coronary anatomy</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>is known and who are proceeding to PCI unless there is a high risk of life-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>threatening bleeding or other contraindications.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Recommendations for oral antiplatelet agents (2)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel (300 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.</td>
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<td>A</td>
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<tr>
<td>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.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>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.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>In patients pre-treated with P2Y₁₂ 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.</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Ticagrelor or clopidogrel should be considered to be (re-)started after CABG surgery as soon as considered safe.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended.</td>
<td>III</td>
<td>C</td>
</tr>
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### Recommendations for oral Antiplatelet Agents

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</table>
Decision-making algorithm in ACS

1. Clinical Evaluation
   - STEMI → reperfusion
   - Evaluation
     - Quality of chest pain.
     - Symptom-orientated physical examination.
     - Short history for the likelihood of CAD.
     - Electrocardiogram (ST elevation?).

2. Diagnosis/Risk Assessment
   - ACS possible
   - Validation
     - Response to antianginal treatment.
     - Biochemistry/troponin.
     - ECG.
     - Echocardiogram.
     - Calculated risk score (GRACE).
     - Risk criteria.
     - Optional: CT, MRI, scintigraphy.

3. Coronary angiography
   - No/CAD
   - urgent < 120 min
   - early < 24 h
   - < 72 h
   - no/elective

www.escardio.org/guidelines