Questions and answers on antithrombotic therapy: a companion document of the 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation†

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The disclosure forms of all experts involved in the development of these guidelines are available on the ESC website http://www.escardio.org/guidelines

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Q1: An 85-year-old woman presented to the emergency room (ER) with recent recurrent interscapular back pain occurring during short walking distance and cold exposure. The discomfort sometimes persisted at rest for few minutes. The last pain episode was 12 h prior to admission and lasted approximately 5 min. She has a prior history of spontaneous gastrointestinal bleeding. Cardiac troponin is negative and electrocardiogram (ECG) shows no ST change. Do you administer aspirin?

No. Aspirin should be administered as soon as possible in patients with a high likelihood of acute coronary syndrome (ACS) and low bleeding risk.

In the case described, anaemia should be ruled out first (sections 4.2.1 and 4.3).

Q2: A 50-year-old man with no prior relevant medical history, active smoker, seeks medical attention for recurrent tearing chest pain episodes, the last one occurring in the last 24 h and lasting a few seconds. He has no symptoms at exercise and takes no medication. ECG shows 0.5 mm ST depression in the lateral leads and is unchanged 1 h later. The first high-sensitivity cardiac troponin is within the normal range. Should this patient receive antiplatelet and/or anticoagulant drugs?

There is neither the need for immediate anticoagulation nor for oral antiplatelet agent (aspirin or P2Y12 inhibitors) administration. You should obtain a second troponin measurement. If the second troponin is negative, the patient should undergo non-invasive functional testing to rule out myocardial ischaemia (sections 3.3.2, 5.2.9 and 5.3.3).

Q3: A 67-year-old diabetic man with suspected non-ST-elevation ACS (NSTE-ACS) is referred to you. His chest pain characteristics are typical and T wave inversions in the anterior leads are detected. He has no co-morbidities. The first high-sensitivity troponin is 100 ng/L [upper limit of normal (ULN) <14 ng/L]. The patient has a prior history of aspirin allergy. Should he receive antiplatelet treatment? If yes, which one? Should he undergo coronary angiography? What about antithrombotic treatment if percutaneous coronary intervention (PCI) is needed?

No prospective data are available to guide the management of patients with aspirin allergy in the setting of NSTE-ACS. First, you should know more about the allergy, particularly whether the patient has had episodes of Quincke oedema or anaphylactic shock. If the aspirin allergy is confirmed, the patient should receive a P2Y12 inhibitor (ticagrelor preferred over clopidogrel, while prasugrel administration is only recommended in patients undergoing PCI at the time of the procedure) and parenteral anticoagulation. Based on the risk profile, the patient qualifies for an early invasive strategy (i.e. coronary angiography within 24 h). If PCI is needed, the procedure should be postponed and aspirin desensitization should be undertaken first. If the patient is treated conservatively (not a likely option in the present case) or if he requires a coronary artery bypass graft (CABG), a P2Y12 inhibitor should be administered instead of aspirin (i.e. ticagrelor if the patient is treated conservatively and clopidogrel if he undergoes CABG). With respect to aspirin desensitization, aspirin is administered at an increasing dose (e.g. 5 mg, 10 mg, 20 mg, 40 mg every 30 min followed by 75–100 mg the day after) in the absence of intolerance.

Such protocol may also be used in patients with prior Quincke oedema/anaphylactic shock. In patients with aspirin allergy requiring immediate PCI [e.g. non-ST-elevation myocardial infarction (NSTEMI) with ongoing myocardial ischaemia or haemodynamic instability], administration of a glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitor in addition to prasugrel or ticagrelor may be an option. In this case, aspirin desensitization may be performed after PCI, once the patient is stabilized (sections 5.2.9 and 5.6.6.2).

Q4: A NSTEMI patient is admitted to the intensive care unit with a ST depression on the anterior leads of 1.5 mm. He has no ongoing chest pain and the last symptoms occurred 12 h earlier. High-sensitivity troponin at hospital admission was 150 ng/L (ULN <14 ng/L). He received aspirin and parenteral anticoagulation in the ER. The resident calls to inform you that he missed the fact that the platelet count on admission was 40 000/µL. How do you handle antithrombotic treatment?

First, recheck the platelet count on a sodium citrate tube to exclude a falsely low platelet count due to platelet aggregate on ethylenediaminetetraacetic acid (EDTA) tubes. If confirmed, stop parenteral anticoagulation and check for liver dysfunction by measuring liver transaminases, spontaneous international normalized ratio (INR) and factor V. Check for a prior history of bleeding to exclude a haematological disorder. Perform a coronary angiogram to assess the extent of coronary artery disease (CAD) and the need for revascularization. If the platelet count remains stable and >40 000/µL and PCI is indicated, a P2Y12 inhibitor should be added. In this setting, bivalirudin would be the anticoagulant of choice. As low platelet count has been an exclusion criterion in randomized studies comparing P2Y12 inhibitors, no data are available to guide the decision with respect to the agent of choice. In this setting, clopidogrel may be advised over ticagrelor or prasugrel, given the lower bleeding risk (section 5.2.9).

Q5: Should the patient just described receive a drug-eluting stent (DES) or a bare metal stent (BMS)?

Recent data suggest that the duration of dual antiplatelet therapy (DAPT) consisting of aspirin and clopidogrel may be shortened to 3–6 months when bleeding risk is high following DES implantation. The Zotarolimus-eluting Endeavor Sprint Stent in Uncertain DES Candidates (ZEUS) study suggested that newer-generation DES safety appears similar to that for BMSs, even in patients at high bleeding risk, while efficacy in terms of recurrent ischaemic event prevention is superior. These findings were observed on a background DAPT as short as 1 month. In the present case, a newer-generation DES may be used (sections 5.2.9 and 5.4.1).

Q6: Would you start antiplatelet and/or parenteral anticoagulation in a 65-year old man with multiple cardiovascular risk factors, a single prolonged typical chest pain episode, a troponin level of 70 ng/L (ULN <14 ng/L), shortness of breath, normal ECG, haemoglobin concentration at 9 g/dL (previous values unknown) and normal renal function?

The patient has NSTEMI. In the absence of an evident source of bleeding (e.g. gastrointestinal, urinary), aspirin and parenteral anticoagulation should be started, while it seems appropriate to withhold P2Y12 inhibitors. Transthoracic echocardiography is indicated to assess left ventricular (LV) function.
function and exclude relevant valvular heart disease. Early diagnostic angiography should be performed and the origin of anaemia should be determined. A proton pump inhibitor should be considered until upper gastrointestinal bleeding is ruled out (sections 5.2.9 and 5.3.3).

Q7: At an internal conference in your cardiology department, a hot discussion took place about whether or not pretreatment with a P2Y12 receptor inhibitor is to be administered in patients with NSTE-ACS scheduled for an invasive strategy. A bright fellow pointed out that <50% of those patients would ultimately undergo PCI. Was she right?

Yes. The proportion of patients with suspected NSTE-ACS that undergo PCI is ~40% in the real-life registries. In patients with an established diagnosis of NSTEMI, the corresponding proportion approaches 70%, while ~6% of patients may require CABG within a few days of admission. This may explain in part the disappointing results of P2Y12 inhibitors given prior to angiography in patients scheduled for early invasive strategy (section 5.2.3).

Q8: Does pretreatment with P2Y12 inhibitors in NSTE-ACS prevent myocardial infarction (MI) prior to diagnostic angiography?

Yes. But the rate of spontaneous MI within a time window of 48 h is extremely low (~0.2%). Overall, the Comparison of Prasugrel at the Time of Percutaneous Coronary Intervention or as Pretreatment at the Time of Diagnosis in Patients with Non-ST Elevation Myocardial Infarction (ACCOAST) study showed no benefit of a pretreatment with prasugrel compared with administration of the agent at the time of PCI in NSTEMI patients (section 5.2.3).

Q9: Does pretreatment with P2Y12 inhibitors in NSTEMI prevent major cardiovascular events compared with administration of the agent at the time of PCI?

The only study designed to address the impact of pretreatment with a P2Y12 inhibitor in NSTE-ACS patients scheduled for an invasive strategy was the ACCOAST trial. The study showed that prasugrel pretreatment did not reduce major cardiovascular events in PCI-treated patients, while major bleeding episodes were significantly increased (section 5.2.3).

Q10: A 67-year-old man with NSTEMI is admitted to an institution with no on-site PCI capability. He is expected to undergo coronary angiography within 24–48 h. Do you administer P2Y12 inhibitors prior to transfer?

As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated. Based on the ACCOAST results, pretreatment with prasugrel is not recommended (section 5.2.3).

Q11: An 80-year-old man with progressive typical chest pain at exercise, ST depression in the inferior leads and Q waves in the anterior leads is admitted to the intensive care unit at 9 P.M. The first high-sensitivity troponin is 500 ng/L (ULN <14 ng/L). He denied chest pain at rest. Coronary angiogram is scheduled for the next morning. Do you administer a P2Y12 inhibitor on top of aspirin and parenteral anticoagulation? If yes, which agent do you choose? What about if it is Friday night and coronary angiography is scheduled for next Monday?

As just mentioned, evidence in support of or against pretreatment with ticagrelor or clopidogrel is lacking. With this limitation in mind, it is reasonable to start a P2Y12 inhibitor (preferably ticagrelor) if a prolonged delay to coronary angiography is expected. However, scheduling coronary angiography on Monday would not be appropriate for this patient. Accordingly, he is at high risk of ischaemic events based on age, previous anterior MI, dynamic ischaemic ECG changes and troponin elevation. Therefore it is recommended that this patient undergo early (i.e. within 24 h) invasive strategy (sections 5.2.3 and 5.6.3).

Q12: Your expertise is requested for a 62-year-old man with no prior history of cardiovascular disease who underwent open surgical cure of an abdominal aortic aneurism 48 h earlier. An increase in high-sensitivity troponin from 100 to 200 ng/L (ULN <14 ng/L) was observed within 24 h of surgery. The patient did not have chest pain but is receiving morphine and ECG is normal. His haemoglobin level is 9.5 g/dL. Echocardiography shows normal LV function in the absence of regional wall motion abnormalities. Should aspirin and/or therapeutic doses of parenteral anticoagulation be started? Is any further investigation needed?

This patient suffered a perioperative MI. Additional information regarding the intraoperative course (e.g. hypotension, major bleeding, arrhythmias) is necessary to differentiate type 1 MI (i.e. due to a coronary atherosclerotic plaque rupture) from type 2 MI (e.g. due to intraoperative hypotension). The patient qualifies for aspirin administration and therapeutic parenteral anticoagulation [e.g., with unfractionated heparin (UFH), because it is easy to titrate and reverse]. However, a Heart Team discussion with the anaesthesiologist and the surgeon is needed to assess the risks and benefits of early antithrombotic therapy in this patient. Subsequently, non-invasive testing should be performed to document myocardial ischaemia (section 2.1.1 and 5.2.1).

Q13: The cardiology fellow on call has admitted a 65-year-old patient with NSTEMI. The patient is scheduled for coronary angiography the next day. The fellow wants to add a P2Y12 inhibitor to aspirin and therapeutic parenteral anticoagulation but notices that you are somewhat reluctant. He questions whether pretreatment with a P2Y12 inhibitor may be harmful in this patient.

Yes, it may be. In the ACCOAST trial, pretreatment with prasugrel was associated with a 30% increase in major bleeding compared with periprocedural drug administration in the absence of ischaemic event decrease. As the optimal timing of ticagrelor or clopidogrel administration in NSTE-ACS patients scheduled for an invasive strategy has not been adequately investigated, no recommendation for or against pretreatment with these agents can be formulated (section 5.2.3).

Q14: Continuing the discussion on the patient just mentioned, the fellow argues that pretreatment should not really matter since, very likely, coronary angiography and PCI if required will be done using a radial approach.

It is correct to say that radial access reduces bleeding complications irrespective of the pretreatment strategy. However, in the ACCOAST trial, pretreatment with prasugrel was associated with an increased bleeding risk. 

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irrespective of the vascular access site, even if the absolute risk increase was lower in patients undergoing radial as compared with femoral access (section 5.2.3).

Q15: A 75-year-old patient with high-risk NSTE-ACS is pre-treated with ticagrelor in addition to aspirin and UFH. ECG shows no ST deviation and no Q waves. Coronary angiography shows advanced three-vessel CAD including a critical left main stenosis, with a high SYNTAX score (34). Heart Team decision is to perform CAGB. The patient is stable, has been free of chest pain for 48 hours and troponin is falling. The LV ejection fraction is 40% in the presence of diffuse hypokinesia. How do you manage perioperative antithrombotic therapy and the timing of CAGB?

Ticagrelor should be stopped, parenteral anticoagulation maintained and CAGB delayed for 5 days, if possible. Platelet function testing prior to CAGB may be considered to shorten the time delay to surgery. It should be noted that CAGB performed on DAPT treatment is associated with a two-fold increase in major bleeding and in reoperation due to bleeding. If the patient was on clopidogrel instead of ticagrelor, the same time delay to CAGB would have applied, while a 7-day drug-free window prior to CAGB is recommended in prasugrel-treated patients (section 5.2.5).

Q16: The intern rotating in the cardiology ward noticed that you routinely stop parenteral anticoagulation after PCI in patients with NSTE-ACS, even if the total time of parenteral anticoagulation is as short as 24–48 h. He asks you why.

Indeed, it is appropriate to stop anticoagulation following PCI in the absence of indications for prolonged/chronic anticoagulation (e.g., mechanical valve, atrial fibrillation, LV thrombus, venous thromboembolic disease or residual intracoronary thrombus). Accordingly, prolonged parenteral anticoagulation after PCI has never been shown to reduce periprocedural ischaemic events while it increases the risk of bleeding (section 5.3.1).

Q17: A 65-year-old woman is admitted for suspected NSTE-ACS based on chest discomfort, non-specific ECG changes and mildly elevated high-sensitivity troponin [47 ng/L (ULN <14 ng/L)]. She is on VKA for atrial fibrillation and the INR is 2.8. The CHA2DS2-VASc score is 3. Her ventricular rate is poorly controlled (140/min) in the absence of signs of heart failure. Kidney function is normal. Echocardiography shows normal LV systolic function in the absence of regional wall motion abnormalities and a moderate LV hypertrophy. What would be the optimal timing for coronary angiography in this patient?

The patient should first undergo non-invasive testing. Accordingly, the elevation in enzymes could be solely related to tachycardia and LV hypertrophy (i.e. type 2 MI) (section 2.1.1).

Q18: The above-mentioned patient needs PCI. Do you add parenteral anticoagulation?

Prospective data are limited but suggest that there is no benefit if parenteral anticoagulation is added to prevent periprocedural ischaemic complications, including catheter thrombosis, when the INR is ≥2.5, while the combination may increase the risk of bleeding (section 5.4.1).

Q19: A 65-year-old hypertensive woman is admitted for suspected NSTE-ACS based on chest discomfort, non-specific ECG changes and mildly elevated high-sensitivity troponin [47 ng/L (ULN <14 ng/L)]. She is on VKA for atrial fibrillation and the INR is 2.8. The CHA2DS2-VASc score is 3. Her ventricular rate is poorly controlled (140/min) in the absence of signs of heart failure. Kidney function is normal. Echocardiography shows normal LV systolic function in the absence of regional wall motion abnormalities and a moderate LV hypertrophy. What would be the optimal timing for coronary angiography in this patient?

Coronary angiography is a procedure at low risk for bleeding that can be performed at though levels of NOAC (i.e. no drug intake on the evening before angiography) while bridging with parenteral anticoagulation is associated with more bleeding complications. Radial access is recommended. If PCI is indicated, additional parenteral anticoagulation with a short-acting agent should be used [the latter recommendation is based on expert opinion; data are scarce (randomized studies are ongoing)]. There is no need to postpone the procedure (section 5.4.1).

Q20: A patient with atrial fibrillation, prior stroke and treated with a non-vitamin K antagonist oral anticoagulant (NOAC) is admitted for suspected NSTE-ACS. Coronary angiography is planned. Do you proceed for angiography without interruption/bridging? If PCI is needed, do you add parenteral anticoagulation or discontinue the NOAC and reschedule the procedure?

Coronary angiography is a procedure at low risk for bleeding that can be performed at though levels of NOAC (i.e. no drug intake on the evening before angiography) while bridging with parenteral anticoagulation is associated with more bleeding complications. Radial access is recommended. If PCI is indicated, additional parenteral anticoagulation with a short-acting agent should be used [the latter recommendation is based on expert opinion; data are scarce (randomized studies are ongoing)]. There is no need to postpone the procedure (section 5.4.1).

Q21: A 70-year-old man with NSTEMI underwent PCI with a DES and needs chronic anticoagulation for atrial fibrillation on top of aspirin and clopidogrel. The intern asks you whether NOACs are an alternative to VKA for this patient.

Yes, NOACs may be used in addition to aspirin and clopidogrel. Since the data are scarce, the recommendation is according to expert opinion and the decision should be made on a case-by-case basis. The lowest dose of NOACs tested in atrial fibrillation trials should be used (i.e., 110 mg twice a day of dabigatran, 2.5 mg twice a day of apixaban and 20 mg/day of rivaroxaban). More effective P2Y12 inhibitors (i.e. prasugrel or ticagrelor) are not recommended in this setting because of the very high risk of bleeding (section 5.4.1).

Q22: A 50-year-old patient with unstable angina underwent stenting with a DES of the proximal left circumflex coronary artery. He has chronic anaemia due to ulcerative colitis but no additional co-morbidities. May DAPT duration be shortened to 3 months in this patient?

Yes, the duration of DAPT may be shortened to 3 months in this patient at lower ischaemic risk (e.g. troponin-negative NSTE-ACS), especially if the bleeding risk is high. Accordingly, ischaemic event rates in troponin-negative patients are similar to those of patients with stable CAD. In
addition, low-risk NSTE-ACS patients have been enrolled in numerous DAPT interruption trials and no excess risk has been identified if a shorter DAPT duration was applied (section 5.2.6).

**Q23: Should the decision of DAPT beyond 1 year be made according to coronary anatomy after NSTE-ACS?**

Guidelines recommend 1 year of DAPT irrespective of the coronary anatomy. According to the DAPT trial, thienopyridines (preferably clopidogrel) may be considered for up to 18 additional months in patients with previous DES implantation and no bleeding event on DAPT treatment for 1 year. According to the Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin (PEGASUS) trial, ticagrelor (60 mg twice a day is preferred over 90 mg twice a day, if available) may also be considered for up to 36 additional months in post-MI patients with increased ischaemic risk, no history of stroke and low bleeding risk. Finally, in selected patients with complex anatomy requiring multiple stents or stents in strategically important locations (i.e. left main trunk, last remaining vessel), prolongation of DAPT may be considered, although prospective data are lacking. Any prolonged DAPT regimen is associated with an increase in major bleeding that is to be weighted against the estimated reduction in ischaemic events (section 5.2.6).

**Q24: Is there a rebound effect (i.e. ischaemic event increase) after interruption of DAPT in NSTE-ACS?**

Yes. However, there is no rebound in platelet reactivity, but a progressive recovery of platelet function that may lead to recurrent ischaemic events. In the DAPT trial, ischaemic events were significantly decreased in the DAPT group compared with the aspirin group during treatment, but a rebound effect was observed within the first 3 months of follow-up after interruption of DAPT. This is in line with previous registry observations. Nonetheless, this rebound effect does not justify a routine prolongation of DAPT because of the associated risk of bleeding (section 5.2.6).

**Q25: Should DAPT duration beyond 1 year after PCI be device specific in NSTE-ACS?**

In the DAPT trial, there was an interaction between DES generation (first versus second) and the benefit of extended DAPT. DAPT beyond 1 year may be recommended in all patients with a first-generation DES. However, no benefit has been evidenced among second-generation DESs, the only currently available platforms (section 5.2.6).

**Q26: A 60-year-old man underwent coronary stenting with a new-generation DES for NSTE-MI. He was on NOAC for intermittent atrial fibrillation in the absence of prior embolic events. Echocardiography shows no valvular disease, normal LV function and a normal-sized left atrium. He is in sinus rhythm at the time of NSTEMI, with a HAS-BLED score of 2 and a CHA2DS2-VASc score of 1. He has been loaded with clopidogrel and aspirin. Do you maintain triple therapy (i.e. aspirin, clopidogrel and NOAC)? Do you switch clopidogrel to a more effective P2Y12 inhibitor (i.e. prasugrel or ticagrelor) if you decide to interrupt NOAC?**

DAPT may be recommended with newer P2Y12 inhibitors for up to 1 year given the clinical presentation of high-risk NSTE-ACS, the low CHA2DS2-VASc score and the lack of prior stroke/embolic event after stopping the NOAC. If permanent atrial fibrillation is diagnosed, ticagrelor/prasugrel may be discontinued and NOAC may be resumed. Clopidogrel may be initiated and continued for the first 6 months. The other option is a combination of aspirin, clopidogrel and NOAC for up to 6 months followed by a combination of NOAC and single antiplatelet therapy up to 1 year and finally NOAC alone after 1 year if the patient has no high-risk features (e.g. three-vessel disease CAD, left main stenting, recurrent ischaemic symptoms) (section 5.4.1).

**Q27: An 80-year-old man underwent coronary stenting with a BMS in the right coronary artery following NSTEMI. He is on VKA therapy because of a prior history of ischaemic stroke with documented persistent atrial fibrillation. The target INR was difficult to maintain. He received loading doses of aspirin and clopidogrel following coronary stenting. He has no prior history of bleeding. The HAS-BLED and CHA2DS2-VASc scores are 4 and 5, respectively. For how long should triple therapy be maintained?**

The HAS-BLED score and the previous stroke put him at increased risk of intracranial haemorrhage. Triple therapy should be administered for no longer than 1 month; after that clopidogrel should be stopped. Beyond 1 year, VKA-only treatment is recommended (section 5.4.1).

**Q28: May an NOAC be used in the patient just described? If yes, what would be the appropriate dose regimen?**

Yes, given labile INR in this patient. However, the administration of NOAC should be a case-by-case decision because comparative data with a VKA-based strategy are missing. The lowest tested dose of NOAC for atrial fibrillation should be applied in this setting (i.e. 110 mg twice a day of dabigatran, 2.5 mg twice a day of apixaban and 15 mg/day of rivaroxaban) (section 5.4.1).

**Q29: What about if a newer-generation DES is implanted in the same patient?**

Although no prospective data are available to guide the management of such a high-risk patient, triple therapy for 1 month may be considered, followed by clopidogrel discontinuation. After 1 year, anticoagulation-only treatment is recommended. Accordingly, the same approach with respect to long-term treatment should be used irrespective of the stent type. Newer-generation DESs have shown better efficacy and similar safety as compared with BMSs (section 5.4.1).

**Q30: A patient with atrial fibrillation, CHA2DS2-VASc score of 2 and gastrointestinal bleeding due to diverticulosis in the past is treated with aspirin and clopidogrel following multiple stent placement. Your intern asks you if an NOAC would be a better choice than VKA as part of triple therapy. What is your answer?**

Probably yes, according to the evidence that NOACs have a better safety profile than VKA overall. However, comparative data are missing. A meta-analysis of studies addressing real-world use showed similar gastrointestinal safety for NOACs and VKA (section 5.4.1).

**Q31: A patient on aspirin and prasugrel following left main coronary stenting for NSTE-ACS develops atrial fibrillation lasting >24 h. The CHA2DS2-VASc score is 2. How do you manage antithrombotic treatment?**
An option would be to leave the patient on aspirin and prasugrel up to 1 year given the high-risk coronary anatomy. However, since it is likely that atrial fibrillation is going to be permanent, it is advisable to start oral anticoagulation without bridging with parenteral anticoagulation (NOACs have an advantage in this respect over VKA) and to switch from prasugrel to clopidogrel without a loading dose (section 5.4.1).

Q32: A 65-year-old man received triple therapy (i.e. aspirin, clopidogrel and VKA) following NSTE-ACS. He has a mechanical mitral valve prosthesis. Coronary angiography shows distal left anterior descending coronary artery stenosis for which a conservative approach is chosen. Do you continue triple therapy?

Although the optimal antithrombotic treatment in this setting has not been studied, it is unlikely that adding clopidogrel to aspirin and VKA would be beneficial in terms of ischaemic event reduction, while it clearly increases bleeding complications. Therefore clopidogrel should be stopped.

Q33: One year after, the patient just described wonders whether he could also stop aspirin. What do you recommend to him?

There are no data to support extended antiplatelet therapy in patients medically managed for NSTEMI if chronic oral anticoagulation is required. Therefore aspirin should be stopped (section 5.4.1).

Q34: A 73-year-old patient with permanent atrial fibrillation and NSTEMI 1 year earlier treated with a single newer-generation DES in the right coronary artery has been on triple therapy (i.e. aspirin, clopidogrel and VKA) for 6 months and then on a combination of aspirin and VKA. He has been symptom-free since then. His primary care physician is asking whether aspirin can be stopped.

Although this question has never been prospectively addressed, based on expert consensus, aspirin may be stopped because there are no high-risk features for a recurrent coronary event (e.g. three-vessel disease CAD, left main stenting, recurrent ischaemic symptoms) (section 5.4.1).

Q35: A troponin-negative NSTE-ACS patient is about to undergo coronary artery stenting for a significant (but not critical) distal left main stenosis immediately after coronary angiography. He had major gastrointestinal bleeding 4 months earlier related to an ulcer that was treated by interventional endoscopy, with no recurrence. He has an increased body weight (body mass index 35 kg/m²) and has insulin-dependent diabetes. Which P2Y₁₂ inhibitor would you choose? Do you adjust treatment based on platelet function testing? Is any additional treatment necessary?

The PCI procedure should be deferred and this complex situation should be discussed within the Heart Team. Characteristics favouring CABG include left main disease, insulin-dependent diabetes and previous gastrointestinal bleeding. If the risk of surgery is deemed to be high, upper gastrointestinal endoscopy should be considered to confirm healing of the ulcer. In any event, a proton pump inhibitor is recommended. Based on the presence of diabetes and overweight, this patient is likely to be a poor responder to clopidogrel. Due to the strategic stenting location (left main) and NSTE-ACS, a more effective P2Y₁₂ inhibitor (i.e. prasugrel or ticagrelor) is recommended, while platelet function testing is not helpful in decision making (section 5.2.4).

Q36: A 67-year-old patient with NSTEMI is about to undergo left anterior descending coronary artery stenting in the presence of a large thrombus burden in the proximal portion of the vessel. He has been given a total of 10 mg intravenous morphine because of persistent chest pain. He was pretreated with ticagrelor 1 h prior to catheterization in addition to aspirin, and bivalirudin was started at the time of coronary angiography. Should any further action be considered from an antithrombotic perspective?

Morphine delays the biological effect of oral P2Y₁₂ inhibitors by slowing intestinal absorption. The use of GPIIb/IIIa inhibitors should be considered due to a large visible intracoronary thrombus (section 5.2.7).

Q37: A first, transient, atrial fibrillation episode of 30 min is recorded in a 75-year-old woman 24 h after PCI of the left main coronary artery in the context of NSTEMI. She is on ticagrelor and aspirin. Echocardiography shows a mild increase in the left atrium volume without valve disease and a preserved LV ejection fraction. Which antithrombotic regimen should you use?

The estimated risk of early stent thrombosis in this patient, ~1.5%, exceeds the one of stroke. Therefore DAPT should be continued for at least 6 weeks (i.e. until the risk of stent thrombosis substantially declines). Anticoagulation at this point is not necessary because the atrial fibrillation episodes lasted for ~24 h. Rhythm should be monitored to track recurrent episodes of atrial fibrillation. If permanent atrial fibrillation is established, oral anticoagulation and clopidogrel (the latter started with a loading dose of 600 mg 12 h after the last ticagrelor dosing and continued at 75 mg/day for up to 1 year according to the estimated bleeding risk) should be started after discontinuation of ticagrelor (sections 5.4.1 and 5.4.3).

Q38: A 65-year-old patient with NSTEMI underwent successful PCI of the right coronary artery with a single, long, newer-generation DES. He is on aspirin and prasugrel. Before discharge he presents with major upper gastrointestinal bleeding treated by interventional endoscopy. How do you handle antiplatelet therapy?

After successful treatment of the cause of bleeding, DAPT should be resumed. A proton pump inhibitor and monitoring of haemoglobin are indicated. In the absence of dedicated studies, but relying on the findings of the TRITON to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel (TRITON), in which gastrointestinal bleeding was higher in prasugrel- as compared with clopidogrel-treated patients, it appears reasonable to administer clopidogrel in this patient instead of prasugrel (section 5.2.2).

Q39: A 56-year-old man underwent primary PCI for NSTEMI. He was discharged home at day 3 on aspirin and ticagrelor. Ten days later he returned because of shortness of breath. Echocardiogram showed preserved LV function with no mitral regurgitation. The internal medicine doctor on the ward decides to switch him from ticagrelor to
clopidogrel and is asking you how to proceed. Is he right? If yes, what should be the clopidogrel dosage?

After excluding alternative causes of dyspnoea, it is reasonable to stop ticagrelor since dyspnoea can be a side effect of the drug. A loading dose of 600 mg clopidogrel 12 h after the last ticagrelor dosing may be appropriate (section 5.2.2).

Q40: If the patient just described was on prasugrel and a P2Y₁₂ inhibitor change was indicated due to a major bleed of unidentified origin (i.e. a drop in haemoglobin of 4 g/dL), how would you dose clopidogrel?

In this particular situation, transitioning from prasugrel to clopidogrel may be performed without a clopidogrel loading dose, as the active metabolites of these thienopyridines have similar potency, allowing a sufficient level of P2Y₁₂ inhibition without any gaps. In addition, the patient has a major bleed, the origin of which needs to be determined (section 5.2.2).

Reference