Antiplatelet Guidelines in Acute Coronary Syndromes and Elective PCI - Morriston Cardiac Centre

- In patients presenting with barn-door **STEMI** (not LBBB) to A&E at Morriston, to referring hospitals, to paramedics, or when STEMI occurs in existing inpatients, Ticagrelor should be considered as a first line antiplatelet in combination with Aspirin where there are no contraindications, and should be given at the first point of contact if possible.

- In patients presenting with **clear-cut Non-STEMI** (typical chest pain + significant troponin T rise >100ng/l +/- dynamic ECG changes), Ticagrelor is now the preferred antiplatelet, in combination with Aspirin, providing there are no contraindications. A single TnT >100ng/l is very likely to indicate a NSTEMI in the appropriate clinical context, and a decision to treat can usually be made without waiting to the repeat test.

- **Where the diagnosis of ACS is less certain** (e.g. atypical pain, questionable ECG changes, TnT <100ng/l) consider using Aspirin and Clopidogrel or review the diagnosis of ACS. Patients may be swapped to Ticagrelor on a post-take ward round or when seen by a cardiologist if appropriate. Seek senior advice and see notes below.

- The decision to give ACS treatment in patients presenting with **LBBB** can be difficult and should be an individualised decision usually made by a senior trainee or consultant, taking into account the potential benefits and risks to the patient. A small proportion should be managed via the STEMI pathway.

- Where Ticagrelor is contraindicated, where bleeding risk is high, or anticoagulation is indicated, Clopidogrel should be considered as an alternative in combination with Aspirin in patients with **STEMI**, Non-**STEMI** and **ACS with LBBB**.

In patient with no indication for anticoagulation (No AF, DVT, PE, LV Thrombus, Prosthetic valve)		
STEMI	Non-STEMI/ other ACS	Elective PCI for stable angina
1) Aspirin for life and 2) Ticagrelor for 1 year Clopidogrel should be considered as an alternative to Ticagrelor in patient with a contraindication e.g. higher bleeding risk or need for anticoagulation	1) Aspirin for life and 2) Ticagrelor for 1 year Clopidogrel should be considered as an alternative to Ticagrelor in patient with a contraindication e.g. higher bleeding risk or need for anticoagulation	1) Aspirin for life and 2) Clopidogrel, Clopidogrel duration usually 6 months, depending on bleeding risk.

Patients requiring anticoagulation.

In all patients with ACS and having an indication for anticoagulation, use Clopidogrel rather than Ticagrelor, in combination with Aspirin, and consider

1) The **risk of stent thrombosis / recurrent coronary events**

2) The risk of **bleeding related to antiplatelet agents**

3) The indication and **benefit of anticoagulation** (e.g. measure CHADS2VASC in AF). Common reasons for anticoagulation in cardiac patients include AF, LV thrombus, prosthetic valves, DVT/PE. Data for one indication does not necessary translate to another indication.

4) The risk of **bleeding related to anticoagulation** (measure HASBLED in AF)

The decision on whether to use Warfarin or a DOAC, and the decision re duration of DAPT should be individualised and usually made by a consultant cardiologist based on the above. Consider routine use of a PPI. See below for more information

General Notes.

- Many patients with underlying stable cardiac or renal disease have a chronically elevated level of troponin and should be borne in mind when assessing these patients. A typical history, a rise and fall in troponin and ECG changes may be required to make the diagnosis of ACS. Most of these patients with have TnT <100ng/l and dual antiplatelet therapy may be inappropriate. Decisions should be individualised based on overall patient assessment. Where doubt exists then seek advice from a senior cardiology trainee or consultant cardiologist.

- The TnT cut off of 100ng/l is an arbitrary value to prevent the indiscriminate use of Ticagrelor in patients presenting with chest pain. A TnT >100ng/l indicates a high probability of NSTEMI, however Ticagrelor may be appropriate for patient with a clear rise and fall in TnT at a level <100ng/l, subject to senior cardiology review.

- Patients may be switched from one antiplatelet to another by giving a stat loading dose of the new drug and continuing with maintainance dose. Acute switching from Clopidogrel to Ticagrelor or Prasugrel should occur irrespective of prior Clopidogrel timing and dose. Switching from Prasugrel or Ticagrelor to Clopidogrel should occur 24hours after the last dose.

- Ticagrelor 180mg stat then 90mg BD.

- Clopidogrel 600mg stat then 75mg OD.

- Prasugrel 60mg stat then 10mg OD may be used as an alternative to Ticagrelor on the advice of a consultant cardiologist.

- Consider using a PPI in patients on DAPT to reduce the risk of gastrointestinal bleeding.

- **DO NOT DISCONTINUE** dual antiplatelet therapy (DAPT) within the recommended period without first agreeing with a Cardiology SpR or Consultant. This can result in stent thrombosis and sudden death. Patients with stents should continue with single antiplatelet drug or Warfarin long term after the period of DAPT. Contact the responsible consultant's team or in an emergency the on call SpR 01792 702222 Bleep 3661.

- Ticagrelor is associated with a 1.4% absolute reduction in all-cause mortality at the expense of a 0.7% increase in bleeding when compared to Clopidogrel. Patients at higher risk of recurrent events (e.g. high atherosclerotic burden, multiple risk factors, but not necessarily complex or left main stenting) and lower risk of bleeding will benefit most compared to Clopidogrel. Use of Ticagrelor should be considered regardless of treatment strategy, as benefit is not only seen in patients receiving stents. Elderly low body weight females do not appear to be at higher risk of bleeding with Ticagrelor. There are currently no effective predictors of bleeding other than a history of bleeding.

- Ticagrelor and Prasugrel may be used in renal failure but there is limited information. Use Aspirin and Clopidogrel routinely in ESRF / dialysed patients unless high risk of stent thrombosis.

- Prior to cardiac surgery, withhold Ticagrelor for 3 days, Clopidogrel for 5 days and Prasugrel for 7 days if clinical stability allows. Post-operatively restart DAPT in ACS patients when the surgeon feels it is safe to do so from a bleeding perspective (usually 24-96hrs) in patients who have not developed AF and do not require anticoagulation. Continue DAPT for 6-12 months post-operatively depending on risk of bleeding. In patients deemed at high risk of recurrent events who have tolerated DAPT well for 1 year, continuation for up to 36 months may be considered.

- In patients with ACS managed medically, with or without angiography, DAPT should be continued in a similar fashion to stented or operated patients, according to bleeding risk. .

- Bleeding risk on DAPT appears predicted by age, low BMI, Smoking, anaemia, low CrCl, triple therapy at discharge, WBC, prior bleeding. Patients at higher risk of bleeding could be considered for discontinuation of DAPT 6 months after ACS.

Notes relating to triple therapy.

- Consider CHADS2VASC, HASBLED, risk of stent thrombosis and risk of DAPT related bleeding in all patients individually. Consider modifiable risk factors.
- Limited tools are available to predict the risk of stent thrombosis or recurrent MI. Age, congestive cardiac failure, low LVEF, vein graft stenting, MI at presentation, prior MI, prior PCI, prior stent thrombosis, diffuse multi-vessel disease, stenting of last remaining artery, at least three stents inserted, at least three lesions treated, bifurcation stenting, total stent length >60mm, CTO treatment, prior CABG, Diabetes, Stent diameter <3mm, smoking, paclitaxel eluting stent used, low CrCl may be predictors in guiding the duration of antiplatelet therapy.
- Patients requiring triple therapy following ACS should be considered high risk for bleeding and should be reviewed and reassessed carefully and followed up closely.
- Triple therapy with Aspirin, Clopidogrel and OAC should be considered for 1 month, thereafter keep the duration as short as possible and consider dual therapy with Clopidogrel and OAC
- Continue triple therapy for up to 6 months in patients considered at high ischaemic risk due to ACS that outweighs the high bleeding risk,
- Dual therapy with clopidogrel and OAC should be considered in patients in whom the bleeding risk outweighs the ischaemic risk
- Ticagrelor and Prasugrel should be avoided as part of triple therapy given limited data, and aspirin and clopidogrel used as routine.
- Consider DOACS instead of warfarin, but if using warfarin (e.g. mechanical prosthetic valves) keep INR in the lower half of the therapeutic range and maximise time in therapeutic range by frequent testing.
- Use the lowest tested DOAC dose for stroke prevention; patient specific factors for drug accumulation should be considered. (Evidence for lower dose Rivaroxaban and Dabigatran available form Pioneer AF, REDUAL-PCI studies.)
    - Rivaroxaban 20mg od (15mg of if CrCl 30-49ml/min)
    - Dabigatran 110mg bd
    - Apixaban 5mg bd (2.5mg bd if two of Age>80, weight <=60Kg, Creatinine >=133umol/l)
    - Edoxaban may also be considered.
- There is no strong evidence for choosing one DOAC over another.
- Uncertainty remains about the efficacy of the Pioneer Study regimens in preventing stroke or stent thrombosis and there was an excess of stroke in the low dose (2.5mg bd) rivaroxaban arm compared to Warfarin at 6 months. This study was primarily powered to look at bleeding risk. The balance of stent thrombosis, stroke and bleeding risk on differing regimens remains unclear, and requires an individualised patient decision.
- Consider discontinuing antiplatelet therapy in patients on OAC at 12 months.
- A PPI should be used routinely in patients receiving triple therapy.

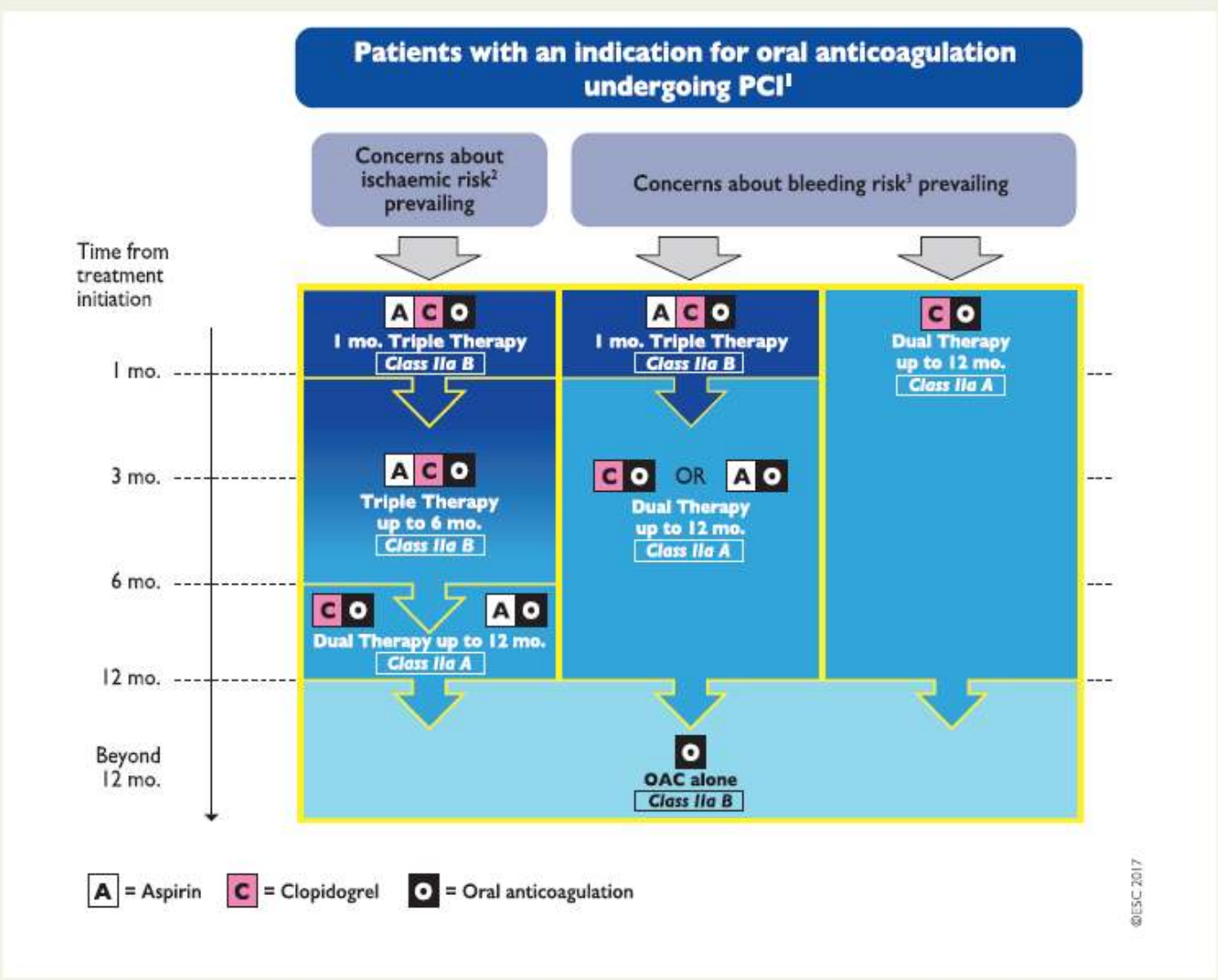

Figure 7 Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation undergoing percutaneous coronary intervention (PCI). Colour-coding refers to the number of concomitant antithrombotic medication(s). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment with a single antiplatelet agent (aspirin or clopidogrel) plus OAC.
ABC = age, biomarkers, clinical history; ACS = acute coronary syndrome; mo. = month(s); PCI = percutaneous coronary intervention.
1: Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy.
2: High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.
3: Bleeding risk can be estimated by HAS-BLED or ABC score.

Cited from 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS European Heart Journal (2018) 39, 213–254

Contraindications to Ticagrelor – see data sheet for full information

- Need for anticoagulation
- History of any bleeding, particularly intracranial bleeding
- Sick sinus syndrome, 2nd or 3rd degree AV block or bradycardia-related syncope
- Need for cytochrome CYP 3A4 inhibitor or inducer e.g. ketoconazole, **clarithromycin,** nefazodone, ritonavir, and atazanavir are contraindications. Diltiazem, erythromycin and fluconazole increase plasma levels of Ticagrelor to a lesser extent and can be considered
- Simvastatin >40mg – not recommended
- Gout related arthritis or nephropathy
- Moderate / severe hepatic impairment
- Caution in asthma/ COPD (may be used but increased dyspnoea reported)
- Monitor closely if using Digoxin
- Caution with SSRIs – may increase bleeding risk
- Limited experience in renal failure. Patients with ESRF were excluded from PLATO but others seemed to benefit
- Side effects - ventricular pauses > 3 sec on Holter 5.8% v. 3.6% (PLATO); Dyspnoea 13.8% v. 7.8% PLATO; minimal increase in creatinine, rarely clinically relevant

Contraindications to Prasugrel – see data sheet for full information

- Need for anticoagulation
- History of any bleeding, particularly intracranial bleeding
- Anaemia, thrombocytopenia
- Previous stroke or TIA
- Concomitant NSAIDS predict bleeding
- Low body weight (<60Kg) (less benefit, more risk)
- Elderly >75yrs (less benefit, more risk)
- Severe hepatic impairment
- Limited experience in renal failure, but no dose adjustment required
- Side effects -TTP, Angio-oedema

Guidelines for Use of Antiplatelet agents in patients presenting to A&E, via Paramedics, via EMERTS, and in existing inpatients

Barn Door STEMI - Appropriate symptoms and clear-cut ECG changes

Give Aspirin 300mg po stat,
Ticagrelor 180mg po stat
Consider Unfractionated Heparin 5000Units IV stat if no contraindication. (Do not give S/C or IV LMWH)

- In Morriston: Activate STEMI call (2222) and prepare the patient for immediate transfer to the catheter lab
- Outside Morriston: Call Morriston CCU Emergency STEMI line 01792 703920 – please notify immediately of all paramedic calls and interhospital transfers as STEMI team may need to be called in from home.

Clear-cut Non-STEMI - Typical chest pain +/- dynamic ECG changes + significant single troponin T usually >100ng/l

Give Aspirin 300mg po stat then 75mg od
Ticagrelor 180mg po stat then 90mg bd
Consider Enoxaparin 1mg/Kg bd**.**

Where the diagnosis of ACS is less certain

e.g. Atypical pain, TnT <100ng/l), questionable ECG changes,

Consider using Aspirin 300mg and Clopidogrel 300mg or review the diagnosis of ACS and give no antiplatelelets. Patients may be swapped to Ticagrelor after repeat TnT testing if appropriate, on a post-take ward round, or when seen by a cardiologist. Seek senior advice and see notes.

See the full guideline or references below for more information

Contraindications to Ticagrelor:
Do not give Ticagrelor and discuss appropriate use of Clopidogrel with on call Cardiology Registrar if

- Already anticoagulated or need for anticoagulation
- History of any bleeding, particularly intracranial bleeding
- Sick sinus syndrome, 2nd or 3rd degree AV block or bradycardia-related syncope
- Need for cytochrome CYP 3A4 inhibitor or inducer e.g. ketoconazole, **clarithromycin,** nefazodone, ritonavir, and atazanavir are contraindications. Diltiazem, erythromycin and fluconazole increase plasma levels of Ticagrelor to a lesser extent and can be considered
- Simvastatin >40mg – not recommended
- Gout related arthritis or nephropathy
- Moderate / severe hepatic impairment
- Caution in asthma/ COPD (may be used but increased dyspnoea reported)
- Monitor closely if using Digoxin
- Caution with SSRIs – may increase bleeding risk
- Limited experience in renal failure. Patients with ESRF were excluded from PLATO but others seemed to benefit

DO NOT DELAY TRANSFER OF STEMI PATIENTS TO THE MORRISTON CARDIAC CENTRE CATHETER LAB IN ORDER TO DISCUSS OPTIONS – IN DIFFICULT CIRCUMSTANCES THE DECISION WILL BE MADE IN THE CATHETER LAB

- The Morriston on call Cardiology SpR can be contacted on 01792 702222 Bleep 3661 for further advice

More information

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS European Heart Journal (2018) 39, 213–254

Long-term dual antiplatelet therapy for secondary prevention of cardiovascular events in the subgroup of patients with previous myocardial infarction: a collaborative meta-analysis of randomized trials European Heart Journal (2016) 37, 390–399

Management of antithrombotic therapy in AF patients presenting with ACS... or with mechanical valves. Y.H. Lip EHJ August 2014

NICE TAG 317 - Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of technology appraisal guidance 182)

NICE TAG 236 - Ticagrelor for the treatment of acute coronary syndromes

NICE TAG 420 - Ticagrelor for preventing atherothrombotic events after myocardial infarction

ESC/EACTS Guidelines on myocardial revascularisation

Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI (Pioneer) NEJM 2016 vol. 375 no. 2

2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation

European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation