POST MYOCARDIAL INFARCTION

LONG TERM MANAGEMENT

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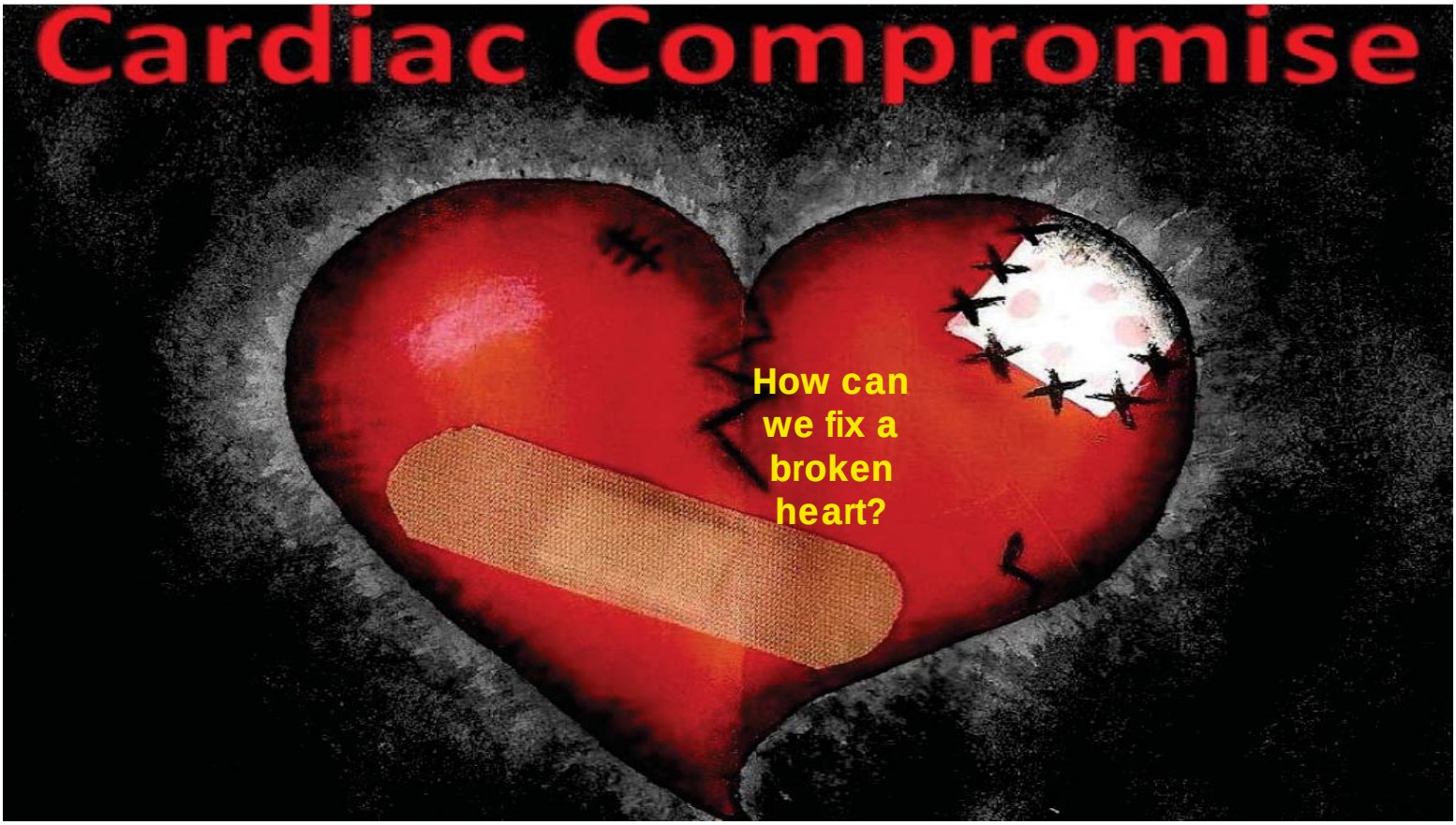
DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

- Consultant and research grants
- Astra-Zeneca, Amgen, Sanofi-Aventis, BMS-Pfizer, Bayer, Boehringer-Ingelheim.



OBJECTIVES

Following this presentation, participants will be able to:

- ✓Understand the use of dual antiplatelet therapy (DAPT),
- ✓Determine who needs Beta Blockers,
- ✓Adjust statins properly.

CASE MR. B

50 y old white male whom you are following for mild hypertension.

Recent admission (1-month) following an inferior myocardial infarct (MI).

Discharge summary:

- non-ST segment elevation inferior MI,
- left ventricular ejection fraction: 50%,
- successful percutaneous coronary intervention (PCI) with drug eluting stents x 2 in the right coronary artery, stenosis of 60% of the proximal left coronary artery (not intervened).

PHYSICAL EXAM AND LAB

- Overweight, BMI: 28
- BP: 140/80, HR: 50, physical exam is otherwise normal
- **LAB on day 0 of MI hospitalization:**
- HDL: 1.3 mmol/L *(N>1.6 mmol/L)*
- LDL: 3.0 mmol/L, non-HDL-C: 3.2 mmol/L
- TG: 1.7 mmol/L *(N<2.0 mmol/L)*
- HbA1c: 6.0 (pre-diabetes range)
- CBC, chem7, creatinine, liver function tests and thyroid profile normal.
- Peak hi-sensitivity troponin I: 1,548 *(N<17)*

MANAGEMENT?

Patient is doing well, back to work, and would like to discuss his medications.

Thinks that he is taking too many pills and questions their uses?

Medications:

- Asaphen 81 daily
- Ticagrelor 90 bid
- Metoprolol 50 bid
- Atorvastatin 80 daily
- Nitroglycerin 0.4 s/l as needed.

QUESTIONS?

In particular, he is scheduled to undergo an elective colonoscopy and would like to know what to do with his antiplatelets?

ASPIRIN

- Lowest dose possible: 80-81 mg.
- Preferably coated (Asaphen).
- For life.
- To continue for non-cardiac interventions/surgeries, unless discontinuation is ABSOLUTELY required.

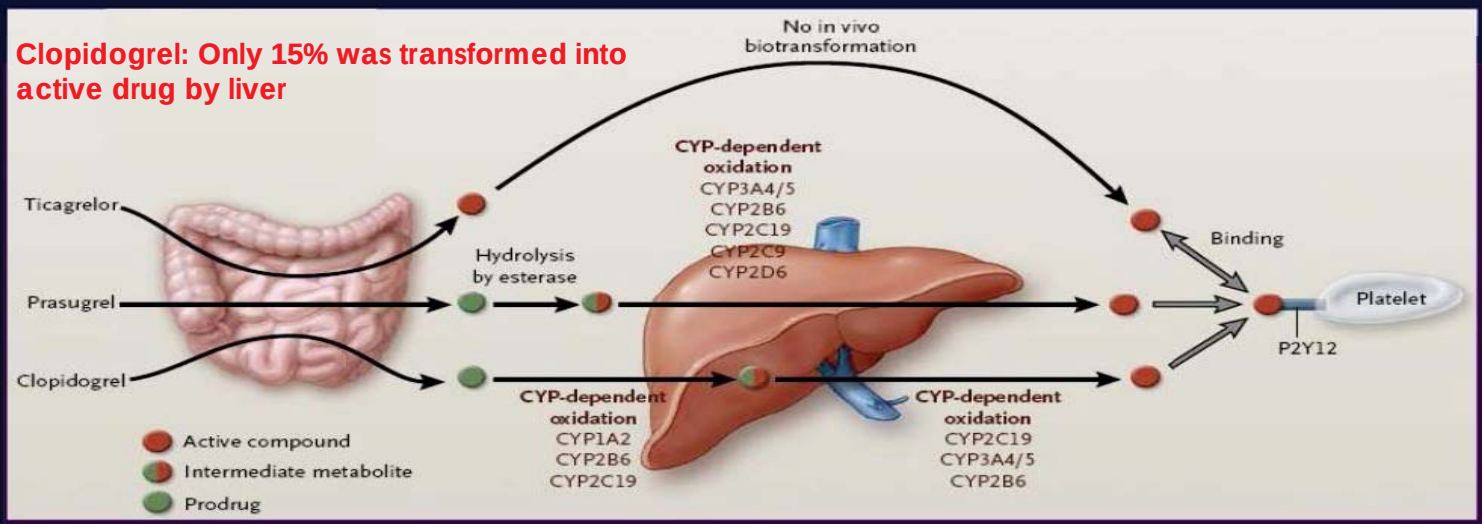
DAPT: Dual anti-platelet
ASA and P2Y12 inhibitors

P2Y12 INHIBITORS

- **P2Y12 receptor = Activation of the platelets.**
- Adenosine-mediated (ADP),
- **Indirect, irreversible**= thienopyridines: ticlodipine, clopidogrel and prasugrel.
- Marked polymorphism: genetic variation in the metabolism of clopidogrel (2% in Whites, 4% in Blacks, 10%-14% in East Asians)= poor responders to clopidogrel.
- **Direct, reversible**: ticagrelor.

Biotransformation and Mode of Action of Clopidogrel, Prasugrel and Ticagrelor

Clopidogrel: Only 15% was transformed into active drug by liver



PLATO

SAFE TIMING FOR TEMPORARY DISCONTINUATION OF DAPT

- If bare metal stent: 1 month post stent,
- If drug eluting stent (DES): 3 months post stent.
- (If no information on type of stent), safe to assume DES (most frequent type of stent), ie. 3 months NOT to stop P2Y12 inhibitors.
- **To continue ASA peri-procedure and intervention.**
- If semi-urgent surgery/intervention (such as cancer), to discuss with cardiologist.

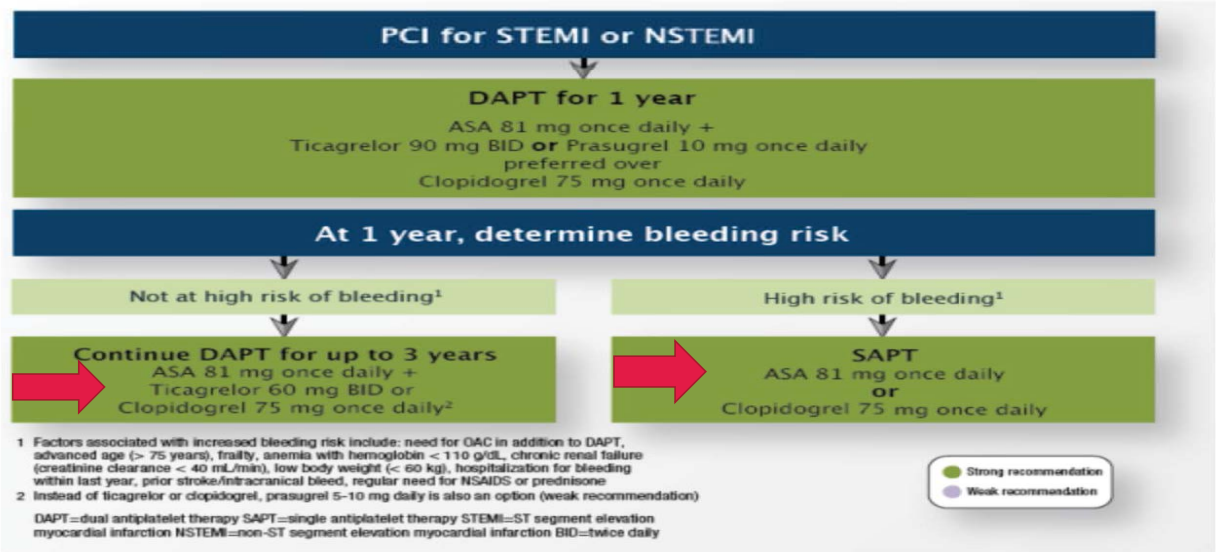
TICAGRELOR NON BLEEDING SIDE EFFECTS

- Increased plasma adenosine may increase dypsnea and bradycardia.
- Dypsnea (not due to heart or pulmonary diseases).
- Approximately 5%-10%, mainly in the first 10 days.
- Transient bradycardia and heart block (benign).
- Can increase uricemia and rarely gout.

DURATION OF P2Y12 INHIBITORS

- At least one year (with/without PCI).
- To consider longer duration depending on the thrombotic/bleeding balance.

Figure 1: Recommendations for duration of DAPT in patients with ACS (STEMI or NSTEMI) who undergo PCI



Recommendations for duration of DAPT in patients with ACS (STEMI or NSTEACS) who undergo PCI. ACS, acute coronary syndrome; ASA, acetylsalicylic acid; BID, twice daily; DAPT, dual antiplatelet therapy; NSAID, nonsteroidal anti-inflammatory drug NSTEMI, non ST-segment elevation myocardial infarction; OAC, oral anticoagulant; OD, once daily; PCI, percutaneous coronary intervention; SAPT, single antiplatelet therapy; STEMI, ST-segment elevation myocardial infarction.

CCS Antiplatelet guidelines 2018

RISK FACTORS FOR RECURRENT CORONARY THROMBOTIC EVENTS

Clinical	Angiographic
Prior myocardial infarction	Multiple stents (≥ 3 stents implanted, ≥ 3 lesions stented)[13] or use of a biodegradable vascular scaffold
Diabetes Mellitus	Long lesion length (> 60 mm total stent length)
Chronic kidney disease (creatinine clearance ≤ 60 ml/min)	Complex lesions (birfurcation treated with 2 stents, stenting of chronic occlusion)
Prior stent thrombosis	Left main or proximal LAD stenting
Current smoker	Multivessel PCI

CCS Antiplatelet guidelines 2018

Factors associated with increased bleeding risk
Oral anticoagulant
Advanced age (> 75 years)
Frailty
Anemia with hemoglobin < 110 g/dL
Chronic renal failure (creatinine clearance < 40 mL/min)
Low Body Weight (< 60 kg)
Hospitalization for bleeding within last year
Prior stroke/intracranical bleed
Regular need for NSAIDS or prednisone

CCS Antiplatelets guidelines 2018

PATIENTS WITH ATRIAL FIBRILLATION

- **Age <65 years or with CHADS2 =0: only DAPT**
- **If anticoagulation required,**
- Try to minimize duration of ASA

(IF in doubt, discuss with cardiologist)

- **Clopidogrel preferred to combine with oral anticoagulants**
- **NOAC or Warfarin**
- Rivaroxaban 2.5 bid +ASA or Rivaroxaban 15 mg.
- Apixaban 5 bid or 2.5 bid without ASA.
- Dabigatran 110 bid or 150 bid without ASA.

PROTON PUMP INHIBITORS

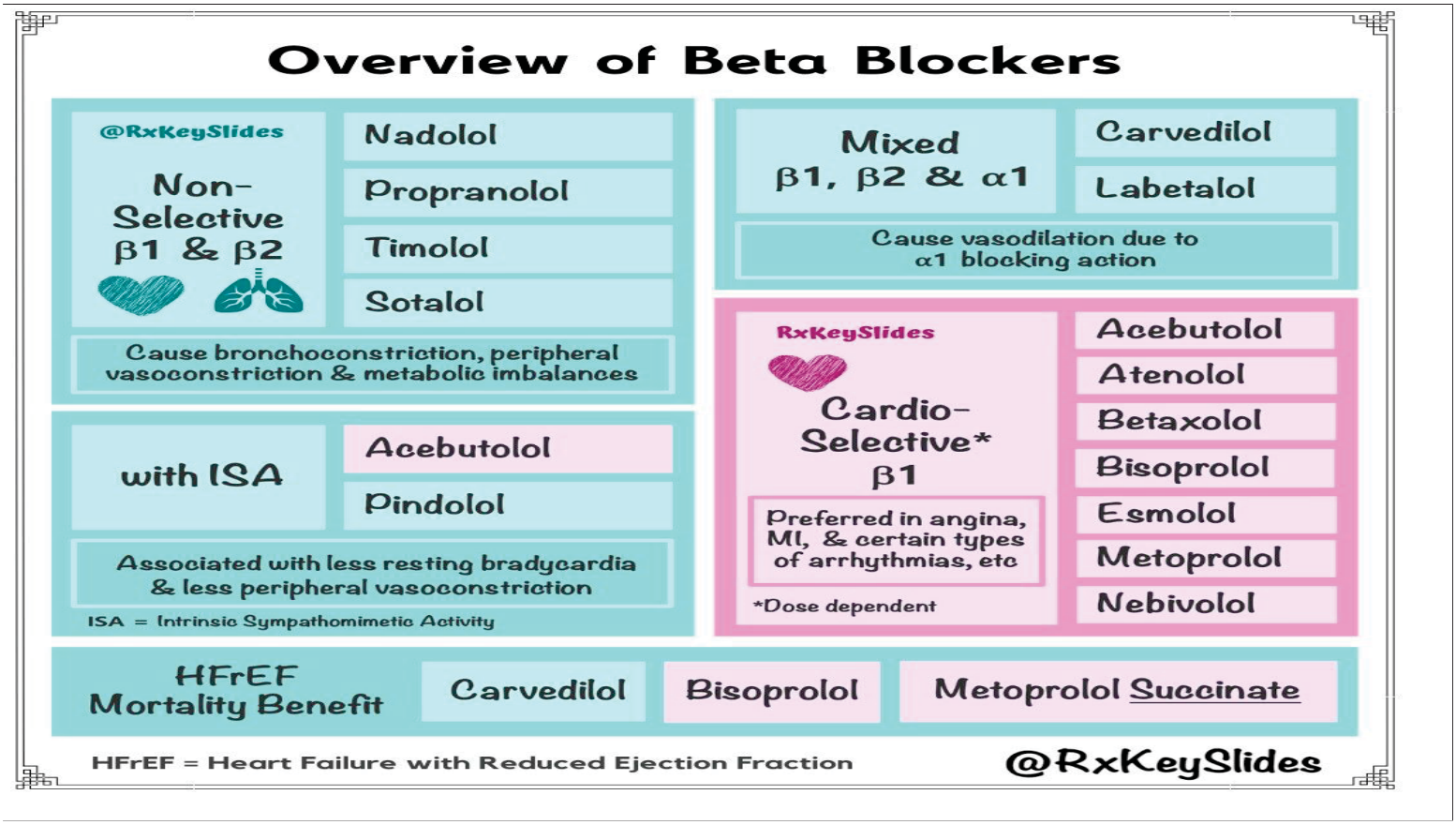
- Recommended in patients with known gastro-intestinal ulcer/reflux.
- DAPT with oral anticoagulant “Triple therapy”.
- Patient on steroids.
- Avoid omesoprazole and lansoprazole with clopidogrel.

QUESTIONS OF MR. B?

- How long will he need to stay on beta-blockers?
- And is this medication crucial?
- If yes, can he have another beta-blocker with less side-effect (fatigue in his case)?

BETA-BLOCKERS

- Most of the benefits were derived before trials of reperfusion, DAPT and statins.
- Still recommended routinely by American Heart Association.
- European Society of Cardiology: mainly in patients with heart failure or LVEF≤40%.
- Optimal duration of therapy?
- Benefits proven up to 3 years post MI.



RESPONSES TO QUESTIONS ABOUT BETA-BLOCKERS

- Reasonable to continue beta-blockers (also for hypertension).
- Consider switch of Metoprolol to Atenolol (hydrosoluble/less CNS side-effects) and once a day (to improve medication adherence).
- Aim for resting heart rate of 60-70/min.
- Worsening of bronchospasm more associated with non-selective beta-blockers.

STATINS

TYPES OF STATINS

In elderly >75 years, may start with moderate intensity

TABLE 3 High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	—	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Percent LDL-C reductions with the primary statin medications used in clinical practice (atorvastatin, rosuvastatin, simvastatin) were estimated using the median reduction in LDL-C from the VOYAGER database (S3.1.1-2). Reductions in LDL-C for other statin medications (fluvastatin, lovastatin, pitavastatin, pravastatin) were identified according to FDA-approved product labeling in adults with hyperlipidemia, primary hypercholesterolemia, and mixed dyslipidemia (S3.1.1-6). **Boldface type** indicates specific statins and doses that were evaluated in RCTs (S3.1.1-7–S3.1.1-19), and the Cholesterol Treatment Trialists' 2010 meta-analysis (S3.1.1-20). All these RCTs demonstrated a reduction in major cardiovascular events.

*Percent reductions are estimates from data across large populations. Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice (S3.1.1-2).

†LDL-C lowering that should occur with the dosage listed below each intensity.

‡Evidence from 1 RCT only: down titration if unable to tolerate atorvastatin 80 mg in the IDEAL (Incremental Decrease through Aggressive Lipid Lowering) study (S3.1.1-18).

§Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA because of the increased risk of myopathy, including rhabdomyolysis.

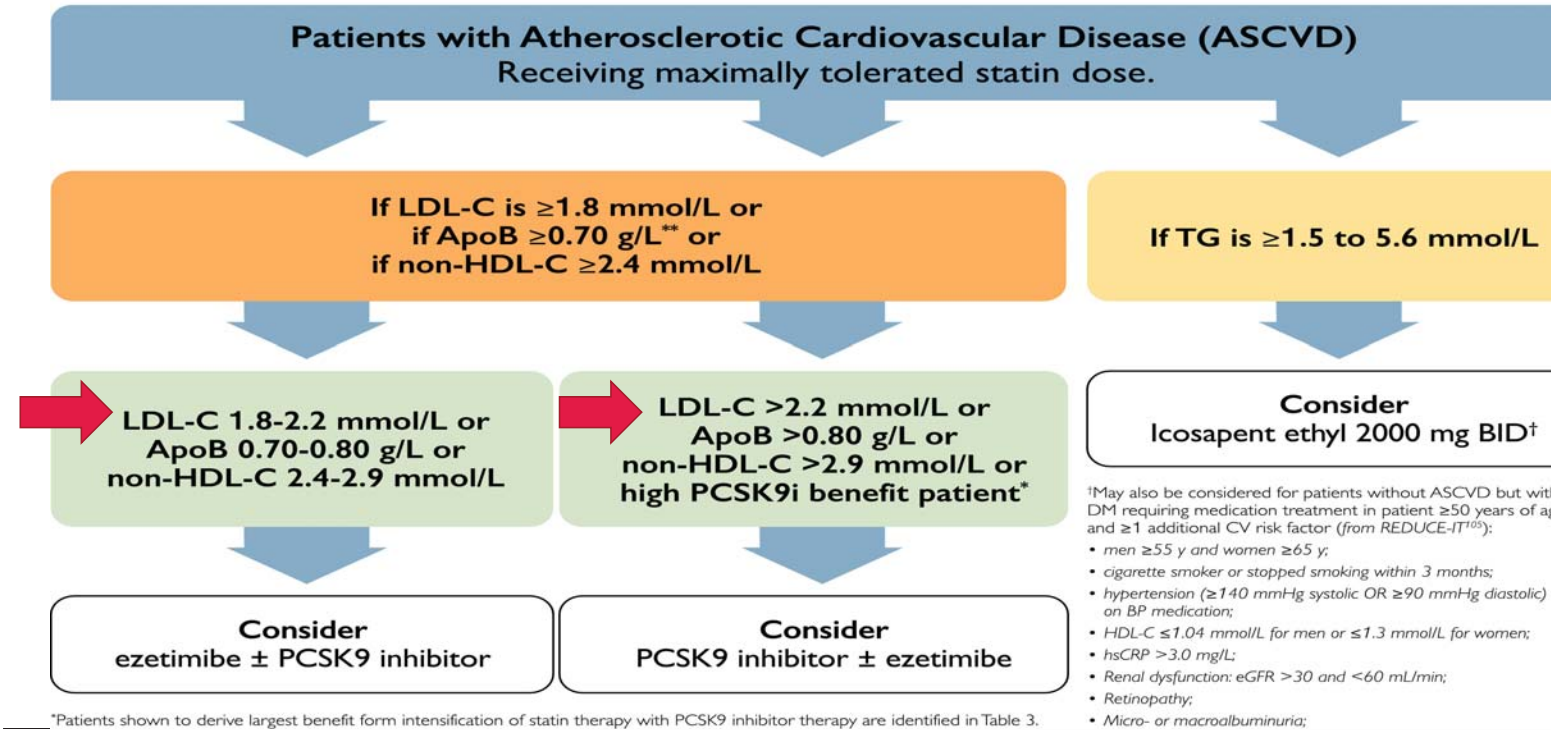
BID indicates twice daily; FDA, U.S. Food and Drug Administration; LDL-C, low-density lipoprotein cholesterol; RCT, randomized controlled trial; VOYAGER, an individual patient data meta-analysis Of statin therapY in At risk Groups: Effects of Rosuvastatin, atorvastatin and simvastatin; and XL, extended release.

AHA GUIDELINES ON THE MANAGEMENT OF CHOLESTEROL 2018

SPECIAL CONSIDERATIONS FOR LIPID MANAGEMENT

CCS Lipid Guidelines 2021

Treatment Intensification Approach for Patients with Atherosclerotic Cardiovascular Disease (ASCVD)



*Patients shown to derive largest benefit form intensification of statin therapy with PCSK9 inhibitor therapy are identified in Table 3.

†May also be considered for patients without ASCVD but wit
DM requiring medication treatment in patient ≥50 years of a
and ≥1 additional CV risk factor (*from REDUCE-IT*[105]):

- *men ≥55 y and women ≥65 y;*
- *cigarette smoker or stopped smoking within 3 months;*
- *hypertension (≥140 mmHg systolic OR ≥90 mmHg diastolic) on BP medication;*
- *HDL-C ≤1.04 mmol/L for men or ≤1.3 mmol/L for women;*
- *hsCRP >3.0 mg/L;*
- *Renal dysfunction: eGFR >30 and <60 mL/min;*
- *Retinopathy;*
- *Micro- or macroalbuminuria;*

TITRATION OF LIPID LOWERING THERAPIES

- Lipid measurement 4-12 weeks following medication adjustment.
- Ezetimibe ± PCSK9 inhibitors.
- Fibrate, cholestyramine and nicotinic acid (benefits less clear post MI).
- **NO side effect associated with low LDL.**
- **No need for down-titration of statins, unless side effect.**

- (European Heart Association 2020 recommends target of LDL <1.4 mmols/L after an acute coronary syndrome, AHA recommends >50% reduction of baseline LDL).

STATIN-INDUCED MYALGIA

- Elderly
- Female sex
- Low BMI
- CYP3A4 inhibitors,
- Grapefruit juice,
- HIV, renal, liver, thyroid related myopathy,
- East Asian (Chinese, Japanese, Vietnamese, Korean…),
- Excess alcohol,
- High levels of physical activity.

Adapted from AHA GUIDELINES ON THE MANAGEMENT OF CHOLESTEROL 2018

EAST ASIANS

- East Asians carry more genetic variants which increase drug exposure with increased myositis, and require less drugs for similar efficacy as Whites.

Table 1. Maximum dose of statins in Japan and U.S.

	Rosuvastatin	Pitavastatin	Atorvastatin	Simvastatin	Pravastatin	Fluvastatin
Japan (mg)	20	4	40	20	20	60
U.S. (mg)	40	4	80	80	80	80

OTHER RARE SIDE-EFFECTS OF STATINS

- Myositis/rhadomyolysis/auto-immune myopathy= RARE
- Transaminitis. (Rare; statins can be used safely in patients with non-alcoholic liver steatosis).
- New onset diabetes mellitus. Mainly in patients with metabolic syndromes, more frequent with high dose statins.

SUMMARY OF MANAGEMENT

- Reassurance Mr. B about his good prognosis, uncomplicated MI with preserved LV ejection fraction.
- Counsel him on the importance of medication adherence, lifestyle modification.
- Instruct him on delaying the colonoscopy (>3 months) and DAPT management peri-colonoscopy (continue ASA).
- Change his metoprolol to atenolol.
- To repeat his lipid profiles and refer him to cardiac rehabilitation/personal trainer.

CONCLUSIONS

- ASA For life.
- DAPT for at least one year, to consider 18 months – 3 years for patients at high risk of recurrent MI.
- Beta-blockers strongly recommended if presence of heart failure, incomplete revascularisation.
- Statins (maximally tolerated doses), aiming for LDL <1.8 mmol/L or non-HDL-C <2.4 mmol/L.