Gastro short cases

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Case 1

- 50 year old Indian male
- 3 month history of epigastric pain
- No weight loss
- No PMHx or regular meds

Question 1: What would you do now?

- A) Start omeprazole 20mg daily
- B) Start omeprazole 20mg bd
- C) Refer gastroscopy
- D) Check Helicobacter

Case 1 (continued)

- He returns 1 month later and reported that the symptoms are unchanged
- What do you do now?
- A) Increase omeprazole
- B) Refer USS
- C) Add ranitidine

Why are some PPIs more effective in some patients than others?

- Approximately 40% of patients will not respond adequately to PPI
  - Due to Cytochrome P450 CYP2C19 genotype differences
  - Rabeprazole and esomeprazole are CYP independent
- 5% Caucasians, 12-23% Asians homozygous for CYP2C19 inactivating mutations → Delayed metabolism of PPI
- Patients homozygous for wild type gene are rapid metabolisers and have lower PPI plasma concentration
- Less likely to have successful treatment (46% success in rapid metabolisers vs 85% in normal metabolisers)

PPIs available in NZ

Omeprazole

Pantoprazole

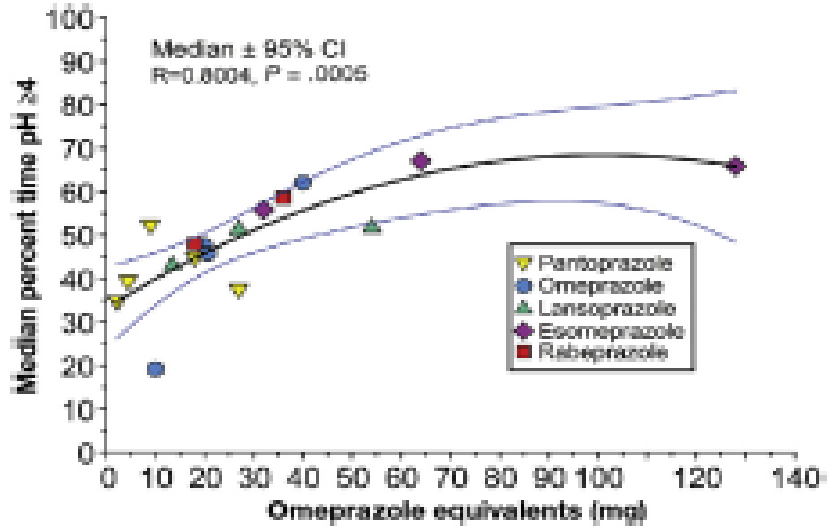
Lansoprazole

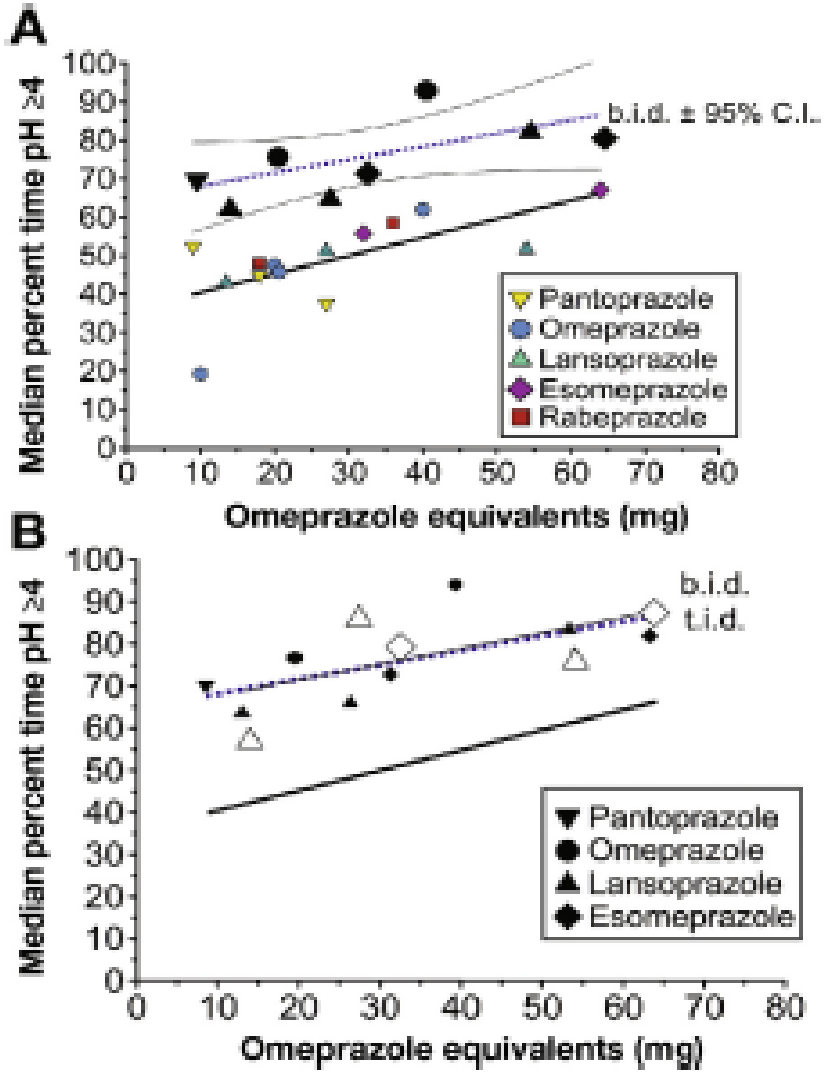
Are they equivalent?

Table 1. Potency of PPIs Based on OE

Drug at lowest available dosage	OE
Pantoprazole 20 mg	4.5 mg
Lansoprazole 15 mg	13.5 mg
Omeprazole 20 mg	20 mg
Esomeprazole 20 mg	32 mg
Rabeprazole 20 mg	36 mg

NOTE. PPIs are listed in order of increasing potency.[17]
OE, omeprazole equivalent; PPIs, proton pump inhibitors.





Graham et al. CGH 2018

Gastroscopy normal

- Patient reports improvement with high dose omeprazole
- How long would you treat him for?

Who should remain on long term therapy?

- Treatment of erosive esophagitis (LA Grade C and D). Risk of relapse is 72% if PPI is stopped
- PPI responsive esophageal eosinophilia
- High risk, long term NSAID users
- Barretts esophagus
- Zollinger-Ellison syndrome

How do I stop long term PPI therapy?

- Patients suitable to stop PPIs include functional dyspepsia, NERD (non erosive reflux disease), laryngopharyngeal reflux, no specific indication identified
- The longer a patient is on a PPI (esp if high dose), the harder it is to stop
- Suddenly stopping PPIs can result in a rebound effect- a sudden rise in gastric acid output due to hypergastrinemia
- Step down approach effective
- On-demand use can continue to be effective in many patients
- H2RAs can also be used to improve symptoms

Dietary advice

- Spicy foods
- Caffeine (coffee, tea, chocolates)
- Fizzy drinks
- Tomatoes
- Citruses

Case 2

- 50 year old Caucasian man, company executive
- Complains of excessive fatigue
- Normal physical examination
- Blood tests show normal Hb, ferritin, TFTs.
- ALT 150, bilirubin and the rest normal

What do you do now?

- A) Hepatitis serology
- B) USS
- C) Observe and repeat ALT in 3 months

Hepatitis C serology positive

- What is the current funded treatment for HCV in NZ?
- A) Viekira Pak
- B) Pegylated interferon/ribavirin
- C) Maviret
- D) Sofosbuvir

Introduction to MAVIRET

Glecaprevir (GLE)

pangenotypic NS3/4A protease inhibitor

Pibrentasvir (PIB)

Pangenotypic NS5A inhibitor

Glecaprevir/pibrentasvir approval was based on clinical trial data in over 2,300 patients including placebo and active-controlled studies

Glecaprevir/pibrentasvir is a fixed-dose combination of glecaprevir, an HCV NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of patients with chronic HCV GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A)

Maviret is indicated for the treatment of adult patients with chronic HCV GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A)

GT=genotype. HCV=hepatitis C virus. NS=non-structural protein.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Formulation & Packaging

- Co-formulated, film-coated tablet of glecaprevir (100mg) and pibrentasvir (40mg)
- **Recommended oral dose is 3 tablets taken once daily with food**
- Tablets should be taken whole and not chewed, crushed or broken

Daily blister sheet

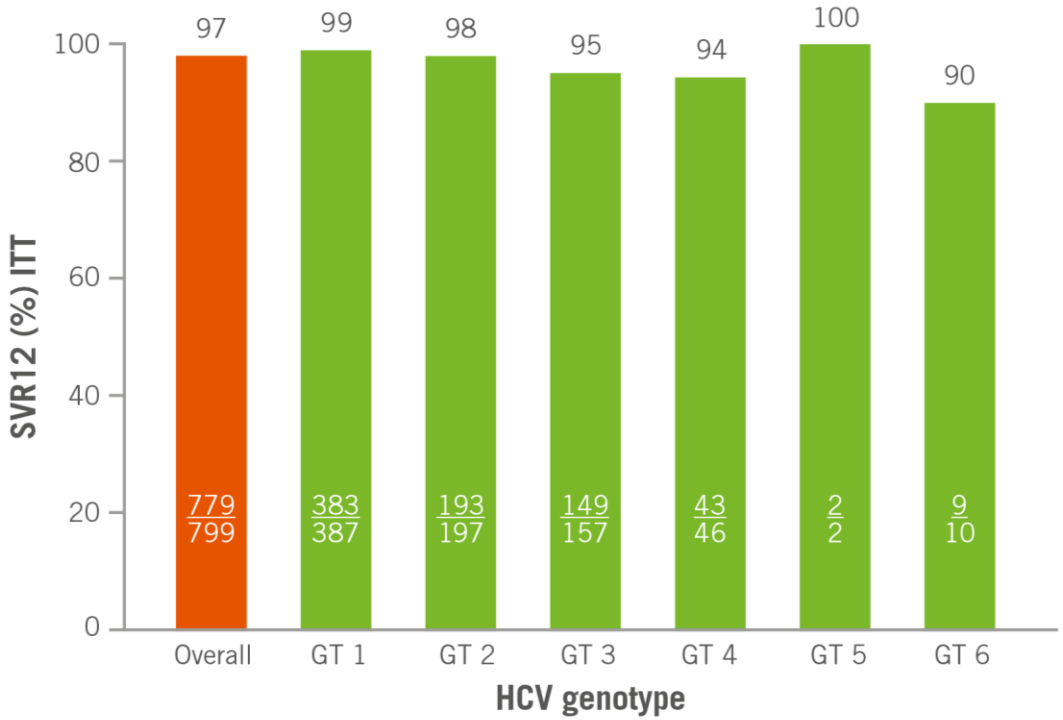
Weekly carton

Monthly carton (28 Days)

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Integrated Analysis of Non-cirrhotic Patients with HCV GT 1–6

MAVIRET once daily for 8 Weeks (ITT)



BT	2	1		1			
Relapse	7		2	5			
Non-VF†	11	3	2	2	3		1

High SVR12 rates were achieved with 8 weeks of MAVIRET in treatment naïve* non cirrhotic patients irrespective of HCV genotype

GT 1, 2, 4, 5 and 6 patients includes patients experienced with prior regimens containing peginterferon, ribavirin, and/or sofosbuvir.

BT=breakthrough. GT=genotype. ITT=intent-to-treat.. SVR=sustained virologic response. TN=treatment-naïve. VF=virologic failure.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

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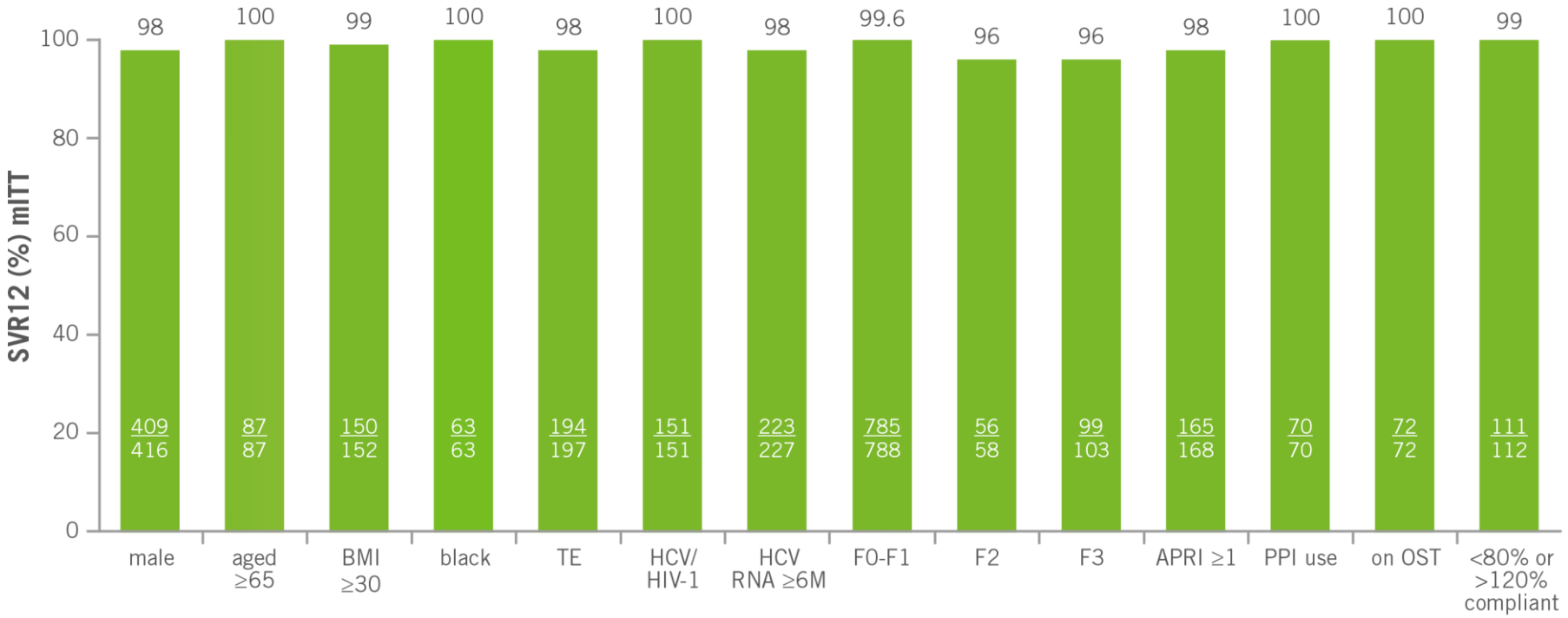


High SVR12 was achieved irrespective of baseline patient and viral characteristics

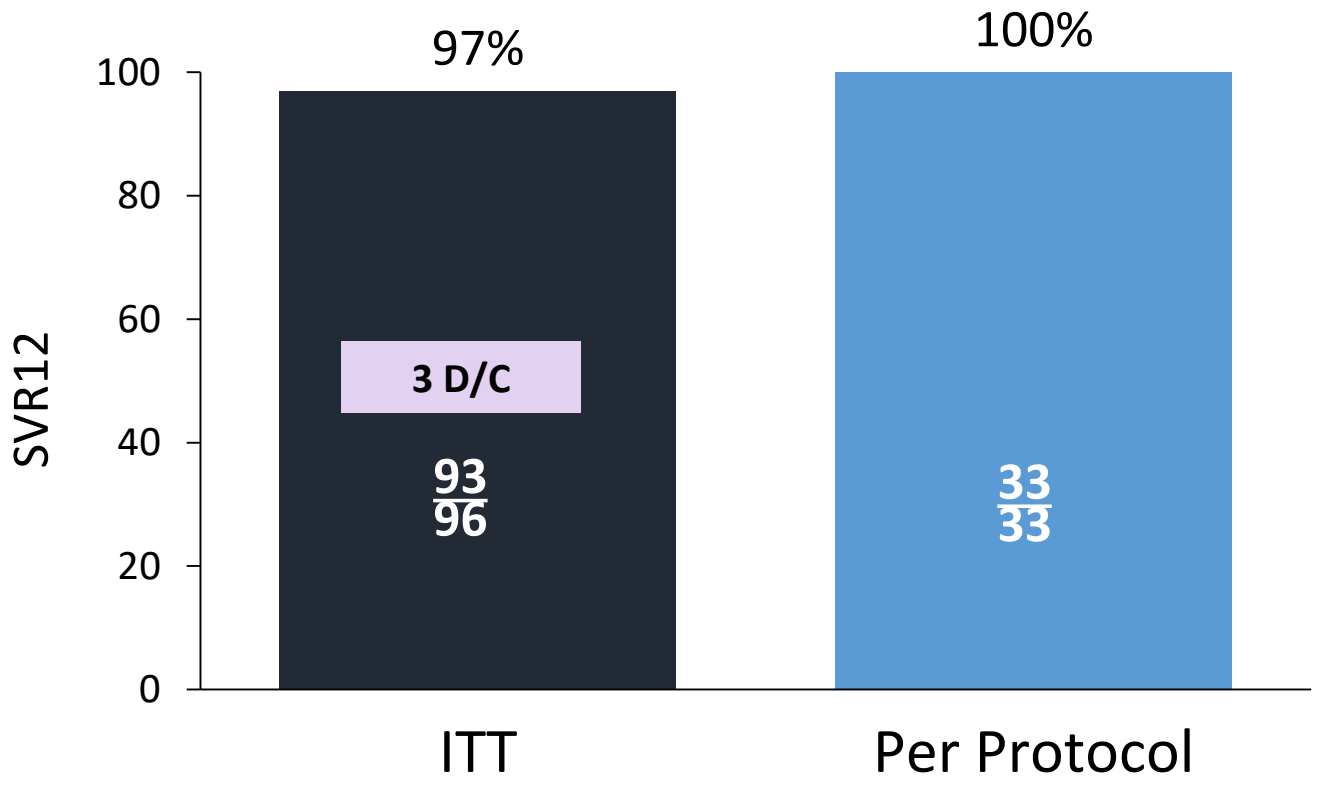
APRI=aspartate aminotransferase to platelet ratio. BMI=body mass index. GT=genotype. HCV=hepatitis C virus. HIV=human immunodeficiency virus. mITT=modified ITT (excludes patients with non virologic failure). OST=opioid substitution therapy. pegIFN=peginterferon. PPI=proton pump inhibitor. RBV=ribavirin. RNA=ribonucleic acid. SVR=sustained virologic response. SVR12=HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment. TE=treatment experienced.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

Real-world safety and efficacy of Glecaprevir-Pibrentasvir

MAVIRET once daily for 8 Weeks (ITT)

- 638 German patients treated since MAVIRET approved in August 2017



Berg T et al ILC 2018;GS-007

Treatment Duration depends on cirrhosis and previous IFN

Patient populations	Recommended Treatment Duration
GT 1,2,3,4,5 or 6 without cirrhosis	8 weeks
GT 1,2,3,4,5 or 6 with cirrhosis	12 weeks
IFN-Failure GT 3 with or without cirrhosis	16 weeks

GT=genotype. HCV=hepatitis C virus. HIV=human immunodeficiency virus

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

VIEKIRA PAK Drug-drug interactions

Contraindicated
Alfuzosin hydrochloride
Aliskerin
Atorvistatin
Bosentan
Budesonide
Carbamazepine
Cisapride
Domperidone
Dronedarone
Efavirenz
Ergotamine
Ethinyloestradiol
Fusidic Acid
Gemfibrozil
Fluticasone
Etravirine
Gemfibrozil
Indinavir
Lopinavir

Contraindicated
Lovastatin
Midazolam (oral)
Nevirapine
Phenytoin
Pimozide
Ranolazine
Rifampicin
Rilpivirine
Ritonavir
Salmeterol
Sildenafil*
Simvastatin
Salmeterol
St. John's Wort
Tacrolimus
Terfenadine
Triazolam
Phenytoin

Contraindicated
Lovastatin
Midazolam (oral)
Nevirapine

Caution/adjust/ monitor
Alprazolam
Ambristentan

Caution/adjust/ monitor
Ezetamide
Fludrocortisone
Fluvastatin
Furosemide
Nelfinavir

Caution/adjust/ monitor
Norethisterone
Phencyclidine
Omeprazole§
Pravastatin

MAVIRET DDIs

Contraindicated
Atazanavir
Rifampicin

Caution/adjust/ monitor
Atorvastatin
Cyclosporin
Dexamethasone
Efavirenz
Ethinyloestrodiol
Ezetimibe
Indinavir
Lopinavir
Nevirapine
St Johns Wort
Dabigatran
Carbamazepine
Digoxin

***This is not an exhaustive list please refer to the full MAVIRET data sheet www.medafe.govt.nz & The University of Liverpool Hep Drug Interactions www.hep-druginteractions.org. In some instances, the recommendations in the data sheet may differ to those on the University of Liverpool Hep Drug Interactions website.**

Staging fibrosis is important pretreatment

- Fibroscan
- Shear wave elastography
- Fibrotest

Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT (U/L)}}} =$$

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Cirrhosis child pugh B and C

- Maviret is not suitable for Childs Pugh B and C – can apply for Harvoni +/- RBV

Side-effects

- Headache, Fatigue and Nausea most commonly reported side effect.
- Most reported side-effects as mild to moderate.
- Most side-effects resolved by EOT

Case 3

- 25 year old male
- Current IVDU
- ALT 30
- antiHCV positive

- What is the treatment for him?

Case 4

- 71 year old male
- G 3a
- Moderate fibrosis
- Treatment naïve
- Peripheral vascular disease, AF, hyperlipidaemia and hypertension
- Meds - Dabigatran 110mg bd, atorvastatin, cilazapril, diltiazem, diazepam, triazolam

www.hep-druginteractions.org

- Glecaprevir/Pibrentasvir + Atorvastatin Coadministration of glecaprevir/pibrentasvir and atorvastatin (10 mg single dose) increased atorvastatin AUC by 8.28-fold and increased Cmax by 22-fold. Coadministration is not recommended due to increased levels of atorvastatin, caused by inhibition of OATP1B1, Pgp and BCRP by glecaprevir/pibrentasvir.

www.hep-druginteractions.org

- Glecaprevir/Pibrentasvir + Dabigatran Coadministration increased dabigatran exposure due to P-gp inhibition by glecaprevir/pibrentasvir. Coadministration of dabigatran (150 mg single dose) and glecaprevir/pibrentasvir increased dabigatran Cmax and AUC by 2.05-fold and 2.38-fold. Coadministration is contraindicated in the European SPC for glecaprevir/pibrentasvir. However, the US Prescribing Information for glecaprevir/pibrentasvir refers to the dabigatran Prescribing Information which suggests no dose adjustment is needed in subjects with normal renal function, but to reduce dabigatran to 75 mg twice daily in subjects with creatinine clearance 30-50 mL/min (or avoid use) and does not recommend coadministration in subjects with creatinine clearance <30mL/min

Treatment

- Dabigatran reduced to 75mg bd
- Atorvastatin withheld
- No other amendments needed/made
- Maviret 8 weeks treatment
- Tolerated treatment well
- CURED

Who Should Get Tested?

IVDU
Prison
Tattoo/piercing
Blood transfusion before 1992
Jaundice/hepatitis/abnormal liver tests
Previous medical treatment in Eastern Europe, South east Asia, Middle East, Indian subcontinent
Family/household member with hepatitis C

Feeling
OLD&TIRED?

What if it was wasn't just ageing?
What if we could fix it?

Get tested for HepC

If you are one of the 1 in 100 who have Hepatitis C a simple blood test and 12 week tablet treatment could see you feeling 20 years younger...

Get Cured!

Ask your Doctor or phone: 0800 33 20 10

SKLLR Hong Kong,

HCV Take home points

- Note some patients with HCV can have normal ALT
- High index of suspicion, test in everyone from at risk geographical areas
- Easy, short course, highly effective treatment now available
- No on treatment monitoring required unless conmeds/cirrhosis
- SVR12 to confirm cure
- Fibrosis staging important- determines follow up after treatment