Initiating treatment in non-cirrhotic patients

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HCV ECHO

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(session #3)

Disclosure

- I have no financial disclosures

CASE

- 30 year old male referred for chronic hepatitis C.
  - Patient's mother was a former patient who I had treated for HCV
  - Believed to be vertical transmission
  - Per notes previously vaccinated for Hep A and B
  - Only Med was MVI

MEDS

- Sofosbuvir/Ledipasvir (Harvoni) - genotype 1,4,5,6
- Sofosbuvir/Velpatasvir (Epclusa) - pangenotypic
- Sofosbuvir/Velpatasvir/voxilaprevir (Vosevi) - pangenotypic
- Glecaprevir/Pibrentasvir (Mavyret) - pangenotypic

Glecaprevir/Pibrentasvir

Figure 1. Next Generation Direct-acting Antivirals

Glecaprevir
(formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Coformulated: G/P

Pibrentasvir
(formerly ABT-530)
pangenotypic NS5A inhibitor

In vitro:[13]
- High barrier to resistance
- Potent against common NS3 polymorphisms (eg, positions 80, 155, and 168) and NS5A polymorphisms (eg, positions 28, 30, 31, and 93)
- Synergistic antiviral activity

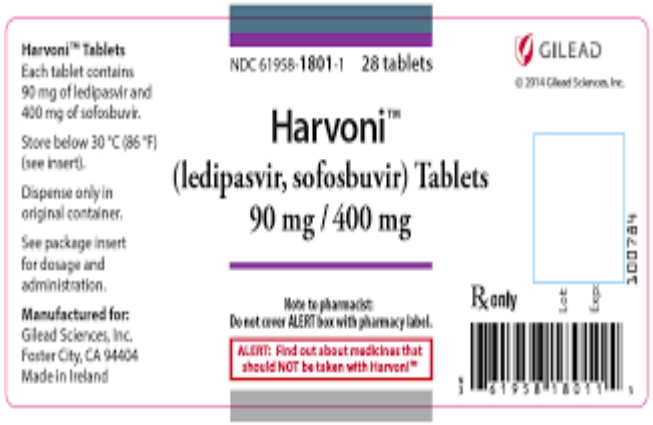
Clinical PK & metabolism:
- Oral dosing of 3 pills once-daily
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is coformulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg.
Note in the phase 2 SURVEYOR-I and SURVEYOR-II studies, once daily GLE (300 mg) + PIB (120 mg) were administered separately.
Glecaprevir was identified by AbbVie and Enanta.

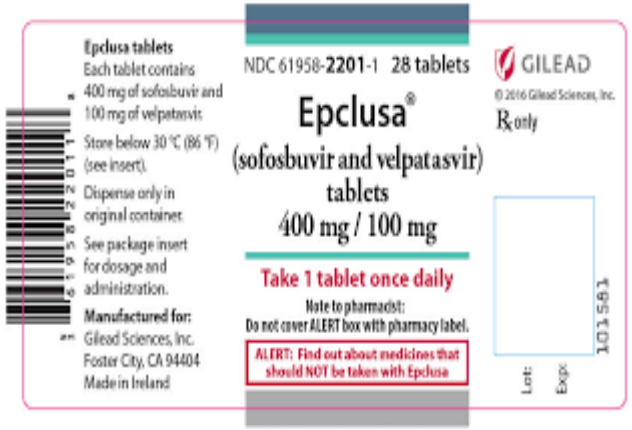
Taken with food

Harvoni/Epclusa

Sofosbuvir/ledipasvir



Sofosbuvir/Velpatasvir



Pretreatment Assessment

- Calculate FIB-4 score.
- Cirrhosis assessment: Liver biopsy is not required. For the purpose of this guidance, a patient is presumed to have cirrhosis if they have a FIB-4 score >3.25 or any of the following findings from a previously performed test.
  - Transient elastography indicating cirrhosis (eg, FibroScan stiffness >12.5 kPa)
  - Noninvasive serologic tests above proprietary cutoffs indicating cirrhosis (eg, FibroSure, Enhanced Liver Fibrosis Test, etc)
  - Clinical evidence of cirrhosis (eg, liver nodularity and/or splenomegaly on imaging, platelet count <150,000/mm^3, etc)
  - Prior liver biopsy showing cirrhosis

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).

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

Interpretation:

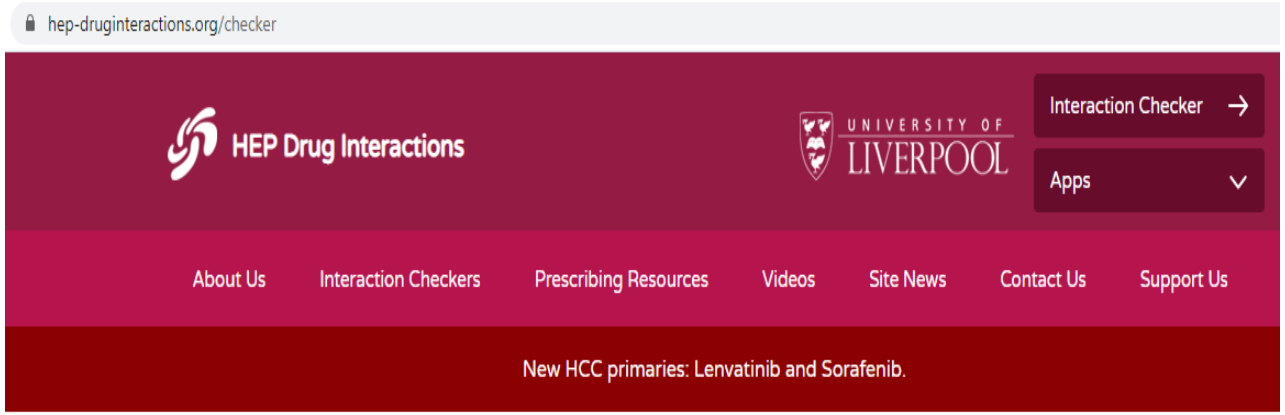
Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced 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%.

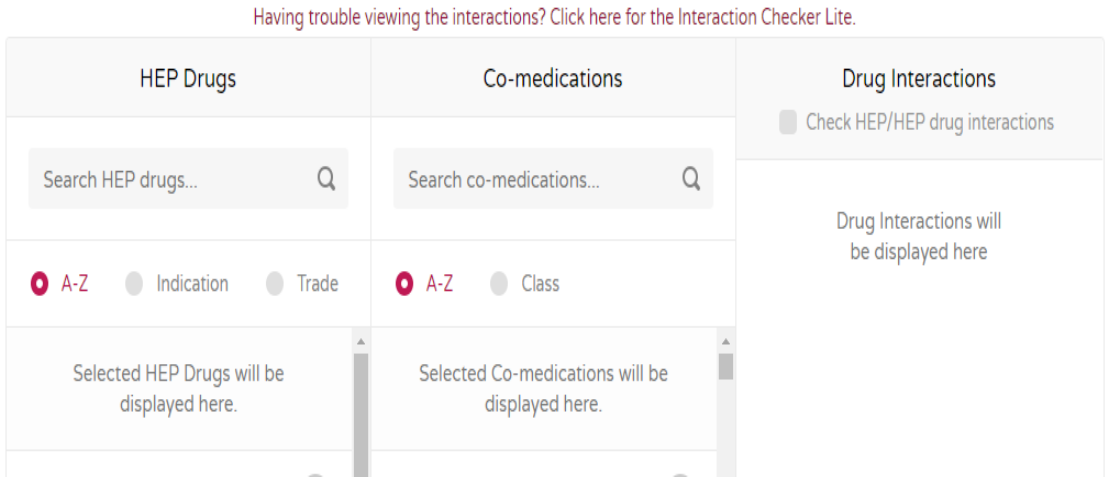
Medications

- Review current medications
- OTC
- Herbal supplements

Drug-drug interactions

- AASLD/IDSA guidance
- University of Liverpool drug interaction checker





MEDICATION ISSUES

- Amiodarone – symptomatic bradycardia
- St. John's wort (decreases HCV meds)
- **PPIs**
- **Statin**
- Anti-seizure meds
- Warfarin

HCV Regimen/Drug	QD PPI*	BID PPI	H_2 Blocker†
Ledipasvir/sofosbuvir[1]	Take LDV/SOF + PPI together on empty stomach	NO	Take LDV/SOF + H_2 blocker together or 12 hrs apart
Sofosbuvir/velpatasvir[2]	Not recommended, but if medically necessary, take SOF/VEL with food 4 hrs before omeprazole 20 mg	NO	Take SOF/VEL + H_2 blocker together or 12 hrs apart
Sofosbuvir/velpatasvir/ voxilaprevir[3]	Take SOF/VEL/VOX + PPI together with food	NO	Take SOF/VEL/VOX + H_2 blocker together with food or 12 hrs apart
Glecaprevir/pibrentasvir[4]	No significant interaction	NO[5]	No data

*Not to exceed omeprazole 20 mg/day. †Not to exceed famotidine 40 mg BID.

Epclusa (sofosbuvir/velpatasvir)

- **Rosuvastatin** (Crestor): may significantly increase the concentration of rosuvastatin which is associated with increased risk of myopathy including rhabdomyolysis. **May be administered at a dose that does not exceed 10mg**
- **Atorvastatin** (Lipitor): may be associated with increased risk of myopathy, including rhabdomyolysis. Monitor closely for adverse reactions such as myopathy and rhabdomyolysis
- **Pravastatin** is considered "safe" with no expected interactions

Mavyret (glecaprevir/pibrentasvir)

- Atorvastatin/lovastatin/simvastatin
  - Coadministration may increase the concentration of these statins. Risk of myopathy including rhabdomyolysis. Coadministration with these statins **is NOT RECOMMENDED.**

- Pravastatin
  - Coadministration my increase the concentrations of pravastatin. May increase risk of myopathy including rhabdomyolysis. **Reduce pravastatin dose by 50% when coadministered**
- Rosuvastatin
  - Coadministration may significantly increase the concentration of rosuvastatin. May increase risk of myopathy including rhabdomyolysis. **May be administered at a dose that dose not exceed 10mg**

Antiepileptic Drugs

Anticonvulsants: carbamazepine phenytoin phenobarbital oxcarbazepine	↓ ledipasvir ↓ sofosbuvir	Coadministration of HARVONI with carbamazepine, phenytoin, phenobarbital, or oxcarbazepine is expected to decrease the concentration of ledipasvir and sofosbuvir, leading to reduced therapeutic effect of HARVONI. Coadministration is not recommended.
Anticonvulsants: carbamazepine phenytoin phenobarbital oxcarbazepine	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.
carbamazepine phenytoin phenobarbital oxcarbazepine	↓ sofosbuvir ↓ velpatasvir ↓ voxilaprevir	Coadministration is not recommended.

Carbamazepine – Tegretol
Phenytoin – Dilantin
Phenobarbital –
Oxcarbazepine – Trilepetal

Anticonvulsants:		
Carbamazepine	↓ glecaprevir ↓ pibrentasvir	Coadministration may lead to reduced therapeutic effect of MAVYRET and is not recommended.

Recommended Regimens

- Glecaprevir/pibrentasvir (Mavyret) to be taken with food for a duration of 8 weeks

- Sofosbuvir/velpatasvir (Epclusa) for a duration of 12 weeks

CASE

- HCV PCR 2,100,000 IU/mL
- Genotype 1a
- FibroScan was unsuccessful
- FIB-4 <1.45
- Liver Fibrosis panel F0
- Started on therapy

SCHEDULE

DATE	TOPIC
2/21/25	HCV screening
3/7/25	Acute HCV
3/21/25	Chronic HCV: workup
4/4/25	Treatment of non-cirrhotic patients
4/18/25	Treatment of cirrhotic patients
5/2/25	Monitoring during treatment
5/16/25	Monitoring post treatment
5/30/25	*By request*
6/13/25	Other hepatitides in the context of HCV/Hepatitis A&B
6/27/25	Treatment of special populations

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