

Initiation of Hepatitis C treatment

- ▶ LISA BOCELLI, DO
- ▶ ASSISTANT PROFESSOR OF MEDICINE
- ▶ University of Massachusetts medical school
- ▶ Department of medicine, Division of gastroenterology
- ▶ Umass Memorial Chan Health Center
- ▶ October 9, 2026



Disclosure

I have no financial disclosures related to this topic



Outline

- ▶ Initial assessment
- ▶ Pre-treatment labs
- ▶ Assessing for liver damage non-invasively
- ▶ Factors to consider
- ▶ Contraindications
- ▶ Treatment options
- ▶ Drug-Drug interactions
- ▶ Life after cure

Initial assessment

Risk of HCV acquisition

Prior HCV treatment (treatment naïve or treatment experienced)

Stigmata of cirrhosis

Alcohol use

IVDU

Review of medications including PRN and OTC (supplements/herbal)

Counseling on modes of transmission



Hepatitis C

Pre-Treatment labs

- ▶ Hepatitis B core total Antibody (HBVcore)
- ▶ Hepatitis B surface Antigen and Antibody (HBVsAg and HBVsAb)
- ▶ HIV
- ▶ TB, ALT,AST, Cr (CMP)
- ▶ Hepatitis A total antibody
- ▶ Pregnancy
- ▶ HCV genotype
- ▶ Synthetic function of liver
 - ▶ PT/INR
 - ▶ Albumin
 - ▶ Platelets/CBC



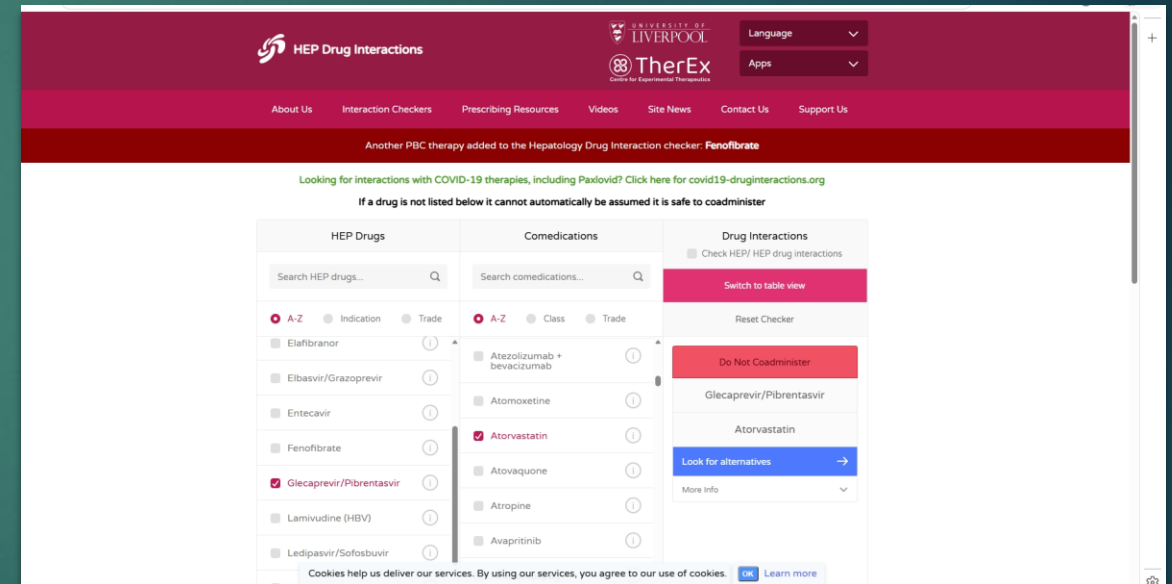
Assess for Liver Damage

- ▶ APRI score (AST to platelet ratio)
- ▶ Fibrosis-4 (FIB-4) Calculator
- ▶ Fibrosure Algorithm (ALT, alpha-2-macroglobulin, haptoglobin, apoprotein A1, TB, GGT, age and sex)
- ▶ Transient Elastography (Fibroscan)
- ▶ MRI elastography



Factors to Consider

- ▶ Drug-Drug interactions: amiodarone, PPI, anticonvulsants, statins, OCPs, St. John's wort (decreases HCV meds)
 - ▶ University of Liverpool drug interaction checker
 - ▶ [Liverpool HEP Interactions](#)
 - ▶ AASLD/IDSA guidance
- ▶ Side effects: headache, fatigue, diarrhea, nausea
- ▶ Compliance: will this person take the medication
- ▶ Other: co-morbidities



Contraindications to treatment

- ▶ With modern direct-acting antiviral (DAA) therapies, there are very few absolute contraindications to treating hepatitis C
- ▶ Treatment is not recommended for patients with an unmodifiable, short life expectancy (less than 12 months) that cannot be improved by HCV treatment or a liver transplant.
- ▶ **Pregnancy and Breastfeeding (if using Ribavirin):** While DAA regimens are generally safe, combination regimens containing **ribavirin** are strictly contraindicated during pregnancy due to severe teratogenic (birth defect-causing) risks. Effective contraception is required during and after ribavirin treatment
- ▶ With modern DAAs, the [AASLD-IDSA HCV Guidance](#) notes that these are **no longer contraindications**: Active or historical substance use (alcohol or injection drugs)
- ▶ Compensated or decompensated cirrhosis (though specific drug choices and monitoring change)
- ▶ Mild-to-severe renal impairment or dialysis
- ▶ HIV or Hepatitis B coinfection



Pregnancy and HCV

- ▶ **Individualized Considerations:** The joint [AASLD-IDSA HCV Guidance](#) states that DAA treatment **can be considered during pregnancy on an individualized basis** after a thorough shared decision-making discussion between the patient and provider. Emerging data shows DAAs are highly effective and safe when used in the second or third trimester, offering a critical window to cure the mother and potentially prevent vertical transmission to the baby. However, outside of these specific, individualized clinical discussions or clinical trials, treatment is typically deferred until the postpartum period



Meds: Direct Acting Antivirals (DAAs)

- ▶ sofosbuvir/ledipasvir (Harvoni) - genotype 1,4,5,6
- ▶ sofosbuvir/velpatasvir (Epclusa) - pangenotypic
- ▶ sofosbuvir/velpatasvir/voxilaprevir (Vosevi) - pangenotypic
- ▶ glecaprevir/pibrentasvir (Mavyret) - pangenotypic

Choosing a DAA

- ▶ Mavyret (glecaprevir/pibrentavir)
 - ▶ 8 week regimen 3 pills PO daily
 - ▶ Taken with food
 - ▶ >95% cure rate
 - ▶ Fatigue and headache
- ▶ Epclusa (sofosbuvir/velpatasvir)
 - ▶ 12 week regimen 1 pill PO daily
 - ▶ With or without food
 - ▶ 95% -100% cure rate
 - ▶ Fatigue and headache



glecaprevir/pibrentasvir (Mavyret)

Figure 1. Next Generation Direct-acting Antivirals

Glecaprevir (formerly ABT-493) pangenotypic NS3/4A protease inhibitor		Pibrentasvir (formerly ABT-530) pangenotypic NS5A inhibitor
Coformulated: G/P		
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.



sofosbuvir/ledipasvir (Harvoni) sofosbuvir/velpatasvir (Epclusa)

► sofosbuvir/ledipasvir



► sofosbuvir/velpatasvir



PPIs

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/velpatavir)

- ▶ **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 may 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 does not exceed 10mg**



Anticonvulsants

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

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.
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Anticonvulsants: carbamazepine phenytoin phenobarbital oxcarbazepine	↓ sofosbuvir ↓ velpatasvir	Coadministration is not recommended.
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carbamazepine phenytoin phenobarbital oxcarbazepine	↓ sofosbuvir ↓ velpatasvir ↓ voxilaprevir	Coadministration is not recommended.
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Next steps to initiate treatment

- ▶ Obtain a Prior authorization (PA)
- ▶ DAAs are a specialty medication
- ▶ Work closely with Specialty pharmacy
- ▶ Monitor Follow up with patient ½ way into treatment
- ▶ Test of cure/(sustained virological response rate) SVR
12 weeks post therapy



Life after HCV Treatment

- ▶ Healthy living + Education
 - ▶ Avoiding risk factors
- ▶ Not immune
- ▶ Will always test positive for HCV Ab because exposed at some point in life
- ▶ Can always get reinfected if exposed to the virus
 - ▶ But you had will not come back (The original virus does not reactivate)



Life after HCV Treatment

▶ Ongoing Liver Care

- ▶ **Existing Scarring:** Antiviral medications clear the virus, but they do not instantly reverse prior liver damage or cirrhosis (severe scarring)
- ▶ **Liver Cancer Screening:** If you had advanced scarring (stage F3 or F4 fibrosis), you need an ultrasound and blood work every six months to watch for liver cancer
- ▶ **Protect Your Liver:** Avoid heavy alcohol use, maintain a healthy weight to prevent fatty liver disease, and check with your doctor before taking new supplements or medications

▶ Preventing Reinfection

- ▶ **Avoid Exposure:** Do not share razors, toothbrushes, or drug injection equipment. Avoid getting tattoos or body piercings in unlicensed or unsanitary settings. Certain high-risk sexual practices that involve blood exposure
- ▶ **Vaccinations:** Get vaccinated against Hepatitis A and Hepatitis B if you have not had them

