Hepatitis C Treatment in 2016

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Disclosures

- I have no financial disclosures.

Learning Objectives

- Discuss the epidemiology and immunology of hepatitis C in the United States.
- Discuss the importance of prior treatment history and liver staging in determining a HCV treatment regimen.
- Discuss current available hepatitis C treatment options.
- Describe common side effects and drug-drug interactions of directly-acting antiviral medications for HCV.
- Describe immunizations related to various types of hepatitis.

Multiple Choice

1. What is the most common barrier to patients accessing hepatitis C treatment currently?
   a) Unstable mental health disorders
   b) Insurance coverage
   c) Drug-drug interactions
   d) A life-expectancy of <1 year

Multiple Choice

2. Which of the following drugs interacts with Ledipasvir/sofosbuvir to decrease serum levels of ledipasvir?
   a) Methadone
   b) Levothyroxine
   c) Levetiracetam
   d) Omeprazole

Multiple Choice

3. Based on the ION trials, which of the following patients might be a candidate for 8 weeks of ledipasvir/sofosbuvir?
   a) GT 1a, treatment naïve, non-cirrhotic, HCV viral load 4 million
   b) GT 3, treatment naïve, non-cirrhotic, HCV viral load 3 million
   c) GT 1b, treatment naïve, cirrhotic, HCV VI 2 million
   d) GT 4, treatment naïve, non-cirrhotic, HCV viral load 6 million
Multiple Choice

4. Which of the following is among the most common noted side effect of daclatasvir?
   a) Nausea
   b) Fatigue
   c) Skin rash
   d) diarhea

Multiple Choice

5. Which of the following measures are important to preventing morbidity associated with chronic hepatitis C?
   a) Weekly lab monitoring
   b) Vaccination against hepatitis B alone
   c) Vaccination against hepatitis A and B
   d) Avoidance of all medications metabolized by the liver

Hepatitis C

First described in 1989, Blood screening began in 1990.
Peak prevalence occurs in those born 1945-1965.
Worldwide 350,000-500,000 people die annually from HCV related causes.
Cirrhosis develops in 10-20% of patients with chronic HCV infection over 20-30 years on average, although rates vary widely (from 2% to 51%).
After cirrhosis due to HCV has developed, the annual risk of developing HCC is 1.5%.

Deaths Due to HCV Infections Now Exceed Those Due to HIV Infection

Number of HCV-related deaths may be over 60,000 because of under-reporting on death certificates.

HCV Strains

- Hepatitis C virus
  - RNA virus–high mutation rates
  - Evolved different genotypes
- 6 known genotypes
  - Genotype 1 (70%)
  - Genotype 2 (10%)
  - Genotype 3 (10%)
- The above 3 are the most common in the United States
- Little difference in mode of transmission or natural history of infection among different genotypes
- Variable geographic distribution

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Chronic HCV Infection May Lead to Chronic Liver Disease and Liver Cancer

**Fibrosis**

- Chronic HCV infection can lead to the development of fibrous scar tissue within the liver.

**Cirrhosis**

- Over time, fibrosis can progress, causing severe scarring of the liver, restricted blood flow, impaired liver function, and eventually liver failure.

**Hepatocellular Carcinoma** (with cirrhosis)

- Cancer of the liver can develop after years of chronic HCV infection.

Chronic liver disease includes fibrosis, cirrhosis, and hepatic decompensation; HCC = hepatocellular carcinoma.


Decompensated cirrhosis:
- Ascites
- Bleeding gastroesophageal varices
- Hepatic encephalopathy
- Jaundice

**Distribution of Fibrosis Scores**

- F0 = 15% — Recently infected and slow progressors
- F1 = 25% — "Advanced fibrosis"
- F2 = 20%
- F3 = 15%
- F4 = 25%

Limits of fibrosis tests:
- Liver biopsies are +/- 1 fibrosis stage
- Noninvasive tests are best at determining a high versus low probability of advanced fibrosis

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Immunizations


Gyarmathy et al.

- Evaluated 186 from Hungary, PWIDs between 2005-2006
  - Co-infection with HAV/HCV was 12%
  - HBV/HCV 9%
  - HAV/HBV 7%, and
  - HAV/HBV/HCV 4%
HAV/HCV Coinfection

Acute hepatitis A infection in patients with chronic hepatitis C virus (HCV) infection can be devastating.

In a prospective study by Vento, 432 patients with chronic hepatitis C (183 with cirrhosis) were observed over a 7-year period.

- Of the 17 patients with concurrent HAV infection, seven (41.4%) developed fulminant hepatitis and six died (35.3%).

Hepatitis A Vaccination

Two doses required

**Havrix**: 1440 ELISA Units (1 ml) IM with a booster dose (1440 units) at 6+ months after the primary immunization

**VAQTA**: 50 units (1 ml) IM with a booster dose (50 units) given at 6-18 months after primary immunization.

HBV/HCV Coinfection

An estimated 7-20 million people worldwide are living with both chronic hepatitis B and hepatitis C infections.

Patients with HBV/HCV coinfection have an increased risk for cirrhosis, hepatocellular carcinoma (HCC) and even death.

Hepatitis B Immunization

**Energix-B**:  
- Immunocompetent hosts:  
  - 1 ml/dose for 3 total doses administered at 0, 1, and 6 months.
- Immunocompromised hosts:  
  - 20 mcg/ml: administer 2 ml per dose at 0, 1, 2 and 6 months.

**Recombivax HB**:  
- Immunocompromised hosts:  
  - 40 mcg/ml: administer 1 ml per dose at 0, 1, and 6 months

**Twinrix**: Hepatitis A and B vaccine

Hepatitis A and recombinant hepatitis B inactivated vaccine

- Hepatitis A virus antigen 720 ELISA units and hepatitis B surface antigen 20 mcg/mL (1 ml)
- Contains aluminum, trace amounts of neomycin, and some yeast protein

Given as 1 mL intramuscular injections at 0, 1, and 6 months (3 doses total)

- Hep A component is ½ that of the Hep A vaccine alone, so it may be less immunogenic after 1 dose.
- Hep B component is likewise ½ that of the Hep B vaccine alone, so it may be less immunogenic after a single dose.
- Should not be used as post-exposure prophylaxis.
Developing a HCV Vaccine: The Challenges

Hepatitis C is highly variable even among strains

HCV mutates quickly

The vaccine likely needs to be specific to only one genotype

Utilization of the T cell response is critical to viral clearance

Specific Targets for HCV Treatment: Protease and Polymerase Inhibition

Abstract

A protective vaccine against hepatitis C virus (HCV) remains an unmet clinical need. HCV infects millions of people worldwide and is a leading cause of liver cirrhosis and hepatocellular cancer. Animal challenge experiments, immunogenicity studies, and assessment of host immunity during acute infection highlight the critical role that effective T cell immunity plays in viral control. In this first-in-man study, we have induced antiviral immunity with functional characteristics analogous to those associated with viral control in natural infection, and impressed upon a vaccine based on adenoviral vectors alone. We assessed a heterologous prime-boost vaccination strategy based on a replication deficient adenoviral vector (ChAd166) and modified vaccinia Ankara (MVA) vector encoding the NS3, NS4A, NS5A, and NS5B proteins of HCV genotype 1b. Analysis used single-cell mass cytometry and human multiplex antigen class peptide beads technology in healthy human volunteers. We show that HLA-specific T cells induced by ChAd166 are optimally boosted with MVA, and generate very high levels of both 1DCC and 2DCC HCV-specific T cells targeting multiple HCV antigens. Sustained memory and effector T cell populations are generated, and T cell memory evolved over time with improvement of quality, persistence, and polyfunctionality after heterologous MVA boost. We have developed an HCV vaccine strategy, with durable, broad, sustained, and balanced T cell responses, characteristic of those associated with viral control, paving the way for the first efficacy studies of a prophylactic HCV vaccine.

Treatment
### December 2013

**FIRST IFN-Free Therapy FDA-approved**

Sofosbuvir

Nucleotide Analogue Inhibitor of HCV NS5B polymerase enzyme

- Potent HCV-specific nucleotide analog (chain terminator)
- Safe and well tolerated
  - Once daily, no food effect
  - No significant drug interactions
  - No safety signals in pregnancy/animal studies
- High barrier to resistance
- No virologic breakthrough to date
- "Game-changer, miracle drug"

Effective for treatment-naïves + pts who failed prior IFN treatment, cirrhotics, decompensated cirrhotics

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**Case #1**

A 56 yo M with diabetes mellitus, peptic ulcer disease due to NSAIDS with prior upper GI bleed, opioid use disorder in remission, tobacco dependence, and chronic hepatitis C genotype 1a, fibrosis stage 2, HCV viral load 2.6 million, presents for evaluation to your office.

Pt's EGD last month shows no active upper GI bleeding and well-healed peptic ulcers. He has never been treated for chronic hepatitis C before, presents today to discuss his treatment options. Pt has no known mental health disorders, is stably housed, and hasn’t used injection drugs in over 10 years, stable on methadone. Pt is found to have early stage (F1) disease.

1. Which of the following directly-acting antivirals are options for treatment?
   - a) Ledipasvir 90 mg/sofosbuvir 400 mg x 8 weeks
   - b) Sofosbuvir 400 mg + weight-based ribavirin x 12 weeks
   - c) Paritaprevir 150 mg/ritonavir 100 mg/ombitasvir 25 mg + dasabuvir 250 mg BID (PRID) + weight-based ribavirin x 12 weeks
   - d) Daclatasvir 60 mg + Sofosbuvir 400 mg x 24 weeks

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   - d) Daclatasvir 60 mg + Sofosbuvir 400 mg x 24 weeks
Case #1

This patient’s med list includes 40 mg omeprazole, levothyroxine 125 mcg, levetiracetam 1000 mg BID, and methadone 90 mg daily.

3. What changes would you suggest to the patient’s gastroenterologist regarding this pt’s medications prior to treatment initiation?
   a) Suggest an alternate anti-convulsant
   b) Reduce omeprazole to 20 mg daily if clinically feasible and advise the patient to take the drug at the same time as Ledipasvir/Sofosbuvir
   c) Increase the levothyroxine
   d) Reduce the pt’s methadone dose
   e) No changes needed here

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   e) No changes needed here
Genotype 1 Trials

Genotype 1: C-EDGE

382 patients received 12 weeks of elbasvir 50 mg + grazoprevir 100 mg for genotype 1 HCV.
- 50% genotype 1a
- 41% genotype 1b

SVR12 was 92% in treatment-naive patients with HCV genotype 1a infection (144/157) without cirrhosis.

SVR12 was 99% in genotype 1b (129/131) without cirrhosis.

Genotype 1: C-WORTHY

74 patients, treatment-naive, non-cirrhotic, included both HCV mono-infected and HIV/HCV co-infected patients who received 12 weeks of elbasvir/grazoprevir without ribavirin.

SVR 12 was 92% (48/52) for GT 1a treatment-naive, non-cirrhotic patients.

SVR-12 was 95% (21/22) for GT 1b treatment-naive non-cirrhotic patients.

Genotype 1: C-EDGE, Cirrhotic pts

92 (22%) patients in the trial had Metavir F4 disease consistent with cirrhosis.

SVR was 97% (90/92) in the subgroup of cirrhotic patients with GT 1 disease.

Presence or absence of compensated cirrhosis does not appear to alter the efficacy of the elbasvir/grazoprevir regimen.

Genotype 1: RAVs

Baseline NS5A Resistance-associated variants (RAVs) significantly reduce rates of SVR12 with a 12-week course of the elbasvir/grazoprevir regimen in GT 1a patients.

NSSA RAVs were identified at baseline in 12% (19/154) of GT 1a patients enrolled in the C-EDGE study.
- 58% (11/19) achieved SVR12 compared to
- 99% (133/135) SVR12 in patients without RAVs
- Both groups got 12 weeks of elbasvir/grazoprevir

Recommendation: Patients should be tested for RAVs to NS5A inhibitors before beginning treatment.

Genotype 1: ION Trials

ION-1: Ledipasvir 90 mg/sofosbuvir 400 mg
865 treatment-naive patients, including pts with cirrhosis.
- SVR12 with LED/SOF was 97% to 99%
- There was no significant difference in SVR12 based on:
  • Use of RBV
  • HCV genotype 1 subtype
  • Length of treatment (12 vs. 24 week regimens)
- 16% of subjects had cirrhosis
  • SVR12 was 97% with cirrhosis
  • SVR12 was 98% for those without cirrhosis
Genotype 1: ION Trials

ION-3: Ledipasvir 90 mg/sofosbuvir 400 mg
647 treatment-naive patients, non-cirrhotic only
- SVR12 was 93%-95% across all treatment groups
- There was no significant difference between 12 and 8 week regimens with or without ribavirin
- There were lower relapse rates in patients receiving 8 weeks of ledipasvir/sofosbuvir who had baseline HCV RNA levels below 6 million IU/mL (2%; 2 of 123)

Genotype 1: PEARL-IV, SAPPHIRE-1, TURQUOISE-II

TURQUOISE-II: PrOD + weight-based ribavirin
261 treatment-naive and experienced patients with genotype 1a and cirrhosis
- 12 versus 24 weeks of PrOD + ribavirin
- SVR12 rates were 89% in the 12-week arm
- SVR12 was 95% in the 24-week arm
  * Treatment failures driven by null responders to PEG-IFN/RBV among treatment-experienced group

Due to at least 2 cases of CTP class A compensated cirrhotic patients dying or requiring liver transplant after receipt of PrOD or PO, this regimen is now contraindicated in patients with Child Turcotte Pugh (CTP) class B or C hepatic impairment (decompensated liver disease).

Genotype 1: ALLY-2

ALLY-2: Daclatasvir + Sofosbuvir x 12 weeks in Co-infected pts with HIV/HCV (genotypes 1-4)
- 123 pts had genotype 1 HCV, 83 (64%) treatment-naive
- SVR12 was 96% in treatment-naive patients (n=71) with GT1a including 9 pts with cirrhosis
  * Of the 88 treatment-naive patients:
    - 21 patients with GT 1a were treated for 24 weeks (including 11 also with ribavirin)
    - 67 were treated for 12 weeks (33 with RBV)
    - There were no virologic relapses in either group
    - Only 14 cirrhotic patients were included, so recommendations for 12 vs. 24 weeks remain unclear.

Genotype 1: PEARL-IV

SAPPHIRE-I: Paritaprevir 150 mg/ ritonavir 100 mg/ ombitasvir 25 mg + Dasabavir 25 mg BID x 12 wks (PrOD) + weight-based ribavirin

322 treatment-naive, non-cirrhotic patients with genotype 1a
- SVR12 was 95% with 12 weeks of PrOD and ribavirin
- Virologic failure was higher in GT1a (7 of the 8 failures were GT 1a)

PEARL-IV:
305 treatment-naive, non-cirrhotic patients with genotype 1a
- SVR12 was lower in ribavirin-free arm
  * 86% for POx alone x 12 weeks
  * 97% for PO + weight-based ribavirin x 12 weeks
- This trial provided the rationale for recommendation to use ribavirin with all GT1a disease if using PrOD

Genotype 1: OPTIMIST-1 and -2

Simeprevir 150 mg and sofosbuvir 400 mg in chronically infected patients with HCV genotype 1

OPTIMIST-1:
310 treatment-naive and experienced patients without cirrhosis
- SVR12 was 97% (150/155) for 12 weeks of SIM/SOF
- SVR12 was 83% (128/155) for 8 weeks of SIM/SOF
- SVR 12 in treatment naive was 97% for the 12 week regimen
- SVR 12 in treatment experienced was 95% for the 12 week regimen

OPTIMIST-2:
103 treatment-naive and experienced patients with cirrhosis
- Overall SVR12 rate was 83% (86/103)
- SVR12 was 88% (44/50) among treatment-naive
- SVR12 was 79% (42/53) among treatment-experienced

Genotype 1: ALLY-1

ALLY-1: Daclatasvir + sofosbuvir + weight-based RBV in 60 patients with advanced cirrhosis
- SVR12 was only 76% in patients with GT1a (n=34) who received 12 weeks of therapy
- SVR12 was 100% in patients with GT1b (n=11) who received 12 weeks of therapy
- Therefore 24 weeks of treatment is recommended for GT1a with cirrhosis, although the SVR12 remains unclear in this group
Case #2

A 65 yo M with history of anemia of chronic disease, GERD, asthma, CAD and chronic hepatitis C genotype 2, fibrosis stage 3, HCV viral load 4 million, presents for evaluation. Pt presents to your office for initial evaluation of hepatitis C. He is interested in treatment. Pt’s anemia has been thoroughly evaluated and appears to be anemia of chronic disease. His last hemoglobin was 9.5. He denies having ever had any bleeding, melena, BRBPR, hematemesis, epistaxis or hemoptysis. Patient uses an albuterol inhaler as needed, omeprazole 20 mg daily, and take metoprolol tartrate 100 mg daily, lisinopril 10 mg daily, aspirin 325 mg daily, and simvastatin 10 mg daily for CAD.

1. Which of the following is a contraindication to the use of ribavirin in this patient?
   a) Drug-drug interaction with omeprazole
   b) Hemoglobin baseline < 11.0
   c) Coronary artery disease history
   d) Patient’s HCV genotype (2)
Genotype 2: FISSION, VALENCE, POSITRON Trials

Sofosbuvir 400 mg daily and weight-based ribavirin

FISSION: 499 treatment-naïve pts with GT 2 or 3, randomized to daily PEG-IFN/RBV x 24 wks vs. Sofosbuvir + RBV x 12 weeks.
- SVR12 was 97% (68/70) in patients in the SOF/RBV GT 2 group
- SVR12 was 78% in the PEG-IFN/RBV arm

POSITRON: 278 interferon-ineligible or unwilling, treatment-naïve and treatment-experienced GT2 and GT3 pts randomized to 12 weeks Sofosbuvir + RBV vs. placebo x 12 weeks.
- SVR12 was 93% (101/109) among GT2s

The overall SVR12 was 94% in a pooled analysis of all 3 trials with SOF/RBV x 12 weeks (for GT 2)
- Patients with cirrhosis tended to do worse in all 3 trials
- Thus therapy was extended to 16 weeks in pts with cirrhosis (despite limited data)

Genotype 3

Case #3

A 45 yo M w/ a seizure disorder, hypothyroidism, and treatment-experienced hepatitis C genotype 3 without cirrhosis (null response to PEG-IFN + RBV after 12 weeks), presents for treatment. His provider decides to treat this patient with 12 weeks of daclatasvir + sofosbuvir. Which of the following drug-drug interactions are you most concerned about?
- Carbamazepine
- Pantoprazole
- Levothyroxine
- Levetiracetam
- Omeprazole

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4/25/2016
**Genotype 3 Trials**

**Genotype 3: ALLY-3 Trial**

**ALLY 3:** 101 treatment-naive patients with and without cirrhosis, daclatasvir 60 mg daily + sofosbuvir 400 mg daily x 12 weeks (no ribavirin)
- Overall SVR12 rate of 90%
- SVR12 was 97% among treatment-naive non-cirrhotic pts
- SVR12 was 58% among treatment-naive cirrhotic pts,
  - This data suggests that cirrhotic patients might benefit from extension of therapy to 24 weeks.

DAC + SOF + RBV x 12 vs. 16 weeks in those with cirrhosis:
- SVR12 rates were 88% (15/17) for those in the 12 week arm versus
- SVR12 of 89% (16/18) in the 16 week arm

**Genotype 3: BOSON Trial**

592 patients total, both treatment-naive and treatment-experienced (IFN-eligible ONLY)
- 196 received sofosbuvir and RBV for 16 weeks
- 199 received sofosbuvir and RBV for 24 weeks
- 197 received sofosbuvir plus PEG-IFN/RBV for 12 weeks

SVR12 rates among treatment-naive patients with GT3:
- 77% (70/91) for SOF + RBV x 16 weeks
- 88% (83/94) for SOF + RBV x 24 weeks
- 82% for those with cirrhosis in SOF + RBV x 24 weeks arm
- 95% (89/94) for SOF + PEG-IFN/RBV x 24 weeks arm
- 91% for those with cirrhosis in SOF + RBV x 24 weeks arm

**Genotype 3: VALENCE Trial**

250 treatment-naive (42%) and -experienced (58%) subjects with genotype 3 (cirrhotic (n=45) and non-cirrhotic (n=100)) received sofosbuvir (400 mg daily) plus weight-based RBV x 24 weeks.
- Overall SVR12 rate was 84%
- SVR12 was 93% in treatment-naive
- SVR12 was 77% in treatment-experienced
- Cirrhosis didn’t impact results significantly.

**Genotype 3: C-SWIFT Trial**

40 patients with GT 3, treatment-naive, with and without cirrhosis, randomized to 8 versus 12 weeks of triple therapy with elbasvir/grazoprevir + sofosbuvir (400 mg) daily.
- SVR12 was 93% (14/15) for 8 weeks (non-cirrhotic)
- SVR12 was 100% (14/14) for 12 weeks of therapy (non-cirrhotic)
- SVR12 was 91% (10/11) for cirrhotics x 12 weeks
Genotype 4

Genotype 4 Trials

Genotype 4: SYNERGY Trial

21 patients with GT4, both treatment-naive and -experienced, both cirrhotic and non-cirrhotic, randomized to 12 weeks of ledipasvir/sofosbuvir - 60% were treatment-naive - 43% had advanced fibrosis (F3 or F4)

Overall SVR12 was 100% for all 20 patients

Genotype 4: PEARL-1 Trial

PEARL-I:
86 treatment-naive GT4 patients, non-cirrhotic received 12 weeks of the daily fixed-dose combination of paritaprevir/ritonavir/ombitasvir (PrO) +/- RBV

- SVR12 was 100% (42/42) in the PrO + RBV group
- SVR12 was 91% (40/44) in the PrO arm
Genotype 4: AGATE-I and −II Trials

**AGATE-I:**
120 treatment-naive and -experienced patients with GT4 + cirrhosis
- 12 versus 16 weeks of paritaprevir/ritonavir/ombitasvir (PrO) + RBV
- SVR12 was 96% in the 12 week PrO + RBV
- SVR12 was 100% in the 16 week PrO + RBV arm

**AGATE-II:**
100 treatment-naive and -experienced non-cirrhotic GT4 patients received 12 weeks of PrO + RBV
- Overall SVR12 was 94% for 12 weeks of PrO + RBV

**AGATE-III:**
60 treatment-naive and -experienced GT4 patients with cirrhosis
- 12 versus 24 weeks of PrO + RBV
- SVR12 was 97% for 12 weeks of PrO + RBV in cirrhotic pts

Genotype 4: C-EDGE Trial

66 treatment-naive GT4 patients, with and without cirrhosis, received elbasvir (50 mg)/grazoprevir (100 mg) x 12 weeks
- 6 were cirrhotic (9.1%)
- 28 were co-infected with HIV (42.4%)
- 10 also received RBV
- 56 did not receive RBV
- Overall SVR12 was 97% (64/66) regardless of status of cirrhosis or coinfection
- 1 treatment failure
- Baseline RAVs did not impact SVR12 rates

Genotype 4: NEUTRINO Trial

28 treatment-naive patients with GT4 with and without cirrhosis received 12 weeks of sofosbuvir 400 mg daily + PEG-IFN 2a + RBV
- SVR12 was 96% (27/28)
- The one treatment failure was in a cirrhotic pt

Ribavirin

**Important to carefully consider the patient’s baseline comorbidities.**
- If you have to stop RBV, you have to stop treatment.
- Pts with prior CAD, CAO, COPD, etc... may be risky candidates due to anemia and low oxygen carrying capacity that can result

Avoid ribavirin in pts w/ anemia or thalassemia
- Anyone with hemoglobin <13.0 should not receive RBV
- Particularly problematic in women (Pregnancy category X); 2 forms of contraception needed

Ribavirin needs to be dosed according to renal function
- CrCl >50: no dose adjustment
- CrCl 30-50: Alternate 200 mg and 400 mg every other day
- CrCl <30: 200 mg once daily
- ESRD: 200 mg once daily

Ribavirin's half-life is very long.
- Capsule, single dose: 64 hours in HCV pts
- Tablet: 120-170 hours

Beware: Drug-Drug Interactions

**Common:**
- Antacids
- H2 blockers
- PPIs
- Herbal medications
- HAART (Pis, NNRTIs)
- Many others

Double check for these, with patient, online, and with pharmacy

Be sure to ask patients about herbal remedies, antacids, OTC meds, etc.

Ledipasvir Solubility Decreases as pH Increases; Products that Increase Gastric pH are Expected to Decrease Concentration of Ledipasvir

- Caltrate (all forms)
- Calcichew (all forms)
- Tums (all forms)
- Vacta
- Omeprazole calcium/vitamin D
- Citracal (all forms)
- Alka-Mints®
- Cal-I®
- Cal–Leef®
- Choos®
- Mirkas®
- Rolia®
- Gas-A-X® with Maalox® (containing Calcium Carbonate, Simethicone)
- Rolaid® Plus Gas Relief (containing Calcium Carbonate, Simethicone)
- Titrax® Plus (containing Calcium Carbonate, Simethicone)
- Alamag®
- Alumina and Magnesia®
- Gen-Alox®
- Kodro®
- M.A.H.
- Makena®
- Magalene®
- Malapath®
- Mylanta®
- Bi-Alox®
- Ruxol®
- Mag-Dx®
- Maal®
- Uro-Mag®

Separate these OTC products and Harvoni administration by at least 4 hours

*** Slide courtesy of Dr. Camilla Graham***
H2 Blockers and Proton Pump Inhibitors with Harvoni

H2 Blockers
- Famotidine 40mg BID
- Ranitidine 150mg BID
- Tagamet 800mg BID

H2 blocker may be administered at the same time with LED/SOF or 12 hours apart from LED/SOF at a dose that does not exceed doses comparable to famotidine 40mg BID.

Proton Pump Inhibitors
- Omeprazole 20mg daily
- Prevacid 30mg daily
- Aciphex 20mg daily
- Protonix 40mg daily
- Nexium 20 to 40mg daily (try to stay with lower dose if possible)

PPI doses comparable to omeprazole 20mg or lower can be administered at the same time with LED/SOF under fasted conditions.

Drug-Drug Interactions

www.hep-druginteractions.org/interactions.asp

Ritonavir: Drug-Drug Interactions
5 Pre/Post Multiple Choice Questions

1. What is the most common barrier to patients accessing hepatitis C treatment currently?
   a) Unstable mental health disorders
   b) Insurance coverage
   c) Drug-drug interactions
   d) A life-expectancy of <1 year

2. Which of the following drugs interacts with Ledipasvir/sofosbuvir to decrease serum levels of ledipasvir?
   a) Methadone
   b) Levothyroxine
   c) Levetiracetam
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3. Based on the ION trials, which of the following patients might be a candidate for 8 weeks of ledipasvir/sofosbuvir?
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   c) GT 1b, treatment naïve, cirrhotic, HCV VL 2 million
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4. Which of the following is among the most common noted side effect of daclatasvir?
   a) Nausea
   b) Fatigue
   c) Skin rash
   d) diarrhea

5. Multiple Choice

   5. Which of the following measures are important to preventing morbidity associated with chronic hepatitis C?
      a) Weekly lab monitoring
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Thank you for your attention.

Questions/Comments?