Cases: Treatment of Hepatitis C in Patients with Cirrhosis and Advanced Liver Disease

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe increasing complexity when evaluating hepatitis C in patients with advanced liver disease
- Describe current guidance regarding hepatitis C treatment in patients with cirrhosis

Case Presentation

- 55 yo man with HCV/HIV
  - AST 48 (Lab normal 10-45)
  - ALT 39 (Lab normal 10-40)
  - Alk Phos 143 (Lab normal 25-140)
  - Total Bili 1.1 (Lab normal .2-1.2)
  - Hgb 13.7 (Lab normal 14)
  - Platelets 133K (Lab normal >140)
  - No symptoms; PE normal
  - CD4+ cell count: 325 cells/mm^3
  - HIV-1 RNA: <50 copies/ml on raltegravir/emtricitbine/tenofovir

ARS Question 1

The patient is found to have HCV genotype 1 (no subtype available), HVL. He wants to know if "the stuff on the HCV commercial would work". You now….

1. Ultrasound
2. Liver Biopsy
3. Other Non-invasive Marker assay
4. Obtain Subtype

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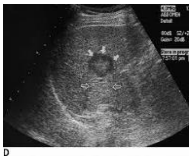
ARS Question 2

An ultrasound is performed. You will now…..

1. Refer to general surgeon for resection
2. Refer to interventional radiology for biopsy
3. Refer to transplant center
4. Start DAA for HCV
5. Order multiphasic CT



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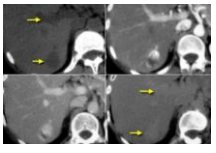
ARS Question 3 (Case)

The multiphasic CT shows the lesion has characteristics of a hemangioma. Enhancement in all phases matches the blood pool. HCCs exhibit "washout" early after peak arterial filling.



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ARS Question 3

- You calculate the FIB-4 which = 3.18
- Transient elastography is also performed and the results are as follows…
  - 17.5 kPascals
  - IQR/M= 26%
- You would now
  - 1. Treat patient with DAAs
  - 2. Obtain liver biopsy
  - 3. Obtain FibroTest

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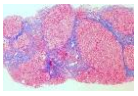
ARS Question 4

- Because you can't believe that this guy has cirrhosis you obtain a liver biopsy



- You would now
  - 1. Obtain EGD for variceal screening
  - 2. Start treatment for HCV
  - 3. Order EGD and start treatment for HCV
  - 4. Refer to hepatologist for treatment/evaluation

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ARS Question 5

- Which one of the following would NOT be an acceptable regimen?
  - 1. Elbasvir/grazoprevir x 12 weeks
  - 2. Ledipasvir/sofosbuvir x 12 weeks
  - 3. Sofosbuvir/velpatasvir x 12 weeks
  - 4. Glecaprevir/Pibrentasvir x 8 weeks

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TN GENOTYPE 1 with Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:

Treatment-Naive Genotype 1a Patients With Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[b] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[c]	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) with weight-based ribavirin for patients with baseline NS5A RASs[b] for elbasvir	16 weeks	IIa, B

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Includes genotype 1a resistance-associated substitutions at amino acid positions 28, 30, 31, or 93 known to confer antiviral resistance.
[c] This is a 3-tablet coformulation. Please refer to the prescribing information.

AASLD/IDSA HCV Guidance Accessed 9/7/2017

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ARS Question 6

While you are waiting for insurance approval and the EGD, the patient calls to say that his ankles are swollen and he has gained 15 lbs.

1. Start furosemide 60 mg/day
2. Repeat Ultrasound
3. Tell him to raise his legs when sitting and wait for approval of HCV meds
4. Call for help—Transplant Center

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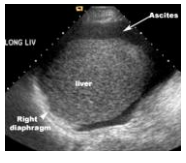
ARS Question 7

- An ultrasound is obtained
- You would now…
  1. Start spironolactone 50 mg and furosemide 20 mg
  2. Do diagnostic tap
  3. Contact transplant center
  4. 1 and 2
  5. 1, 2, and 3
  6. Send for TIPSS



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ARS Question 8

Which regimen would you use for HCC screening in this patient?

1. AFP every six months and US yearly
2. AFP every 6 months only
3. US every 6 months
4. US and AFP every 6 months
5. CT yearly
6. Would not surveil HCC

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ARS Question 9

How would you stage the liver disease?

1. Childs-Pugh
2. MELD
3. No need to stage. When patient looks ill enough, will refer to transplant center

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ARS Question 10

Do you think liver transplantation is an option for your HIV-infected patients with liver disease?

1. Yes
2. No
3. Don't Know

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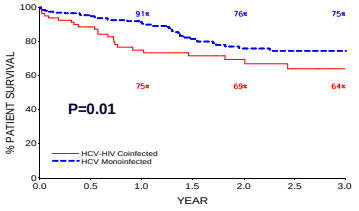
Patient Survival: HCV



Terrault et al. HEPATOLOGY 2009 Abs AASLD

HCV mono-infected	N=135	N=67	N=22
HCV-HIV co-infected	N=46	N=28	N=14

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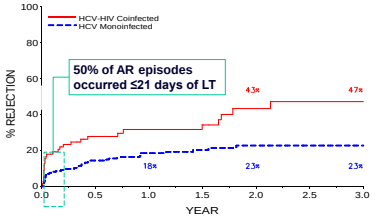
Time to First Acute Rejection



Stock , HIV and Liver Disease 2010

HCV mono-infected:	N=106	N=52	N=17
HCV-HIV co-infected:	N=31	N=14	N=7

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ARS Question 11

- The patient has an appointment in transplant hepatology in 8 weeks…
  1. You should treat HCV while waiting
  2. You should NOT treat HCV without transplant center approval

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Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Eligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I, A[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) with weight-based ribavirin[c]	12 weeks	I, A[d]
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[e] plus sofosbuvir (400 mg) with low initial dose of ribavirin (600 mg, increase as tolerated)	12 weeks	I, B

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.
[b] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.
[c] Low initial dose of ribavirin (600 mg) is recommended for patients with CTP class C cirrhosis; increase as tolerated.
[d] Only available data for genotype 6 are in patients with compensated cirrhosis.
[e] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

Recommended regimens listed by evidence level and alphabetically for:

Patients With Decompensated Cirrhosis[a] Who Have Genotype 1, 4, 5, or 6 Infection and Are Ribavirin Ineligible

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	24 weeks	I, A[b]
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	24 weeks	I, A[c]
Genotype 1 or 4 infection only: Daily daclatasvir (60 mg)[d] plus sofosbuvir (400 mg)	24 weeks	II, C

[a] Includes CTP class B and class C patients who may or may not be candidates for liver transplantation, including those with hepatocellular carcinoma.
[b] Only available data for genotypes 5 and 6 are in a small number of patients with compensated cirrhosis.
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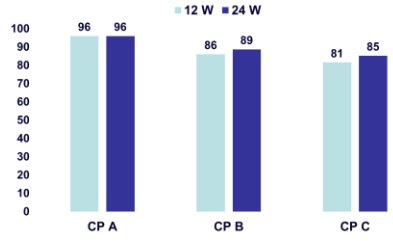
[d] The dose of daclatasvir may need to be increased or decreased when used concomitantly with cytochrome P450 3A/4 inducers and inhibitors, respectively. Please refer to the prescribing information for daclatasvir.

SOLAR-1: LDV/SOF + RBV in Decompensated Cirrhosis



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TIMING OF TREATMENT IN HCV-ASSOCIATED DECOMPENSATED CIRRHOSIS

- Background: Optimal timing for HCV treatment not known and highly controversial in those with ESLD
- Virtual Trial Model Simulation
  - Markov Model of SIM-LT (simulation of liver transplant candidates)
  - Evaluated Outcomes Based Upon Timing of HCV Treatment (before or after OTLTx)
    - Expected Life Years
    - QALYs
    - 1 and 5 year patient survival
    - Death from background and Liver-related causes
    - UNOS region
- RESULT:
  - Optimal threshold is MELD of 22-26 depending upon UNOS region
  - MELD >22 is more cost-effective to treat AFTER transplant
  - MELD below threshold favor HCV treatment before OTLTx

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Samur S et al, CLIN GASTROENTEROL HEPATOL, 2018

Summary: Management of Liver Disease

- Staging helps determine not only viral disease management, but liver disease management
- Compensated cirrhotics can and should be treated BUT
  - Must remember issues of surveillance
  - Must be constantly aware of risk of decompensation
- Liver transplant is a viable option for both decompensated liver disease and HCC in many patients with HIV

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Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!

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