Cases: Treatment of and Monitoring for Hepatitis C in Patients with Cirrhosis

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe disease severity and mortality risk in patients with cirrhosis
- Describe the current guidance in HCV treatment in patients with cirrhosis

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Case 1:

- 48 yo female infected with HCV diagnosed 20 years ago
  - IDU, significant alcohol for 15 years, none now
  - Fatigue, loss of energy on disability
  - PH upper GI bleed 1 year ago
- She saw a commercial where people born between 1945 and 1965 with HCV are riding horses and talking about being cured of HCV
- She is interested in treatment

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Case 1 : Labs

- ALT 54; AST 68; bilirubin 2.7; albumin 3.2;
- INR 1.4; AFP 22.4; creatinine 0.8
- WBC 3,000; Hgb 14; platelets 82,000
- HCV RNA 607,509 IU/mL
- HCV genotype 1a

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Case 1: ARS Question 1

Which statement is **NOT** true?

1. She likely has cirrhosis
2. She needs an upper endoscopy
3. She needs HCC screening
4. She should not be treated with an NS5a inhibitor
5. She should be screened for HBV and HIV

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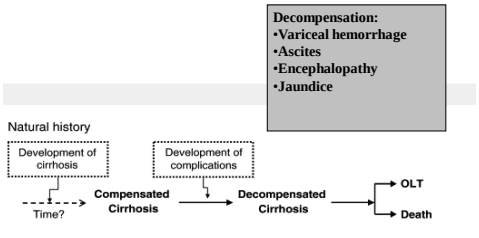
The Natural History of Cirrhosis in HCV



D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44:217-231.

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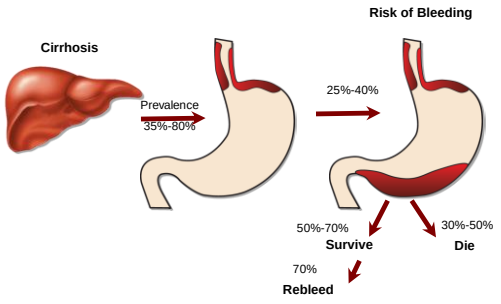
Risk of Bleeding from Esophageal Varices



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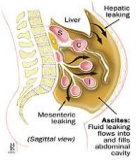
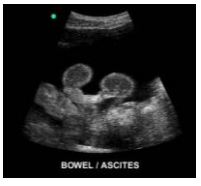
Ascites

- Fluid within the peritoneal cavity
- Occurs in 50-60% of patients with cirrhosis over 10-15 years
  - 1 yr survival 50%
- Mixture of liver and intestinal lymph





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Hepatic Encephalopathy

- Results from a combination of :
  - Portosystemic shunting and failure to metabolize neurotoxic substances
  - Ammonia remains the most important neurotoxic substance but poorly correlates with stage
- Treatment to reduce production of NH3 from the colon via
  - nonabsorbable disaccharides
    - lactulose: 3-4 BM per day
  - nonabsorbable antibiotics
    - rifaximin 550 mg bid, neomycin rarely used
- Protein restriction promotes protein degradation and, if maintained for long periods, worsens nutritional status and decreases muscle mass
    - No longer recommended

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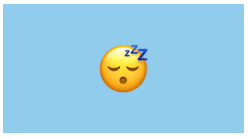
Things to remember about HE



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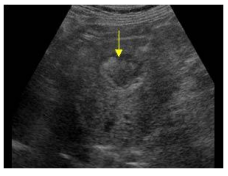
Case 1: ARS Question 2

- A right upper quadrant ultrasound is ordered for RT. Which showed:



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Case 1: ARS Question 2

A mass is noted in a cirrhotic appearing liver. The next step should be:

1. Ultrasound guided liver biopsy
2. Triple phase CT scan
3. PET Scan
4. Repeat ultrasound in 3 months to confirm stability

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Hepatocellular Carcinoma

- Late complication of end-stage liver disease
  - Exceptions: HBV seen in non cirrhotics
- Diagnosis by CT scan, MRI
  - Histology is not essential
- Alpha-fetoprotein level may be elevated
  - 20-40% with HCC have normal AFP
  - 20-30% without HCC have abnormal AFP
  - The higher the AFP, the more likely the diagnosis of HCC

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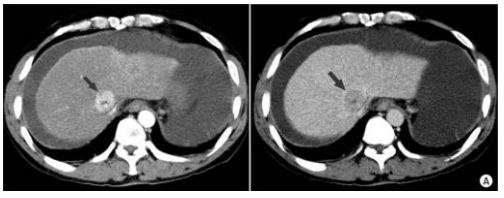
Triple phase CT scan



Arterial Phase Portal venous Phase washout

Hypervascular lesion that washes out on portal venous phase

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Health Maintenance for Cirrhosis

1. EGD to screen for varices
2. Ultrasound +/- AFP q 6 months
   - May want to alternate with CT or MR
3. MELD score q 3-6 months
   - INR, Creatinine, Bili
4. Screen for decompensation
   - Bleeding, volume, encephalopathy

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Big Questions in HCV and Cirrhosis

- What are the treatment options for patients with cirrhosis?
- Who should be treated by non hepatologists?
- When is a patient too sick to be treated?

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Case 2

55 year old woman with Genotype 1b HCV who is naïve to treatment. Staging via transient elastography reveals kPa 15.6. She has no evidence of decompensation. EGD is normal. CTP score is A. MELD score is 8.

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Case 2: ARS Question 3

Which of the following is **TRUE**?

1. This patient should be referred to a transplant center prior to treatment
2. If she is cured, she can discontinue HCC screening
3. Ribavirin will be necessary for most regimens in cirrhosis
4. Glecaprevir / pibrentasvir x 12 weeks would be a safe and effective regimen to treat her

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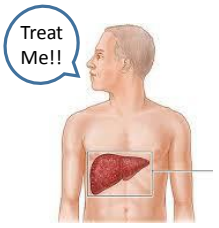
Compensated Cirrhosis

- Treatment options are essentially the same
- May be some differences in duration of therapy
- Protease inhibitors OK
  - But only for use in Childs A
- In most cases can be treated outside of transplant setting



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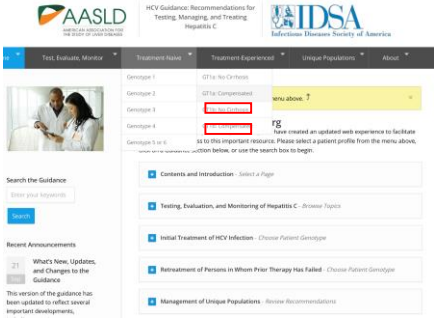
One Stop Shopping…



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Treatment in Noncirrhotic vs Cirrhotic

No Cirrhosis

Recommended and alternative regimens listed by evidence level and alphabetically for:
Treatment-Naive Genotype 1a Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A RASs[a] for elbasvir	12 weeks	I, A
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)[f]	8 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL	8 weeks	I, B
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

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)[f]	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

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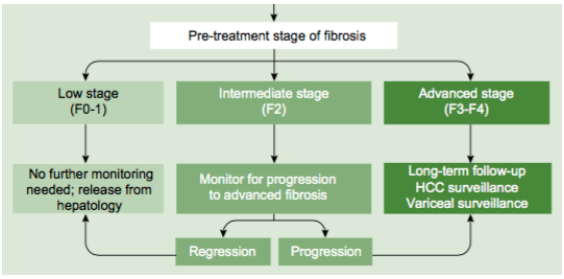
Post Treatment Management



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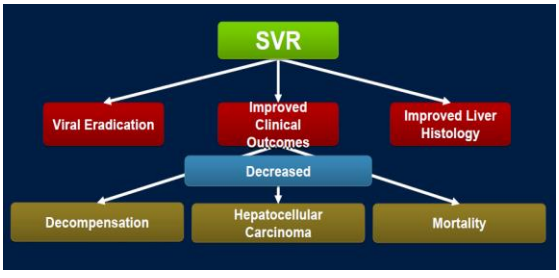
Terrault J Hep 2016

Treatment Effect in Cirrhosis



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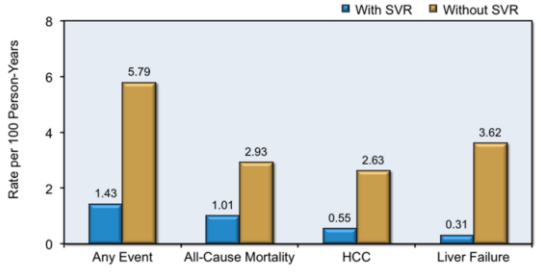
Benefits of Treatment



Van der Meer et al JAMA 2012

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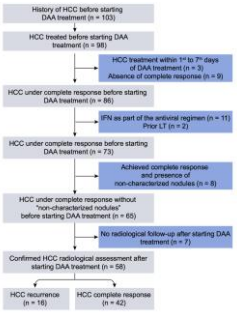
Controversy: HCV Treatment and HCC



- Hypothesis: immune dysregulation
- Highly effective DAA therapy eradicates HCV but may dismantle the immune "brake" on HCC

Reig et al 2016 J Hep

Survival Free of HCC Recurrence

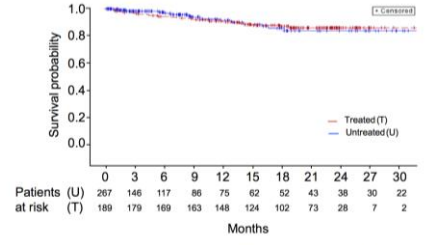


Fig. 2. Recurrence of HCC according to DAA treatment in the ANRS CO22 HEPATHER cohort. Pseudo-survival curves were plotted for time-dependent DAA treatment.

ANRS Collaboration, J Hepatology 2016

Case 3

62 year old female infected with HCV genotype 2 who is a nonresponder to interferon based therapy. She has no evidence of encephalopathy and mild ascites which is controlled with low dose lasix and aldactone. Bilirubin= 2.7, Albumin 2.2, INR = 2.

Case 3: ARS Question 4

What is this patient's Childs Classification?

1. A
2. B
3. C
4. D

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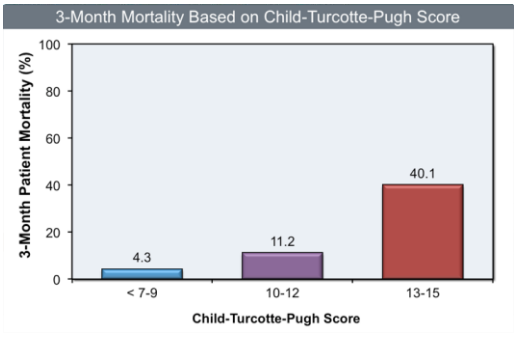
Childs-Turcotte-Pugh Review



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https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp

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Case 3 Continued: ARS Question 5

Would you…

1. Treat this patient
2. Refer the patient to a transplant center
3. Arrange for palliative care / hospice services

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Childs B and C

Recommended for All Patients With HCV Infection Who Have Decompensated Cirrhosis

RECOMMENDED	RATING
Patients with HCV infection who have decompensated cirrhosis—moderate or severe hepatic impairment, ie, Child-Turcotte-Pugh (CTP) class B or class C—should be referred to a medical practitioner with expertise in that condition, ideally in a liver transplant center.	I, C

www.hcvguidelines.org

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Avoiding Protease Inhibitors in Decompensated Cirrhosis

Regimens not recommended for:

Patients With Decompensated Cirrhosis (Moderate or Severe Hepatic Impairment; Child-Turcotte-Pugh Class B or C)

NOT RECOMMENDED	RATING
Paritaprevir-based regimens	III, B
Simeprevir-based regimens	III, B
Elbasvir/grazoprevir-based regimens	III, C
Glecaprevir/pibrentasvir	III, C
Sofosbuvir/velpatasvir/voxilaprevir	III, C

www.hcvguidelines.org

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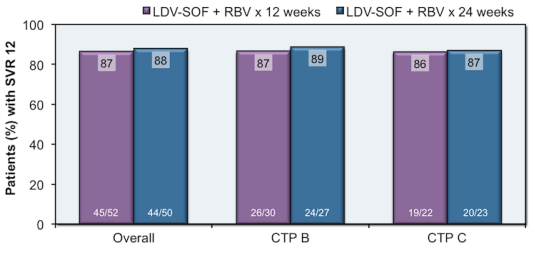
Treatment In Decompensated Cirrhosis: SOLAR 1



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Charlton et al Gastroenterology 2015

SOLAR-1/2: Overall Safety Summary in CPT B and C Cirrhosis

Patients, n (%)	CTP B + C (n=215)
Any AE	208 (97)
Grade 3–4 AE	51 (24)
Serious AE	61 (28)
Serious treatment-related AE	5 (2)
AE leading to D/C of LDV/SOF	9 (4)
Death	10 (5)
Liver transplantation	11

- Treatment-related SAEs were mostly related to RBV treatment
- Deaths and AEs that led to D/C of LDV/SOF were not attributed to study treatment

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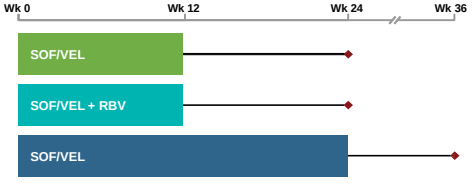
Samuel D, et al. EASL 2015, P0774

Sofosbuvir / Velpatasvir in Decompensated Cirrhosis



- Open-label, randomized (1:1:1) US study (NCT02201901)
- HCV GT 1–6 treatment-naïve or -experienced patients with Child-Pugh-Turcotte (CPT) B cirrhosis
- Key eligibility criteria: creatinine clearance (CL_{cr}) >50 mL/min, platelets >30,000/mm^3; no hepatocellular carcinoma or liver transplant

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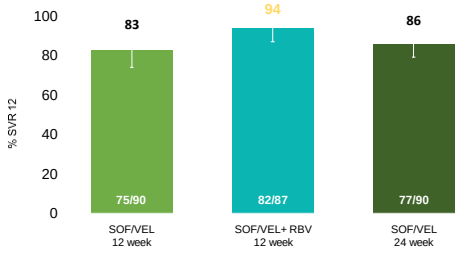
Curry et al NEJM 2015

Overall SVR12



P-value < 0.001 for comparison of SVR12 rate to 1% for each treatment group
Error bars represent 95% confidence intervals.

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Curry et al NEJM 2015

Treatment in Decompensated Cirrhosis

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

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

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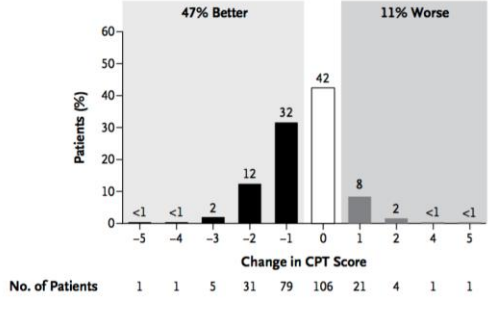
CTP Score In Decompensated Patients After SVR



Curry et al NEJM 2015

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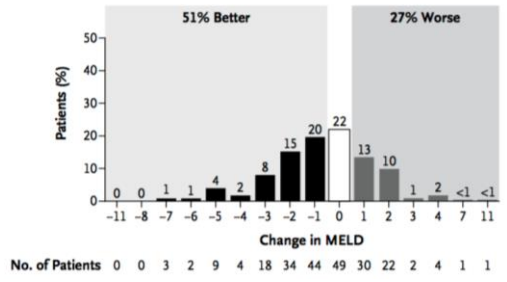
MELD Score (Baseline <15) Post SVR



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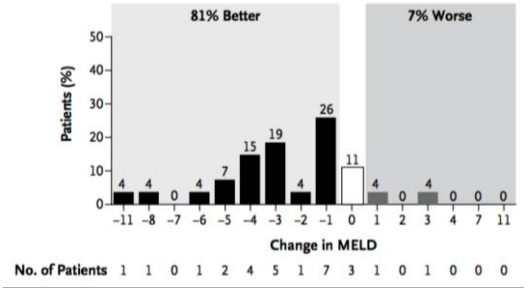
Curry et al NEJM 2015

MELD Score (Baseline <15) Post SVR



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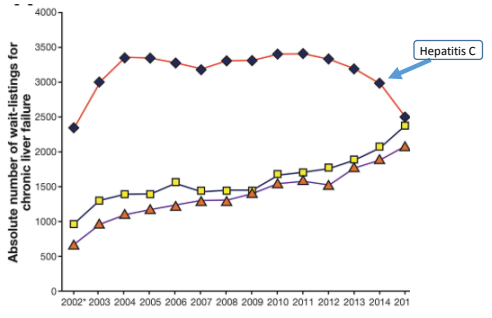
Curry et al NEJM 2015

Decrease in Wait list additions for HCV



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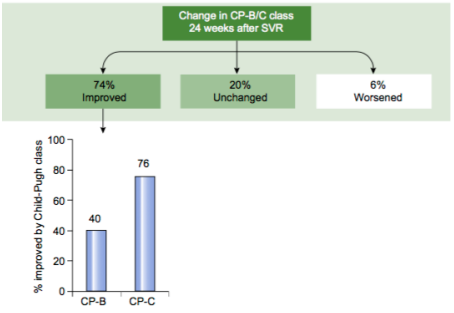
Goldberg et al Gastro 2017

What to Tell Patients



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Take Home: HCV and Cirrhosis

- In most cases Low MELD (<15) and Childs A are OK to treat in non transplant setting
- In cirrhosis (compensated and decompensated) outcomes improve, on all metrics, after SVR
- All patients with cirrhosis require HCC monitoring, variceal screening– even after SVR

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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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