ACTHIV 2018: A State-of-the-Science Conference for Frontline Health Professionals
Pre-Treatment Evaluation of Hepatitis C

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Learning Objectives
Upon completion of this presentation, learners should be better able to:

• Review the steps the healthcare team should follow from HCV diagnosis to treatment
• Discuss the importance of fibrosis assessment in HCV management and how to assess fibrosis.
• Describe when hepatocellular cancer (HCC) screening is an essential part of post-cure care.

HCVguidelines.org (AASLD/IDSA)
Faculty and Planning Committee Disclosures
Please consult your program book.

Off-Label Disclosure

There will be no off-label/investigational uses discussed in this presentation.
Do you treat HCV patients?

• A. yes, I treat HCV in my HIV/HCV co-infected patients

• B. Yes, I treat HCV mono and HIV/HCV co-infected patients in my practice

• C. I do not treat HCV and refer to other specialists
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https://api.cvent.com/polling/v1/api/polls/sp-npvkvz

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Deaths From Hepatitis C Have Surpassed Deaths From HIV Infection

Age-adjusted Mortality Rates of HIV and Hepatitis C: United States, 1999-2010

Rate per 100,000 Persons

1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010

Hepatitis C
HIV

16,600 deaths
8369 deaths

HCV is increasing in the younger population:

Source: CDC, National Notifiable Diseases Surveillance System (NNDSS)
Projected Cases of Hepatocellular Carcinoma and Decompensated Cirrhosis Due to HCV


![Graph showing projected cases of hepatocellular carcinoma and decompensated cirrhosis due to HCV. The graph indicates a peak incidence of 145,000 cases/year for hepatocellular cancer in 2020 and 14,000 cases/year for decompensated cirrhosis in 2019.](image-url)
HIV Disease Progression in the Setting of HCV Co-infection

Although most studies demonstrate increased mortality among co-infected individuals, a recent meta-analysis of over 30 studies with over 100,000 patients found no increase in mortality in co-infected patients in the pre-HAART era. Post-HAART, co-infection increased risk of overall mortality but not of AIDS-defining conditions [22]. In contrast, an Italian cohort study found a twofold increased AIDS risk among co-infected patients [23]. The Women’s Interagency HIV Study (WIHS) found an almost twofold increased AIDS risk among co-infected women without a CD4 count <200 cells/μL and for ART-naïve women [24].

The Italian cohort showed increases in bacterial and mycotic infections and WIHS found increases in bacterial pneumonia, HIV encephalopathy, and wasting syndrome, suggesting the need for earlier and more aggressive HIV and HCV treatment in co-infected individuals [23, 24]. Recent studies found high levels of T-cell activation in co-infected compared to HIV monoinfected individuals even following HAART [24, 25, 26]. Chronic immune activation may lead to immune dysfunction and cytokine production, causing enhanced HIV and HCV replication and lower T-cell counts [25]. The WIHS study showed that high levels of activated CD8 T cells are associated with incident AIDS among HCV-viremic women but not HCV-uninfected women, and CD4 activation predicted AIDS in both groups [24]. Suppression of HCV with therapy reduces activation [26]. These results again support early treatment of HIV and HCV.

Several pathways for active HCV infection impacting HIV infection have been proposed (Table 1). HCV co-infection may increase immune activation, leading to CD4 T-cell apoptosis in HIV-untreated patients and more rapid...
Risk Factors Associated with Faster Fibrosis Progression in Chronic HCV

**Disease State Factors**
- Fibrosis stage
- Inflammation grade
- Persistently elevated ALT

**Host/Viral Factors**
- Male gender
- Age
- Obesity
- Diabetes
- Metabolic syndrome
- HIV, HBV co-infection
- Immune system compromise
- Steatosis
- Iron overload
- Genotype 3

**Lifestyle Factors**
- Heavy alcohol consumption
- Tobacco use

Extrahepatic Manifestations of HCV

**Strongly associated**
- Mixed cryoglobulinemia
- Sjögren (sicca) syndrome
- Lymphoproliferative disorders
- Porphyria cutanea tarda
- Neuropathy
- Membranoproliferative glomerulonephritis
- Cryoglobulinemic vasculitis

**Possibly associated**
- Corneal ulcers (Mooren ulcers)
- Thyroid disease
- Lichen planus
- Pulmonary fibrosis
- Type 2 diabetes
- Systemic vasculitis (polyarteritis nodosa, microscopic polyangiitis)
- Arthralgias, myalgias, inflammatory polyarthritis
- Autoimmune thrombocytopenia

**STEP 1: SCREENING**

-HCV SCREENING AT ENTRY INTO CARE (A1) AND....

| Recommendation for HCV Testing for Persons With Ongoing Risk Factors |
|----------------------------------------------------------|------------------|
| RECOMMENDED                                               | RATING           |
| Annual HCV testing is recommended for persons who inject drugs and for HIV-infected men who have unprotected sex with men. | IIa, C           |
| Periodic testing should be offered to other persons with ongoing risk factors for HCV exposure. |                  |
Mr HK

- Social hx: has history of recreational marijuana use and occasional “other drugs”; denies significant etoh
- Meds: Darunavir/cobi+Dolutegravir+FTC/TDF, Metformin, atorvastatin, pantoprazole for heartburn
- PE: normal
- Labs: ALT 45, AST 78, TB 1.8, GFR 90. Plts 138K
- Imaging: ultrasound shows hyperechoic liver consistent with steatosis
- Has “great” private insurance and wants to start HCV therapy ASAP
Case (cont’d)

- Viral testing is done for patient and his HCVRNA is 3.2 million IU/ml

- He wants treatment for HCV but what other counseling do you need to do?
### Recommendations for Counseling Those with Current (Active) HCV Infection

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons with current (active) HCV infection should receive education and interventions aimed at reducing progression of liver disease and preventing transmission of HCV.</td>
<td>IIa, B</td>
</tr>
<tr>
<td>1. Abstinence from alcohol and, when appropriate, interventions to facilitate cessation of alcohol consumption should be advised for all persons with HCV infection.</td>
<td>IIa, B</td>
</tr>
<tr>
<td>2. Evaluation for other conditions that may accelerate liver fibrosis, including HBV and HIV infections, is recommended for all persons with HCV infection.</td>
<td>IIb, B</td>
</tr>
<tr>
<td>3. Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate an appropriate decision regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see When and in Whom to Initiate HCV Therapy).</td>
<td>I, A</td>
</tr>
<tr>
<td>4. Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection.</td>
<td>IIa, C</td>
</tr>
<tr>
<td>5. Vaccination against pneumococcal infection is recommended to all patients with cirrhosis (Marrie, 2011).</td>
<td>IIa, C</td>
</tr>
<tr>
<td>6. All persons with HCV infection should be provided education on how to avoid HCV transmission to others.</td>
<td>I, C</td>
</tr>
</tbody>
</table>
The AASLD/IDSA Recommendations for Patients with Active HCV

- Abstinence from alcohol
- Evaluation for other conditions that may lead to fibrosis (e.g. HIV, HBV, NASH)
- Evaluation for advanced fibrosis
  - APRI, Fib4, imaging
- Vaccination against HAV, HBV and pneumococcal infection (in patients with cirrhosis)
- Education on avoidance of transmission

www.hcvguidelines.org
**STEP 2:**
**LINKAGE TO CARE AND FIBROSIS ASSESSMENT**

<table>
<thead>
<tr>
<th>Recommendation for Linkage to Care</th>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>All persons with active HCV infection should be linked to a clinician who is prepared to provide comprehensive management.</td>
<td>RECOMMENDED</td>
<td>IIa</td>
</tr>
</tbody>
</table>
What more information do you need before you treat him?

- A. Confirm genotype and start treatment since his insurance covers the payment?
- B. Assess fibrosis severity before treatment initiation
- C. Order baseline resistance test to check for RAVs with genotype order
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https://api.cvent.com/polling/v1/api/polls/sp2mnmtu

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HCV RNA positive—What do you need to know?

- HCV Genotype
- Hepatitis B status - BsAg, cAb, sAb
- Alcohol use?
- Active substance use?
- Liver fibrosis severity.
- If cirrhotic-child’s class. Compensated or decompensated?
- Prior treatment experience
- Renal function
- Medication list
- Insurance status
Stateofhepc.org

Courtesy: NVHR
National Viral Hepatitis Roundtable.
nvhr.org
FDA Warning: Risk of HBV Reactivation in HCV-Patients Treated with DAAs

- 29 cases from November 2013 – Oct 2016
  - 2 deaths, 1 liver transplant
  - Reactivation typically 4–8 weeks after HCV treatment initiation
  - Baseline HBV characteristics:
    - 9 +HBsAg and HBV DNA
    - 7 +HBsAg; undetectable HBV DNA.
    - 3 HBsAg and HBV DNA negative; presumed isolated core +
    - 10 HBV testing not reported/available
  - HCV patients should be screened for HBV infection before starting DAA treatment and should be monitored for HBV flare-ups or reactivation during and following treatment

Suggestions for chronic HBV Management/Monitoring

1. +sAg and detectable HBV DNA
   • HBV treatment prior to HCV therapy

2. +sAg, undetectable HBV DNA
   • Close monitoring (ALT/AST q2weeks; HBV DNA monthly)
   • Duration?

3. Isolated core +, HBV DNA negative
   • Close monitoring
   • Double dose vaccine?

Slide courtesy of David L Wyles, MD
What about routine resistance testing?
## Occurrence of Resistance Mutations

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Protease (Linear)</th>
<th>Protease (Macro cyclic)</th>
<th>NS5A Inhibitor</th>
<th>NS5B Nucleoside</th>
<th>NS5B Palm</th>
<th>NS5B Thumb</th>
<th>NS5B Finger</th>
<th>Interferon</th>
<th>Ribavirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>V36M</td>
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<td>L28V</td>
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<td>Y93H</td>
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<td>S282T</td>
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<td>C136Y</td>
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<td>R422K</td>
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<td>P495S</td>
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</tr>
</tbody>
</table>

= Resistance mutation

HCV DrAG ResisSS. 2012;1.2. http://www.hivforum.org
### Regimen-Specific Recommendations for Use of RAS Testing in Clinical Practice

<table>
<thead>
<tr>
<th>Regimen</th>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elbasvir/grazoprevir</strong></td>
<td><strong>NSSA RAS testing is recommended</strong> for genotype 1a-infected, treatment-naive or -experienced patients being considered for elbasvir/grazoprevir. If present, weight-based ribavirin should be added and treatment should be extended to 16 weeks, or a different recommended therapy used.</td>
<td>I, A</td>
</tr>
</tbody>
</table>
| **Ledipasvir/sofosbuvir**   | **NSSA RAS testing can be considered** for genotype 1a-infected, treatment-experienced patients without cirrhosis being considered for ledipasvir/sofosbuvir. If >100-fold resistance is present, treatment should include 12 weeks of therapy with weight-based ribavirin, or a different recommended therapy.  
  **NSSA RAS testing can be considered** for genotype 1a-infected, treatment-experienced patients with cirrhosis being considered for ledipasvir/sofosbuvir. If >100-fold resistance is present, treatment should include 24 weeks of therapy with weight-based ribavirin, or a different recommended therapy used. | I, A   |
| **Sofosbuvir/velpatasvir**  | **NSSA RAS testing is recommended** for genotype 3-infected, treatment-experienced patients (with or without cirrhosis) and treatment-naive patients with cirrhosis being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added. | I, A   |
| **Daclatasvir plus sofosbuvir** | **NSSA RAS testing is recommended** for genotype 3-infected, treatment-experienced patients without cirrhosis being considered for 12 weeks of daclatasvir plus sofosbuvir. If Y93H is present, weight-based ribavirin should be added.  
**NSSA RAS testing is recommended** for genotype 3-infected, treatment-naive patients with cirrhosis being considered for 24 weeks of daclatasvir plus sofosbuvir. If Y93H is present, treatment should include weight-based ribavirin, or a different recommended therapy used. | I, B   |
Important to Assess Severity of Liver Disease

- Liver biopsy: very infrequently done since 2014
- Fibroscan: transient elastography
- Fibrotest/Fibrosure: biochemical
- MR elastography

- Determining fibrosis level is important as it may affect duration of treatment and determines the need for HCC screening post-cure

MR = magnetic resonance; HCC = hepatocellular carcinoma.
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Importance of Assessing Fibrosis in Hepatitis C Treatment

- Determines urgency of therapy for some payors
- Selects patients in need of additional screening with cirrhosis
  - Varices
  - Hepatocellular carcinoma
- Allows for selection of proper treatment plan and duration of therapy
- May be used by many payors as a way to restrict access to therapy or to prioritize therapy
Standard Lab Tests Suggesting Cirrhosis

- AST:ALT ratio > 1
- Elevated total bilirubin > 2 mg/dL
- INR > 1.5
- Platelet count < 125,000/μL

Note: If the AST:ALT ratio > 2, then alcohol-related liver injury is likely!
https://www.hepatitisc.uw.edu/page/clinical-calculators

- Clinical Calculators
  - CTP Calculator
  - APRI Calculator
  - BMI Calculator
  - CrCl Calculator
  - FIB-4 Calculator
  - Glasgow Coma Scale
  - GFR Calculator
  - MELD Calculator
  - SAAG Calculator
- Substance Use Screening Tools
  - AUDIT-C Questionnaire
  - CAGE Questionnaire
How do you assess fibrosis severity in your practice?

- A. Transient elastography (Fibroscan)
- B. Serum biomarkers- fibrotest/fibrosure
- C. MR elastography
- D. Liver biopsy
- E. Do not routinely assess fibrosis
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Liver Stiffness Measurement (LSM) Ranges in Chronic Liver Disease

<table>
<thead>
<tr>
<th>METAVIR Score</th>
<th>Liver Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0 – F1</td>
<td>Mild</td>
</tr>
<tr>
<td>F2</td>
<td>Moderate</td>
</tr>
<tr>
<td>F3</td>
<td>Severe</td>
</tr>
<tr>
<td>F4</td>
<td>Cirrhosis</td>
</tr>
</tbody>
</table>

- LSM 2.5 – 7.0 kPa → Mild or absent fibrosis is likely
- LSM > 12.5 kPa → Cirrhosis is likely


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Pitfalls of liver stiffness measurement

1. Obesity
2. Operator experience
3. Acute liver injury
4. Extrahepatic cholestasis
5. Increased CVP
6. Ascites
7. Narrow intercostal spaces
### Fibroscan results

<table>
<thead>
<tr>
<th>Stage</th>
<th>Fibroscan Score (kPa)</th>
<th>CAP  (mmHg)</th>
<th>E (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>&lt;7.1</td>
<td>248</td>
<td>12.1</td>
</tr>
<tr>
<td>2</td>
<td>7.1-9.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9.5-12.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>&gt;12.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Comments:**

FibroScan® Touch (SN: F60411) - Probe M (SN: 71005) - 2.0.5

FibroScan® is a medical device intended as an aid for the management of patients with liver disease. Measurements should be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical records of the patient, the number of valid measurements and their scatter. Probes must be calibrated according to the manufacturer’s recommendations.

**Exam M (Liver)**
- Operator: WINSTON
- Valid measurements: 10
- Total measurements: 10
- SWS MEDIAN = 2.01 m/s
- SWS IQR = 0.18 m/s
- CAP MEDIAN = 197 mmHg
- CAP IQR = 4.3 mmHg

**Comments:**

FibroScan® Touch (SN: F60411) - Probe M (SN: 71005) - 2.0.5

FibroScan® is a medical device intended as an aid for the management of patients with liver disease. Measurements should be interpreted by a physician experienced in dealing with liver disease, taking into account the complete medical records of the patient, the number of valid measurements and their scatter. Probes must be calibrated according to the manufacturer’s recommendations.
## Invasive and Noninvasive Fibrosis Tests

<table>
<thead>
<tr>
<th>Methodology</th>
<th>Liver Biopsy</th>
<th>Serum Markers</th>
<th>Transient Elastography</th>
<th>MRE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measuring methods</td>
<td>Direct observation</td>
<td>Measures direct and indirect serum markers* of fibrosis</td>
<td>Liver stiffness by detection of ultrasound-propagated shear waves</td>
<td>Liver stiffness by MRI of vibration-propagated shear waves</td>
</tr>
<tr>
<td>Accuracy for detecting cirrhosis</td>
<td>High</td>
<td>Moderate (APRI) to high (FibroSURE™, ELF)</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Accuracy for detecting intermediate fibrosis</td>
<td>High</td>
<td>Low (APRI) to moderate (FibroSURE™, ELF)</td>
<td>Moderate to high</td>
<td>High</td>
</tr>
<tr>
<td>Risk of complications</td>
<td>Risk of pain/bleeding</td>
<td>Minimal</td>
<td>Minimal</td>
<td>Minimal</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Coagulopathy</td>
<td>Minimal</td>
<td>Obesity; narrow rib spaces</td>
<td>Claustrophobia; other MRI contraindications</td>
</tr>
<tr>
<td>Limitations</td>
<td>Sampling error</td>
<td>False-positives with hemolysis, inflammation, Gilbert’s syndrome</td>
<td>False-positives with inflammation, congestion</td>
<td>False-positives with inflammation, congestion</td>
</tr>
<tr>
<td>Longitudinal monitoring</td>
<td>Unsuitable</td>
<td>Indices may change with disease progression / therapy</td>
<td>Liver stiffness changes with disease progression / therapy</td>
<td>Liver stiffness changes with disease progression / therapy</td>
</tr>
<tr>
<td>Cost</td>
<td>Highest per-test cost</td>
<td>Low per-test cost</td>
<td>High initial equipment cost</td>
<td>Very high initial equipment cost</td>
</tr>
</tbody>
</table>

*Serum tests that incorporate markers of fibrogenesis are generally more accurate.

APRI=AST-to-platelet ratio index; AST=aspartate aminotransferase; ELF=enhanced liver fibrosis; MRE=magnetic resonance elastography, MRI=magnetic resonance imaging.

### Indirect Serum Tests for Fibrosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Test Components</th>
<th>Sensitivity (%)*</th>
<th>Specificity (%)*</th>
<th>PPV (%)*</th>
<th>NPV (%)*</th>
<th>Cirrhosis Discrimination</th>
<th>Fibrosis Discrimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST/ALT ratio(^1)</td>
<td>AST, ALT</td>
<td>53</td>
<td>100</td>
<td>100</td>
<td>81</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>APRI(^2)</td>
<td>AST/platelet count</td>
<td>77</td>
<td>72</td>
<td>70</td>
<td>79</td>
<td>+</td>
<td>+/- (moderate)</td>
</tr>
<tr>
<td>FIBROspect II(^3,4)</td>
<td>HA, TIMP-1, α2-macroglobulin</td>
<td>72</td>
<td>74</td>
<td>61</td>
<td>82</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>FIBROSURE(^5,6) <strong>FibroTest</strong></td>
<td>α2-macroglobulin, haptoglobin, Apo A1, GGT, total bilirubin, ALT</td>
<td>84</td>
<td>95</td>
<td>76</td>
<td>91</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>HepaScore(^7)</td>
<td>Age, gender, bilirubin, GGT, HA, γ2-macroglobulin</td>
<td>77</td>
<td>70</td>
<td>71</td>
<td>77</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>ELF(^8)</td>
<td>HA, N-terminal propeptide of type III collagen, TIMP-1</td>
<td>86</td>
<td>62</td>
<td>80</td>
<td>70</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

ALT=alanine aminotransferase; Apo A1=apolipoprotein A1; GGT=gamma-glutamyl transpeptidase; HA=hyaluronic acid; NPV=negative predictive value; PPV=positive predictive value; TIMP-1=tissue inhibitor of metalloproteinase. *Sensitivity, specificity, PPV, and NPV values are for significant fibrosis, with the exception of AST/ALT ratio, where the values are for cirrhosis.

### Detection of Cirrhosis: Transient Elastography versus FibroTest & AST-Platelet Ratio Index (APRI)

<table>
<thead>
<tr>
<th></th>
<th>Transient Elastography</th>
<th>FibroTest (FibroSURE)</th>
<th>APRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cut-off value</td>
<td>≥ 12.5 kPa</td>
<td>≥ 0.75</td>
<td>≥ 1.0</td>
</tr>
<tr>
<td>AUROC (95% CI)</td>
<td>0.92 (0.86-0.98)</td>
<td>0.78 (0.66-0.89)</td>
<td>0.73 (0.58-0.88)</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>76.9</td>
<td>61.5</td>
<td>77</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>86.4</td>
<td>73.8</td>
<td>72.8</td>
</tr>
<tr>
<td>Positive Predictive Value (%)</td>
<td>41.7</td>
<td>22.9</td>
<td>26.3</td>
</tr>
<tr>
<td>Negative Predictive Value (%)</td>
<td>96.7</td>
<td>93.8</td>
<td>96.2</td>
</tr>
<tr>
<td>Correctly classified (%)</td>
<td>85.3</td>
<td>72.4</td>
<td>68.1</td>
</tr>
</tbody>
</table>

Choosing a Regimen 2018

- You may not have a choice: the choice may be made by the payors
- Deciding factors
  - **SVR rates** – all > 95%, similar among existing regimens
  - **Duration of therapy** – 8-12 weeks naïve, longer for cirrhosis patients and non-responders
  - **Impaired renal function (GFR, 30 ml/min)**; Protease/NS5a inhibitors may be used safely
  - **Genotype** also guides the choice of regimen
Case (cont’d)

- He gets transient elastography
  - 15.4 kPa (stage 4 fibrosis/cirrhosis)
  - Gets an EGD- no varices
  - Child’s A compensated cirrhosis
- Treatment is initiated
  - SVR achieved with 12 weeks of treatment
  - Repeat fibroscan post cure is 11.0 (stage 3 fibrosis)
- What else do you need to do for him?
  - Cancer surveillance
Screening EGD and follow up

**CIRRHOSIS**

- Upper gastrointestinal endoscopy

**Esophago-gastric varices present**

- **NO**
  - Repeat upper GI endoscopy every 2 year

- **SMALL** (grade 1)
  - Repeat upper GI endoscopy every 1 year
  - Contraindication for beta-blockers?
    - **NO**
      - Start non-cardio selective beta-blockers
    - **YES**
      - Endoscopic ligation
        - If side effect or no effect

- **LARGE** (grade 2-3)

**Screening EGD at diagnosis of cirrhosis**

- **No varices**
  - Repeat EGD in 3 years

- **Small varices**
  - Not at high risk of bleeding

- **High risk of bleeding**
  - Beta blockers can be used, long term benefit not established
  - Add beta blocker for prevention of first variceal hemorrhage

- **Not yet bled but at high risk of bleeding**
  - Beta blockers or EVL

- **Not yet bled and without high risk of bleeding**

**If not on beta blockers, repeat EGD in 2 years**

**Follow up EGD not necessary**

Beta blockers preferred, EVL can be used if there are contraindications, blockers intolerance or non-compliance to beta blockers

* High risk of bleeding: Child B/C cirrhosis, red wale marks on varices seen on endoscopy.

http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/hepatology/variceal-hemorrhage/
Cirrhosis and HCC Screening

- Cirrhosis is the most important risk factor for developing HCC in patients with chronic hepatitis C infection.
- Less commonly, HCC will occur in patients who have advanced fibrosis but without cirrhosis.
- The AASLD practice guidelines recommend surveillance for HCC using abdominal ultrasound every 6 months for all HCV-infected patients who have cirrhosis (or advanced fibrosis).
- Some experts still recommend using AFP in addition to ultrasound, but it is strongly recommended not to use AFP as the sole screening tool.
# HCC Screening

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Association for the Study of Liver Diseases</td>
<td>US every 6 months</td>
</tr>
<tr>
<td>European Association for the Study of the Liver</td>
<td>US every 6 months</td>
</tr>
<tr>
<td>Asian-Pacific Association for the Study of the Liver</td>
<td>AFP + US every 6 months</td>
</tr>
<tr>
<td>National Comprehensive Cancer Network</td>
<td>AFP + US every 6-12 months</td>
</tr>
<tr>
<td>US Department of Veterans Affairs</td>
<td>AFP + US every 6-12 months</td>
</tr>
</tbody>
</table>

AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma; US, ultrasonography.

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td>Results are superior to serological tests, but are operator-dependent</td>
</tr>
<tr>
<td>Alpha fetoprotein (AFP)</td>
<td>AFP has a known imbalance between sensitivity and specificity</td>
</tr>
<tr>
<td></td>
<td>A rising AFP level &gt; 200 ng/mL positively predicts HCC in patients with cirrhosis and a liver mass</td>
</tr>
<tr>
<td>Ultrasonography + AFP</td>
<td>Although the combination improves the sensitivity, it is not recommended, due to increased costs and false-positive rates</td>
</tr>
</tbody>
</table>
Persistent Elevation In ALT Post Cure of HCV

• Elevated ALT in patients with SVR:
  – 2-8% of patients treated with PEGINF
  – 1% of patients treated with oral anti-viral therapy

• What causes this?
  – NAFLD, did they gain weight?
  – Another co-existent liver disease
  – Alcohol consumption, is AST elevated?
  – re-infection, always need to consider this
Key Messages

– Need to assess fibrosis stage prior to treatment initiation
– Need for continued HCC screening post cure with advanced fibrosis (stage 3 and 4).
– Indications for baseline resistance testing well laid out.
– Screening for and monitoring for HBV reactivation during DAA Rx
– Counseling on reinfection post Cure remains important.

– Visit hcvguidelines.org OFTEN
Thanks for your attention