2019 AL/MS ACP CHAPTER MEETING

“UPDATES IN HEPATITIS C”

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DISCLOSURES

• I have received funds for research support, paid to UAB, from Gilead, Janssen and Merck; and consulting fees from Abbvie (updated 05/17/2019).
LEARNING OBJECTIVES

In the end of this activity, participants will:

- Understand how direct-acting antivirals work
- Appraise the revolutionary medical impact of DAAs
- Become aware of the benefits of timely diagnosis and treatment
- Identify challenges and opportunities of HCV control in the US
- Capture local realities of HCV control in Alabama
WHICH ONE OF THESE OPTIONS BEST DESCRIBE YOUR CURRENT PRACTICE SETTING?

A. I don’t screen patients or even see HCV infection
B. I look for HCV infection, but rarely diagnose it
C. I refer patients outside for treatment
D. I refer patients to my clinic partner for treatment
E. I see quite a bit of HCV infection and I have prescribed DAAs
A 60-year-old man presents for health insurance evaluation. He is otherwise healthy.

- Past medical hx is unremarkable
- Social Hx unremarkable
- Normal PE
- Normal labs, including LFTs

Is this patient at increased risk of infectious hepatitis?
VIRAL HEPATITIS TESTING

Acute N/V, abd pain, fever, jaundice

- Acute hep panel
  - HAV IgM
  - HBsAg
  - HBcIgM
  - Anti-HCV

Screening of asymptomatic patients

- HBsAg, Anti-HBc, Anti-HBs
  - Asian ethnicity, high risk sexual behavior, IVDU, HD, HCWs

- Anti-HCV
  - Baby boomers, IVDU hx, HD
**TESTING ALGORITHM FOR HCV INFECTION**

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**ELISA Screening Tests**
- Sensitivity (97%-100%)
- Positive predictive value
  - 95% with risk factors + elevated ALT
  - 50% without risk factors + normal ALT
- False-positive results
  - More likely in patients with low risk of HCV infection
- False-negative results
  - More likely in severely immunocompromised patients

**HCV RNA Assays**
- Use sensitive quantitative assay w reflex genotyping
- When to test?
  - If anti-HCV Ab test is positive
  - If treatment is being considered
  - If unexplained liver disease and anti-HCV Ab test result is negative and person is immunocompromised
  - If acute HCV infection is suspected

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HCV SCREENING

HCV AB + + HCV VL + = Acute or Chronic HCV → Counselling Linkage to Care

HCV AB + + HCV VL - = Spontaneous Clearance Cure by treatment False (+) AB test

HCV AB - + HCV VL + = IC populations HIV co-infection → Counselling Linkage to Care

CASE 2

- A 60-year-old man presents for routine primary care visit

- Past medical hx: HTN, DM, CAD, CHF, HLD
- Med list: omeprazole, rosuvastatin, ASA, metoprolol, insulin
- Social Hx: occasional drinking (3-4 beers per week)
- Normal PE
- Normal labs, except for mildly elevated LFTs
  - Anti-HCV +, HCV VL 1,500,000
  - What to do next?
COUNSELLING

In 2019, cure is possible for the vast majority of patients

Encourage patients to seek treatment early

Refer (or treat at your own practice)
COUNSELLING NEWLY DIAGNOSED PATIENTS WITH HCV

- Educate regarding HCV transmission
  - Screen sexual partners, but CDC does not recommend barrier methods for monogamous heterosexual partners
  - Higher risk of sexual transmission among MSM especially with HIV co-infection
  - Children born to HCV-positive mothers should be screened (~3% risk)
- Screen for hepatitis A (Ab total) and hepatitis B (HBsAb) and vaccinate if non-immune
- Assess alcohol use in all patients with HCV (CDC guidelines)
  - There is no “safe” amount of alcohol consumption for patients with HCV
  - Refer patients with risky use for alcohol treatment
    - Men: >2 drinks/day (>14/week) or more than 4 in one day
    - Women: >1 drink/day (>7/week) or more than 3 in one day
- Advise on a liver-healthy diet, which equates to a normal body mass index
DIRECT-ACTING ANTIVIRAL TARGETS

Structural Proteins (Capsid and Envelope)

- Core
- E1
- E2
- NS2
- NS3
- 4A
- NS4B
- NS5A
- NS5B
- 3'UTR

Ribavirin

NS3 Protease Inhibitors

NS5A Inhibitors

Non-NUC Inhibitors

NS5B Non-NUC Inhibitors

Protease Polyprotein Processing

Protease Cofactors

Viral Assembly

RNA Polymerase

Non- Structural Proteins (Replication Complex)

Covalent Binding

Allosteric Binding

NS5B NUC Inhibitors NUC analogues
HCV LIFE CYCLE AND THERAPEUTIC TARGETS

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Abbrev.</th>
<th>Activity</th>
<th>Potency</th>
<th>Resistance Barrier</th>
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<tbody>
<tr>
<td><strong>Protease Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simeprevir</td>
<td>SIM</td>
<td>GT1</td>
<td>High</td>
<td>Low (1a&lt;1b)</td>
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<td>Paritaprevir</td>
<td>PTV</td>
<td>GT 1,4 &amp; 6</td>
<td>Moderate</td>
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<tr>
<td>Grazoprevir</td>
<td>GZR</td>
<td>Pan-genotypic</td>
<td>High</td>
<td></td>
<td></td>
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<tr>
<td>Glecoprevir</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voxilaprevir</td>
<td>VOX</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>NS5A Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>DCV</td>
<td>GT 1,3 &amp; 4</td>
<td>High</td>
<td>Low (1a&lt;1b)</td>
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</tr>
<tr>
<td>Ledipasvir</td>
<td>LDV</td>
<td>GT 1,4</td>
<td></td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Ombitasvir</td>
<td>OBR</td>
<td>GT 1,4 &amp; 6</td>
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<td>Very high</td>
<td></td>
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<td>Elbasvir</td>
<td>EBR</td>
<td></td>
<td></td>
<td></td>
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<td>Velpatasvir</td>
<td>VEL</td>
<td>Pan-genotypic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pibrentasvir</td>
<td>PIB</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>NUC Analogue</strong></td>
<td>Sofosbuvir</td>
<td>Pan-genotypic</td>
<td>Intermediate</td>
<td>Very High</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>SOF</td>
<td></td>
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</tr>
<tr>
<td>Dasabuvir</td>
<td>DSV</td>
<td>GT1</td>
<td>Intermediate</td>
<td>Low</td>
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<tr>
<td><strong>Non-Nuc</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Dasabuvir</td>
<td>DSV</td>
<td></td>
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</tbody>
</table>
A 60-year-old man presents for routine primary care visit

Past medical hx: HTN, DM, CAD, CHF, HLD
Med list: omeprazole, rosuvastatin, ASA, metoprolol, insulin
Social Hx: occasional drinking (3-4 beers per week)
Normal PE
Normal labs, including LFTs
  Anti-HCV +, HCV VL 1,500,000, GT1a
  Pre-treatment evaluation key points?
STAGING LIVER FIBROSIS

- **APRI** =
  \[
  \frac{\text{AST/ULN}}{\text{Platelets}(10^9/L) \times 100}
  \]
  - \(< 0.7 = \text{F0-1}\)
  - \(> 0.7 = \text{F2 or F3}\)
  - \(> 2.0 = \text{F4 (cirrhosis)}\)

- **FIB-4** =
  \[
  \frac{\text{Age (years) \times AST U/L}}{\text{Platelets}(10^9/L) \times \text{ALT U/L}}
  \]
  - \(< 1.45 = \text{F0-1}\)
  - \(> 1.45, < 3.25 = \text{F2 or greater}\)
  - \(> 3.25 = \text{F4 (cirrhosis)}\)

- **Fibrosure (or Fibrotest)**
  - \(\alpha 2\) macroglobulin
  - Apolipoprotein A1
  - GGT, ALT, Haptoglobin
  - Total bilirubin

- **Liver Stiffness**
  - \(7.2 \text{ Kpa} = \text{F0-1}\)
  - \(> 7.2 \text{ Kpa}, \leq 9.3 \text{ Kpa} = \text{F2}\)
  - \(> 9.3 \text{ Kpa}, \leq 12.2 \text{ Kpa} = \text{F3}\)
  - \(> 12.2 \text{ Kpa} = \text{F4 (cirrhosis)}\)

Zhu X. Dig Dis Sci 2011;56:2742-49
Protease Inhibitors are contraindicated

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points*</th>
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<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin time</td>
<td></td>
</tr>
<tr>
<td>Seconds prolonged</td>
<td>&lt;4</td>
</tr>
<tr>
<td>International normalized</td>
<td>&lt;1.7</td>
</tr>
<tr>
<td>ratio</td>
<td></td>
</tr>
</tbody>
</table>

Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)
Class A = 5 to 6 points (least severe liver disease)
Class B = 7 to 9 points (moderately severe liver disease)
Class C = 10 to 15 points (most severe liver disease)

T Bili = 2
INR = 1.7
Alb = 3.4
CPT = 8
Class B

Rx plan changes
May need RBV
Needs referral
<table>
<thead>
<tr>
<th>Interaction</th>
<th>LDV/SOF</th>
<th>SOF/VEL</th>
<th>EBV/GZR</th>
<th>GLE/PIB</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-acids (PPIs, H2 blockers, others) ↔</td>
<td>↓</td>
<td>↓</td>
<td>-</td>
<td>-</td>
<td>Dose reduction and/or med change</td>
</tr>
<tr>
<td>Amiodarone ↑</td>
<td>↔</td>
<td>↔</td>
<td>-</td>
<td>-</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Anticonvulsants (phenytoin, CBZ, barbiturates) ↔</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Contraindicated, med change</td>
</tr>
<tr>
<td>Digoxin ↑</td>
<td>↔</td>
<td>↔</td>
<td>-</td>
<td>↔</td>
<td>Use lowest dose, monitor levels</td>
</tr>
<tr>
<td>Ethinyl estradiol–containing products ↑</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>↔</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Rifamycins (rifampin, rifabutin) ↔</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>St John’s wort</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Milk thistle</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Statins ↑</td>
<td>↔</td>
<td>↔</td>
<td>↔</td>
<td>↔</td>
<td>Dose reduction or statin change</td>
</tr>
</tbody>
</table>

Other notable interactions:
LDV/SOF: tenofovir (↑ - especially w concominant HIV protease inhibitor use); rosuvastatin use is contraindicated
SOF/VEL: tenofovir (↑ - especially w concominant HIV protease inhibitor use); rosuvastatin use OK (5mg max); efavirenz (↓)
EBV/GZR: nafcillin, ketoconazole, bosentan, tacrolimus, efavirenz, etravirine, modafinil (↓); cyclosporine, HIV protease inhibitors, cobicistat (↑)
GLE/PIB: efavirenz (↓); HIV protease inhibitors (↑)

Adapted from DAA Package Inserts
### DAAS AND STATINS

<table>
<thead>
<tr>
<th></th>
<th>LDV SOF</th>
<th>SOF VEL</th>
<th>EBV GZR</th>
<th>GLE PIB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Lowest dose</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Lowest dose</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Reduce by 50%</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Lowest dose</td>
<td>Lowest dose</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Lowest dose</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Monitor</td>
<td>Monitor</td>
<td>Avoid &gt; 20mg</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Not recommended</td>
<td>Avoid &gt; 10mg</td>
<td>Avoid &gt; 10mg</td>
<td>Avoid &gt; 10mg</td>
</tr>
</tbody>
</table>

Adapted from DAA Package Inserts
http://www.hep-druginteractions.org/checker

<table>
<thead>
<tr>
<th>HEP Drugs</th>
<th>Co-medications</th>
<th>Drug Interactions</th>
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<tr>
<td>Search HEP drugs...</td>
<td>Search co-medications...</td>
<td>Check HEP/HEP drug interactions</td>
</tr>
<tr>
<td>A-Z</td>
<td>A-Z</td>
<td>Switch to table view</td>
</tr>
<tr>
<td>Class</td>
<td>Class</td>
<td>Reset Checker</td>
</tr>
<tr>
<td>Trade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine (HBV)</td>
<td></td>
<td>Potential Interaction</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir</td>
<td></td>
<td>Telaprevir</td>
</tr>
<tr>
<td>OBV/PTV/r.</td>
<td></td>
<td>Tipranavir</td>
</tr>
<tr>
<td>OBV/PTV/r + DSV</td>
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<td></td>
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<tr>
<td>Peg-IFN alfa</td>
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<tr>
<td>Ribavirin</td>
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<td></td>
</tr>
<tr>
<td>Simeprevir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticarcillin</td>
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<td>No Interaction Expected</td>
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<tr>
<td>Ticlopidine</td>
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<td></td>
</tr>
<tr>
<td>Timotol</td>
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<td>Telaprevir</td>
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<tr>
<td>Almotriptan</td>
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<td>Private</td>
<td>Medicare</td>
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<tr>
<td><strong>Baseline Labs</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Staging</strong></td>
<td>No restrictions in most</td>
<td>No restrictions</td>
</tr>
<tr>
<td><strong>US imaging</strong></td>
<td>Required in most</td>
<td>Optional</td>
</tr>
<tr>
<td><strong>Negative UDS and ETOH</strong></td>
<td>No</td>
<td>No</td>
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<tr>
<td><strong>Sobriety &gt; 6m in chart</strong></td>
<td>Encouraged</td>
<td>Encouraged</td>
</tr>
<tr>
<td><strong>HIV and HBV status</strong></td>
<td>Required in most</td>
<td>Encouraged</td>
</tr>
</tbody>
</table>
Case 2: A 60-year-old man presents for routine primary care visit

Past medical hx: HTN, DM, CAD, CHF, HLD. Med list: omeprazole, rosuvastatin, ASA, metoprolol, insulin

Normal PE, normal labs, including LFTs

Social Hx: occasional drinking (3-4 beers per week)

Anti-HCV +, HCV VL 1,500,000, GT1a, F2 per Fibroscan, US wnl

<table>
<thead>
<tr>
<th>HCV Genotype</th>
<th>Regimens</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EBR/GZR* (elbasvir/grazoprevir)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>GLE/PIB (glecaprevir/pibrentasvir)</td>
<td>8 weeks</td>
</tr>
<tr>
<td></td>
<td>LDV/SOF** (ledipasvir/sofosbuvir)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF/VEL (sofosbuvir/velpatasvir)</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

*Only if no baseline NS5A elbasvir RASs detected.

** 8 weeks OK for patients who are non-black, HIV-uninfected, and whose HCV RNA level is <6 million IU/mL.
## TREATMENT MONITORING - SUMMARY

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>Wk 4</th>
<th>Wk 8</th>
<th>Wk 12</th>
<th>SVR12</th>
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</thead>
<tbody>
<tr>
<td>Medical, social and behavioral status</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Pregnancy (category B risk)</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>prn</td>
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<tr>
<td>Check DDIs</td>
<td>yes</td>
<td>prn</td>
<td>prn</td>
<td>prn</td>
<td>prn</td>
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<tr>
<td>Liver Disease Staging</td>
<td>yes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Adherence, side effects, new medications</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
<td>-</td>
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<tr>
<td>CBC, creat, eGFR, hepatic function</td>
<td>yes</td>
<td>prn</td>
<td>prn</td>
<td>prn</td>
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<tr>
<td>HIV status</td>
<td>yes</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>HBV Status (HbsAg; anti-HBc; anti-HBs)</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>HCV VL</td>
<td>yes**</td>
<td>yes</td>
<td>prn</td>
<td>prn</td>
<td>yes</td>
</tr>
<tr>
<td>HCC screening in cirrhotics (US)</td>
<td>yes</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>yes</td>
</tr>
</tbody>
</table>

*X for RBV. If taking RBV need to avoid pregnancy for 6 months post HCV treatment

**HCV VL with genotype at baseline
MANAGING TREATMENT

• Monthly calls and/or clinic visits to assure compliance

• Side effect management (infrequent ~ 10%)
  • Fatigue (hydration – at least 40 oz of water daily)
  • Headache (acetaminophen prn - <2g daily)
  • Skin itching or rash (topical anti-histamine and/or steroids)

• Check HCV VL at baseline, rx week 4 and 3-6m post-rx

Adapted from: Dore G, Feld JJ. Clin Infect Dis. 2015;60(12):1829-1836.
ASSESSING READINESS FOR TREATMENT: PREP-C

Motivation
Information
Medication adherence
Self-efficacy
Social support and stability
Alcohol and substance use
Psychiatric stability
Energy level
Cognitive functioning

Pschosocial Readiness

HCV Treatment Adherence

www.prepc.org
EXPANDED ACCESS TO SPECIAL POPULATIONS

- Compensated cirrhosis
- ESLD and post-TX
- CKD, ESRD and post-TX
- HIV co-infection
- HBV co-infection
- Patients who failed first-line DAAs
CHRONIC HCV INFECTION IS ASSOCIATED WITH APPROXIMATELY HOW MANY YEARS OF LOST LIFE EXPECTANCY?

A. 1-5 years
B. 6-8 years
C. 10-12 years
D. 15-25 years
E. Life expectancy is similar to general population
HCV DEATHS EXCEED THOSE FROM 60 OTHER INFECTIOUS CONDITIONS COMBINED (DEATH CERTIFICATE DATA)

Includes HIV, *Pneumococcus*, TB

AIDS in 1995 = 55,000
Vietnam War = 57,000
Drug overdoses in 2017 = 72,000
Flu season in 2017 = 80,000

Source: Center for Disease Control and Prevention
The highest average annual mortality rate for those with HCV was among the 50 to 54 year age group, with 38 deaths per 100,000.
Liver-related mortality rate in CHeCS cohort = 12,854/100,000 persons
Liver related mortality rate in general pop = 1,046/100,000 persons
SVR REDUCES ALL-CAUSE AND LIVER-RELATED MORTALITY

530 patients
Stage 3/4 fibrosis

5 year liver-related mortality without SVR is ~10%

van der Meer A, JAMA, 2013
SVR “RESETS” ALL –CAUSE MORTALITY TO GENERAL POPULATION RATES

van der Meer AJ. JAMA 2014.
THE DISEASE BURDEN MODELLING SIMULATES DISEASE PROGRESSION OVER TIME

Acute hepatitis → Spontaneous clearance

Chronic hepatitis — F0 → Chronic hepatitis — F1 → Chronic hepatitis — F2 → Chronic hepatitis — F3 → Compensated cirrhosis

Hepatocellular carcinoma → Liver-related death

Decompensated cirrhosis → Liver transplantation

 DOES HCV TREATMENT IMPACT LIFE EXPECTANCY?

Markov model of HCV progression toward advanced liver disease

Table 1. Life year (LY) gained for treated vs. non-treated patients by age and initial fibrosis stage.

<table>
<thead>
<tr>
<th>Age</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>2.84</td>
<td>6.09</td>
<td>9.85</td>
<td>10.20</td>
</tr>
<tr>
<td>45</td>
<td>1.89</td>
<td>4.36</td>
<td>7.47</td>
<td>8.35</td>
</tr>
<tr>
<td>50</td>
<td>1.19</td>
<td>2.98</td>
<td>5.45</td>
<td>6.64</td>
</tr>
<tr>
<td>55</td>
<td>0.70</td>
<td>1.92</td>
<td>3.80</td>
<td>5.10</td>
</tr>
<tr>
<td>60</td>
<td>0.38</td>
<td>1.16</td>
<td>2.50</td>
<td>3.76</td>
</tr>
<tr>
<td>65</td>
<td>0.19</td>
<td>0.65</td>
<td>1.55</td>
<td>2.64</td>
</tr>
<tr>
<td>70</td>
<td>0.08</td>
<td>0.33</td>
<td>0.89</td>
<td>1.74</td>
</tr>
<tr>
<td>75</td>
<td>0.03</td>
<td>0.15</td>
<td>0.47</td>
<td>1.07</td>
</tr>
<tr>
<td>80</td>
<td>0.01</td>
<td>0.06</td>
<td>0.23</td>
<td>0.62</td>
</tr>
</tbody>
</table>

The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response (SVR).
WHEN AND IN WHOM TO INITIATE HCV THERAPY\textsuperscript{1,A}

Treatment is recommended for \textit{all patients with chronic HCV infection}, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

\textsuperscript{a}Rating: Class I, Level A.

ACCORDING TO WHO, HCV ELIMINATION AS A PUBLIC HEALTH THREAT IS ACHIEVABLE. ALL OF THE FOLLOWING COUNTRIES ARE CONSIDERED ON TRACK TO ELIMINATE HCV BY 2030, EXCEPT:

A. Australia
B. Brazil
C. Egypt
D. Republic of Georgia
E. United States

**Global targets for 2030**

- **Expand and enhance services**
  - 90% diagnosed
  - 90% of eligible people treated
  - 90% of those treated are cured
  - 50% of PWID covered by harm reduction services by 2020

- **Decrease new infections**
  - 70% reduction in HCV incidence
    - 50% reduction by 2020
  - Zero new infections due to unsafe blood transfusions
  - 75% reduction in new infections due to unsafe medical practices by 2020

- **Decrease deaths**
  - 60% reduction in HCV-related deaths

- **Reduce global suffering and costs**

Focus on high risk groups: PWIDs, HIV/MSM, Prisoners, Cirrhotics

THE UNITED STATES
will be a place where new viral hepatitis infections have been eliminated, where all people with chronic hepatitis B and C know their status, and everyone with chronic hepatitis B and C has access to high quality health care and curative treatments, free from stigma and discrimination.
HCV – 20% diagnosed, yet major Tx gap; cost reductions <$150/cure

Sources – WHO, work conducted by Center for Disease Analysis
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ever Infected Persons</td>
<td>Prevalence</td>
</tr>
<tr>
<td></td>
<td>Estimate</td>
<td>Estimate</td>
<td>Estimate</td>
</tr>
<tr>
<td>NHANES</td>
<td>241,152,600</td>
<td>3,721,000</td>
<td>1.5%</td>
</tr>
<tr>
<td>Additional Populations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incarcerated</td>
<td>2,131,000</td>
<td>344,100</td>
<td>16.1%</td>
</tr>
<tr>
<td>Unsheltered homeless</td>
<td>160,600</td>
<td>23,700</td>
<td>14.7%</td>
</tr>
<tr>
<td>Active-duty military</td>
<td>1,288,600</td>
<td>13,500</td>
<td>1.0%</td>
</tr>
<tr>
<td>Nursing homes</td>
<td>1,425,500</td>
<td>18,900</td>
<td>1.3%</td>
</tr>
<tr>
<td>Additional populations subtotal</td>
<td>5,005,700</td>
<td>400,100</td>
<td></td>
</tr>
<tr>
<td>NHANES modified estimate excluding additional populations</td>
<td>239,864,100</td>
<td>3,701,100</td>
<td>1.5%</td>
</tr>
<tr>
<td>Total</td>
<td>244,869,800</td>
<td>4,101,200</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

VA: > 92,000 HCV-INFECTED VETERANS FROM JAN 14 – JUN 17
CURE RATES > 90%; MAY ELIMINATE HCV BY MAY 2019?

Number of veterans with HCV infection in VA care requiring HCV antiviral treatment over time

Effect of availability of HCV drug funding on the number of HCV treatment regimens at the VA System / week

HCV TREATMENT UPTAKE: 2015-2016

3 to 5-fold increase in dx and/or rx rates from baseline

CDA 2017: Polaris Observatory (http://centerforda.com/polaris/)

Kirby Institute 2017
(http://kirby.unsw.edu.au/research-programs/vhcrp-newsletters)
MODELLING HCV ELIMINATION IN AUSTRALIA

- Annual number of people receiving HCV treatment

<table>
<thead>
<tr>
<th>Treatment Scenario</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Post-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pessimistic</td>
<td>7,296</td>
<td>32,400</td>
<td>18,510</td>
<td>13,890</td>
<td>13,890</td>
</tr>
<tr>
<td>Intermediate</td>
<td>7,296</td>
<td>32,400</td>
<td>27,770</td>
<td>23,143</td>
<td>18,510</td>
</tr>
<tr>
<td>Optimistic</td>
<td>7,296</td>
<td>32,400</td>
<td>32,400</td>
<td>32,400</td>
<td>32,400</td>
</tr>
</tbody>
</table>

- Estimated year Australia meets World Health Organization target compared to 2015 estimates

<table>
<thead>
<tr>
<th>WHO target</th>
<th>Treatment scenario</th>
</tr>
</thead>
<tbody>
<tr>
<td>80% reduction in new chronic infections</td>
<td>Pessimistic 2028</td>
</tr>
<tr>
<td>80% of people living with chronic HCV treated</td>
<td>Intermediate 2026</td>
</tr>
<tr>
<td>65% reduction in HCV-related deaths</td>
<td>Optimistic 2021</td>
</tr>
</tbody>
</table>

- Status quo: Pre-DAA era scenario
  - Number on treatment kept at 2015 levels
    - Elimination by 2030 unlikely

Kwon A, et al. AVHEC 2017
MODELLING HCV ELIMINATION IN THE US (260,000 PATIENTS TREATED IN 2016)

Increase dx from 50 – 80%  
Unrestricted access  
Treat 150,000 patients/year

LOWEST PRICES FOR SOFOSBUVIR REPORTED BY ORIGINATOR AND GENERIC COMPANIES IN LOW- AND LOWER-MIDDLE-INCOME COUNTRIES, PER 28-DAY SUPPLY, 2015–2017

Drug cost in US
~ $95,000/rx in 2014
~ $25,000/rx in 2018

Countries on track to elimination - 2017
- Australia
- Brazil - $1399 / 28d
- Egypt - $50 / 28d
- Georgia - donation
- Iceland
- Japan
- Morocco - $300 / 28d
- Netherlands
- Qatar

PROGRESS REPORT ON ACCESS TO HEPATITIS C TREATMENT. WHO, March 2018
December 26, 2017

President Donald J. Trump
The White House
1600 Pennsylvania Avenue NW
Washington, DC 20500

Re: America Falls Behind in Hepatitis Elimination Efforts

Dear Mr. President,

It was announced at the Summit that nine countries (Australia, Brazil, Egypt, Georgia, Iceland, Japan, the Netherlands, and Qatar) are on track to reach the 2030 WHO elimination goals for HCV. Unfortunately, the United States is not one of them. It was also announced that only one third of countries with national hepatitis plans invest any funding in their plan. The United States, one of the richest countries in the world, is shamefully not one of them.

It is long overdue for the Administration and Congress to invest in the Department of Health & Human Services Viral Hepatitis Action Plan¹ and to commit in words and action to the elimination of HBV and HCV in the United States by 2030.
We cannot afford these prices! Let’s ban laws that prohibit Medicare from negotiating prices with drug companies! Make negotiated drug prices public! Open our borders to importation of generic drugs! Contact your representatives! Visit them in DC!

“Our healthcare system doesn't promote healthcare”
Mike Saag, TEDxBirmingham, May 2017 (with permission)
IN 2016, CDC FUNDING TO ALABAMA INCLUDED HIV ($6.5M), STD (2.4M) AND TUBERCULOSIS ($1.2M). IN THE SAME YEAR, HOW MUCH CDC FUNDING WAS AVAILABLE TO SUPPORT HCV CONTROL IN ALABAMA?

A. $1,000,000
B. $750,000
C. $500,000
D. $250,000
E. $100,000
A. Medicaid will only cover patients with F2 or greater
B. Uninsured patient have access to DAA (compassionate use)
C. Cirrhotics can receive shorter DAA courses (8 weeks)
D. Harm reduction through syringe exchange services is prohibited by law
E. Sobriety from drugs and alcohol for 6 months is required by Medicaid
THINK GLOBAL, ACT LOCAL: ALABAMA

• Estimated AB prevalence is 1.44% (52,400 individuals exposed)
  • 37,000 with active infection (viremia)

• Rates of acute HCV increased by 200% in 2014

• Top-ranked state in key opioid use indicators
  • number of 30-day supply of opioids per Medicaid Part D enrollee
  • morphine mg equivalents per capita
  • percentage of people in need but not receiving addiction treatment (90%)

- amfAR Opioid and Health Indicator Database. http://opioid.amfar.org/
• Alabama has not expanded Medicaid programs

• State law prohibit the sale or distribution of drug paraphernalia – including syringes and needles without exceptions - not allowing syringe exchange programs (AL Statute 13-A-12-260)

amfAR Opioid and Health Indicator Database. http://opioid.amfar.org/
Universal HCV screening Pilot

HCV AB Prevalence in Baby Boomers
Private Insurance = 5%
Uninsured = 17%

COUNTIES HIGHLY VULNERABLE FOR OUTBREAKS OF BLOOD-BORNE INFECTIONS AMONG PWID

Scott County, Indiana (ranked 32nd) Walker County, Alabama (ranked 37th)


Figure 2. Geospatial Assessment of Central Alabama IDU Indicators and PWID Infectious Disease Transmission. A) Vulnerable Alabama counties for an HIV and HCV outbreak among PWIDs (VanHandel:2016sep) B) EMS naloxone administration events per 10,000 county residents in 2014. C) High-risk HCV prevalence zip codes for persons born after 1965 identified through the UAB Emergency Department universal HCV testing.

* denotes Walker County
- State-wide, community-based test and treat program
- Disease awareness, testing, patient navigation and treatment co-location in Primary Care

Partners: QOLHS, Quality of Life Health Services; ARMS, Alabama Regional Medical Services; CGMHS, Cooper Green Mercy Health Services; CHC, Christ Health Center; CNALHS, Central North Alabama Health Services Inc.; UABH, University of Alabama at Birmingham – Huntsville Campus; CRH, Capstone Rural Health; MCHD, Mobile County Health Department; HSI, Health Services Inc.; MAO, Medical Advocacy Outreach; UMC-UA, University Medical Center at University of Alabama; WHS, Whatley Health Services.
<table>
<thead>
<tr>
<th>ACTIVE-C at a Glance (2015-2017)</th>
<th>UAB, Community Health Centers, Health Departments, 12 organizations in 7 cities and over 40 satellite locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CME credits provided</td>
<td>900+ credit hours to 250 providers at reach</td>
</tr>
<tr>
<td>UAB Health System</td>
<td>&gt;84,000 HCV AB tests</td>
</tr>
<tr>
<td>HCV AB (+) tests</td>
<td>&gt;9,500 (11%)</td>
</tr>
<tr>
<td>Patients linked to care</td>
<td>&gt;6,500 (68%)</td>
</tr>
<tr>
<td>Patients treated</td>
<td>1897 (29%)</td>
</tr>
</tbody>
</table>
ACKNOWLEDGMENTS

Partners: QOLHS, Quality of Life Health Services; ARMS, Alabama Regional Medical Services; CGMHS, Cooper Green Mercy Health Services; CHC, Christ Health Center; CNALHS, Central North Alabama Health Services Inc.; UABH, University of Alabama at Birmingham – Huntsville Campus; CRH, Capstone Rural Health; MCHD, Mobile County Health Department; HSI, Health Services Inc.; MAO, Medical Advocacy Outreach; UMC-UA, University Medical Center at University of Alabama; WHS, Whatley Health Services.
THANK YOU!

Ricardo Franco, MD
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rfranco@uabmc.edu