Clinical Pearls on Chronic C Infection: Special Consideration and Current Treatments

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- AbbVie: consultant, speakers bureau
- Gilead: consultant, speakers bureau
Learning Objectives

- Recognize the important steps in the evaluation of patient with hepatitis C antibody positivity
- Recognize strategies to best stage patient’s liver disease prior to initiation of hepatitis C treatment
- Identify medications and duration for chronic hepatitis C treatment
Case 1: A New Referral

- 22 year old male with history of cocaine abuse who is currently in a drug rehabilitation program who presents to the clinic for evaluation of hepatitis C Ab positivity. What are the next steps to consider in the management of patient?
Hepatitis C Genotypes in U.S.

- Type 1: 72%
- Type 2: 17%
- Type 3: 10%
- Other: 1%

Sources of Infection for Persons with Hepatitis C: USA

- Injection drug use: 60%
- Sexual: 15%
- Transfusion (before screening): 10%
- Occupational: 4%
- Other: 1%
- Unknown: 9%

*Nosocomial; iatrogenic; Perinatal
Adapted from CDC Hepatitis Slide Kit [http://www.cdc.gov/ncidod/diseases/hepatitis/slideset](http://www.cdc.gov/ncidod/diseases/hepatitis/slideset)
Who Should You Screen?

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
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</thead>
<tbody>
<tr>
<td>Persons who ever injected illegal drugs</td>
<td></td>
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<tr>
<td>HIV-infected patients</td>
<td></td>
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<tr>
<td>Persons who have received tattoos from unlicensed or unregulated environments</td>
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<tr>
<td>Those with certain medical conditions, including:</td>
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<tr>
<td>- Persons who received clotting factor concentrates produced before 1987</td>
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<tr>
<td>- Persons who were ever on long-term hemodialysis</td>
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<tr>
<td>- Persons with persistently abnormal alanine transaminase levels</td>
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<tr>
<td>Prior recipients of transfusions or organ transplants, including:</td>
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<tr>
<td>- Persons who were notified that they received blood from a donor who later tested positive for HCV infection</td>
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<tr>
<td>- Persons who received a blood transfusion, blood components, or an organ transplant before July 1992</td>
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<tr>
<td>Healthcare, emergency medical, and public safety workers after needlesticks, sharps, or mucosal exposures to HCV-positive blood</td>
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<td>Children born to an HCV-positive mother</td>
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### Age Cohort Screening for Hepatitis C

<table>
<thead>
<tr>
<th></th>
<th>Birth</th>
<th>1945 - 1965</th>
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<tbody>
<tr>
<td>US Population (millions)</td>
<td>78.8</td>
<td></td>
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<tr>
<td>Anti-HCV Prevalence</td>
<td>3.29%</td>
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<tr>
<td>Percent anti-HCV identified</td>
<td>74.5%</td>
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**Gender**

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<tr>
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<tbody>
<tr>
<td>Male</td>
<td>4.35%</td>
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</tr>
<tr>
<td>Female</td>
<td>2.23%</td>
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**Race/Ethnicity**

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<tbody>
<tr>
<td>White</td>
<td>2.93</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>6.31</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.92</td>
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</tbody>
</table>
Mortality Risk with Hepatitis C

Hepatitis C: A Systemic Illness

INCREASED RISK FOR:
- Depression
- Carotid atherosclerosis/atherothrombosis
- Type 2 diabetes mellitus
- Hypertension
- Congestive heart failure
- Chronic kidney disease
- End-stage renal disease
- Kidney cancer
- Other renal manifestations (e.g., glomerulonephritis, proteinuria)\(^a\)
- Low bone mineral density (BMD)
- Rheumatologic manifestations (e.g., polyarthritis, polyarthralgia)\(^a\)
- Fatigue

POSSIBLE INCREASED RISK FOR:
- Neurologic impairment/disorders
- Stroke
- Coronary artery disease/ischemic heart disease

\(^a\) References

Mortality: HCV vs HIV

Clinical Pearl #1

- Among patients with hepatitis C antibody positivity, follow-up hepatitis C RNA quantitative and hepatitis C genotype should be sent to confirm chronic hepatitis C infection.
Clinical Pearl #2

- Due to similar mode of transmission of hepatitis C, hepatitis B, and HIV, it is important to send for:
  - Hepatitis B sAg, Hepatitis B sAb, Hepatitis B cAb total
  - HIV screening
Case #2: Staging of Liver Disease

- 48 year old male with a history of chronic hepatitis C infection. Patient is treatment naïve.

- His lab results are as follows:
  - CBC—Hgb 13.0, WBC 5.0, platelet count 120,000
  - Hepatitis BsAg, BcAb, BsAb all negative
  - Hepatitis C Ab was positive
  - HCV RNA 4,000,000 IU/ml
  - HCV genotype 1a

- What are your next considerations prior to offering patient treatment for hepatitis C?
Outcome Following Hepatitis C Infection

- Acute hepatitis C: 55 - 85%
- Chronic infection: 70%
- Chronic hepatitis: 20%
- Cirrhosis: 1 - 4%/yr
- Cirrhosis: 4 - 5%/yr
- HCC: 1 - 4%/yr
- Decompensation: 4 - 5%/yr
Staging of Liver Disease

- FIB-4
- AST to platelet ratio index (APRI)
- Fibrosure
- Ultrasound with dopplers
- Ultrasound-based transient hepatic elastography
- Upper endoscopy
- Liver Biopsy
Risk of Hepatocellular Carcinoma: Platelet Count < 150,000

Screening for HCC

Risk factor: Cirrhosis (Platelet count < 150,000/mm³)

Ultrasound of liver every 6-12 months
Clinical Pearl #3

- It is important to stage patient’s liver disease prior to initiation of hepatitis C treatment because it affects treatment duration and post-treatment monitoring.

- If you are using a non-invasive marker to determine cirrhotic liver disease, it is important to use at least 2 markers to rule out existing advanced fibrosis or cirrhosis.
Case #3: Treatment Decisions

- A 55 year old male with a history of prior IV drug use who presents to the clinic for evaluation of abnormal liver function testing. He underwent extensive work-up which included:
  - CBC—Hgb 13.0, WBC 5.0, platelet count 120,000
  - Hepatitis BsAg, BcAb, BsAb all negative
  - Hepatitis C Ab was positive
  - HCV RNA 4,000,000 IU/ml
  - HCV genotype 1a
  - Liver biopsy shows: Grade 3, Stage 3 disease

- What are additional history to considered prior to recommendation of treatment of hepatitis C?
Qualify of Life After SVR12

HRQL outcomes in 3486 patients with SVR12

SF-36 summary scores

Greatest HRQL gains consistently observed
General Health and Vitality domains

Improvement in HRQL after achieving SVR is maintained in the long-term follow up

Younossi ZM et al AASLD 2017, Ab 64
Survival Curves for CLD Patients With and Without SVR

Overall

HCC Disease Free Survival

Log Rank P-Value <0.001

Time Since DAA End of Treatment (Years)

Survival Rate

SVR
No SVR

No SVR
1067 923 650 326 105
SVR 13992 12939 9521 5437 1875

HCC Disease Free Survival Rate

Time Since DAA End of Treatment (Years)

SVR
No SVR

No SVR
871 844 650 425 181
SVR 13153 13070 10759 7482 3588

Increasing access to DAAs for ACLD patients should result in fewer overall deaths

Veterans Affairs HCV Clinical Case Registry
Retrospective study in 167 medical centers including 35,871 IFN-only regimens, 4,535 DAA+IFN and 21,948 DAA-only (80% SOF-based regimens); mean f/u of 6.1 years (range: 2-18); incident HCCs=3,271

DAA-induced SVR is associated with 71% reduction in HCC risk

Ioannou et al, AASLD, 2017, oral 142
HCC Recurrence after DAA Treatment

Nguyen DL et al, ACG 2018
Why is Hep C Curable?
Hepatitis C Treatment Evolution

1970's
- Non-A, non-B hepatitis was recognized

1989
- Hepatitis C Virus identified

1991
- 1st Hepatitis C treatment is approved by the FDA – Schering-Plough’s Intron A

1997
- FDA approves Infergen (interferon alfacon-1) injection

1998
- FDA approves Merck’s Rebetol (ribavirin)

1999
- Merck’s Peginteron (peginterferon alfa-2b) injections are approved by the FDA

2001
- FDA approves Victrelis (boceprevir) and Incivek (telaprevir)

2011
- FDA approves Olysio (simeprevir) capsules and Sovaldi (sofosbuvir) tablets

2013
- FDA approves Daklinza (daclatasvir), was approved as the first 12-week, all-oral treatment option for patients with chronic hepatitis C virus genotype 3

2014
- Zepatier, a combination of elbasvir and grazoprevir earned FDA approval

- Epclusa (sofosbuvir/velpatasvir) approved as the first all-oral, single tablet regimen for the treatment of adults with genotype 1-6 chronic hepatitis C virus infection

- Technivie (ombitasvir, paritaprevir and ritonavir) first drug approved to treat genotype 4 HCV infection without interferon

2015
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2016
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Important Initial Treatment Considerations

- Treatment status
  - Treatment naïve vs. treatment experienced
  - Prior failure of DDA
  - Prior failure of interferon-based therapy

- Hepatitis C genotype

- Hepatitis C baseline viral load

- Co-existing advanced renal disease

- Stage of liver disease
  - Non-cirrhotic, compensated cirrhosis, decompensated cirrhosis

Nguyen DL et al, Open Medicine, 2016
Pan-Genotypic Regimens

1. 12-week regimen for all genotypes
2. Decompensated cirrhosis add in RBV for 12-weeks. If RBV ineligible, then 24-weeks
3. Decompensated cirrhosis with prior failure of sofosbuvir or NS5A-based treatments, 24 weeks with RBV
4. Treatment experienced:
   - GT 1—NS5A w/o NS3/4A: 16 weeks
   - NS3/4A w/o NS5A: 12 weeks (non-cirrhotic); 16 weeks (cirrhotic)
   - GT 1,2,4,5,6 PRS—8 weeks (non-cirrhotic); 12 weeks cirrhotic
   - GT 3 PRS—16 weeks (non-cirrhotic, compensated cirrhotic)

1. 8-week Treatment-naïve, non-cirrhotic
2. 12-week Treatment naïve, compensated cirrhotic
3. Not indicated for decompensated cirrhosis
G/P Real World Data: German Hepatitis Registry

- 1 patient had virologic relapse; 2 patients had reinfections post treatment
- 2 patients discontinued due to AEs
- 12 patients were lost to follow-up

*Includes unknown GTs and mixed GT populations (GT1 + GT2 and GT1 + GT3)
AE, adverse event; d/c, discontinuation; ITT, intent-to-treat; mITT, modified intent-to-treat.
TRIO Real World Cohorts for HCV Patients with GT 1-6

LDV/SOF data is excluded from this slide
Curry, AASLD 2018, 678
TRIO Real World Data for GT 1-6

**SVR12, % (PP)**

<table>
<thead>
<tr>
<th></th>
<th>SOF/VEL</th>
<th>GLE/PIB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>98/98</td>
<td>98/98</td>
</tr>
<tr>
<td><strong>F0-3</strong></td>
<td>98/99</td>
<td>99/98</td>
</tr>
<tr>
<td><strong>F4</strong></td>
<td>96/98</td>
<td>95/82</td>
</tr>
<tr>
<td><strong>F0-3</strong></td>
<td>50/52</td>
<td>37/39</td>
</tr>
<tr>
<td><strong>F4</strong></td>
<td>85/87</td>
<td>28/34</td>
</tr>
<tr>
<td><strong>PPI</strong></td>
<td>79/79</td>
<td>135/138</td>
</tr>
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</table>

LDV/SOF data is excluded from this slide

Cure: AASLD 2018. 678
TRIO Real World Data for SOF-VEL-VOX

SOF/VEL/VOX for 12 weeks resulted in high real world efficacy, irrespective of genotype and prior treatment regimen

Bacon AASLD 2018, #706
Linkage to Care

Differences in linkage to care with HCV specialists at health center (2016 – 1Q/2017)

**Linkage to Care**

- **Baby Boomers**: 52/244 (%: 21.3)
- **Non-Baby Boomers**: 37/326 (%: 11.3)

**Multivariate Analysis for Association with Linkage**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>aOR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth cohort</td>
<td>2.3 (1.4–3.7)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Clinical Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient</td>
<td>1.0</td>
<td>Ref</td>
</tr>
<tr>
<td>ED</td>
<td>0.7 (0.3–1.4)</td>
<td>0.3162</td>
</tr>
<tr>
<td>Inpatient</td>
<td>0.5 (0.3–0.8)</td>
<td>0.009</td>
</tr>
<tr>
<td>Jail</td>
<td>0.4 (0.04–3.9)</td>
<td>0.430</td>
</tr>
<tr>
<td>Risk Factor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1.0</td>
<td>Ref</td>
</tr>
<tr>
<td>Active IVDU</td>
<td>0.4 (0.2–0.7)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Remote IVDU</td>
<td>1.0 (0.6–1.7)</td>
<td>0.9364</td>
</tr>
<tr>
<td>Psychiatric Illness</td>
<td>0.8 (0.5–1.1)</td>
<td>0.1831</td>
</tr>
</tbody>
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Overall, only 43% of patients were linked to care with HCV specialists
CONCLUSIONS

Identify

Treat

Follow-Up
Questions?