Evaluation and Care of the HCV Patient Prior to or in the Absence of Treatment

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

✓ Identify the indications and contraindications for antiviral therapy.
✓ Advise patients who are currently ineligible for therapy.

Off-Label Disclosure
✓ This presentation will include discussion of investigational agents.
Faculty and Planning Committee Disclosures

✓ I have received grant support from Abbott, Gilead, Genentech, Janssen, Merck and Vertex.
✓ I serve on the Speaker’s Bureau for Gilead, Genentech, Merck and Vertex.
✓ I have served on a grant review committee for Vertex.
Outline

✓ Indications for therapy
✓ Contraindications for therapy
✓ Getting ready for therapy
✓ Keeping the liver healthy
AASLD Guidelines

✓ Decision to treat needs to be made on a case-by-case basis!
✓ General recommendation that stage 3 or more on liver biopsy be prioritized

Weighing the Risks and Benefits of Therapy

Disease Progression
Likelihood of Treatment Response
  - Virologic
  - Host Specific

Side Effects
Competing Mortality
Costs

TREAT

DEFER THERAPY

Adapted from Thomas DL CROI 2007
## Indications for Therapy

### 2009 AASLD Guidelines

<table>
<thead>
<tr>
<th>Characteristics of Persons in Whom HCV Therapy is Widely Accepted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 18 years and older</td>
</tr>
<tr>
<td>HCV RNA positive in serum</td>
</tr>
<tr>
<td>Liver biopsy showing significant fibrosis (bridging fibrosis or higher)</td>
</tr>
<tr>
<td>Compensated liver disease:</td>
</tr>
<tr>
<td>▪ Total bilirubin &lt;1.5 mg/dL, and</td>
</tr>
<tr>
<td>▪ INR &lt;1.5, and</td>
</tr>
<tr>
<td>▪ Serum albumin &gt;3.4 g/dL, and</td>
</tr>
<tr>
<td>▪ Platelet count &gt;75,000/mm³, and</td>
</tr>
<tr>
<td>▪ No evidence of hepatic decompensation (hepatic encephalopathy or ascites)</td>
</tr>
<tr>
<td>Acceptable hematological and biochemical indices:</td>
</tr>
<tr>
<td>▪ Hemoglobin &gt;13 g/dL for men and &gt;12 g/dL for women, and</td>
</tr>
<tr>
<td>▪ Neutrophil count &gt;1500/mm³, and</td>
</tr>
<tr>
<td>▪ Serum creatinine &lt;1.5 mg/dL</td>
</tr>
<tr>
<td>Willing to be treated and to adhere to treatment requirements</td>
</tr>
<tr>
<td>No absolute contraindications</td>
</tr>
</tbody>
</table>

Other Special Situations to Strongly Consider Therapy

✓ HCV-associated lymphomas
✓ Symptomatic cryoglobulinemia
✓ Membranoproliferative glomerulonephritis
✓ Pre-renal transplant
✓ Acute hepatitis C

A 46-year-old schoolteacher wants a second opinion about treatment of his hepatitis C virus (HCV) infection. He was diagnosed with hepatitis C in the late 1990s by antibody testing done because routine laboratory studies showed an alanine aminotransferase (ALT) level of 65 IU/L (range 8-35 IU/ml). He now brings laboratory slips showing testing over the ensuing six years as follows:
Question

- ALT levels between 32 and 74 IU/L
- HCV RNA levels 6.1 log copies/ml, then more recently 5.4 log IU/ml
- HCV genotype 1a
- Liver biopsy done 6 months ago showing septate fibrosis (ranked stage 3 of 4 by Metavir scoring system) with mild portal and lobular inflammation
- Serum creatinine 0.8 mg/dL
- Albumin 4.6 mg/dL
- Total bilirubin 0.8 mg/dL
- Platelet count 134,000/mm3
- Other ‘routine tests,’ including hematocrit and serum chemistries, normal.
Question

The patient acknowledges some illicit drug use in late 1970s, but not since. He used to drink alcohol but stopped drinking 10 years ago. He has been treated in the distant past for depression with paroxetine (Paxil), but is not currently on treatment and he has no symptoms of depression. He is taking no medications and is not aware of any other medical problems. He is married with two children. His review of systems is negative and his physical examination is normal.
Which of the following statements is TRUE regarding the decision to start hepatitis C treatment for this patient?

A. Before starting therapy, it is essential to update the patient's liver fibrosis status by performing a noninvasive test for liver fibrosis, such as transient elastography.

B. The patient's baseline HCV RNA level is the best predictor of treatment response.

C. The degree of hepatic fibrosis correlates with treatment response.

D. Monitoring serum aminotransferase levels plays a critical role in determining disease progression.
SVR = Better Health Outcomes

✓ Liver Histology improves
  • Patients w/ SVR have 87% chance of decreased inflammation and 44% chance of less fibrosis after cure; compared to 36% and 14% in relapsers

✓ Survival improves
  • 60-70% reduction in mortality!

✓ Can cure lymphoma w/o chemotherapy

✓ Reduces chance of diabetes developing by 50%

SVR Increases Survival!


Contraindications

2009 AASLD Guidelines

<table>
<thead>
<tr>
<th>Characteristics of Persons in Whom HCV Therapy is Currently Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major uncontrolled depressive illness</td>
</tr>
<tr>
<td>Solid organ transplant (renal, heart, or lung)</td>
</tr>
<tr>
<td>Autoimmune hepatitis or other autoimmune condition known to be exacerbated by peginterferon and ribavirin</td>
</tr>
<tr>
<td>Untreated thyroid disease</td>
</tr>
<tr>
<td>Pregnant or unwilling to comply with adequate contraception</td>
</tr>
<tr>
<td>Severe concurrent medical disease such as severe hypertension, heart failure, significant coronary heart disease, poorly controlled diabetes, chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Age less than 2 years</td>
</tr>
<tr>
<td>Known hypersensitivity to drugs used to treat HCV</td>
</tr>
</tbody>
</table>

Gray Areas

✓ Substance Abuse
✓ Mental Health Issues
✓ Social Issues
Substance Abuse

- Patients with a history of past injection drug use (> 6 mo) should not be treated any differently than patients without a history
- Active substance abuse is a relative contraindication per AASLD guidelines, but should not in itself be reason for withholding therapy
Concerns with Active IDU

✓ Adherence?

• Modestly decreased in IDU. 6.8% of active IDUs on IFN were non-compliant vs. 4.9% of non-IDUs
• Active IDU completion rate=71%
  • Recent meta-analysis showed 83%!
• Non IDU completion rate = 79%
• Enrollment in agonist maintenance therapy can improve treatment completion

Concerns with Active IDU

✓ Poorer Outcomes?

• SVR for active IDU with chronic infection was 54-55% (vs. 54-63% in clinical trials)
• SVR for active IDU with acute infection was 68.5% (vs. 82% in non IDU)

Concerns with Active IDU

✓ Risk of reinfection?
  • Modestly elevation, 5.3 reinfection events per 100 person-years
  • Safer injection practices may mitigate risk

✓ Reduction of transmission?
  • Mathematical models suggest that treating active IDUs would result in a reduction in HCV transmission

Alcohol Abuse

✓ Progression to advanced fibrosis is faster with heavy EtOH and HCV

  • 36% of cirrhosis in HCV+ pts is attributable to alcohol

✓ Even if HCV clears, liver fibrosis can worsen if heavy alcohol use continues

✓ General consensus: 6 mos of sobriety prior to starting treatment (but little evidence to support this duration)

Opioid Abuse

✓ Does not seem to speed progression of liver disease

✓ Effective therapies are methadone and buprenorphine

  • Drug interactions are difficult to predict with methadone and telaprevir/boceprevir
  • Withdrawal sxs can be similar to IFN side effects
  • No drug interactions with PIs and buprenorphine


Stimulant Abuse

✓ Cocaine and methamphetamine use do not seem to have effects on liver (more cardiac)
✓ Tends to be more sporadically used, but a/w poor adherence, depression and concurrent alcohol abuse
✓ Mirtazapine and possibly bupropion may be beneficial for reducing MA use

Marijuana Use

• Two large, independent studies have shown that daily cannabis users are ~3x more likely to have advanced fibrosis
  – Controlled for other factors, like alcohol

• Biologic plausibility
  – CB1 and CB2 receptors found on liver
  – Cannabis activates CB1 and promotes both fibrosis and steatosis in mice
  – CB2 is antifibrogenic

• CB1 receptors were highly induced in human cirrhotic samples and in liver fibrogenic cells

Marijuana and Effect on SVR

UCSF observational study of 71 ex-substance users on therapy
31% used cannabis, 69% did not
More AA, GT 1 pts in non-user group, used std IFN

<table>
<thead>
<tr>
<th></th>
<th>Cannabis</th>
<th>Non-user</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stopped early</td>
<td>1/22 (5%)</td>
<td>23/49 (47%)</td>
</tr>
<tr>
<td>SVR</td>
<td>12/22 (54%)</td>
<td>9/49 (18%)</td>
</tr>
</tbody>
</table>

Cannabis may improve cure rate

Tobacco Use

• Risk factor for developing hepatocellular carcinoma
• Good tobacco cessation therapies available: buproprion or varenicline
• Paired with behavioral support
Mental Health Issues: Depression

✓ Estimates are that HCV tx-emergent depression is a complication in 25-28% of cases

✓ Most of these cases occur in the first 12wks of HCV tx

✓ Multiple studies have failed to find a difference in IFN tx adherence /SVR rates in comparing pts with a pre-tx h/o depression vs. control HCV pts

✓ The best (and perhaps only validated) predictor for HCV tx emergent depression is baseline depressive symptoms prior to starting tx

METHODS

- Germany: patients screened from hepatology depts of 10 universities, 11 academic hospitals, enrolled betw 2004-08
- Requirements:
  - tx-naïve
  - ≥ 18yo
  - HCV RNA ≥ 1000 IU/ml
• **Schaefer M et al, 2012**

• Exclusions:
  - prior Ψ hx of a mood d/o or other Axis I condition;
  - illicit drugs w/in past 12mos
  - antidepressant use in past 3y
  - prior IFN tx history, prior immunotherapy, or prior h/o any other chronic infection, autoimmune, or ‘severe’ medical comorbidity

• double-blind, prospective, randomized, placebo-controlled, phase 3 study
• identical appearing escitalopram (LEXAPRO) tabs & placebo tabs

• pre-observation:
  - 12 wks monitoring

• antidepressant initiation:
  - escitalopram 10 mg/d, n=90 (or placebo, n=91)
• Schaefer M et al, 2012

• HCV tx
  • 2wks after antidepressant: peg-IFN2α + RBV
  • GT 1 or 4:
    • 48wks, 180 mcg Qwk & 1000 mg/d, respectively
  • GT 2 or 3:
    • 24wks, 180 mcg Qwk & 800 mg/d, respectively
• Schaefer M et al, 2012

• Outcomes
  • Primary outcome was incidence of depression (i.e., MADRS of 13+) during IFN tx.
  • Ad-hoc outcome measures included: time to depression, incidence of DSM-IV-defined MDE, severe depression, HRQOL measures, SVR, tolerability, safety.

• Power calculation suggested minimum N req’d was 182 pts (for 80% power).

• Conflicts of interest:
  • Roche & Lundbeck supplied funding Rxs, but were NOT allowed to influence data collection, manuscript prep’n, decision to publish.
RESULTS

- Primary outcome was incidence of depression (i.e., MADRS of 13+)
Schaefer M et al, 2012

- Received escitalopram (n = 90)
  - Plus PEG-IFN-α2a plus ribavirin
  - Genotype 1: 54
  - Genotype 2: 9
  - Genotype 3: 19
  - Genotype 4: 8

- Received placebo (n = 91)
  - Plus PEG-IFN-α2a plus ribavirin
  - Genotype 1: 59
  - Genotype 2: 5
  - Genotype 3: 21
  - Genotype 4: 6

Reasons for early discontinuation:
- HCV treatment failure: 12
- Severe adverse events: 5
- Nonadherence: 2

Therapy completed (n = 83)
- Lost to follow-up (n = 5)

Follow-up completed (n = 78)

Included in the efficacy analysis: 90
Included in the safety analysis: 90

Reasons for early discontinuation:
- HCV treatment failure: 17
- Severe adverse events: 5
- Other reasons: 2

Therapy completed (n = 84)
- Lost to follow-up (n = 4)

Follow-up completed (n = 80)

Included in the efficacy analysis: 91
Included in the safety analysis: 91
• Schaefer M et al, 2012

- After imputation of missing data, 32% of the escitalopram group v. 59% of the placebo group became depressed (MADRS of 13+). NNT = 3.7, p<0.001.

- by multivariate LR, factors assoc’d w/ depression were:
  - female (p=0.027)
  - baseline MADRS score (p<0.001)

- NO assocn’s w/ BMI, genotype, site
Figure 3. Montgomery–Asberg Depression Rating Scale scores during hepatitis C virus therapy.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Placebo</th>
<th>Escitalopram</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>91</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>91</td>
<td>89</td>
</tr>
<tr>
<td>24</td>
<td>86</td>
<td>80</td>
</tr>
<tr>
<td>36</td>
<td>76</td>
<td>77</td>
</tr>
<tr>
<td>48*</td>
<td>45</td>
<td>45</td>
</tr>
</tbody>
</table>

Escitalopram, n = 45, Placebo, n = 48

Significant group differences were seen at weeks 12 (P = 0.004), 24 (P = 0.002), and 48 (P = 0.001, genotypes 1 and 4).

* Only genotypes 1 and 4.
Schaefer M et al, 2012

Secondary outcomes (cont’d):

- SVR

<table>
<thead>
<tr>
<th></th>
<th>Genotypes 1&amp;4</th>
<th>Genotypes 2&amp;3</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>escitalopram</td>
<td>42%</td>
<td>73%</td>
<td>56%</td>
</tr>
<tr>
<td>placebo</td>
<td>35%</td>
<td>86%</td>
<td>46%</td>
</tr>
</tbody>
</table>

- Mirtazapine rescue: 3% v. 18% (escitalo v. placebo), p=0.004.
- NO suicidal ideation, attempts, reported.
- Fewer escitalo pts developed fatigue (p=0.040), insomnia (p=0.015)
- 87% of escitalo group completed HCV tx, 88% of placebo group.
- Medical complications:
  - 3 in escitalo (renal, brain tumor, jaundice)
  - 2 in placebo (retinopathy, brain tumor)
Schizophrenia

• 1% lifetime prevalence (general population & across cultures)
• male = female
• sex differences in age of onset
  • male: 15-25 yo
  • female: 25-35 yo

from Kaplan and Sadock’s Synopsis of Psychiatry, 2005 ed.; Strahl NR, 2005; & Grinker RR, 2007
Schizophrenia and HCV

- most studies ‘lump’ schizophrenia together w/ other severe mental illnesses (including substance use disorders)
- one exception is Huckans M et al (2010).
  - small retrospective study of VA patients (OR, WA, ID, AK)
  - n=30 HCV pts dx’d w/ schizophrenia + 30 age, genotype- & histologically-matched HCV (non-schizophrenic) controls

### Table 2. Antiviral Therapy Completion and Response Rates by Genotype for Patients with Hepatitis C

<table>
<thead>
<tr>
<th>All genotypes</th>
<th>Total Sample</th>
<th>Controls</th>
<th>Schizophrenics</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total N</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td>—</td>
</tr>
<tr>
<td>Treatment completion (100%)</td>
<td>36 (60.0%)</td>
<td>20 (66.7%)</td>
<td>16 (53.3%)</td>
<td>0.292</td>
</tr>
<tr>
<td>Treatment completion (80%)</td>
<td>39 (65.0%)</td>
<td>23 (76.7%)</td>
<td>16 (53.3%)</td>
<td>0.058</td>
</tr>
<tr>
<td>ETR (intention to treat)</td>
<td>37 (61.7%)</td>
<td>16 (53.3%)</td>
<td>21 (70.0%)</td>
<td>0.184</td>
</tr>
<tr>
<td>SVR (intention to treat)</td>
<td>26 (43.3%)</td>
<td>9 (30.0%)</td>
<td>17 (56.7%)</td>
<td>0.037*</td>
</tr>
<tr>
<td>Genotype 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>28</td>
<td>14</td>
<td>14</td>
<td>—</td>
</tr>
<tr>
<td>Treatment completion (100%)</td>
<td>14 (50.0%)</td>
<td>8 (57.1%)</td>
<td>6 (42.9%)</td>
<td>0.450</td>
</tr>
<tr>
<td>Treatment completion (80%)</td>
<td>15 (53.6%)</td>
<td>9 (64.3%)</td>
<td>6 (42.9%)</td>
<td>0.256</td>
</tr>
<tr>
<td>ETR (intention to treat)</td>
<td>12 (42.9%)</td>
<td>6 (42.9%)</td>
<td>6 (42.9%)</td>
<td>1.000</td>
</tr>
<tr>
<td>SVR (intention to treat)</td>
<td>8 (28.6%)</td>
<td>3 (21.4%)</td>
<td>5 (35.7%)</td>
<td>0.678</td>
</tr>
<tr>
<td>Genotypes 2 and 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>28</td>
<td>15</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>Treatment completion (100%)</td>
<td>22 (78.6%)</td>
<td>12 (80.0%)</td>
<td>10 (76.9%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Treatment completion (80%)</td>
<td>24 (85.7%)</td>
<td>14 (93.3%)</td>
<td>10 (76.9%)</td>
<td>0.311</td>
</tr>
<tr>
<td>ETR (intention to treat)</td>
<td>23 (82.1%)</td>
<td>10 (66.7%)</td>
<td>13 (100.0%)</td>
<td>0.044*</td>
</tr>
<tr>
<td>SVR (intention to treat)</td>
<td>16 (57.1%)</td>
<td>6 (40.0%)</td>
<td>10 (76.9%)</td>
<td>0.049*</td>
</tr>
<tr>
<td>Antiviral therapy type</td>
<td>Total Sample</td>
<td>Controls</td>
<td>Schizophrenics</td>
<td>( P )</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------------</td>
<td>----------</td>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td><strong>Total N</strong></td>
<td>60</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Monotherapy</td>
<td>2 (3.3%)</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>58 (96.7%)</td>
<td>29 (96.7%)</td>
<td>29 (96.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Peginterferon alfa-2a</td>
<td>35 (58.3%)</td>
<td>19 (63.3%)</td>
<td>16 (53.3%)</td>
<td>0.432</td>
</tr>
<tr>
<td>Peginterferon alfa-2b</td>
<td>6 (10.0%)</td>
<td>6 (20.0%)</td>
<td>0 (0.0%)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Nonpegylated interferon</td>
<td>19 (31.7%)</td>
<td>5 (16.7%)</td>
<td>14 (46.7%)</td>
<td>0.012*</td>
</tr>
<tr>
<td><strong>Reasons for early discontinuation from</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>antiviral therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (patients with early discontinuation)</td>
<td>24</td>
<td>10</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Neuropsychiatric side effects</td>
<td>5/24 (20.8%)</td>
<td>3/10 (30.0%)</td>
<td>2/14 (14.3%)</td>
<td>0.615</td>
</tr>
<tr>
<td>Alcohol/substance-abuse relapse</td>
<td>0/24 (0.0%)</td>
<td>0/10 (0.0%)</td>
<td>0/14 (0.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Medical side effects</td>
<td>9/24 (37.5%)</td>
<td>3/10 (30.0%)</td>
<td>6/14 (42.9%)</td>
<td>0.678</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>3/24 (12.5%)</td>
<td>1/10 (10.0%)</td>
<td>2/14 (14.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Noncompliance with treatment</td>
<td>6/24 (25.0%)</td>
<td>0/10 (0.0%)</td>
<td>6/14 (42.9%)</td>
<td>0.024*</td>
</tr>
<tr>
<td>Inadequate viral response</td>
<td>7/24 (29.2%)</td>
<td>5/10 (50.0%)</td>
<td>2/14 (14.3%)</td>
<td>0.085</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>1/24 (3.3%)</td>
<td>1/10 (10.0%)</td>
<td>0/14 (0.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Adverse events during antiviral therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Emergency room visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td>2 (3.3%)</td>
<td>0 (0.0%)</td>
<td>2 (6.7%)</td>
<td>0.492</td>
</tr>
<tr>
<td>Medical</td>
<td>11 (18.3%)</td>
<td>3 (10.0%)</td>
<td>8 (26.7%)</td>
<td>0.095</td>
</tr>
<tr>
<td>Inpatient hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td>2 (3.3%)</td>
<td>0 (0.0%)</td>
<td>2 (6.7%)</td>
<td>0.492</td>
</tr>
<tr>
<td>Medical</td>
<td>5 (8.3%)</td>
<td>1 (3.3%)</td>
<td>4 (13.3%)</td>
<td>0.353</td>
</tr>
<tr>
<td>Alcohol abuse(^{a})</td>
<td>0/38 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Drug abuse(^{b})</td>
<td>5/30 (16.7%)</td>
<td>2/12 (16.7%)</td>
<td>3/18 (16.7%)</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Selected treatment factors present during antiviral therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N</td>
<td>60</td>
<td>30</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Alcohol/substance-abuse therapy</td>
<td>1 (1.7%)</td>
<td>0 (0.0%)</td>
<td>1 (3.3%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Mental health services</td>
<td>46 (76.7%)</td>
<td>17 (56.7%)</td>
<td>29 (96.7%)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Psychotropic medications</td>
<td>51 (85.0%)</td>
<td>22 (73.3%)</td>
<td>29 (96.7%)</td>
<td>0.026*</td>
</tr>
<tr>
<td>Psychotropic medication changes</td>
<td>37 (61.7%)</td>
<td>17 (56.7%)</td>
<td>20 (66.7%)</td>
<td>0.426</td>
</tr>
<tr>
<td>Antiviral dose adjustments</td>
<td>21 (35.0%)</td>
<td>12 (40.0%)</td>
<td>9 (30.0%)</td>
<td>0.417</td>
</tr>
<tr>
<td>Growth factor prescriptions</td>
<td>6 (10.0%)</td>
<td>5 (16.7%)</td>
<td>1 (3.3%)</td>
<td>0.195</td>
</tr>
</tbody>
</table>

Bipolar Disorder

• Depression occurs first and most often
• Increased suicide risk (15 x gen pop)
• Lifetime prevalence of Bipolar I = 1%
  – Mean age of first mood symptoms = 18 years
  – M = F
• Lifetime prevalence of Bipolar II = 1%
  – Mean age of first mood symptoms = 20 years
  – F > M
Bipolar Disorder and HCV

- Retrospective study in Oregon of pts w/o psychiatric dz, those w/ depression and those w/ BPD
- 8/22 (36%) depressed pts had adverse psychiatric event
- 8/11 (73%) with bipolar d/o had adverse psychiatric event
- SVR rate not affected

Social Issues

• Homelessness
• Work and income
• Legal issues
Predictors of SVR

- HCV Genotype
- HCV RNA Level
- Race
- *IL28B* genotype
- Age
- Gender
- Weight
- Fibrosis Level
- Prior Treatment Response
IL28B genotype explains 50% of variability in Response between AA and Caucasians!

## Checklist Prior to Starting Therapy

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>❑ No history of decompensated cirrhosis (CPT score &gt; 7, ascites, variceal bleeding)</td>
</tr>
<tr>
<td>❑ Psychiatrically stable</td>
</tr>
<tr>
<td>❑ No active drug abuse or problem alcohol use</td>
</tr>
<tr>
<td>❑ No baseline cytopenias</td>
</tr>
<tr>
<td>❑ Normal thyroid infection</td>
</tr>
<tr>
<td>❑ No active autoimmune disease</td>
</tr>
<tr>
<td>❑ Good evidence of adherence and willing to comply with follow-up</td>
</tr>
<tr>
<td>❑ Perform dilated retinal exam if history of diabetes mellitus, hypertension, or retinal issues</td>
</tr>
<tr>
<td>❑ If HIV+, HIV is well-controlled</td>
</tr>
<tr>
<td>❑ Potential drug-drug interactions addressed and plan in place to monitor</td>
</tr>
<tr>
<td>❑ Adequate psychosocial support</td>
</tr>
<tr>
<td>❑ Financial aspects of therapy and ability to work addressed</td>
</tr>
<tr>
<td>❑ Not pregnant or planning to become pregnant during therapy and for 6 months afterwards</td>
</tr>
<tr>
<td>❑ If patient or partner of child-bearing potential, has ≥2 reliable methods of birth control</td>
</tr>
<tr>
<td>❑ No significant cardiac or respiratory issues</td>
</tr>
</tbody>
</table>
Timing of Treatment

• Waiting for newer antivirals
  – Several Qd protease inhibitors expected in next year
  – Polymerase inhibitor (GS7977) expected at end of 2013
  – IFN free regimen possible for GT 2,3 but not for GT 1,4 (probably 2014-15)
• Issue of competing morbidity and mortality
Keeping the liver healthy

• Alcohol cessation
  – MD discussing alcohol use with HCV+ patients leads to a reduction in alcohol consumption
  – Naltrexone via monthly injection is most promising pharmacotherapy option
  – Multidisciplinary support

Keeping the liver healthy

- Hepatitis A/B vaccination
- If cirrhotic, vaccinate with Pneumovax (>5 yrs), screen for varices and HCC
- Limiting acetaminophen intake, esp. for cirrhosis
- Avoiding fatty liver or trying to lose weight if NAFLD present

- For HIV+ pts, taking ARVs!

Winning the Race

ACTHIV 2013: A State-of-the-Science Conference for Frontline Health Professionals
Thank You!

Questions?