Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment: PREP-C

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Presenter Disclosure

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Vertex Pharmaceuticals Inc.

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Hepatitis C disproportionately impacts marginalized groups

Rates of infection:

- IDU > 10 years of use: 90%
- IDU < 10 years of use: 50%
- Homeless persons: 35%
- HIV-positive: 25-30%
- Prisoners: 29%
- Severely mentally ill: 19%
- US population: 2%

Chak et al. Liver Int. 2011
‘Stigma is the process by which the reaction of others spoils normal identity'.

E. Goffman, *STIGMA: Notes on the Management of Spoiled Identity* 1963
Natural History of HCV Infection

Acute Infection
- Resolved
- Chronic
  - Stable/Slowly Progressive
  - Slowly Progressive
    - Liver failure, HCC
      - Transplant
      - Death

HIV, Alcohol, Age, Male gender, Fatty liver DO influence progression

HCV viral load and genotype DO NOT influence progression
Neuro-psychiatric Context

There are higher rates of psychiatric and substance use disorders and cognitive impairment (risk factors for non-adherence) in persons with chronic HCV infection than in the general population.

HCV treatment causes neuro-psychiatric symptoms (depression, anxiety, emotional lability, irritability, insomnia) in a high percentage of treated patients.

HCV treatment side effects often result in early treatment discontinuation which reduces rates of cure.
Time Course of IFN Side Effects

Severity

IFN Treatment (Weeks)

Flu-like symptoms

Fatigue

Depressive/ anxiety symptoms
# Boceprevir Adverse Event Data Presented to FDA

## Pooled Phase 2 and Phase 3 trials

### Adverse Events

<table>
<thead>
<tr>
<th>Neuro-psychiatric AEs:</th>
<th>Boceprevir-containing Arm</th>
<th>P-R Control Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=1548</td>
<td>N=547</td>
</tr>
<tr>
<td>Suicidal Ideation</td>
<td>1 %</td>
<td>&lt; 1 %</td>
</tr>
<tr>
<td>Homicidal ideation</td>
<td>&lt; 1%</td>
<td>0 %</td>
</tr>
<tr>
<td>Anxiety</td>
<td>19%</td>
<td>15%</td>
</tr>
<tr>
<td>Depression</td>
<td>29%</td>
<td>26%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>48%</td>
<td>41%</td>
</tr>
</tbody>
</table>

### Most common AEs:

<table>
<thead>
<tr>
<th></th>
<th>Boceprevir-containing Arm</th>
<th>P-R Control Arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=1548</td>
<td>N=547</td>
</tr>
<tr>
<td>Fatigue</td>
<td>57%</td>
<td>57%</td>
</tr>
<tr>
<td>Anemia</td>
<td>49%</td>
<td>29%</td>
</tr>
<tr>
<td>Nausea</td>
<td>45%</td>
<td>40%</td>
</tr>
<tr>
<td>Headache</td>
<td>44%</td>
<td>43%</td>
</tr>
</tbody>
</table>
Age-Adjusted Rates of Mortality Associated with Hepatitis B, Hepatitis C, and HIV
United States, 1999 – 2007

HIV/HCV-co-infection

- HIV/HCV-co-infected patients have twice the risk of developing cirrhosis and a six-fold increased risk of liver failure compared to those with HCV alone

- End-stage liver disease is now a leading cause of mortality in HIV-infected persons as a result of high rates of untreated chronic HCV-co-infection

- HCV can be cured and the effectiveness of HCV treatment has dramatically increased with the DAAs: SVR12 45% vs. 74% with telaprevir Dieterich et al. CROI 2012
HIV/HCV-co-infection

- The uptake of HCV treatment in HIV/HCV-co-infected patients remains unacceptably low - estimated at 10%

- Progress in developing effective behavioral interventions to successfully engage and retain HIV-co-infected patients in HCV care has not kept pace with the rapid pharmacologic advances made in HCV treatment

- There are multiple barriers to HCV treatment initiation at patient, provider, and structural levels
Patient level barriers to HCV treatment initiation in HIV/HCV-co-infected patients

- Adequate knowledge about HCV disease course, HCV treatment, and relationship to HIV infection
  

- Low motivation for HCV treatment
  
  Mehta et al. AIDS 2005, Wagner et al. AIDS Pat Care STDs 2009, Osilla et al. AIDS Pat Care STDs 2009

- Negative and/or incorrect attitudes and beliefs regarding HCV infection and treatment
  
  Osilla et al. AIDS Pat Care STDS 2011, Salmon-Ceron et al. BMC Health Serv Res 2012

- Low perceived self-efficacy to tolerate HCV treatment side effects and obtain adequate support during treatment
  
Provider Barriers: Low Rates of Referral/Treatment of HCV

Providers are hesitant to refer and treat HCV in patients for many reasons:

- Current/History of depression/psychiatric illness
- Current/History of Substance use problems
- Cognitive impairment
- Suspected poor adherence
- High burden of treatment side effects
- Perceived low likelihood of treatment success
Structural Barriers

- Poor access to HCV testing (49% tested for HCV in Miami cohort of 15,000 HIV+ patients in care, Deeb et al. CROI 2012).
- Provider inexperience in treating HCV
- Lack of collaborative relationships across disciplines (HIV primary care provider, liver specialist, psychiatrist/psychologist)
- Inadequate insurance coverage for HCV treatment

Wagner & Ryan, AIDS, 2005; Wagner et al. AIDS Patient Care STDs 2009
Differences between HCV and HIV: Implications for Intervention

- Goal of HCV treatment is cure; whereas cure is not (yet) possible in HIV
- HCV treatment is time-limited; whereas HIV treatment is life-long
- If patient is adherent, HIV treatment works whereas this is not necessarily the case with HCV treatment
- HCV treatment is not accompanied by a ‘Lazarus effect’; to the contrary
Cost of HCV medication alone

- 48 weeks PEG-IFN + RBV = $30,000
- 12 weeks telaprevir = $49,200 (12 wk course) OR
- 48 weeks boceprevir = $48,400 (28-48 wk course)
- **Total Medication Cost = $80,000**

- Cost-effectiveness of behavioral interventions to promote treatment readiness and adherence

*Garcia-Retortillo et al., AASLD 2011, Poster 938*
Continuum of Care for Persons Chronically infected with HCV

• Awareness of HCV infection
• Linkage to and engagement in HCV Care
• Preparation for HCV Treatment
• HCV Treatment (Adherence)
Prevalence and Patient Awareness of Medical Comorbidities in an Urban AIDS Clinic

- All patients attending the Mount Sinai HIV outpatient clinic during the summer of 2005 were invited to participate.

- 200 subjects were recruited and asked whether they had each of 15 medical conditions and if so, whether they were getting treated and taking medication for it.

- Demographic information and permission to access medical records were obtained.

- Subsequently, their medical charts were independently reviewed by a physician to determine concordance between patient self-report and chart documentation.

Weiss et al. (2010) AIDS Patient Care & STDs, 24, 39-48
HIV+ Patients Awareness of chronic HCV infection

- 102/200 (51%) of HIV+ patients in HIV care chronically infected with HCV – chart documentation
  - 68/102 (67%) were aware of HCV infection
  - 19/102 said they were not infected
  - 15/102 said they did not know

1/3 of HIV+ patients in HIV care with chronic HCV infection could not correctly report this
HCV medication adherence is even more critical in the DAA era:

• Risk of development of resistance

• Increased regimen complexity (pill burden, dosing frequency, dietary requirement)

• Increased side effects

• HCV Adherence - Definitional Confusion
Adherence decreases as dosing frequency increases

Systematic Review 1986-2007 – 20 studies
Prospective design, Chronic Disease, MEMS adherence assessment

Dose and Dose Interval Adherence to TID regimens Assessed With MEMS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Participants on TID Regimen</th>
<th>Dose Adherence (Mean ± SD)</th>
<th>Dose Interval Adherence (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>59</td>
<td>85.7%*</td>
<td>45%*</td>
</tr>
<tr>
<td>Heart disease</td>
<td>68</td>
<td>66 ± 29%</td>
<td>46 ± 31%</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>36</td>
<td>80 ± 18%</td>
<td>40 ± 19%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15</td>
<td>65.8 ± 30.1%</td>
<td>5.3 ± 5.3%</td>
</tr>
<tr>
<td>Heart failure</td>
<td>26</td>
<td>88.9 ± 13.9%</td>
<td>52.6 ± 27.7%</td>
</tr>
</tbody>
</table>

*Only median available

Lower SVR Rates were observed in RESPOND-2 previous treatment failure patients who adhered to the dosing interval < 60% of the time

### Table 4. SVR by adherence of BOC to TID 7-9-hour dosing interval

<table>
<thead>
<tr>
<th>Adherence, %</th>
<th>SPRINT-2</th>
<th>RESPOND-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOC RGT</td>
<td>n=368</td>
<td>n=162</td>
</tr>
<tr>
<td>&lt;60</td>
<td>45/73 (61.6)</td>
<td>12/25 (48.0)</td>
</tr>
<tr>
<td>60 to &lt;70</td>
<td>22/31 (71.0)</td>
<td>13/20 (65.0)</td>
</tr>
<tr>
<td>70 to &lt;80</td>
<td>26/41 (63.4)</td>
<td>2/20 (60.0)</td>
</tr>
<tr>
<td>≥80</td>
<td>77/103 (74.8)</td>
<td>43/62 (69.4)</td>
</tr>
<tr>
<td>BOC/PR48</td>
<td>n=366</td>
<td>n=161</td>
</tr>
<tr>
<td>&lt;60</td>
<td>39/58 (67.2)</td>
<td>15/30 (50.0)</td>
</tr>
<tr>
<td>60 to &lt;70</td>
<td>25/30 (83.3)</td>
<td>10/13 (76.9)</td>
</tr>
<tr>
<td>70 to &lt;80</td>
<td>23/30 (76.7)</td>
<td>13/18 (72.2)</td>
</tr>
<tr>
<td>≥80</td>
<td>73/115 (63.5)</td>
<td>47/66 (71.2)</td>
</tr>
<tr>
<td>Combined BOC arms</td>
<td>n=734</td>
<td>n=323</td>
</tr>
<tr>
<td>&lt;60</td>
<td>84/131 (64.1)</td>
<td>27/55 (49.1)</td>
</tr>
<tr>
<td>60 to &lt;70</td>
<td>47/61 (77.0)</td>
<td>23/33 (69.7)</td>
</tr>
<tr>
<td>70 to &lt;80</td>
<td>49/71 (69.0)</td>
<td>25/38 (65.8)</td>
</tr>
<tr>
<td>≥80</td>
<td>150/218 (68.8)</td>
<td>90/128 (70.3)</td>
</tr>
</tbody>
</table>

Gordon et al. 2011. EASL Poster: Adherence To Assigned Dosing Regimen and Sustained Virologic Response Among Hepatitis C-Genotype 1 Previously Untreated and Peginterferon/Ribavirin Treatment-Failure Patients Treated With Boceprevir Plus Peginterferon Alfa-2b/Ribavirin
New concepts introduced to HCV treatment with DAAs

- No dose reductions with DAAs
- TID (every 7-9 hours) with food
- Increased pill burden
- DDIs with ARVs and other medications
- Risk of resistance
- Increased side effects
- Increased focus on virologic response
- Increased rate of cure
The Decision to Treat HCV

- Age
- Stage of liver disease
- HCV genotype, IL28B gene
- Prior response to treatment (side effects, adherence, and virologic outcome)
- Control of other co-morbid illnesses
- Psychosocial readiness
Parallel Work-ups

• Medical work-up for Hepatitis C treatment is usually a lengthy process that involves assessment, referral for further evaluation, and intervention to improve medical condition prior to HCV treatment initiation.
• A psychosocial work-up should occur in parallel to the medical work-up being conducted.
• Identifying psychosocial factors that could potentially interfere with treatment adherence prior to treatment initiation can result in delivery of interventions to improve these areas of functioning prior to treatment.
• The parallel psychosocial work-up also provides support for patients to complete the medical work-up.
Research from HCV mono-infection

- Providing treatment for psychiatric and substance use disorders increases rates of HCV treatment initiation

- Patients who are receiving treatment for mental health and substance use disorders do as well on treatment as those without these disorders when adequate treatment and support is provided
Several studies find that IDUs (including active users) can do well on:

- Adherence to HCV treatment
- Outcome of HCV treatment — SVR

Context of adequate access to food, housing, medical care, medication, psychiatric care, syringe exchange, opioid substitution therapy, Safer Injection Facilities (8 countries).

Robaeys et al. (2006) Eur J Gastroenterol Hepatol (Benelux)
Bruggmann et al. (2008) J Viral Hepatitis (Switzerland)
Grebely et al. (2010) Eur J Gastroenterol Hepatol (Vancouver)
PREP-C

• Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment (PREP-C) is a clinical interview that healthcare providers from diverse disciplines can be trained to administer.

• It provides an assessment of a patient’s psychosocial readiness to begin HCV treatment and identifies domains of functioning which require intervention to improve treatment readiness.
PREP-C

• Background
  – Developed in response to lack of guidelines and screening tools to meet clinicians’ needs for assessing patient’s preparedness to begin chronic HCV therapy

• Description
  – Clinical interview (30 – 45 minutes)
  – Assessment of 9 areas of psychosocial functioning

• Implementation
  – Used over last 2 years to evaluate chronic HCV patients
  – Continually revised over this period
PREP-C
Psychosocial Readiness Evaluation and Preparation for hepatitis C treatment

WELCOME
A brief, friendly introduction to what PREP-C is. As this is for the general public, we don't want to be too technical here. Brevi vel toto est iunior anno. Utor permissio, caudaeque pilos ut equinae paulatim vello unum, iemo etiam unum. Si meliora dies, ut vina, poemata reddit, scire velim, chartis perficit quotus pretium quotus arroget annus. Scriptor abhinc reddit misso annos centum qui decidunt, inter perfectos veteresque referri iebet an inter viis atque perfectos novos? Excludat iurgia finis. "Est iurus atque probus, centum qui perficit annos." Quid, qui deperiti nihis perfectos uno mense vel anno?

LOGIN

Forgot your password? You can reset your password here »
PREP-C Pilot Data

PREP-C was administered to 50 patients in 2011 being evaluated for HCV treatment at primary-care based liver clinic and HIV Clinic.

The patients were 50% male; 46% Hispanic, 42% black, 12% white; 30% HIV-co-infected.

A clinically derived scoring algorithm was used to rate the completed interviews on each of the 9 domains.

The median number of domains on which patients received a rating of ‘Satisfactory’ is 5 (range = 1-8).

The number of domains rated ‘Satisfactory’ did not differ by sex, race/ethnicity, or by HIV-co-infection status.

Weiss et al. Poster 79354 presented at Second International Conference on Viral Hepatitis New York, March 2012
PREP-C Category Scores (n=50)
21/50 patients (42%) began HCV treatment within 6 months of PREP-C

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Beginning HCV Treatment in 6 months</th>
<th>P value – Fisher’s Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>40%</td>
<td>1.0</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>HIV-negative</td>
<td>43%</td>
<td>1.0</td>
</tr>
<tr>
<td>Black</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>50%</td>
<td>0.86</td>
</tr>
</tbody>
</table>
21/50 patients (42%) began HCV treatment within 6 months of PREP-C

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Beginning HCV Treatment in 6 months</th>
<th>P value – Fisher’s Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motivation - Satisfactory</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>Motivation - CBI/NFE</td>
<td>14%</td>
<td>0.22</td>
</tr>
<tr>
<td>Information - Satisfactory</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>Information – CBI/NFE</td>
<td>37%</td>
<td>0.12</td>
</tr>
<tr>
<td>Med Adh - Satisfactory</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Med Adh – CBI/NFE</td>
<td>32%</td>
<td>0.25</td>
</tr>
<tr>
<td>Self-efficacy - Satisfactory</td>
<td>53%</td>
<td></td>
</tr>
<tr>
<td>Self-efficacy – CBI/NFE</td>
<td>19%</td>
<td>0.03</td>
</tr>
<tr>
<td>Soc Support - Satisfactory</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>Soc Support – CBI/NFE</td>
<td>44%</td>
<td>0.75</td>
</tr>
</tbody>
</table>
21/50 patients (42%) began HCV treatment within 6 months of PREP-C

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<tr>
<th>Variable</th>
<th>% Beginning HCV Treatment in 6 months</th>
<th>P value – Fisher’s Exact Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol and Substance Use - Satisfactory</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>Alcohol and Substance Use - CBI/NFE</td>
<td>44%</td>
<td>1.0</td>
</tr>
<tr>
<td>Psychiatric - Satisfactory</td>
<td>30%</td>
<td></td>
</tr>
<tr>
<td>Psychiatric – CBI/NFE</td>
<td>50%</td>
<td>0.24</td>
</tr>
<tr>
<td>Energy - Satisfactory</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>Energy – CBI/NFE</td>
<td>43%</td>
<td>1.0</td>
</tr>
<tr>
<td>Cognitive - Satisfactory</td>
<td>46%</td>
<td></td>
</tr>
<tr>
<td>Cognitive – CBI/NFE</td>
<td>33%</td>
<td>0.54</td>
</tr>
</tbody>
</table>
Goals of Using PREP-C

• Identify modifiable areas of psychosocial functioning which are predictive of HCV treatment adherence prior to HCV treatment initiation in order to be able to improve functioning in these areas prior to HCV treatment initiation.

• Identify non-modifiable areas of psychosocial functioning which are predictive of HCV treatment adherence prior to HCV treatment initiation in order to be able to plan for and take these factors into account during treatment.

• Level of support and resources available in treatment setting can be used to inform evaluation of readiness
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