What’s new in HCV/HIV coinfection therapy?

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Disclosures

PI for research grants related to HCV
   – Funds paid to Johns Hopkins University
   – AbbVie, BMS, Gilead, Janssen, Merck

DSMB related to HBV
   – Funds paid to Johns Hopkins University
   – Gilead

Scientific advisor/Consultant related to HCV
   – AbbVie, Achillion, BMS, Gilead, Janssen, Merck

The terms of this arrangement are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.
Typical comment from my colleagues in the era of highly effective DAAs

“Hey, great work on hepatitis C; simply amazing results.....now, that hep C is done, what are you going to do with the rest of your career?”
Hepatitis C: Challenges and Opportunity in the 21st Century

• **Challenge #1:** High disease burden
• **Challenge #2:** Low rates of diagnosis and treatment despite available HCV cure
• **Challenge #3:** Development of and access to better HCV treatments
• **Challenge #4:** Prevention of new HCV infection and re-infection
• **Challenge #5:** HCV vaccine
Global prevalence: 130–150 million people have chronic HCV infection -- at least 5 million with HIV coinfection

North America
Europe, Western
Europe, Central
Europe, Eastern
Asia, Central
Asia Pacific, High Income
Asia, South
Asia, Southeast
Asia, East
Australasia
North Africa/Middle East
Sub-Saharan Africa, West
Sub-Saharan Africa, Central
Sub-Saharan Africa, Southern
Latin America, Andean
Latin America, Tropical
Latin America, Southern
Caribbean
Latin America, Central

Prevalence (Viremic)
- 0.0%-0.6%
- 0.6%-0.8%
- 0.8%-1.3%
- 1.3%-2.9%
- 2.9%-7.8%

Total Infected (Viremic)
- 0-200K
- 200K-650K
- 650K-1.9M
- 1.9M-3.5M
- 3.5M-9.2M

Global number of deaths in 2010 –
Hepatitis B and C ≈ HIV

Global Burden of Disease Study 2010 Lozano et al, Lancet 2012
Hepatitis C: Challenges and Opportunity in the 21st Century

- Challenge #1: High disease burden
- **Challenge #2:** Low rates of diagnosis and treatment despite available HCV cure
- Challenge #3: Development of and access to better HCV treatments
- Challenge #4: Prevention of new HCV infection and re-infection
- Challenge #5: HCV vaccine
HCV cure decreases the incidence of liver transplant, hepatocellular carcinoma, and death

5-year risk of death (all-cause) by SVR

5-year risk of hepatocellular carcinoma by SVR

Meta-analysis of 129 studies of 34,563 patients

Hill A. Clinical Infectious Disease 2015
Diagnosis and treatment rates are low in most countries.
Hepatitis C: Challenges and Opportunity in the 21st Century

• Challenge #1: High disease burden
• Challenge #2: Low rates of diagnosis and treatment despite available HCV cure
• **Challenge #3: Development of and access to better HCV treatments**
• Challenge #4: Prevention of new HCV infection and re-infection
• Challenge #5: HCV vaccine
Interferon-based treatments have been a major barrier to effectiveness of treatment.
1. Entry
2. Endosomal release and IRES dependent translation
3. Protease cleavages
4. Membranous web formation
5. NS5B RNA dependent polymerase (RdRp)
6. Lipoprotein assembly linked to NS5A
7. Cellular targets
HCV suppression by NS3 protease inhibitors

Rapid and potent HCV suppression with BILN2061 (2003)

Selection of telaprevir resistant variants with monotherapy x 14 days

Lamarre Nature 2003
Kieffer Hepatology 2007
HCV Drug Development Advisory Group
HCV suppression by NS5A inhibitors

Rapid and potent antiviral activity with a single dose of daclatasvir (2010)

Selection of daclatasvir resistant variants with monotherapy x 14 days

Gao Nature 2010
Nettles Hepatology 2011
HCV Drug Development Advisory Group;
HCV suppression by non-nucleoside NS5B polymerase inhibitors (non-nuc)

Binding sites for non-nucleoside HCV NS5B polymerase inhibitors

HCV RNA suppression over 3 days with dasabuvir (ABT-333) monotherapy (~ 1 log₁₀)

Poordad EASL 2012
HCV cure with variable combinations of Paritaprevir/r + Ombitasvir + Dasabuvir + Ribavirin
(NS3 ± NS5A ± non-nuc NS5B ± Ribavirin)

Kowdley NJEM 2014
Ribavirin prevents HCV virologic failure in patients with genotype 1a infection and is not required for 1b infection

Ombitasvir/Paritaprevir + Dasabuvir with or with Ribavirin

| Genotype 1b | 1 patient with breakthrough* |
| Genotype 1a - No Ribavirin | 16 patients with virologic failure (6 breakthrough and 10 relapse)* |
| Genotype 1a plus Ribavirin | 2 patients with virologic failure (1 breakthrough and 1 relapse)* |

*Variants in patients with virologic failure:
NS3, D168V
NS5A, M28T and Q30R
NS5B,S556G

Ferenci NEJM 2014
C-EDGE treatment-naive study: 12-week regimen of grazoprevir/elbasvir (GZR/EBR) in G1/4/6 patients

- Good safety and tolerability profile: No drug-related SAE; 2 deaths unrelated to drugs
- Lab: No concurrent ALT/Bili increase, no anemia

Zeuzem S, et al. EASL 2015, Vienna. #G07
### C-EDGE treatment-naive study: 12-week regimen of grazoprevir/elbasvir (GZR/EBR) in G1/4/6 patients

- SVR was achieved by 95% of pts
- Lower SVR in G1a accounted for by high-level (>5x fold) NS5A RAVs in G1a
- Although such RAVs uncommon (6% of G1a), BL NS5A testing with high BL VL might be needed to identify need for RBV, longer duration, or selection of a different regimen
- Well tolerated, with similar safety profile and similar efficacy in cirrhotic and non-cirrhotic patients

All pts with virologic failure had BL HCV RNA of >800,000 IU/mL

<table>
<thead>
<tr>
<th>NS5A RAVs</th>
<th>RAV status in pts with BL sequence % (n/m)</th>
<th>SVR12 All pts % (N/n)</th>
<th>SVR12 NS5A RAVs ≤5-fold potency loss</th>
<th>SVR12 NS5A RAVs &gt;5-fold potency loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>G1a RAVs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BL NS5A RAVs</td>
<td>12 (19/154)</td>
<td>58 (11/19)</td>
<td>90 (9/10)</td>
<td>22 (2/9)</td>
</tr>
<tr>
<td>No BL NS5A RAVs</td>
<td>88 (135/154)</td>
<td>99 (133/135)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>G1b RAVs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BL NS5A RAVs</td>
<td>14 (18/130)</td>
<td>94 (17/18)</td>
<td>100 (1/1)</td>
<td>94 (16/17)</td>
</tr>
<tr>
<td>No BL NS5A RAVs</td>
<td>86 (112/130)</td>
<td>100 (112/112)</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

m: pts with evaluable BL sequence; n: number of pts with/without BL RAVS; N: pts who achieved SVR

Zeuzem S, et al. EASL 2015, Vienna. #G07
GZR/EBR ± RBV for 12 weeks in G1/4 patients who previously failed PegIFN/RBV: C-EDGE treatment-experienced trial

SVR according to baseline factors

<table>
<thead>
<tr>
<th></th>
<th>12-wk no RBV</th>
<th>12-wk + RBV</th>
<th>16-wk no RBV</th>
<th>16-wk + RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>92%</td>
<td>90%</td>
<td>89%</td>
<td>91%</td>
</tr>
<tr>
<td>G1a</td>
<td>94%</td>
<td>93%</td>
<td>92%</td>
<td>91%</td>
</tr>
<tr>
<td>Non-cirrhotic</td>
<td>92%</td>
<td>97%</td>
<td>93%</td>
<td>94%</td>
</tr>
<tr>
<td>Cirrhotic</td>
<td>97%</td>
<td>96%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Partial or null reponse</td>
<td>92%</td>
<td>100%</td>
<td>94%</td>
<td>100%</td>
</tr>
</tbody>
</table>

SVR according to BL NS3 and NS5 RAVs

<table>
<thead>
<tr>
<th></th>
<th>SVR12 n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NS3 variants not detectable</td>
</tr>
<tr>
<td>Total</td>
<td>92/112 (96%)</td>
</tr>
<tr>
<td>G1a</td>
<td>95%</td>
</tr>
<tr>
<td>G1b</td>
<td>99%</td>
</tr>
<tr>
<td></td>
<td>NS5A variants not detectable</td>
</tr>
<tr>
<td>G1a</td>
<td>95%</td>
</tr>
<tr>
<td>G1b</td>
<td>99%</td>
</tr>
</tbody>
</table>

- GZR/EBR FDC ± RBV was safe and effective in PR non-responders
- 16 weeks + RBV achieved 100% SVR in cirrhotic null responders
- 12/14 G1 failures had high-level NS5A RAVS at baseline
- An intensified regimen is needed to overcome impact of baseline NS5A RAVs, especially in G1 pts
- Baseline NS5A testing advisable with this regimen now that commercially available

Kwo P, et al. EASL 2015, Vienna. #P0886
C-SURFER: GZR + EBR in treatment-naive and treatment-experienced patients with HCV G1 infection and CKD

Virologic response (ITG)

<table>
<thead>
<tr>
<th>Patients (HCV RNA &lt; LLQ, %)</th>
<th>TWk2</th>
<th>TWk4</th>
<th>TWk12 (EOT)</th>
<th>FWk4</th>
<th>FWk12 (SVR12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>81/122</td>
<td>109/121</td>
<td>119/119</td>
<td>118/118</td>
<td>115/116</td>
<td></td>
</tr>
</tbody>
</table>

SVR12 subgroup analyses (ITG)

<table>
<thead>
<tr>
<th>All patients</th>
<th>115/116</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6/6</td>
</tr>
<tr>
<td>No</td>
<td>109/110</td>
</tr>
<tr>
<td>HCV genotype</td>
<td></td>
</tr>
<tr>
<td>G1a</td>
<td>61/61</td>
</tr>
<tr>
<td>G1b</td>
<td>54/55</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>58/59</td>
</tr>
<tr>
<td>African-American</td>
<td>51/51</td>
</tr>
<tr>
<td>Previous tx</td>
<td></td>
</tr>
<tr>
<td>Naive</td>
<td>96/96</td>
</tr>
<tr>
<td>Experienced</td>
<td>19/20</td>
</tr>
<tr>
<td>CKD stage</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>22/22</td>
</tr>
<tr>
<td>5</td>
<td>93/94</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40/41</td>
</tr>
<tr>
<td>No</td>
<td>75/75</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>86/87</td>
</tr>
<tr>
<td>No</td>
<td>29/29</td>
</tr>
</tbody>
</table>

SVR12 (95% CI) 70 80 90 100

1 G1b, non-cirrhotic, patient relapsed at FWk12

ITG: Immediate treatment group

Roth D, et al. EASL 2015, Vienna. #LP02
HCV suppression by nucleos(t)ide analogue NS5B polymerase inhibitors

Sofosbuvir, β-d-2' ‑deoxy-2' ‑α-fluoro-2' ‑β-C- methyluridine nucleotide prodrug (2010)

Potent HCV suppression with sofosbuvir alone, with ribavirin or with both interferon/ribavirin (2010)

Sofia J Med Chem 2010
Gane NEJM 2013
HCV Drug Development Advisory Group
OPTIMIST-1: 8- or 12-week regimen of simeprevir (SIM) + sofosbuvir (SOF) in G1 patients without cirrhosis

- High overall SVR12 rate (97%) for 12-week treatment duration
- Q80K was not impactful in this non-cirrhotic population
- Lower overall SVR12 rate (83%) for 8-week duration – not a viable option, unlike LDV/SOF, for treatment naive G1 non-cirrhotics
- Reason for lower efficacy of SMV than LDV with SOF for 8 weeks unclear – do NS5A inhibitors degrade the replicase complex faster?
OPTIMIST-2: A Phase 3, open-label, single-arm study to evaluate the efficacy and safety of 12 weeks of SMV + SOF in treatment-naive or -experienced G1 cirrhotic patients

SVR12: SMV + SOF 12 weeks

- SVR12 did not differ between IL28B genotypes
- Expands COSMOS + TRIO/TARGET data in clinical trials
  - No RBV; Q80K adversely influenced response; would need BL testing before using regimen in cirrhotics
- 18% increase in bilirubin
- Lost opportunity to explore (approved) 24-week regimen

Lawitz E, et al. EASL 2015, Vienna. #LP04
HCV eradication with the fixed-dose combination of Ledipasvir/Sofosbuvir (NS5A/nuc NS5B)

Persons with no prior HCV treatment

8 weeks
20 patients with relapse, 4.6%
HCV RNA < 6 million IU/mL, 2%

12 weeks
4 patients with relapse, 0.6%

24 weeks
1 patient with relapse, 0.2%

*Variants in patients with virologic failure:
NS5A, L31V/M/I, Y93H, Q30R
NS5B, None

HCV cure – genotypes 1, 2, 3, 4, 5 and 6 – with the combination of sofosbuvir/GS5816 (nucNS5B/NS5A)

- Sofosbuvir - potent antiviral activity HCV genotype 1 – 6
- GS5816 - potent antiviral activity HCV genotype 1 – 6
- Phase 3 clinical trials are underway for the fixed dose combination of Sofosbuvir/GS5816

Everson EASL 2014
There has been great progress toward more efficacious HCV treatments but…

56-year-old man with HIV/HCV genotype 1/subtype A

- Cirrhosis: MELD 15 with Cr 1.6, INR 1.3, bili 1.3; IL28B TT

- HIV: Atazanavir/r + raltegravir + TDF/FTC with CD4 249 and HIV RNA < 20 c/mL

- HCV treatment
  - 2011: PegIFN/RBV + telaprevir → breakthrough
    - At treatment week 4, HCV RNA = 46 IU/mL; week 12, HCV RNA = 1,299 IU/mL
  - 2014: Sofosbuvir + ribavirin → breakthrough
    - Baseline HCV RNA = 2,506,896 IU/mL
    - Week 4 = 36 IU/mL
    - Week 12 = not detected
    - Week 16 = Detected < 43 IU/mL
    - Week 24 = 2,119 IU/mL (on-treatment) despite 100% adherence
$\log_{10} [\text{HCV RNA}]_{\text{plasma}}$ per mL absolute

- Nonresponse
- Breakthrough
- Relapse

Courtesy of Dr. Stuart Ray
Retreatment of patients who failed 8 or 12 weeks of LDV/SOF-based regimens with LDV/SOF for 24 weeks

- Shorter therapies produce less-frequent treatment-emergent RAVs
- More complex RAV pattern = less likely to achieve response
- Retreatment with longer duration more likely to be successful with fewer NS5A RAVs or RAVS with smaller shifts in EC$_{50}$

Lawitz E, et al. EASL 2015, Vienna. #O005
The prevalence and effect of HCV NS5A resistance-associated variants in subjects with compensated cirrhosis treated with LDV/SOF ± RBV

- 513 patients with G1 and compensated cirrhosis were pooled from Phase 2 and 3 LDV/SOF ± RBV studies
- 20/513 failed to achieve SVR12
  - 18 patients relapsed
  - 2 patients excluded from resistance analysis (1 lost to FU, 1 death)

**Overall SVR12 rates in patients with and without NS5A RAVs***

*Presence of RAVs was evaluated by deep sequencing with assay cutoffs of 1%; error bars represent 95% CIs

Sarrazin C, et al. EASL 2015, Vienna. #P0773
Ribavirin prevents the emergence of resistance associated variants during antiviral therapy

HCV breakthrough with or without ribavirin during telaprevir/peginterferon

Zeuzem Hepatology 2012
Hezode NEJM 2009
Treatment with GS-9857 + SOF/GS-5816 in treatment-naive and DAA-experienced G1 patients with and without cirrhosis

- **Aim**: Triple therapy with SOF plus 2nd-gen NS5A inhibitor (GS-5816) and NS3/4A (GS-9857) could reduce treatment duration across patient populations.

**Study design**

<table>
<thead>
<tr>
<th>Week 0</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>6 weeks</th>
<th>16</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>G1</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TN no cirrhosis n=30</td>
<td>SOF/GS-5816 + GS-9857</td>
<td>SOF/GS-5816 + GS-9857</td>
<td><strong>SVR12</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TN cirrhosis n=15</td>
<td>SOF/GS-5816 + GS-9857</td>
<td>SOF/GS-5816 + GS-9857</td>
<td><strong>SVR12</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAA failure n=30</td>
<td>SOF/GS-5816 + GS-9857</td>
<td>SOF/GS-5816 + GS-9857</td>
<td><strong>SVR12</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Baseline Characteristics**

<table>
<thead>
<tr>
<th>4 weeks n=15</th>
<th>6 weeks n=15</th>
<th>6 weeks n=15</th>
<th>6 weeks n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age, y (range)</strong></td>
<td>54 (40–64)</td>
<td>50 (24–65)</td>
<td>59 (51–66)</td>
</tr>
<tr>
<td><strong>Male, n (%)</strong></td>
<td>9 (60)</td>
<td>7 (47)</td>
<td>11 (73)</td>
</tr>
<tr>
<td><strong>White, n (%)</strong></td>
<td>12 (80)</td>
<td>14 (93)</td>
<td>14 (93)</td>
</tr>
<tr>
<td><strong>Mean BMI, kg/m² (range)</strong></td>
<td>27 (20–33)</td>
<td>25 (21–32)</td>
<td>27 (20–39)</td>
</tr>
<tr>
<td><strong>IL28B CC, n (%)</strong></td>
<td>5 (33)</td>
<td>5 (33)</td>
<td>8 (53)</td>
</tr>
<tr>
<td><strong>Cirrhosis, n (%)</strong></td>
<td>0</td>
<td>0</td>
<td>15 (100)</td>
</tr>
<tr>
<td><strong>Mean HCV RNA, log₁₀ IU/mL (range)</strong></td>
<td>6.3 (5.2–7.1)</td>
<td>6.0 (4.4–6.7)</td>
<td>6.0 (3.9–7.1)</td>
</tr>
<tr>
<td><strong>HCV G1a, n (%)</strong></td>
<td>11 (73)</td>
<td>11 (73)</td>
<td>14 (93)</td>
</tr>
</tbody>
</table>

**DAA failures**

- Delobuvir + faldaprevir + RBV (n=2)
- Telaprevir + VX222 ± RBV (n=4)
- LDV/SOF + RBV (n=1)
- DCV + VX135 (n=3)
- Danoprevir + mericitabine (n=14)
- Danoprevir + mericitabine + ritonavir ± RBV (n=6)

Gane E, et al. EASL 2015, Vienna. #LP03
Short-duration treatment with GS-9857 + SOF/GS-5816 in treatment-naive and DAA-experienced G1 patients with and without cirrhosis

**Predictors of SVR (univariate)**
- Younger age, lower BL HCV RNA
- Not IL28B C, AUC, or BL RAVs

**Safety**
- AEs mild, non-specific
- Any AE in 58/75 (77%)
- No Grade 3/4 AE, SAE or d/c
- Lab abnormality in 7 pts (4 transient ↑ lipase)

Gane E, et al. EASL 2015, Vienna. #LP03

**Results: SVR12**

<table>
<thead>
<tr>
<th></th>
<th>4 weeks</th>
<th>6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN NC G1</td>
<td>27</td>
<td>93</td>
</tr>
<tr>
<td>TN cirrhotic</td>
<td>87</td>
<td>67</td>
</tr>
</tbody>
</table>

**Impact of BL RAVs (deep sequencing)**

- **Treatment naive ± cirrhosis, n=43**
  - 60% without n=26/43
  - 40% with n=17/43
  - 82% SVR12
  - 14/17

- **Prior DAA failure ± cirrhosis, n=30**
  - 57% without n=17/30
  - 43% with n=13/30
  - 69% SVR12
  - 9/13

† Only 3/10 subjects have been sequenced

**RAVs at virologic failure (relapse)**

<table>
<thead>
<tr>
<th></th>
<th>NS3</th>
<th>NS5A</th>
<th>NS5B</th>
</tr>
</thead>
<tbody>
<tr>
<td>TN NC G1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TN cirrhotic</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DAA failures</td>
<td>0†</td>
<td>0</td>
<td>0†</td>
</tr>
</tbody>
</table>

[^] Only 3/10 subjects have been sequenced

- SOF/GS-5816 + GS-9857 is safe and well tolerated
- In G1 TN without cirrhosis, 6 weeks triple DAA was effective, but shortening to 4 weeks was associated with >70% relapse without RAVs
- In G1 cirrhotics and DAA failures, duration longer than 6 weeks should be considered
- Threshold for duration regardless of DAA number?
Hepatitis C: Challenges and Opportunity in the 21st Century

• Challenge #1: High disease burden
• Challenge #2: Low rates of diagnosis and treatment despite available HCV cure
• Challenge #3: Development of and access to better HCV treatments
• Challenge #4: Prevention of new HCV infection and re-infection
• Challenge #5: HCV vaccine
HCV is a sexually transmitted disease among HIV-infected MSMs

Incidence of HCV in HIV-infected MSM from 12 cohorts within CASCADE

Incidence of hepatitis C reinfection following SVR: 7-year follow-up of Scandinavian patients infected through injecting drug use

Patients

- 2004–05: Multicentre study comprising 428 Scandinavian G2 or G3 patients
  - SVR 76%; 68% PWID, abstinent from drug use ≥6 months prior to treatment
- 2012-14: 94 PWID and 44 non-PWID with SVR
  - Median f/u of 7.1–7.5 years

Results

- 37 of 94 (39%) PWID relapsed to active injection after SVR
- HCV reinfection in 12 patients; of whom 11 were active PWID

Incidence of reinfection

Midgard H, et al. EASL 2015, Vienna. #O061
Incidence of HCV infections in young adults in the US

Increases in Hepatitis C Virus Infection Related to Injection Drug Use Among Persons Aged ≤30 Years — Kentucky, Tennessee, Virginia, and West Virginia, 2006–2012
Hepatitis C: Challenges and Opportunity in the 21st Century

• Challenge #1: High disease burden
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• Challenge #3: Development of and access to better HCV treatments
• Challenge #4: Prevention of new HCV infection and re-infection
• **Challenge #5: HCV vaccine**
rs12979860 C IL-28B allele associated with higher probability of natural clearance of HCV

Shorter duration of viremia during reinfection among PWID with prior infection/spontaneous clearance

$P = 0.019$

Osburn et al. Gastroenterology 2010;138:315–324
HCV Prophylactic Vaccine Based on Sequential Use of Chimpanzee Adenovirus AdCh3 and MVA with NS

- Cross reactivity of AdCh3 with human anti-adenovirus Abs is 12%
- MVA boosts well in Phase I trials
- Double-blinded, randomized, placebo-controlled two stage study.
- Subjects: HCV Ab and RNA negative, active IDU’s at high risk for HCV, 18 -45 y.o.
- Two Sites (UCSF, JH)
Hepatitis C: Challenges and Opportunity in the 21st Century

• Globally, chronic infection with HCV is a major cause of death
  – HCV cure is associated with improved survival
• Oral, interferon-free HCV treatment regimens involving two or more directly acting antivirals which target unique viral mechanism have been developed
  – Rapid, remarkable translation of laboratory discoveries into approved drugs
  – If treated, most individuals can be cured
  – Unanswered questions about drug resistance in persons who are not cured
• Current challenge: Translation of clinical trial findings into global community effectiveness
• HCV vaccine is needed