SHOULD EVERYONE WITH HCV/HIV COINFECTION BE TREATED NOW?

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Disclosures

 страхование.

1. Contracted Research (with institution): AbbVie, Anadys, BMS, Genentech, Gilead, Merck
2. Advisory Board/Consulting (w/i 12 months): MedImmune, Merck
3. DSMB and Endpoint adjudication Board: Janssen, Synteract
DO WE NEED TO TREAT NOW? Factors to Consider

- Risk of progression to a critical stage
- Drugs available now, versus later
  - Patient preference
- Public Health Issues
  - Treatment as Prevention
  - Cost
  - Lack of providers
Effect Of HAART on Liver Related Mortality In HCV/HIV Infected Patients


Liver-related Mortality

Patients with HAART
Patients with ART
Untreated Patients

$P=0.018$

Cumulative Survival
Observation Time (Days)
Fibrosis Progression Rate by HIV Viral Load


<table>
<thead>
<tr>
<th>HIV RNA Status</th>
<th>HIV Viral Load</th>
<th>IshFU / yr</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-negative</td>
<td>HIV RNA &lt;400</td>
<td>0.128</td>
<td>0.52</td>
</tr>
<tr>
<td>HIV-negative</td>
<td>HIV RNA &gt;400</td>
<td>0.136</td>
<td>0.29</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>HIV RNA &lt;400</td>
<td>0.128</td>
<td>0.151</td>
</tr>
<tr>
<td>HIV-negative</td>
<td>HIV RNA &gt;400</td>
<td>0.122</td>
<td>0.015</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>HIV RNA &lt;400</td>
<td>0.133</td>
<td>0.013</td>
</tr>
<tr>
<td>HIV-positive</td>
<td>HIV RNA &gt;400</td>
<td>0.145</td>
<td>0.013</td>
</tr>
</tbody>
</table>

n = 382

P = 0.013

P = 0.053

P = 0.053

P = 0.044

P = 0.005

IshFU / yr

P = 0.005

P = 0.015

P = 0.044

P = 0.005

0.08 0.1 0.12 0.14 0.16 0.18 0.2 0.22

HIV-negative  HIV-positive  HIV-negative  HIV RNA <400  HIV RNA >400  HIV RNA <400  HIV RNA >400  HIV RNA >99K  HIV RNA >100K
HCV/HIV Coinfected Patient on Effective cART at 0.122 Metavir U/year
FIBROSIS CHANGE
Paired Sample Analysis

Sherman et. al., JAIDS 2010
Rapid Progression of Liver Disease in HIV/HCV-Coinfected Patients

- Prospective study of fibrosis progression in 67 coinfected patients
- 2 biopsies; median time between biopsies was 2.84 years

**Patients With Mild Fibrosis (≤F1) on First Biopsy**

- >25% of patients with mild fibrosis on initial biopsy had ≥2 stage progression in fibrosis score

**Change in Ishak Score From First to Second Biopsy**

- No Change
- 1
- 2
- 3
- 4
- 5
- 6

Sulkowski M et al. AIDS, 2007
EXPANDED FIBROSIS PROGRESSION STUDY- JH

- 282 HCV/HIV without cirrhosis
  - 69.2% Receiving cART at time of first bx and 69% over paired bx period
  - Alcohol abuse 49.7% during pair biopsy period

- Paired Biopsy Performed
  - Median Length 1.2-1.3 cm

- Progression to 2 Stages (2 Metavir U) or More
  - 39/282= 13.8% over Median Interval of 2.5 Years
  - Predictors of “rapid” fibrosis
    - Elevated BMI
    - Diabetes
    - Steatosis
    - ALT or AST > 100 on >25% of Interval Tests but AST stronger predictor (alcohol)

Konerman MA et al. HEPATOLOGY 2014
### DAAs AVAILABLE NOW

**Genotype 1**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HCV</th>
<th>HIV/HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOC</td>
<td>67/63</td>
<td>40/64</td>
</tr>
<tr>
<td>TPV</td>
<td>75/74</td>
<td>28/38</td>
</tr>
<tr>
<td>SMV (Naive)</td>
<td>80/79</td>
<td>419/521</td>
</tr>
<tr>
<td>SMV (Relapser)</td>
<td>77/87</td>
<td>206/260</td>
</tr>
<tr>
<td>SMV (Partial)</td>
<td>65/70</td>
<td>13/15/15</td>
</tr>
<tr>
<td>SMV (Null)</td>
<td>53/57</td>
<td>9/17</td>
</tr>
<tr>
<td>P/R/SOFx12</td>
<td>89/89</td>
<td>260/292</td>
</tr>
<tr>
<td>SOF/R</td>
<td>68/76</td>
<td>17/17</td>
</tr>
</tbody>
</table>

**SVR Rate**

**NOT DIRECT COMPARISON WITHIN TRIALS** (provided by Susannah Naggie, MD)

DAAs for HCV/HIV

- Telaprevir - Globally Available
- Boceprevir - Globally Available
- Simeprevir - US, Approved EU May 16, but not marketed until second half, under review in Australia
- Faldaprevir - Not available
- Sofosbuvir (and Ledipasvir) - Sofosbuvir available in U.S., Europe, under review in Australia, but Ledipasvir NOT available
- MK-5172 + MK-8742 - Not available
- Daclatasvir - No data
- ABT-450/r - No data
Sofosbuvir/Ledipsavir in HCV/HIV (ERADICATE)

- NIH Open Label Phase II
- N = 50
- SOF/LDV qd x 12 weeks
  - GT1
  - TN with or w/o cART
- “Difficult” Cohort
  - G1a = 78%
  - A-A = 84%
  - F3 = 26%
  - BMI = 26%

Osinusi et al, EASL 2014
MK-5172 + MK8742 + Riba (C-WORTHY)

- Phase II Open Label
- N= 59 HCV/HIV G1
  - Treatment Naïve
  - F0-F2
- Two Arms HCV/HIV
  - MK-5172 100 mg + MK-8742 50 mg + RBV x 12 Wks
  - MK-5172 100 mg + MK-8742 50 mg x 12 Wks

**PATIENT PREFERENCE**

- N= 284 HCV-infected
- 5 Countries (UK, France, US, Germany, Spain)
- Methodology: Choice-format conjoint analysis to study trade-off

Kauf TL et al, PATIENT 2012
COST ISSUES

In U.S. 250-300K coinfected with HCV/HIV
- Genotype 1 Approx. 200,000

Treatment Cost (not including labs and physician fees)
- Sof/Riba x 24 Weeks= $172,000/case= 34 Billion Dollars
  • At least 48,000 uncured and will need next gen therapy
- Sof/Sim x 12 Weeks (never tested)= $28 Billion Dollars

US Direct Healthcare Expenditure= Approx $600 Billion

If we treat everyone NOW, costs will exceed 5% of all U.S. Federal Healthcare expenditures
Gastroenterologists in U.S. 10,390 but short 1,050 by 2020 just to meet colorectal Ca screening needs (Lewin Group Report, 2009)
- Includes 300-400 dedicated Hepatologists

Infectious Disease in U.S. ?how many
- Shortage Predicted by 2020 due to less people entering the field (M. Tapper, Infectious Dis News accessed 6/6/2014)

Primary Care
- Few interested or knowledgeable
- Project ECHO- 90 trained over multiyear period
Conclusion

- Treatment of all HIV infected with effective cART is appropriate
- TARGETED and SELECTIVE treatment with current agents is warranted
- New BETTER (more efficacious and possibly cheaper) therapies are coming
- NOW IS NOT THE TIME TO TREAT EVERYONE