Best of HCV from AASLD

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Abstract #194

Effectiveness of Hepatitis C Virus (HCV) Testing for Persons Born during 1945-1965 – Summary Results from Three Randomized Controlled Trials

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Background & Aims

- CDC and the U.S. Preventive Services Taskforce recommend 1-time HCV testing for persons born during 1945-1965 (birth cohort).

- We present summary results from 3 independent trials to determine the relative probability of identifying HCV infections using birth cohort (BC) testing versus current screening protocol.
Methods

• From December 2012 to February 2014, we conducted HCV (BC) testing trials at 3 large primary care healthcare centers using variations of the randomized controlled trial design.

• Across centers, patients born during 1945-1965 with no clinical documentation of prior HCV test or infection were randomly assigned (individually or in defined clusters) to receive a 1-time HCV test (intervention) or the prevailing screening protocol (control).

• We estimated the risk ratio (RR) of identifying patients with HCV antibody or RNA positive results (HCV+) using BC testing versus control for each trial, with adjustment for correlated data.

• We applied meta-analysis to summarize individual risk ratios into a pooled effect estimate.
Conclusions

• HCV testing of persons born during 1945-1965 without prior ascertainment of HCV risk was 5 times more effective in identifying persons with previous or current HCV infection compared with standard of care.

Abstract #116

The Use of All Oral Regimens for Treatment of Chronic Hepatitis C (CHC) Coupled with Birth Cohort Screening Is Highly Cost Effective: The Health and Economic Impact on the U.S. Population

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Background & Aims

• As new treatments for HCV are being developed, it is important that these regimens are assessed beyond the cost of a pill and assessed for their “cost per cure” and incremental cost effectiveness ratio (ICER)

• The economic impact of an effective screening strategy followed by highly effective treatment of HCV(+) patients with all oral anti-HCV regimens have not been fully evaluated
Methods

• The cost and health benefits of a hepatitis C screening/treatment program were examined by computer simulation

• The birth cohort (1945-1965) was modeled over time using a Markov decision analytic model

• Health outcomes and costs were compared between Birth Cohort Screening and Risk-Based Screening

Results

• Birth cohort screening followed by treating all HCV positive patients with all oral anti-HCV regimens save more than 4 million life years at an incremental cost of ~$37,000 per QALY

• This strategy is the most cost-effective strategy from the societal perspective (ICER<$50,000 per QALY)

• Even when considering a very pessimistic scenario, birth cohort screening-treat all strategy remains the most cost-effective strategy
Abstract #46

Evaluation of Sofosbuvir and Simeprevir-based Regimens in the TRIO Network Academic and Community Treatment of a Real-world, Heterogeneous Population

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SOF/PEG/RBV or SOF/SMV +/- RBV for 12 Weeks: SVR 12 For Treatment Naïve GT 1 (ITT)

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SOF/PEG/RBV or SOF/SMV +/- RBV for 12 Weeks: SVR 12 For Treatment Experienced GT 1 (ITT)

Dieterich D, et al. Abstract #46, AASLD 2014
## Treatment Discontinuation

<table>
<thead>
<tr>
<th>Discontinuation Rates by Reason</th>
<th>GT1 SOF + PEG/RBV</th>
<th>GT1 SMV + SOF +/- RBV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Events*</td>
<td>2.0% (6)</td>
<td>1.4% (4)</td>
</tr>
<tr>
<td>Non-Adherence</td>
<td>4.1% (12)</td>
<td>1.8% (5)</td>
</tr>
<tr>
<td>Financial</td>
<td>0%</td>
<td>0.4% (1)</td>
</tr>
<tr>
<td>Total</td>
<td>6.1% (18)</td>
<td>3.6% (10)</td>
</tr>
</tbody>
</table>

*General intolerance, rash

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*Dieterich D, et al. Abstract #46, AASLD 2014*
Summary

- SOF + PEG/RBV lead to 81% SVR12 in treatment naïve GT 1 patients in real world setting
- SOF + PEG/RBV in GT 1 treatment experienced
  - No Phase 3 registration trial was conducted
  - SVR 12 results consistent with what was predicted by FDA
  - Although not shown, cirrhosis was most important predictor of response
  - Safety consistent with clinical trial data

Dieterich D, et al. Abstract #46, AASLD 2014
Abstract #82

An Integrated Safety and Efficacy Analysis of >500 Patients with Compensated Cirrhosis Treated with Ledipasvir/ Sofosbuvir with or without Ribavirin

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Methods

- 513 patients with GT 1, compensated cirrhosis
- Pooled data from Phase 2 and 3 LDV/SOF + RBV studies
  - LONESTAR, ELECTRON, ELECTRON-2, 337-0113, ION-1, ION-2, SIRIUS
## Baseline Demographics

<table>
<thead>
<tr>
<th>Patients, %</th>
<th>Treatment Naïve (n=161)</th>
<th>Treatment Experienced (n=352)</th>
<th>Total (n=513)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>63%</td>
<td>68%</td>
<td>67%</td>
</tr>
<tr>
<td>Black</td>
<td>8%</td>
<td>4%</td>
<td>5%</td>
</tr>
<tr>
<td>Asian</td>
<td>17%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>GT 1a</td>
<td>53%</td>
<td>63%</td>
<td>60%</td>
</tr>
<tr>
<td>Prior PI Failure</td>
<td>NA</td>
<td>68%</td>
<td>47%</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>50%</td>
<td>31%</td>
<td>37%</td>
</tr>
<tr>
<td>Ex-US</td>
<td>50%</td>
<td>69%</td>
<td>63%</td>
</tr>
</tbody>
</table>

Bourlière M, et al. Abstract #82, AASLD 2014
**SVR12: LDV/SOF for 12 vs 24 Weeks in Compensated Cirrhotics**

- **Overall:** 96% (493/513 patients)
- **12 Weeks:** 95% (305/322 patients)
- **24 Weeks:** 98% (188/191 patients)

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Subgroup Observations

• Among treatment-experienced patients, 12 weeks of LDV/SOF resulted in a 90% SVR rate
  – Adding RBV or extending treatment duration increased this rate to ≥96%

• Platelet count <75 x 10^3/uL was associated with a lower SVR rate among treatment-experienced patients with cirrhosis
Abstract #LB-6

Ledipasvir/Sofosbuvir Fixed-Dose Combination is Safe and Efficacious in Cirrhotic Patients Who Have Previously Failed Protease-Inhibitor Based Triple Therapy

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6. CHRU Lille, Lille, France
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Study Design

- Double-blinded
- Treatment-experienced patients with compensated cirrhosis who did not achieve SVR following sequential PEG/RBV and PI/PEG/RBV regimens
- 2 Arms
  - Placebo 12 weeks followed by LDV/SOF + RBV for 12 weeks
  - LDV/SOF + Placebo RBV for 24 weeks
SVR12: LDV/SOF + RBV for 12 Weeks vs LDV/SOF for 24 Weeks in GT 1 Cirrhotics Who Previously Failed PI Based Triple Therapy

Safety Summary

- Only 2 AEs occurred at a higher frequency with LDV/SOF compared with placebo (comparison during first 12 weeks of placebo-controlled double blind portion)
  - Headache: 21% placebo vs 35% LDV/SOF
  - Fatigue: 4% placebo vs 17% LDV/SOF
Abstract #77

Treatment with Interferon (IFN) and Ribavirin (RBV)-Free Regimens with Ledipasvir (LDV) and Sofosbuvir (SOF) Improves Patient-Reported Outcomes (PRO) for Patients with Genotype 1 (GT1) Chronic Hepatitis C (CH-C): Results from the ION-1,2 and 3 Clinical Trials

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Background & Aims

- Patient reported outcomes (PROs) assessment can add to the efficacy data to capture the full impact of treatment on patients’ experience
- Patients with chronic hepatitis C have significant baseline PRO impairment
- This impairment worsens with PEG/RBV; however, the impact of IFN-free and RBV-free regimens on PROs has not been assessed
- Aim:
  - To assess PROs in the clinical trials of LDV/SOF with and without RBV (ION-1, ION-2 and ION-3)
Methods

• 4 validated instruments were used for assessment (CLDQ-HCV, SF-36, FACIT-F and WPAI:SHP)

• PRO scores compared between RBV-free and RBV-containing regimens

• Change in PRO scores were compared to patients own baseline

• Analysis included 1952 GT 1 subjects
Conclusions

• IFN-free and RBV-free LDV/SOF regimens are associated with significant improvement of PROs during treatment

• This improvement occurs as early as 2 weeks after the initiation of treatment

• This is the first treatment for HCV that shows improvement of PROs during treatment

• Achieving SVR12 is associated with significant PRO improvement
Abstract #83

Integrated Efficacy Analysis of Four Phase 3 Studies in HCV Genotype 1a-Infected Patients Treated with ABT-450/r/Ombitasvir and Dasabuvir With or Without Ribavirin

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8. Consultants for Clinical Research, Cincinnati, OH
9. St. James’s Hospital, Dublin, Ireland
10. Johns Hopkins University, Baltimore, MD
Background

The 3D regimen includes:

• ABT-450 - a potent NS3/4A protease inhibitor. Co-dosing of ABT-450 with ritonavir* (r; ABT-450/r) increases the peak, trough, and overall drug exposures of ABT-450

• Ombitasvir - a potent NS5A inhibitor

• Dasabuvir - a non-nucleoside NS5B polymerase inhibitor

Methods

- Patients infected with GT 1a in the PEARL-IV, SAPPHIRE-I, SAPPHIRE-II, or TURQUOISE-II trials
- 363/1058 (25%) of GT 1a treated patients had cirrhosis

SVR12 in GT 1a Non-cirrhotic Patients Treated with 3D Regimen for 12 Weeks (+/- RBV)

SVR12 in GT 1a Cirrhotic Patients Treated with 3D Regimen + RBV for 12 vs 24 Weeks

Logistic regression: IL28B TT, prior null, North American region and history of IDU were significant variables for not achieving SVR

Conclusions

- GT 1a patients without cirrhosis benefit from RBV inclusion in 12 week treatment regimen (SVR12=96%)

- GT 1a patients with cirrhosis achieved SVR12 rates >90% with 3D + RBV regimen
  - Difference between 12 and 24 week duration?

Abstract #81

TURQUOISE-II: Regimens of ABT-450/r/Ombitasvir and Dasabuvir With Ribavirin Achieve High SVR12 Rates in HCV Genotype 1-Infected Patients with Cirrhosis, Regardless of Baseline Characteristics

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Summary

• This multi-targeted, IFN-free regimen of ABT-450/r/ombitasvir and dasabuvir with RBV achieves high SVR12 rates across a broad range of treatment-naïve and treatment-experienced GT1 patients with cirrhosis, irrespective of most host, viral, or disease characteristics
  - 91.6% (239/261) GT1a patients achieved SVR12
  - 99.2% (118/119) GT1b patients achieved SVR12
• In a logistic regression, the only factors associated with a lower likelihood of SVR included GT1a, prior null response to PEG/RBV, and IL28B TT genotype
• Importantly, demographics (eg, age, gender, race, BMI, diabetes), viral factors (baseline HCV RNA), disease related factors (albumin, platelets) were not associated with lower SVR rates