Abstract GS-006

EXPEDITION-I: Efficacy and Safety of Glecaprevir/Pibrentasvir in Adults with Chronic Hepatitis C Virus Genotype 1, 2, 3, 4, 5 or 6 Infection and Compensated Cirrhosis

Xavier Forns* 1, Sam Lee 2, Joaquin Valdes 3, Sabela Lens 1, Reem Ghalib 4, Humberto Aguilar 5, Franco Felizarta 6, Tarek Hassanein 7, Holger Hinrichsen 8, Diego Rincon 9, Rosa Morillas 10, Stefan Zeuzem 11, Yves Horsmans 12, David Nelson 13, Yao Yu 3, Tami Pilot-Matias 3, Chih-Wei Lin 3, Federico Mensa 3

1. Liver Unit, Hospital Clinic, CIBEREHD, IDIBAPS, Barcelona, Spain
2. University of Calgary, Calgary, Canada
3. ABBVIE, North Chicago
4. Texas Digestive Disease Consultants, Arlington
5. Louisiana Research Center, LLC, Shreveport
6. Private Practice, Bakersfield
7. Southern California Liver Centers and Southern California Research Center, Coronado, United States
8. Gastroenterology-Hepatology Center Kiel, Kiel, Germany
9. Liver Unit, Hospital General Universitario Gregorio Marañón, Madrid
10. Liver Section and CIBERehd, Department of Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain
11. J.W. Goethe University, Frankfurt, Germany
12. Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium
13. Division of Gastroenterology, Hepatology and Nutrition, Department of Medicine, College of Medicine, University of Florida, Gainesville, United States
Next Generation Direct-Acting Antivirals

Glecaprevir (formerly ABT-493)
pangenotypic NS3/4A protease inhibitor

Pibrentasvir (formerly ABT-530)
pangenotypic NS5A inhibitor

**In vitro:**
- High barrier to resistance
- Potent against common NS3 polymorphisms (e.g., positions 80, 155, and 168) and NS5A polymorphisms (e.g., positions 28, 30, 31, and 93)
- Synergistic antiviral activity

**Clinical PK & metabolism:**
- Once-daily oral dosing
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is coformulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg;
Glecaprevir was identified by AbbVie and Enanta
EXPEDITION-1: Objective and Study Design

Objective
Evaluate the efficacy and safety of G/P for 12 weeks in patients with HCV GT1, 2, 4, 5 or 6 infection and compensated cirrhosis *

Open-Label Treatment
G/P is coformulated and dosed once daily as three 100 mg/40 mg plus for a total dose of 300 mg/120 mg.

Patients were enrolled at 40 study sites in Belgium, Canada, Germany, South Africa, Spain, and the United States

* GT3 patients with compensated cirrhosis enrolled in a separate study (SURVEYOR-II, part 3; n=40, 98% SVR12)
### Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>12-Week G/P N = 146</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>90 (62)</td>
</tr>
<tr>
<td>Age, median (range), years</td>
<td>60 (26-88)</td>
</tr>
<tr>
<td>White race, * n (%)</td>
<td>120 (82)</td>
</tr>
<tr>
<td>BMI, median (range), kg/m²</td>
<td>29 (18-55)</td>
</tr>
<tr>
<td>HCV genotype, n (%)†</td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>48 (33)</td>
</tr>
<tr>
<td>1b</td>
<td>39 (27)</td>
</tr>
<tr>
<td>2</td>
<td>34 (23)</td>
</tr>
<tr>
<td>4</td>
<td>16 (11)</td>
</tr>
<tr>
<td>5</td>
<td>2 (1)</td>
</tr>
<tr>
<td>6</td>
<td>7 (5)</td>
</tr>
</tbody>
</table>

G/P, glecaprevir/pibrentasvir; BMI, body mass index

* Race and ethnicity are self-reported
†Genotype determined by the Versant HCV Genotype Inno-LiPA Assay Version 2.0.
## Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>12-Week G/P N = 146</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV RNA</strong>, median (range) log(_{10}) IU/mL</td>
<td>6.1 (3.1–7.4)</td>
</tr>
<tr>
<td>Treatment-naïve</td>
<td>110 (75)</td>
</tr>
<tr>
<td>Treatment-experienced</td>
<td>36 (25)</td>
</tr>
<tr>
<td>IFN-based (IFN/pegIFN ± RBV)</td>
<td>25 (69)</td>
</tr>
<tr>
<td>SOF-based (SOF + RBV ± pegIFN)</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Platelet count &lt;100,000, 10(^9)/L</td>
<td>29 (20)</td>
</tr>
<tr>
<td>INR &lt;1.7</td>
<td>144 (99)</td>
</tr>
<tr>
<td>Total bilirubin ≥2, mg/dL</td>
<td>5 (3)</td>
</tr>
<tr>
<td>Albumin ≥ LLN</td>
<td>145 (99)</td>
</tr>
<tr>
<td>Child-Pugh score at screening</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>133 (91)</td>
</tr>
<tr>
<td>6</td>
<td>13 (9)</td>
</tr>
</tbody>
</table>

IFN, interferon; SOF, sofosbuvir; INR, international normalized ratio; LLN, lower limit of normal (33)

SVR12 by Intent-to-Treat (ITT) Analysis

- No treatment-emergent substitutions were present in NS3
- In NS5A, Y93N was present at baseline; Y93N, Q30R and H58D were present at the time of failure

*Patient with HCV GT1a infection relapsed at PTW8
Abstract PS-095

Real World Experience with Elbasvir/Grazoprevir in the Veterans Affairs Healthcare System

Jennifer R. Kramer¹,², Amy Puenpatom³, Kevin Erickson¹,², Yumei Cao², Hashem El-Serag¹,², Fasiha Kanwal¹,²

1. Department of Medicine, Baylor College of Medicine
2. Center for Innovations in Quality, Effectiveness and Safety, Michael E. DeBakey VA Medical Center, Houston, TX
3. Center for Observational and Real-World Evidence, Merck Sharp & Dohme Corp., Kenilworth, NJ, United States
Methods

• Nationwide retrospective observational cohort study of HCV patients seen at the US Department of Veterans Affairs (VA) using the VA Corporate Data Warehouse (includes laboratory, pharmacy, hospitalizations, and clinical diagnoses).

• The study population included patients with positive HCV RNA who received EBR/GRZ from January-July 2016.

• Examined demographic, virologic, and clinical characteristics, overall and by CKD stage estimated from the most recent estimated glomerular filtration rate (eGFR).

• Chi-square test was used to examine differences by CKD stage.

Results

- 95.6% (2,328/2,436) in the evaluable population achieved SVR.
- The SVR rates by genotype (GT): all GT1, 95.4% (2218/2324); GT1a, 93.4% (788/844); GT1b, 96.6% (1379/1428); and GT4, 96.9% (62/64).
- The SVR rates by baseline viral load (BVL) were as follows: BVL greater than 800,000 IU/ml, 94.7% (1497/1580); and BVL less than or equal to 800,000 IU/ml, 97.3% (726/746).
- SVR rates by baseline patient characteristics were as follows:
  - Male, 95.5% (2,245/2,350); female, 96.5 percent (83/86);
  - African American, 95.9% (1,342/1,400); Hispanic, 95.1% (77/81); White, 95.0% (783/824);
  - Previously untreated, 96.1% (1,910/1,988); treatment-experienced, 93.8% (418/448);
  - Cirrhosis, 95.5% (772/808); without cirrhosis, 95.6% (1556/1628);
  - Stage 3 chronic kidney disease (CKD) (eGFR 30 to 59 mL/min/1.73m$^2$), 96.7% (380/393); stage 4-5 CKD (eGFR less than 30 mL/min/1.73m$^2$), 96.3% (392/407);
  - HIV positive, 98.6% (73/74); HIV negative, 95.5% (2255/2362);
  - History of alcohol abuse, 95.9% (1412/1473); no history of alcohol abuse, 95.1% (916/963);
  - History of drug abuse, 95.3 % (1251/1313); no history of drug abuse, 95.9% (1077/1123).
Abstract PS-096

Long-Term Follow-up After IFN-Free Therapy of Advanced HCV-Associated Liver Cirrhosis: Continued Improvement of Liver Function Parameters – Results from the German Hepatitis C-Registry (DHC-R)

Katja Deterding¹, Stefan Mauss², Anita Pathil³, Peter Buggisch⁴, Eckart Schott⁵, Markus Cornberg¹, Tim Zimmermann⁶, Karl-Georg Simon⁷, Hartwig Klinker⁸, Rainer Günther⁴, Heike Pfeiffer-Vornkahl¹⁰, Dietrich Hueppe¹¹, Christoph Sarrazin¹², Stefan Zeuzem¹³, Michael P. Manns¹, Heiner Wedemeyer¹, Thomas Berg¹⁴, German Hepatitis C-Registry¹⁵

1. Hannover Medical School, Hannover
2. Center for HIV and Hepatogastroenterology, Düsseldorf
3. Internal Medicine IV, Gastroenterology and Hepatology, University Clinic of Heidelberg, Heidelberg
4. ifi-Institute for Interdisciplinary Medicine, Hamburg
5. Charité Campus Virchow-Klinikum (CVK), Berlin
6. University Hospital Mainz, Mainz
7. MVZ Dres. Eisenbach, Simon, Schwarz GbR, Leverkusen
8. University Hospital Würzburg, Würzburg
9. Department of Internal Medicine I, UK S-H, Campus Kiel, Kiel
10. e.factum GmbH, Butzbach
11. Center of Gastroenterology, Herne
12. St. Josef-Hospital, Wiesbaden
13. University Hospital Frankfurt, Frankfurt
14. University Hospital Leipzig, Leipzig
15. Leberstiftungs-GmbH Deutschland, Hannover, Germany
Methods

• The DHC-R (German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients recruited by more than 250 centers including both specialists in private practice as well as academic centers.

• Patients are treated at the discretion of the physician.

• Advanced liver cirrhosis was defined by presence of at least one of the following criteria: FibroScan $>20$ kPa, thrombocytes $<90,000/\mu l$, albumin $<35$ g/l or signs of liver decompensation.

Results

- Advanced liver cirrhosis was present in 974 patients; follow-up data after therapy were available for 863 patients.

- Child-Pugh classification revealed 69.9% class A (n = 680), 13.7% class B (n = 133) and 1.7% class C (n = 17).

- Most patients were infected with HCV-genotype 1 (n = 743). Patients received a variety of different treatment regimens with (n = 512) or without (n = 462) ribavirin.

- Overall, SVR was achieved in 88.3% of the patients.

- 96 serious adverse events were reported, 40 of these were liver related.

- De novo HCCs were reported in 12 patients during treatment and follow-up.

- Overall, 9 patients died during treatment and follow-up (8 due to liver related events).

- Liver function and portal hypertension parameters including albumin, bilirubin and platelet counts all improved in most patients during and after antiviral therapy.

- Factors associated with disease progression (defined as increase in MELD by 3 or more points, variceal bleeding, ascites, encephalopathy, liver transplantation or death) were Child Pugh Score and non-response to antiviral treatment while exposure to HCV protease inhibitors or ribavirin were not associated with decompensation.

Conclusions

• This analysis of a large real-world-cohort of patients with clinically advanced liver cirrhosis confirmed the efficacy of currently available antiviral treatment options in compensated and decompensated disease.

• The continued improvement of liver function parameters and portal hypertension justifies antiviral therapy – even though parameters associated with clinical disease progression should be considered.

Abstract PS-102

Utilization of Sofosbuvir/Velpatasvir in Genotype 2-6 HCV: Real-World Experience from the TRIO Network

Michael Curry*, 1, Bruce Bacon2, Douglas Dieterich3, Steven Flamm4, Kris Kowdley5, Scott Milligan6, Naoky Tsai7, Zobair Younossi8, Nezam Afdhal1

1. Beth Israel Deaconess Medical Center, Boston
2. Saint Louis University School of Medicine, Saint Louis
3. Icahn School of Medicine at Mount Sinai, New York
4. Northwestern University Feinberg School of Medicine, Chicago
5. Liver Care Network, Swedish Medical Center, Seattle
6. Trio Health Analytics, LaJolla
7. Queens Medical Center, University of Hawaii, Honolulu
8. Department of Medicine, Center for Liver Diseases, Inova Fairfax, Falls Church, United States
Study Data

Inclusion criteria:
- 18 year or older patients
- Not enrolled in a clinical trial
- Initiated anti-HCV therapy in 2016
- GT2-6 HCV

Data collection as of Mar 1 2017

Representation from 40 US states and DC

Majority of care in community practice

<table>
<thead>
<tr>
<th>Metric</th>
<th>Academic</th>
<th>Community</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>338</td>
<td>1489</td>
<td>1827</td>
</tr>
<tr>
<td>Physicians</td>
<td>111</td>
<td>652</td>
<td>763</td>
</tr>
</tbody>
</table>
Per Protocol SVR12
SOF + RBV and SOF-VE +/- RBV for Genotype 2 HCV

Per Protocol SVR12

DCV + SOF +/- RBV and SOF-VEL +/- RBV for Genotype 3 HCV

Patient Disposition
LDV-SOF +/- RBV and SOF-VEL +/- RBV for Genotype 4-6 HCV

LDV-SOF +/- RBV n=204 (113 GT4, 1 GT5, 90 GT6)
- In therapy n=2
- Discontinued n=1
- LTFU n=11
- Death n=2
- Completed Therapy n=188
  - SVR Pending n=53
  - SVR Not Achieved n=8
  - SVR Achieved n=127

SOF-VEL +/- RBV n=38 (13 GT4, 25 GT6)
- In therapy n=1
- Discontinued n=2
- LTFU n=0
- Death n=0
- Completed Therapy n=35
  - SVR Pending n=24
  - SVR Not Achieved n=1
  - SVR Achieved n=10

SVR (PP): 94% (127/135)
SVR (PP): 91% (10/11)

Abstract PS-097

Sustained Virological Response for 94% of People Treated with Low-Cost, Legally Imported Generic Direct Acting Antivirals for Hepatitis C: Analysis of 1087 Patients in 4 Treatment Programmes

James Freeman¹, Giten Khwairakpam², Julia Dragunova³, Sergey Golovin³, James Wang⁴, Andrew Hill⁵, Vicky Houghton-Price⁶, Rachel Smith⁶, Roxanna Korologou-Linden⁷, Greg Jefferys⁸

1. GP2U Telehealth FixHepC, Hobart, Australia
2. TREAT Asia/amfAR, Bangkok, Thailand
3. International Treatment Preparedness Coalition Russia, St Petersburg, Russia
4. Ci Run Health Information Consulting Co. Ltd, Kunming, China
5. St Stephens AIDS Trust
6. METAIVIROLOGY LTD
7. Faculty of Medicine, Imperial College London, London, United Kingdom
8. University of Tasmania, Hobart, Australia
Background and Aims

• High prices of branded DAAs prevent universal access to treatment in most countries. However, 12-weeks of generic sofosbuvir/daclatasvir (SOF/DCV) can be purchased for US$450 in India or Bangladesh.

• Several generic DAAs have been approved by international donor agencies, meeting quality control standards.

Methods

• Generic versions of sofosbuvir (SOF), ledipasvir (LDV), daclatasvir (DCV) and velpatasvir were sourced from generic suppliers in India, Bangladesh, Egypt and China.

• Four treatment access programmes in Russia, South East Asia and Australia were included in the analysis.

• The choice of DAAs and treatment length were determined from baseline HCV genotype and stage of fibrosis.

• This analysis includes available data from 1087 patients being monitored in hospitals, private doctors and clinics in 42 countries worldwide.

Results

• 1087 patients were treated; 524 received SOF/DCV, 462 SOF/LDV, 99 received SOF/RBV, 1 received SOF/VEL and 1 received SOF/LDV/DCV. The median length of treatment was 12 weeks.

• Overall, the patients were 60% male with a mean age of 43.7 years; 56% were Genotype 1 and the mean baseline HCV RNA was 6.9 log IU/mL.

<table>
<thead>
<tr>
<th></th>
<th>SOF/RBV</th>
<th>SOF/LDV (+/- RBV)</th>
<th>SOF/DCV (+/- RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVR</td>
<td>52/58 (90%)</td>
<td>208/252 (83%)</td>
<td>253/300 (84%)</td>
</tr>
<tr>
<td>EOT</td>
<td>42/42 (98%)</td>
<td>293/299 (98%)</td>
<td>298/302 (99%)</td>
</tr>
<tr>
<td>SVR4</td>
<td>31/31 (100%)</td>
<td>235/249 (94%)</td>
<td>224/241 (99%)</td>
</tr>
<tr>
<td>SVR12</td>
<td>21/23 (91%)</td>
<td>194/212 (92%)</td>
<td>184/213 (86%)</td>
</tr>
</tbody>
</table>

Abstract PS-098

Ledipasvir/Sofosbuvir for 12 Weeks Is Safe and Effective in Patients with Chronic Hepatitis C and Hepatitis B Coinfection: A Phase 3 Study in Taiwan


E-mail: benedetta.massetto@gilead.com

1. Graduate Institute of Clinical Medicine, Hepatitis Research Center and Department of Internal Medicine, National Taiwan University College of Medicine and Hospital, Taipei
2. Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung
3. Chang Gung Memorial Hospital (CGMH), Taoyuan
4. Mackay Memorial Hospital, Taipei
5. Chia-Yi Christian Hospital
6. Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Chia-Yi
7. National Cheng Kung University Hospital, Tainan, Taiwan
8. Gilead Sc., Foster City, United States
9. Chang Gung Memorial Hospital (CGMH), Kaohsiung
10. Changhua Christian Hospital, Changhua
11. E-DA Hospital, Kaohsiung
12. Taipei Veterans General Hospital, Taipei
13. Chi Mei Hospital, Tainan
14. China Medical University Hospital, Taichung
15. Chang Gung Memorial Hospital, Keelung
16. National Taiwan University College of Medicine and Hospital, Taipei, Taiwan
Background and Aims

• Patients coinfected with HCV/HBV have more rapid liver disease progression and worse outcomes than patients monoinfected with either HBV or HCV.

• Taiwan has among the highest prevalence of chronic HCV/HBV coinfection in Southeast Asia.

• In Taiwan the standard of care for HCV/HBV coinfection is PEG/RBV for 24 or 48 weeks.

• This study evaluated the safety and efficacy of an all-oral treatment with ledipasvir (LDV)/sofosbuvir (SOF) for 12 weeks in patients with chronic HCV and HBV coinfection.

Methods

• Patients with or without compensated cirrhosis chronically infected with HCV GT1 or GT2 and HBV (positive for serum HBsAg) not currently receiving HBV treatment were enrolled into this open-label, ongoing study to receive LDV 90 mg/SOF 400 mg (once daily) for 12 weeks.

• HBV DNA was monitored at all study visits during treatment.

• The start of HBV treatment was based on the APASL guidelines.
Results

- A total of 111 patients (68 [61%] with GT1 and 43 [39%] with GT2) were enrolled and treated. The majority were female (62%), treatment naive (67%), and non-cirrhotic (85%), with a mean age of 55 years (range 32-76) and mean BMI of 24.5 kg/m2 (range 17.3-33.8). All but one were HBeAg negative.

- SVR12 = 100%

- HBV reactivation: 63%

- ALT elevations: 5%

- 2% started HBV therapy

- No patients discontinued treatment due to adverse events (AEs).

- Three patients had serious AEs, one each of optic neuritis, post procedural bleeding and duodenal ulcer bleeding; none was considered drug related. The most common AEs reported (≥5% of patients) were headache, upper respiratory infection, and fatigue.
Abstract PS-032

HCV Eradication Reduces the Occurrence of Major Adverse Cardiovascular Events in Hepatitis C Cirrhotic Patients: Data from the Prospective ANRS CO12 CirVir Cohort

Patrice Cacoub¹, Pierre Nahon², Richard Layese³, Valérie Bourcier⁴, Carole Cagnot⁴, Patrick Marcellin⁵, Dominique Guyader⁶, Stanislas Pol⁷, Dominique Larrey⁸, Françoise Roudot-Thoraval⁹, Etienne Audureau⁸ and ANRS CO12 CirVir group

1. Internal Medicine, CHU Pitié-Salpêtrière, Paris
2. Hepatology, CHU Bondy, Bondy
3. Santé Publique, CHU Henri Mondor, Créteil
4. ANRS, Paris
5. Hepatology, CHU Beaujon, Clichy
6. CHU Rennes, Rennes
7. CHU Cochin, Paris
8. CHU Montpellier, Montpellier
9. CHU Henri Mondor, Créteil, France
Methods

- 878 patients with the following inclusion criteria were enrolled in 35 French centres between 2006 and 2012:
  - Biopsy-proven HCV cirrhosis
  - Child-Pugh A
  - Positive viremia (B or C)
  - No prior liver complication
- All patients received HCV treatment after inclusion.
- Major adverse cardiovascular events (MACE) included stroke, myocardial infarction, ischemic heart disease, heart failure, peripheral arterial disease, cardiac arrest, and cardiovascular death.
The ANRS CO12 CirVir Cohort: Inclusion Criteria – Design

- Biopsy-proven, Child-Pugh A cirrhosis
- HCV- or HBV-related cirrhosis
  - Anti-HCV+ or Ag HBs +
- Absence of previous decompensation or hepatocellular carcinoma (HCC)

Inclusions: n=1822

FOLLOW-UP
Median: 51.5 months
March 2006 – June 2012
January 2015
End Point

62 out of 878 (7.1%) Patients Presented with a Total of 79 Major Adverse Cardiovascular Events

<table>
<thead>
<tr>
<th>Cardiovascular Event</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>23</td>
</tr>
<tr>
<td>Stroke</td>
<td>16</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>12</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>9</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>8</td>
</tr>
<tr>
<td>Cardiovascular deaths</td>
<td>7</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>4</td>
</tr>
</tbody>
</table>

The analysis of heterogeneity of characteristics and outcome by center size (≤ 10 patients vs. >10 patients enrolled) did not reveal any significant differences across centers.

Predictors of Major Adverse Cardiovascular Events in Patients with Compensated HCV-Related Cirrhosis

(\textit{multivariate Cox proportional hazards model})

<table>
<thead>
<tr>
<th>Features</th>
<th>HR</th>
<th>95% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial hypertension</td>
<td>3.24</td>
<td>[1.78; 5.91]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tobacco consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>Ref</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Past</td>
<td>1.75</td>
<td>[0.76; 3.91]</td>
<td>0.18</td>
</tr>
<tr>
<td>Ongoing</td>
<td>4.20</td>
<td>[2.11; 8.64]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ethnic Origin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EUR</td>
<td>Ref</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AFR</td>
<td>1.14</td>
<td>[0.36; 2.80]</td>
<td>0.80</td>
</tr>
<tr>
<td>EAS</td>
<td>9.20</td>
<td>[2.46; 24.95]</td>
<td>0.003</td>
</tr>
<tr>
<td>Serum Albumin ≤35 g/L</td>
<td>2.78</td>
<td>[1.30; 5.56]</td>
<td>0.009</td>
</tr>
<tr>
<td>SVR*</td>
<td>0.35</td>
<td>[0.09; 0.97]</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Compensated HCV-Related Cirrhotic Patients with SVR Showed Lower Incidence of Major Adverse Cardiovascular Events (MACE)

Occurrence of Hepatocellular Carcinoma in Patients with Hepatitis C Virus Related Liver Disease Treated with Direct-acting Antivirals

Vincenza Calvaruso* 1, Giuseppe Cabibbo1, Irene Cacciola2, Salvatore Petta1, Salvatore Madonia1, Alessandro Bellia3, Marco Di Stefano4, Lydia Giannitrapani1, Fabio Tiné1, Antonio Magro5, Antonio Davi6, Licia Larocca3, Annalisa Ardiri3, Antonio Digiacomo7, Maria Gussio3, Luigi Guarneri8, Ignazio Scalis9, Giovanni Mazzola1, Fabio Cartabellootta1, Francesca Savalli10, Maurizio Russello3, Gaetano Scifo4, Giovanni Squadrito2, Calogero Cammà1, Giovanni Raimondo2, Antonio Craxi1, Vito Di Marco1 and RESIST-HCV (Rete Sicilia Selezione Terapia - HCV)

Email: giuseppe.cabibbo78@gmail.com

1. RESIST-HCV, Palermo
2. RESIST-HCV, Messina
3. RESIST-HCV, Catania
4. RESIST-HCV, Siracusa
5. RESIST-HCV, Agrigento
6. RESIST-HCV, Modica
7. RESIST-HCV, Comiso
8. RESIST-HCV, Enna
9. RESIST-HCV, Castelvetrano
10. RESIST-HCV, Trapani, Italy
Methods

• Between 3/2015 and 10/2016, the RESIST-HCV database included 10,123 patients with HCV chronic liver disease of which 5,130 started treatment.

• Each physician established DAA regimen and use of RBV and performed HCC surveillance as indicated by guidelines before and after treatment.

• Evaluated HCC occurrence in 3,447 patients who concluded DAA treatment.

• The primary endpoints of this analysis were the time to HCC occurrence from start of DAA and the pattern of HCC at the diagnosis.

Results

- Patients had a mean age of 64.3 years, 58% were males and 47% were naïve to antiviral therapy.

- 2363 patients (68.6%) had Child-Pugh A cirrhosis and 320 patients (9.2%) had Child-Pugh B cirrhosis.

- Diabetes was present in 802 patients (23%).

- Ribavirin was used in 1577 patients (45.7%)

- Treatment duration: 63.7% received 12 week DAA regimen and 36.3% received 24 week DAA regimen.
Results (Cont.)

• During the observation (mean 34.2 weeks, range 8-72) 55 patients developed HCC with an overall rate of 1.44%.

• The occurrence of HCC was 0.13%, 1.69% and 4.37% in non-cirrhotics, Child-Pugh A cirrhosis and Child-Pugh B cirrhosis, respectively ($p < 0.001$).

• At the time of HCC diagnosis, 49 patients (89.1%) meet Milan criteria and 6 patients (10.9%) were Milan-out.

• The rate of HCC occurrence was 1.48% (26/1752) in patients who achieved SVR and 4.0% (10/249) in patients who maintained HCV viremia ($p = 0.0089$).

Identifying Residual Risk of Hepatocellular Carcinoma Following Hepatitis C Virus Eradication in Compensated Cirrhosis: Decision-tree and Random Forest Models Developed in the French Multicenter Prospective ANRS CO12 CirVir Cohort

Etienne Audureau* 1, Valérie Bourcier2, Richard Layese1, Carole Cagno3, Patrick Marcellin4, Dominique Guyader5, Stanislas Pol6, Dominique Larrey7, Françoise Roudot-Thoraval8, Pierre Nahon2 and ANRS CO12 CirVir group

1. Public Health, CHU Henri Mondor, Créteil
2. Hepatology, CHU Bondy, Bondy
3. ANRS, Paris
4. Hepatology, CHU Beaujon, Clichy
5. Hepatology, CHU Rennes, Rennes
6. Hepatology, CHU Cochin, Paris
7. Hepatology, CHU Montpellier, Montpellier
8. CHU Henri Mondor, Créteil, France
Methods

- Data were collected from 1253 patients with compensated biopsy-proven HCV-cirrhosis recruited in 35 centres and prospectively followed-up.
- During a median follow-up of 54.2 months, 179 (14.3%) patients developed HCC and 637 (50.8%) achieved SVR.
- SVR is most important variable for predicting HCC.
- 5 additional variables independently associated with occurrence of HCC:
  - Age>50 years
  - Past excessive alcohol intake
  - Low platelet count
  - Increased AFP and GGT serum levels

Figure. Decision Tree from CART Survival Analysis

AFP: Alpha-fetoprotein; GGT: Gamma-Glutamyl Transpeptidase; PT: Prothrombin Time; SVR: Sustained Virological Response

Conclusions

• Risk factors for hepatocarcinogenesis differ according to SVR status.

• In patients with compensated cirrhosis, HCV eradication should be achieved before the onset of liver function impairment and HCC surveillance be implemented after 50 years in all cases following SVR.

Among Cirrhotic Patients with a Hepatitis C Sustained Viral Response, the Risk of De-Novo Hepatocellular Carcinoma Relates to Baseline Factors and Not the Use of Direct Acting Antivirals: Results from a Nationwide Cohort

Hamish Innes* 1, Stephen T. Barclay2, Peter C. Hayes3, Andrew Fraser4, John F. Dillon5, Adrian Stanley2, Andy Bathgate3, Scott McDonald1, David Goldberg6, Heather Valerio1, Ray Fox7, Nick Kennedy8, Pete Bramley9, Sharon J. Hutchinson1

Email: hamish.innes@nhs.net

1. School of Health and Life Sciences, Glasgow Caledonian University
2. Glasgow Royal Infirmary, Glasgow
3. Royal Infirmary Edinburgh, Edinburgh
4. Aberdeen Royal Infirmary, Aberdeen
5. Ninewells Hospital and Medical School, Dundee
6. Health Protection Scotland
7. The Brownlee Centre, Glasgow
8. Monklands Hospital, Lanarkshire
9. Stirling Royal Infirmary, Stirling, United Kingdom
### Background

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal, Year</th>
<th>Recurrence or Occurrence?</th>
<th>Country, Setting</th>
<th>Sample</th>
<th>Frequency of HCC Occurrence/Recurrence</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reig, et al</td>
<td><em>J Hepatol</em>, 2016</td>
<td>Recurrence</td>
<td>4 referral hospitals, Spain</td>
<td>Treated with IFN-free regimen after successfully treated HCC, N=59</td>
<td>28% after median follow-up of 5.7 months</td>
<td>None</td>
</tr>
<tr>
<td>Conti, et al</td>
<td><em>J Hepatol</em>, 2016</td>
<td>Recurrence</td>
<td>Liver clinics in Bologna, Italy</td>
<td>Treated with IFN-free regimen after successfully treated HCC, N=58</td>
<td>29% by 24 weeks post-treatment follow-up</td>
<td>None</td>
</tr>
<tr>
<td>Conti, et al</td>
<td><em>J Hepatol</em>, 2016</td>
<td>Occurrence</td>
<td>Liver clinics in Bologna, Italy</td>
<td>Cirrhotic patients treated with IFN-free therapy, N=285</td>
<td>3.2% HCC occurrence by 24 weeks post treatment follow-up</td>
<td>None</td>
</tr>
<tr>
<td>Cardoso, et al</td>
<td><em>J Hepatol</em>, 2016</td>
<td>Occurrence</td>
<td>One clinic in Portugal</td>
<td>Cirrhotic patients achieving SVR via IFN-free therapy, N=54</td>
<td>7.4% after median 12 months follow-up</td>
<td>None</td>
</tr>
</tbody>
</table>

Methods: Study Fundamentals

• Retrospective cohort study using
  - Scottish HCV clinical database (downloads @ April 2016)
  - Subsequent medical chart review (carried out February–March 2017)

• Definition of study cohort
  - Inclusion criteria
    • SVR attainment in 1997–2016
    • Liver cirrhosis at time of starting treatment
  - Exclusion criteria
    • Diagnosis of HCC prior to treatment
    • HBV/HIV co-infection
    • Attendance at a clinic with incomplete database or otherwise not able to participate in medical chart review

Methods: Study Fundamentals

• Primary outcome event: first time diagnosis of HCC by cross-sectional imaging or biopsy

• Wide range of baseline patient characteristics extracted:
  – Age; gender; ethnicity; postcode deprivation score; Child Pugh score; thrombocytopenia; alphafetoprotein; diabetes; alcohol history; smoking history; drug use history; prior genotype; clinic attended; number of prior treatment failures

• Survival analysis approach adopted
  – Start time=commencement of treatment
  – Stop time=earliest of: HCC occurrence; death; or reaching 31 Jan 2017.
  – Used Cox regression to assess univariate and multivariate association between regimen (IFN-free Vs. IFN-containing) and HCC.

# Results: Baseline Description of the Cohort (N=857)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% of Cohort (N=857)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Average age</td>
<td>Mean: 49 years (sd: 8)</td>
</tr>
<tr>
<td>White ethnicity</td>
<td>92%</td>
</tr>
<tr>
<td>Male gender</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Health Behaviours</strong></td>
<td></td>
</tr>
<tr>
<td>History of heavy alcohol use</td>
<td>44%</td>
</tr>
<tr>
<td>Current tobacco smoker</td>
<td>73%</td>
</tr>
<tr>
<td>History of intravenous drug use</td>
<td>70%</td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;100/ 10^9 /L)</td>
<td>28%</td>
</tr>
<tr>
<td>Child Pugh B/C</td>
<td>15%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Treatment experienced</td>
<td>35%</td>
</tr>
<tr>
<td>IFN-free regimen</td>
<td>32%</td>
</tr>
</tbody>
</table>

# Key Differences in Characteristics IFN-Containing Patients and IFN-Free Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Regimen</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IFN-containing (N=585)</td>
<td>IFN-free (N=272)</td>
</tr>
<tr>
<td>Mean age</td>
<td>48.1 years</td>
<td>52.1 years</td>
</tr>
<tr>
<td>Thrombocytopenic (&lt;100 per 10^9/L)</td>
<td>22%</td>
<td>39%</td>
</tr>
<tr>
<td>Child Pugh B or C</td>
<td>9%</td>
<td>30%</td>
</tr>
<tr>
<td>Number of prior failed treatment episodes</td>
<td>0 73% 48%</td>
<td>1 21% 35%</td>
</tr>
</tbody>
</table>

## Follow-up Time and Outcome Events, by Treatment Regimen

<table>
<thead>
<tr>
<th>Regimen</th>
<th>IFN-containing (N=585)</th>
<th>IFN-free (N=272)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up, person years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2697</td>
<td>475</td>
</tr>
<tr>
<td>Median per patient (IQR)</td>
<td>3.5 (2.2-5.6)</td>
<td>1.7 (1.4-2.0)</td>
</tr>
<tr>
<td>Outcome events (i.e. HCC occurrence)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total #</td>
<td>34</td>
<td>12</td>
</tr>
<tr>
<td># occurring &lt;24 weeks post-treatment</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td># occurring ≥24 weeks post-treatment</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Median time to event (min-max range)</td>
<td>2.5 yrs (0.3-8.5)</td>
<td>0.9 yrs (0.5-2.0)</td>
</tr>
<tr>
<td>Crude rate, per 100 persons years</td>
<td>1.26</td>
<td>2.52</td>
</tr>
</tbody>
</table>

Patient Characteristics Associated with HCC Occurrence in Univariate Analysis

- **Hazard Ratio**
- **IFN-Free**: No, Yes
- **Age, Years**: <40, 40-49, 50-59, 60+
- **Child-Pugh**: A, B/C
- **Thrombocyt Openia**: No, Yes
- **# Prior Treatment Episodes**: 0, 1, 2

Association Between IFN-Free Versus IFN-Containing Therapy and HCC Occurrence, in Univariate and Multivariate Analysis

* Multivariate analysis includes adjustment for: age, gender, ethnicity, Child Pugh score, thrombocytopenia, alpha-fetoprotein, genotype, treatment experience, and clinic location.

Conclusions

1. There is no evidence that IFN-free therapy increases the risk of HCC occurrence in patients achieving an SVR

2. Baseline characteristics of patients treated with IFN-free regimens differ from those treated with IFN-containing regimens

3. Multivariate analysis demonstrated that the risk of HCC occurrence was equivalent between these two groups of patients

This enduring activity is supported by educational grants from AbbVie and Gilead Sciences, Inc.