The International Liver Congress™ 2016
Press Conference

14 April, 2016
Chair: Dr Laurent Castera
EASL Secretary General
Introductions and welcome

Dr Laurent Castera, EASL Secretary General
Housekeeping

• Please turn your mobile phones onto silent

• Please hold questions until the Q&A at the end of the session

• Photos are permitted in this press conference

• In the event of a fire, please go to the nearest fire exit
<table>
<thead>
<tr>
<th>Content</th>
<th>Abstract</th>
<th>Speaker</th>
<th>Time</th>
<th>Embargo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welcome and official opening of ILC 2016 press conference</td>
<td></td>
<td>Dr Laurent Castera</td>
<td>08:00</td>
<td></td>
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<tr>
<td>Impact of direct anti-viral agents on inactivation/de-listing of liver transplant candidates listed for decompensated C cirrhosis: a European study</td>
<td>PS036</td>
<td>Dr Luca Belli</td>
<td>08:10</td>
<td>Thu 14 April 07.00 CET</td>
</tr>
<tr>
<td>High sustained virological response rates using generic direct acting antiviral treatment for Hepatitis C, imported into Australia</td>
<td>LB03</td>
<td>Dr James Freeman</td>
<td>08:20</td>
<td>Sat 16 April 07:00 CET</td>
</tr>
<tr>
<td>A genome-wide association study identifies <em>PNPLA3</em> and <em>SLC38A4</em> as risk loci for alcoholic hepatitis</td>
<td>GS03</td>
<td>Dr Stephen Atkinson</td>
<td>08:30</td>
<td>Thu 14 April 07:00 CET</td>
</tr>
<tr>
<td>Development of hepatocellular carcinoma in HCV cirrhotic patients treated with direct acting antivirals</td>
<td>LBP506</td>
<td>Professor Stefano Brillanti</td>
<td>08:40</td>
<td>Wed 13 April 07:00 CET</td>
</tr>
<tr>
<td>Question and answer session &amp; closing remarks</td>
<td></td>
<td>All authors &amp; Professor Laurent Castera</td>
<td>08:50</td>
<td></td>
</tr>
<tr>
<td>Session close</td>
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<td>09:00</td>
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</table>
Impact of direct anti-viral agents on inactivation/de-listing of liver transplant candidates listed for decompensated C cirrhosis: A European study

Dr Luca Belli, Niguarda Hospital Milan, Italy
Abstract number: PS036
Impact of direct anti-viral agents on inactivation/de-listing of liver transplant candidates listed for decompensated C cirrhosis: a European study

study promoted by ELITA

Luca S Belli
SC Epatologia e Gastroenterologia
Ospedale Niguarda
MILANO.

ILC, Barcelona, 14 April 2016
Background

All oral Direct-Acting Antivirals have been shown to improve the liver function of patients with decompensated cirrhosis but it is presently unknown whether this clinical improvement may lead to the delisting of some patients.

M Charlton et al. SOLAR 1 study. Gastroenterology 2015
Patients and methods

11 European Centres*
134 consecutive patients with decompensated cirrhosis w/o HCC listed for LT between Feb 2014 and Feb 2015

103 were treated with DAAs while listed.
   52/103 single DAA (SOF/RBV)
   51/103 dual DAAs (SOF/DCV or SOF/LDV)

31 were not treated
   Too close to LT  →  21 patients (MELD > 25 → 13  MELD 18-24 → 8)
   Pre-emptive protocol  →  6 patients
   Other reasons  →  4

Median follow up with or w/o LT  →  52 weeks

**Parigi Mondor, Parigi Paul Brousse, Montpellier, Vienna, Valencia, Torino, Bologna, Mi Niguarda, Mi Policlinico, Bergamo, Palermo.**
End points & definitions

End-points

Primary end point: Probability do be inactivated and then delisted

- **Inactivated** → patient is placed “on hold” due to clinical improvement.

- **Delisted** → patient is off the list after a variable period of inactivation.

Secondary end points:

- Virological efficacy
- Description of criteria taken into account by the investigators for considering inactivation/delisting
- Predictors of inactivation
RESULTS
End points

- **Primary end point**: Probability do be inactivated and then delisted
- **Secondary end points**:
  - Virological efficacy
  - Description of criteria taken into account by the investigators for considering inactivation/delisting
  - Predictors of inactivation/delisting
Competing risk analysis of “treated patients”

Inactivated

Delisted

A

B

At risk

0

103

100

72

47

60

29

11

3

2

1

0

Weeks

0

12

24

36

48

60

72

84

96

108

Cumulative Incidence (%)
End points

- **Primary end point:** Probability do be inactivated and then delisted

- **Secondary end points:**
  - Virological efficacy
  - Description of criteria taken into account by the investigators for considering inactivation.
  - Predictors of inactivation/delisting
## Delta MELD, Child Pugh and albumin after 24 weeks

<table>
<thead>
<tr>
<th></th>
<th><strong>Non inactivated</strong></th>
<th><strong>Inactivated</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>67 patients</strong></td>
<td><strong>34 patients</strong></td>
</tr>
<tr>
<td>MELD at start of therapy</td>
<td>16 (14-19)</td>
<td>14 (12-16)</td>
</tr>
<tr>
<td>MELD after 24 weeks</td>
<td>16 (13-19)</td>
<td>11 (9-13)</td>
</tr>
<tr>
<td><strong>Delta MELD</strong></td>
<td>0 (-2-2)</td>
<td><strong>-3.3 points (-5--1)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p&lt;0.0001</strong></td>
</tr>
<tr>
<td>CPT at start of therapy</td>
<td>10 (9-10)</td>
<td>9 (8-10)</td>
</tr>
<tr>
<td>CPT after 24 weeks</td>
<td>9 (8-11)</td>
<td>7 (6-7)</td>
</tr>
<tr>
<td><strong>Delta CPT</strong></td>
<td>0 (-1-1)</td>
<td><strong>-2 points (-4--1)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p&lt;0.0001</strong></td>
</tr>
<tr>
<td>Albumin at start of therapy g/dL</td>
<td>3 (2.8-3.3)</td>
<td>3.1 (2.8-3.55)</td>
</tr>
<tr>
<td>Albumin at 24 weeks d/dL</td>
<td>3.1 (2.8-3.5)</td>
<td>3.5 (3.35-4.3)</td>
</tr>
<tr>
<td><strong>Delta Albumin</strong></td>
<td>0.1 (-0.1-0.4)</td>
<td><strong>+ 0.5 g/dL (0.25-0.85)</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>p&lt;0.0002</strong></td>
</tr>
</tbody>
</table>
## Change of ascites and HE after 24 weeks in 34 inactivated patients

<table>
<thead>
<tr>
<th>Ascites at start of therapy</th>
<th>Ascites after 24 weeks</th>
<th>Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>16 (47)</td>
<td></td>
</tr>
<tr>
<td>2*</td>
<td>18 (53)</td>
<td></td>
</tr>
<tr>
<td>3*</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Total N (%)</td>
<td>7 (20)</td>
<td>19 (54)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HE at start of therapy</th>
<th>HE after 24 weeks</th>
<th>Total N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>31 (91)</td>
<td></td>
</tr>
<tr>
<td>2*</td>
<td>3 (9)</td>
<td></td>
</tr>
<tr>
<td>3*</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Total N (%)</td>
<td>21 (62)</td>
<td>13 (38)</td>
</tr>
</tbody>
</table>

* LEGENDA 1= no ascites, 2= moderate ascites, 3= refractory ascites

Regression or improvement of ascites and HE in all inactivated patients

* LEGENDA 1= no HE, 2= moderate HE, 3= chronic HE
End points

• **Primary end point:** Probability do be inactivated and then delisted

• **Secondary end points:**
  – Virological efficacy
  – Description of criteria taken into account by the investigators for considering inactivation.
  – Predictors of inactivation
Table 3. Competing risk analyses of inactivation from list: multivariable model.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>HR (IC95%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta MELD at 12 weeks</td>
<td>c.v.</td>
<td>1.349 (1.2-1.516)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>MELD at baseline</td>
<td>&lt;16</td>
<td>1</td>
<td>ref</td>
</tr>
<tr>
<td></td>
<td>16-20</td>
<td>0.12 (0.036-0.396)</td>
<td>0.0005</td>
</tr>
<tr>
<td></td>
<td>&gt;20</td>
<td>0.042 (0.013-0.138)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Delta Albumin at 12 weeks</td>
<td>c.v.</td>
<td>0.307 (0.13-0.724)</td>
<td>0.0069</td>
</tr>
</tbody>
</table>

*c.v. = continuous variable*
Estimated cumulative incidence of inactivation based baseline MELD, 12w Delta MELD and 12w Delta albumin.
Clinical Features of 21 delisted patients (21/34, 62%)

• Regression of signs of hepatic decompensation
  → 21/21 no HE
  → 16/21 no ascites and off diuretics.

• MELD <15 → 21/21
  MELD improvement of at least 3 pts → 19/21

• Median time of delisting → 48 weeks

• 6 more patients possibly delisted in the near future (27/34=79%)
• Second generation DAAs favoured the inactivation due to clinical improvement of about 30% of treated patients (after 60 weeks).

• 62% of the inactivated patients could be eventually delisted.

• A careful evaluation of
  - MELD score at start of therapy
  - delta MELD and delta albumin after 12 weeks of therapy, predicts the chances be first inactivated and then delisted.
A word of caution is to be mentioned regarding how long the clinical improvement will last. It will be critical to assess the long-term risks of death, further re-deterioration and development of HCC more specifically. These factors still need to be verified.
<table>
<thead>
<tr>
<th>Centres</th>
<th>Investigators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parigi Mondor</td>
<td>Frede<strong>rique</strong> Franco and Christophe Duvoux</td>
</tr>
<tr>
<td>Parigi “Paul Brousse”</td>
<td>Audrey Coilly</td>
</tr>
<tr>
<td>Montpellier</td>
<td>Fréde<strong>rique</strong> Franco and Georges Pageaux</td>
</tr>
<tr>
<td>Wien</td>
<td>Susanne Rockenschaub</td>
</tr>
<tr>
<td>Valencia</td>
<td>Carmen Vinaixa and Marina Berenguer</td>
</tr>
<tr>
<td>Torino</td>
<td>Silvia Martini</td>
</tr>
<tr>
<td>Bologna</td>
<td>Cristina Morelli</td>
</tr>
<tr>
<td>Milano Policlinico</td>
<td>Fr<strong>ancesca</strong> Donato</td>
</tr>
<tr>
<td>Milano Niguarda</td>
<td>Giov<strong>anni</strong> Perricone and Luca Saverio Belli</td>
</tr>
<tr>
<td>Palermo</td>
<td>Riccardo Volpes</td>
</tr>
<tr>
<td>Bergamo</td>
<td>Luisa Pasulo and Stefano Fagiuoli</td>
</tr>
</tbody>
</table>
High sustained virological response rates using generic direct acting antiviral treatment for hepatitis C, imported into Australia

Dr James Freeman, Founder GP2U Telehealth, Australia

Abstract number: LB03
High sustained virological response rates using generic direct antiviral treatment for Hepatitis C

REDEMPTION-1

James Freeman\textsuperscript{1}, Richard Sallie\textsuperscript{2}, Adam Kennedy\textsuperscript{3}, Pham Thi Ngoc Nieu\textsuperscript{1}, John Freeman\textsuperscript{4}, Greg Jeffreys\textsuperscript{5}, Andrew M. Hill\textsuperscript{6}

\textsuperscript{1}GP2U Telehealth, Hobart, \textsuperscript{2}Hepatology, Nedlands, \textsuperscript{3}Kingswood Pharmacy, \textsuperscript{4}Nephrology, Sandy Bay, \textsuperscript{5}University of Tasmania, Hobart, Australia, \textsuperscript{6}St Stephens AIDS Trust, Chelsea and Westminster Hospital, London, United Kingdom

International Liver Congress 2016 13-18 April, Barcelona, Spain
A Global Tragedy

- In a breakthrough that rivals the invention of penicillin drugs called Direct Acting Antivirals (DAAs), which cure the Hepatitis C Virus (HCV) with minimal side effects and a 95% success rate, have reached the market.

- Together with HIV, HBV, TB and Malaria, HCV is one of the 5 major causes of infectious disease death worldwide.

- Tragically this new cure is not being deployed:
  - We have 150,000,000 infected with HCV worldwide\(^1\), and
  - We have 500,000 deaths from HCV annually\(^1\), but
  - We have only 500,000 patients treated for HCV with DAAs annually\(^2,3\)

The Deployment Problem Is Price

The high prices of these new medications prevent patient access to highly effective HCV treatment.

Generic versions of the DAAs sofosbuvir, ledipasvir, daclatasvir are being mass produced for 1% of the current US retail price\(^1\)

Under the laws of Australia\(^2\), the UK\(^3\), and many other countries, individuals have the right to import a three month supply of medication, for their personal use.

The Legal Basis Of Personal Importation

- Patents provision monopoly rights, however...
- Article 60 of TRIPS - De Minimis Imports – states:
  - Members may exclude from the application of the above provisions small quantities of goods of a non-commercial nature contained in travellers' personal luggage or sent in small consignments
- In line with Article 60 most countries allow some form of personal medication importation
- http://fixhepc.com/ helps patients access medication and discuss their treatment online
Methods

- Generic DAAs were first evaluated for quality using HPLC, NMR and Mass Spectrometry.
- Patients enrolled on an intention to treat basis via the fixhepc.com website and were assisted in making a personal importation of affordably priced medication.
- Patients were assessed pre-treatment, during treatment, and then for SVR (cure) following treatment using the gp2u.com.au Telemedicine platform.
- The objective of this analysis was to assess the safety and effectiveness of the generic medications legally imported by patients.
SOFosbuvir NMR
Over 400 Patients Worldwide Enrolled
Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>448</td>
</tr>
<tr>
<td>SOF+RBV</td>
<td>0.9% (4/448)</td>
</tr>
<tr>
<td>SOF+LDV</td>
<td>45.8% (205/448)</td>
</tr>
<tr>
<td>SOF+LDV+RBV</td>
<td>4.7% (21/448)</td>
</tr>
<tr>
<td>SOF+DCV</td>
<td>42.6% (191/448)</td>
</tr>
<tr>
<td>SOF+DCV+RBV</td>
<td>6.0% (27/448)</td>
</tr>
<tr>
<td>Naïve</td>
<td>51.6%</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>31.3%</td>
</tr>
<tr>
<td>Male</td>
<td>54.2%</td>
</tr>
<tr>
<td>Mean Age</td>
<td>54.4 years</td>
</tr>
<tr>
<td>Mean HCV RNA</td>
<td>6.46 log IU/ml, 2878793 IU/ml</td>
</tr>
</tbody>
</table>

Genotype Distribution:
- GT1: 63.9%
- GT3: 27.5%
- GT2: 5.45%
- GT4: 2.27%
- GT5/6: 0.909%
SOF+PEG+RBV kinetics data source: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(13)70033-1/fulltext
SOF+LDV+RBV for GT3? (Ed Gane 2015$^1$)

100% (13/13)

Percentage SVR

GT1  GT2  GT3  GT4  GT5/6

1) http://www.ncbi.nlm.nih.gov/pubmed/26261007
REDEMPTION-1 HCV RNA < LLOQ at EOT and SVR4
Published SVR12 Results SOF+LDV and SOF+DCV

- **GT1**: 96% (3520/3654)
- **GT2**: 94% (49/52)
- **GT3**: 90% (365/406)
- **GT4**: 94% (102/109)
- **GT5/6**: 95% (41/43)
Note: Some small percentage loss of SVR is expected during the SVR4 to SVR12 period.
Patient Safety

- No new or unknown side effects were reported with headache, fatigue and insomnia being the most common.
- 3 patients with compensated cirrhosis temporarily decompensated on treatment initiation but continued.
- 4 patients who enrolled died, all from HCC:
  - 1 patient died prior to treatment commencement.
  - 2 withdrew early in treatment and entered palliative care.
  - 1 patient died prior to SVR4.
In this interim analysis, treatment with legally imported generic DAAs led to high SVR rates. These SVR rates are similar to those seen in the Phase 3 trials of branded treatments. Mass global treatment with generic DAAs is a feasible alternative where high prices prevent access to branded treatment.
Conclusions

- Generic cure for Hepatitis C is available now for $1000 and works as expected.
- Given current API pricing and production costs $200/patient treatment with SOF+DCV is possible, not in the future, but right now\(^1\).
- Without treatment the future for millions of patients infected with HCV looks like this...

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More Information

- http://fixhepc.com
- https://gp2u.com.au
- https://clinicaltrials.gov/ct2/show/NCT02657694
- HCV Decision Support Tool with expected SVR
A genome-wide association study identifies *PNPLA3* and *SLC38A4* as risk loci for alcoholic hepatitis

Dr Stephen Atkinson, Imperial College London
Abstract number: GS03
A Genome-Wide Association Study Identifies *PNPLA3* and *SLC38A4* as Risk Loci for Alcoholic Hepatitis

Stephen Atkinson¹, Michael J Way²,³, Andrew McQuillin³, Marsha Morgan², Mark Thursz¹

¹Hepatology, Imperial College London; ²UCL Institute for Liver & Digestive Health & ³Molecular Psychiatry Laboratory, University College London, London, United Kingdom
Alcohol-related liver disease

- Alcohol misuse is the leading cause of cirrhosis in the Western world

- Approximately half of all cirrhosis related deaths are attributable to alcohol

- Alcohol-related liver disease comprises a spectrum of clinical presentations and histopathological lesions with variability in disease progression
Predisposition to ALD

- Single gene
- Mendelian
- Reduced penetrance
- Multifactorial with single major locus
- Multifactorial
- Polygenic
- Environmental

Alcoholic liver disease
Genome–Wide Association Studies (GWAS)

Several 100k SNPs, common variation, ‘hypothesis generating’, correction for stratification

Compare allele frequencies to identify disease associations
Alcoholic hepatitis

- Clinical syndrome
- Recent onset jaundice/other features of liver failure
- Ongoing, heavy alcohol misuse
- May already have cirrhosis
- At least 20% die in the first month
Alcoholic hepatitis – additional genetic risk?

Normal liver → Steatosis → Inflammation → Cirrhosis

Drinking? Food intake? Genetic variants?

Alcoholic hepatitis
### GWAS of alcoholic hepatitis - two-stage design

#### Exploratory stage
- **Cases**
- **Controls**

#### Replication stage
- **Cases**
- **Controls**

#### Identification of top hits

#### Reporting of independent associations

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases Exploratory</th>
<th>Controls Exploratory</th>
<th>Cases Replication</th>
<th>Controls Replication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>332</td>
<td>318</td>
<td>528</td>
<td>873</td>
</tr>
<tr>
<td>Male gender</td>
<td>223 (67%)</td>
<td>241 (76%)</td>
<td>321 (61%)</td>
<td>504 (65%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.6 ± 9.3</td>
<td>48.4 ± 10.5</td>
<td>49.7 ± 10.7</td>
<td>45.7 ± 10.5</td>
</tr>
</tbody>
</table>
GWAS of alcoholic hepatitis exploratory results

- PNPLA3
  - rs738409
  - $P_{\text{genome-wide}} = 5 \times 10^{-8}$

- SLC38A4
  - $P_{\text{suggestive}} = 5 \times 10^{-5}$
## Alcoholic hepatitis GWAS - replicated hits

<table>
<thead>
<tr>
<th>Locus</th>
<th>CHR</th>
<th>MAF Cases</th>
<th>MAF Controls</th>
<th>p-value</th>
<th>MAF Cases</th>
<th>MAF Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNPLA3</td>
<td>22</td>
<td>31%</td>
<td>18%</td>
<td>1.62E-08</td>
<td>28%</td>
<td>19%</td>
<td>7.00E-08</td>
</tr>
<tr>
<td>SLC38A4</td>
<td>12</td>
<td>55%</td>
<td>43%</td>
<td>4.05E-05</td>
<td>51%</td>
<td>46%</td>
<td>0.023</td>
</tr>
</tbody>
</table>

MAF = minor allele frequency
Alcoholic Hepatitis GWAS: Conclusions

• The first GWAS of alcoholic hepatitis:

  Confirmed rs738409 in PNPLA3 as a risk factor for the development of severe alcohol-related liver disease

  Identified SLC38A4 as a novel, independent risk locus for alcoholic hepatitis

• The gene at the novel locus is implicated in biological processes likely to be relevant to the pathogenesis of alcoholic hepatitis

• Allows us to work towards build profiles of patients at increased risk of severe alcohol-related liver disease
People

Study participants
STOPAH Investigators
UCL Alcohol Genetics Consortium
Danielle Walker & Lucy Hildyard (WTSI)

Funding

NIHR Imperial BRC
Translating research into patient benefits
Development of hepatocellular carcinoma in HCV cirrhotic patients treated with Direct Acting Antivirals

F. Buonfiglioli ¹, F. Conti ¹, P. Andreone ¹, C. Crespi ², F. G. Foschi ³, M. Lenzi ¹, G. Mazzella ¹, G. Verucchi ¹, and S. Brillanti ¹

¹ DIMEC, University of Bologna;
² Medicina Interna, Policlinico S.Orsola-Malpighi, Bologna;
³ Medicina Interna, Ospedale di Faenza, Italy

Contact Information: Stefano Brillanti, MD, Gastroenterologia, Via Massarenti 9, 40138 Bologna, Italy. stefano.brillanti@unibo.it
BACKGROUND

- Advanced chronic hepatitis C progresses to hepatocellular carcinoma (HCC) in a significant proportion of patients (2-5%/yr)
- Cured HCV infection has been associated with a reduced incidence of HCC, but patients who achieve sustained virological response (SVR) remain at risk for HCC
- Direct acting antivirals (DAAs) have dramatically improved SVR rates in cirrhotics, but very little is known about the effect of these therapies on the development of HCC.
The aim of this large retrospective cohort study was to evaluate the effect of therapy with DAAs on the development of HCC in patients with HCV-related liver cirrhosis.
344 consecutive, HIV negative patients, with Child-Pugh A or B cirrhosis, treated with different DAAs, and followed for 24 weeks after therapy

Liver cirrhosis assessed by transient elastography (Fibroscan, Kpa > 12.0) and/or liver histology

Contrast-enhanced ultrasonography at baseline to exclude active HCC. If no definite result, CT-Scan and/or MRI performed to confirm absent HCC

Contrast-enhanced ultrasonography between 12 and 24 week post-treatment follow-up. Suspected HCC confirmed by CT-Scan and/or MRI
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n. (%)</td>
<td>207 (60.2)</td>
</tr>
<tr>
<td>Age, yrs. (median, range)</td>
<td>63 (29-85)</td>
</tr>
<tr>
<td>HCV genotype, n.</td>
<td></td>
</tr>
<tr>
<td>1 / 4</td>
<td>237 / 29</td>
</tr>
<tr>
<td>2 / 3</td>
<td>40 / 38</td>
</tr>
<tr>
<td>Antiviral Treatment, n.</td>
<td></td>
</tr>
<tr>
<td>Naive</td>
<td>153</td>
</tr>
<tr>
<td>Experienced</td>
<td>191</td>
</tr>
<tr>
<td>Child-Pugh A / B, n.</td>
<td>305 / 39</td>
</tr>
<tr>
<td>Liver stiffness, Kpa (mean, SEM)</td>
<td>23.6 (0.8)</td>
</tr>
<tr>
<td>HBsAg positive, n. (%)</td>
<td>7 (2.0)</td>
</tr>
<tr>
<td>History of previous HCC, n. (%)</td>
<td>59 (17.2)</td>
</tr>
</tbody>
</table>
## Baseline Characteristics According to HCC

<table>
<thead>
<tr>
<th></th>
<th>Without HCC after DAAs (n= 318)</th>
<th>With HCC after DAAs (n= 26)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Males, n. (%)</strong></td>
<td>189 (59.4%)</td>
<td>18 (69.2%)</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Age, yrs. (median, range)</strong></td>
<td>64 (29-85)</td>
<td>57.5 (48-82)</td>
<td>0.32</td>
</tr>
<tr>
<td><strong>Diabetes, n. (%)</strong></td>
<td>62 (19.5%)</td>
<td>6 (23.1%)</td>
<td>0.61</td>
</tr>
<tr>
<td><strong>BMI, median (range)</strong></td>
<td>25.6 (17-40)</td>
<td>25.2 (21-30)</td>
<td>0.37</td>
</tr>
<tr>
<td><strong>Child-Pugh class B, n. (%)</strong></td>
<td>32 (10.1%)</td>
<td>7 (26.9%)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Liver stiffness, Kpa</strong></td>
<td>23.2 (0.8)</td>
<td>28.1 (2.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>(mean, SEM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Liver stiffness, Kpa</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 21.3</td>
<td>134</td>
<td>5</td>
<td>0.005</td>
</tr>
<tr>
<td>&gt; 21.3</td>
<td>101</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td><strong>Platelets, x1000/mm³</strong></td>
<td>124.4 (3.9)</td>
<td>102.3 (13.7)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
**BASELINE CHARACTERISTICS ACCORDING TO HCC**

<table>
<thead>
<tr>
<th></th>
<th>Without HCC after DAAs (n= 318)</th>
<th>With HCC after DAAs (n= 26)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCV Genotype</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 / 4</td>
<td>224 / 25</td>
<td>13 / 4</td>
<td>0.15</td>
</tr>
<tr>
<td>2 / 3</td>
<td>35 / 34</td>
<td>5 / 4</td>
<td></td>
</tr>
<tr>
<td><strong>SOF+SMV / 3D</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOF+RBV / SOF+DCV</td>
<td>135 / 54</td>
<td>7 / 2</td>
<td>0.22</td>
</tr>
<tr>
<td>SOF+LDV / DCV+SMV</td>
<td>52 / 51</td>
<td>10 / 6</td>
<td></td>
</tr>
<tr>
<td><strong>SVR 12</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>292</td>
<td>22</td>
<td>0.26</td>
</tr>
<tr>
<td>No</td>
<td>26</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td><strong>Previous treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naive</td>
<td>146</td>
<td>7</td>
<td>0.07</td>
</tr>
<tr>
<td>Experienced</td>
<td>172</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td><strong>History of previous HCC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>42</td>
<td>17</td>
<td>0.0001</td>
</tr>
<tr>
<td>No</td>
<td>276</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>
Among patients with history of previous HCC, those who developed HCC after DAAs:

- were significantly younger (median age 56 vs. 73 yr.)
- more frequently treatment experienced (88.2% vs. 61.9%)
- with more advanced liver fibrosis (Fibroscan, Kpa > 21.5)
In a large cohort of 344 consecutive patients with HCV cirrhosis treated with DAAs, SVR was obtained in 89% during 24 week post-treatment follow-up, 26 patients (7.6%) developed HCC. HCV genotype and DAA regimen did not affect HCC development. History of previous HCC was the strongest predictor of the development of HCC after therapy. A more advanced liver disease and younger age were risk factors for HCC recurrence. Cirrhotic patients should be closely monitored after treatment, and the biological significance of our findings.
Questions and answers
Closing remarks

Dr Laurent Castera, EASL Secretary General
Thank you