UEG 2015: Liver

Jean-Francois Dufour, MD

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Disclosures
CHOLESTATIC LIVER DISEASES
CHOLESTATIC LIVER DISEASE

PBC: primary biliary cholangitis

Obeticholic acid

Hirschfield et al. Gastroenterology 2015
175 PSC patients
Compared to controls, no differences were found in total bile acid concentration (mM%), or between individual bile acids. Phospholipid concentration were also similar in controls and in PSC UDCA therapy: ↑ of UDCA in bile with ↓ biliary cholesterol content, while the total phospholipid content remained unchanged. Proportion of both the primary bile acids, DCA and CDCA were ↓ Of the secondary bile acids, CA ↓, but LCA remained unchanged.

No correlation between disease severity judged by ERC findings and biliary bile acid changes during UDCA therapy.
692 PSC patients in population based PSC cohort from the Netherlands. The median follow-up time was 85 months.

\[
\text{PI} = 1.374 \times \text{PSC type}(0/1)^1 + 0.023 \times \text{Age at diagnosis PSC} - 2.643 \times \log \text{Albumin} \times \text{ULN} + 2.029 \times \text{abs}(\log \text{Thrombocytes} \times \text{ULN} - 0.5) + 0.544 \times \log \text{AST} \times \text{ULN} + 0.683 \times \log \text{ALP} \times \text{ULN} + 0.430 \times \log \text{Total bilirubin} \times \text{ULN}
\]

\(^1\): PSC type: Large duct = 1; Small duct = 0

The PI yielded a c-statistic of 0.7180.
FIBROSIS
Liver stiffness quantification
- M-mode visualization of the region of interest (ROI)
- Quantitative data
121 consecutive patients, 30% with cirrhosis
Same session TE (Fibroscan, Echosens) and ElastPQ (Philips, Affinity) 10 measurements
Cut-off values: TE 7.2 – 14.5 kPa  ElastPQ 5.9 – 12 kPa

Considering TE as the reference method

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Fibrosis</td>
<td>58%</td>
<td>91%</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>83%</td>
<td>96%</td>
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</table>
248 patients with HBV (30 decompensated cirrhosis) (only 37 had a liver biopsy)

AUROC for ≥ F2, ≥F3 and F4: 0.891, 0.921, 0.947
Better than APRI and FIB4

SWE values correlate with BMI, GGT, bilirubin
COMPLICATIONS CIRRHOSIS
Position Paper

Expanding consensus in portal hypertension
Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension

Roberto de Franchis*, on behalf of the Baveno VI Faculty†

Department of Biomedical and Clinical Sciences, University of Milan, Gastroenterology Unit, Luigi Sacco University Hospital, Milan, Italy

See Editorial, pages 543–545
- Endoscopic therapy with tissue adhesive (e.g. N-butylcyanoacrylate) is recommended for acute bleeding from isolated gastric varices (IGV) (1b;A) and those gastroesophageal varices type 2 (GOV2) that extend beyond the cardia (5;D).
- To prevent rebleeding from gastric varices, consideration should be given to additional glue injection (after two to four weeks), beta-blocker treatment or both combined or TIPS (5;D). More data in this area are needed.
- EVL or tissue adhesive can be used in bleeding from gastroesophageal varices type 1 (GOV1) (5;D).
Questionnaire to 336 hepatologists. 32% responded

Primary prophylaxis: beta-blockers 96%

Control active bleeding: 78% obliteration (glue migration 60%), 34% band ligation, early TIPS proposed by 56%

Secondary prophylaxis: 74% beta-blockers, 66% obliteration, 14% TIPS

Management of gastric varices very heterogeneous
HEPATIC ENCEPHALOPATHY

Rifaximin (Xifaxan) ist seit August 20125 in der Schweiz zur Verminderung des Wiederauftretens von Episoden einer manifesten hepatischen Enzephalopathie bei Erwachsenen mit hepatischer Zirrhose erhältlich. Das Antibiotikum wird oral kaum resorbiert und wirkt auf Darmbakterien, welche Harnstoff zu Ammoniak abbauen. Die empfohlene Dosierung beträgt zweimal täglich eine Filmtablette zu 550 mg zu oder ausserhalb der Mahlzeiten.

EASL GUIDELINES 2014

Recommendations

25. Lactulose is recommended for prevention of recurrent episodes of HE after the initial episode (GRADE II-1, A, 1)

26. Rifaximin as an add-on to lactulose is recommended for prevention of recurrent episodes of HE after the second episode (GRADE I, A, 1)

27. Routine prophylactic therapy (lactulose or rifaximin) is not recommended for the prevention of post-TIPS HE (GRADE III, B, 1)
14 cirrhotic patients admitted in ICU for HE, 27 control

LC-HRMS methods led to the characterization of 150 metabolites in CSF, which were mainly amino acids and organic acids. 40% of those metabolites were not reported as present in CSF before.

HE patients could be easily discriminated from controls
Concentrations of 102 metabolites significantly altered in HE patients
Alterations in several major metabolite classes: ammoniac, bile acids, amino-acids, acylcarnitines, and nucleosides.
Accumulations of acetylated compounds, which could be due to a defect of the Krebs cycle.
ALCOHOL-INDUCED LIVER DISEASE
Steroids or Pentoxifylline for ETOH Hepatitis
STOPAHE Trial

28 day Mortality

<table>
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<tr>
<th>Group</th>
<th>Mortality Rate</th>
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</thead>
<tbody>
<tr>
<td>Placebo/Placebo</td>
<td>16.7%</td>
</tr>
<tr>
<td>Placebo/Pred</td>
<td>14.3%</td>
</tr>
<tr>
<td>PTX/Placebo</td>
<td>19.4%</td>
</tr>
<tr>
<td>PTX/Pred</td>
<td>13.5%</td>
</tr>
</tbody>
</table>

Multivariate analysis:
- Prednisolone: OR = 0.61 (95% CI: 0.41-0.90)
- Pentoxifylline: OR = 1.09 (0.74-1.63)

Steroids = 39% ↓ mortality at 28 days
(but not at 90 days & 1 year)
PTX is of no benefit in ETOH hepatitis

NOD2 MUTATIONS AND ALCOHOLIC LIVER CIRRHOSIS: IS THERE A LINK?

Carvalhiero, Oliveira, Cardoso, Donato, ..

Case-control study involving the research of the 3 main NOD2 mutations (3020insC, R702W e G908R) in 202 patients with ALC and in 202 healthy controls

NOD2 mutations 43 patients (21.3%), 27 controls (13.4%) (p=0.064)

Age at diagnosis of ALC with mutation 48±12 vs. 58±12 years; p=0.008

Ø associations with HCC, HRS, encephalopathy, variceal bleeding
June 2010 - September 2013, 100 consecutive patients from 2 liver and alcoholology units

At a mean BAC dosage of 40mg/day [30–210], mean daily alcohol consumption (DAC) was reduced from 106 to 18g/day (p<0.001). A decrease of the DAC>50% was observed in 77 patients. No predictive factor of response was identified. 20 patients reported minor side effects. No liver or renal function deterioration occurred in cirrhotic patients.
HEPATOCELLULAR CARCINOMA
NAFLD associated HCC over time

Dyson et al., J Hepatol 2014
Serum samples of 132 cirrhotic (Child A or B) patients collected between 1995 and 2005 were analyzed, 70% Hepatitis

Significant ↑ of the mean baseline GCT value in the patients who developed a HCC during follow up (p < 0.001).

An optimal cutoff for the GCT was defined (at 1.6) and the hazard ratio for the development of HCC was 3.88 (95% CI: 1.81-8.29) for patients with a baseline GCT above this threshold.
CHRONIC HEPATITIS C
BEHANDLUNG DER CHRONISCHEN HEPATITIS C

http://www.rantpets.com/2015/04/15/10-terrifying-jungle-animals-to-give-you-nightmares/
**SVR OF 96% IN HCV GNT 1A-INFECTED PATIENTS TREATED WITH OMBITASVIR/PARITAPREVIR/R AND DASABUVIR WITH RIBAVIRIN**

Wedemeyer, Pckros, Lee, Gane, Moreno,...

<table>
<thead>
<tr>
<th>VR12 by baseline factors, n/N (%)</th>
<th>GT1a with no cirrhosis 3D+RBV for 12 weeks</th>
<th>GT1a with cirrhosis 3D+RBV for 24 weeks</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>569/593 (96)</td>
<td>115/121 (95)</td>
<td>684/714 (96)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>353/370 (95)</td>
<td>84/89 (94)</td>
<td>437/459 (95)</td>
</tr>
<tr>
<td>Female</td>
<td>216/223 (97)</td>
<td>31/32 (97)</td>
<td>247/255 (97)</td>
</tr>
<tr>
<td>Treatment-naïve</td>
<td>403/420 (96)</td>
<td>53/56 (95)</td>
<td>456/476 (96)</td>
</tr>
<tr>
<td>Prior PegIFN/RBV non-response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>47/50 (94)</td>
<td>13/13 (100)</td>
<td>60/63 (95)</td>
</tr>
<tr>
<td>Partial response</td>
<td>36/36 (100)</td>
<td>10/10 (100)</td>
<td>46/46 (100)</td>
</tr>
<tr>
<td>Null response</td>
<td>83/87 (95)</td>
<td>39/42 (93)</td>
<td>122/129 (95)</td>
</tr>
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</table>
99.7% SVR IN 369 HCV GNT 1B-INFECTED PATIENTS TREATED WITH OMBITASVIR/PARITAPREVIR/R AND DASABUVIR WITH OR WITHOUT RIBAVIRIN

Dufour, Wedemeyer, Bernstein, Colombo,...

<table>
<thead>
<tr>
<th>12 by baseline factors, n/N (%)</th>
<th>GT1b without cirrhosis 3D for 12 weeks</th>
<th>GT1b with cirrhosis 3D+RBV for 12 weeks</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>301/301 (100)</td>
<td>67/68 (98.5)</td>
<td>368/369 (99.7)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>141/141 (100)</td>
<td>44/45 (97.8)</td>
<td>185/186 (99.5)</td>
</tr>
<tr>
<td>Female</td>
<td>160/160 (100)</td>
<td>23/23 (100)</td>
<td>183/183 (100)</td>
</tr>
<tr>
<td>Treatment-naïve</td>
<td>210/210 (100)</td>
<td>22/22 (100)</td>
<td>232/232 (100)</td>
</tr>
<tr>
<td>Prior PegIFN/RBV non-response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>33/33 (100)</td>
<td>14/14 (100)</td>
<td>47/47 (100)</td>
</tr>
<tr>
<td>Partial response</td>
<td>26/26 (100)</td>
<td>6/7 (85.7)</td>
<td>32/33 (97.0)</td>
</tr>
<tr>
<td>Null response</td>
<td>32/32 (100)</td>
<td>25/25 (100)</td>
<td>57/57 (100)</td>
</tr>
</tbody>
</table>
IS RIBAVIRIN ACTUALLY USEFUL FOR GENOTYPE 1 CIRRHOTIC PATIENTS WHO RECEIVE DAAS COMBINATION?
A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

Di Martino, Richou, Cervoni, Weil-Verhoven, Vanlemmens, ....

10 RCTs including 1307 G1 cirrhotic patients (573 TN, 734 TE)
SIM+SOF (COSMOS, N=168), 3D Abbvie (TURQUOISE II, N=380),
DCV-TRIO BMS (UNITY 2, N=202), GPV+EBV (C-WORTHY, N=253),
and LDV+SOF (6 RCTs, N=496).

In TN neither ribavirin nor an extended duration increased SVR12.
In TE ribavirin did not increase SVR12, extended duration
was associated with higher SVR rates

SVR gain was similar between the different DAA regimen
23.10.2015
FDA Drug Safety Communication: FDA warns of serious liver injury risk with hepatitis C treatments Viekira Pak and Technivie
TEAM

www.swissliver.ch