Hepatitis C in the Netherlands including *the Rotterdam experience*

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Disclosures

Honoraria for consulting or speaking (last 5 years):
AbbVie, BMS, Gilead, Janssen-Cilag, Medtronic,
Merck/Schering-Plough, Norgine, Roche

Research grants (last 5 years):
BMS, Janssen Cilag, Medtronic, Roche
The Dutch view: Close to extinction
The Dutch view: Healthy foods for the liver

Coffee

Turmeric

Cacao

Greek diet
The Dutch view: A revolution in therapy ...
Treatment of hepatitis C always beneficial, no matter fibrosis-stage

In hepatitis C higher liver-related mortality, but also higher non-liver-related mortality
Effects of SVR on outcome in F3-F4

international cohort
N=530

- IFN treatment 1990-2003
- FU 8.4 yrs (6.1-11.4)
- 70% men
- SVR in 192 (36%)

-all cause mortality rate/10 yrs :
  - 8.9% (SVR) (N=13)
  - 26% (no SVR) (N=100)

-HCC (N=83) (7 vs 76)
  - 7 SVR
  - 76 no SVR

vd Meer et al; JAMA. 2012;308(24):2584-2593
Thanks to ...
Current available options

- **Viekirax** (ombitasvir/paritaprevir/ritonavir)
  - NS3/NS4A

- **Exviera** (dasabuvir)
  - NS5B

- **Olysio** (simeprevir)
  - NS3/NS4A

- **Daklinza** (daclatasvir)
  - NS5A

- **Harvoni** (sofosbuvir/ledipasvir)
  - NS5B/NS5A

- **Sovaldi** (sofosbuvir)
  - NS5B
How to choose the most optimal treatment

HCV-richtsnoer

- Collaboration between all Dutch societies
- Updates every 3 months
- Online availability
- Based upon evidence-based guidelines

www.hcvrichtsnoer.nl
HCV-SVR-predictor
www.liverdoc.nl

BIBHEP: Tools facilitating treatment

HCV SVR-predictor
Find out which licensed hepatitis C antiviral therapy generates the highest Sustained Virological Response (SVR).

LiverDoc
Find out now

V 1.0 / data authorized by NASL

In four easy steps we show you the SVR percentages of antiviral therapies by patient type.

- HCV type
- Hepatitis C
- Hepatitis C + HIV
- Hepatitis C + Liver TX

- Treatment status
- Genotype
- Cirrhosis

http://hcvsvrpredictor.liverdoc.com/#/
www.liverdoc.nl
Patient

- Mrs. A, 52 years
- HCV genotype 1a
- Child-Pugh A liver cirrhosis
- Failed on PegIFN-RBV
Casus 1 – SVR predictor

SVR % of antiviral therapies for:
- HCV monoinfection
- Previous therapy without SVR
- Genotype 1
- Cirrhosis - Yes

Quality of evidence:
- High: Green
- Moderate: Yellow
- Low: Red

Exclude low quality results

<table>
<thead>
<tr>
<th>Therapy</th>
<th>12wk</th>
<th>24wk, riba</th>
<th>24wk</th>
<th>12wk, riba</th>
<th>12wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ombitasvir-Paritaprevir/ r-Dasabuvir</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LEDIPASVIR-SOFOSBUVIR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFOSBUVIR-SIMEPREVIR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir/r</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Casus 1 – SVR predictor

### SVR % of antiviral therapies for:
- **HCV monoinfection**
- **Previous therapy without SVR**
- **Genotype 1**
- **Cirrhosis – Yes**

#### Quality of evidence:
- **High**: Green
- **Moderate**: Yellow
- **Low**: Red

#### Exclude low quality results

<table>
<thead>
<tr>
<th>Therapy组合</th>
<th>24wk</th>
<th>12wk</th>
<th>48wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ombitasvir-Paritaprevir/r-Dasabuvir</td>
<td>97%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir</td>
<td>98%</td>
<td>95%</td>
<td>92%</td>
</tr>
<tr>
<td>Sofosbuvir-Simeprevir</td>
<td>85%</td>
<td>81%</td>
<td></td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir/r</td>
<td>81%</td>
<td>86%</td>
<td></td>
</tr>
<tr>
<td>PegIFN-Riba-Simeprevir</td>
<td>71%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PegIFN-Riba-Sofosbuvir</td>
<td></td>
<td>64%</td>
<td></td>
</tr>
<tr>
<td>PegIFN-Riba</td>
<td></td>
<td>10%</td>
<td></td>
</tr>
</tbody>
</table>
HCV genotypic distribution in the Netherlands

Genotype

Razavi H. Centerforda.com/polaris
HCV epidemiology in the Netherlands
Predictions based on ‘aggressive’ therapy

Razavi H. Centerforda.com/polaris
Patients with F3-F4, or after liver transplantation
the Rotterdam experience

130 started treatment

60 week 4 FU

30 week 12 FU
# Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CPA (n=49)</th>
<th>CPB + C (n=11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58 (37-77)</td>
<td>56 (41-71)</td>
<td>0.565</td>
</tr>
<tr>
<td>Male</td>
<td>36 (74%)</td>
<td>11 (100%)</td>
<td>0.054</td>
</tr>
<tr>
<td>Caucasian</td>
<td>32 (65%)</td>
<td>5 (46%)</td>
<td>0.221</td>
</tr>
<tr>
<td>DM</td>
<td>9 (18%)</td>
<td>2 (18%)</td>
<td>0.571</td>
</tr>
<tr>
<td>BMI</td>
<td>27.1 (19.0-41.5)</td>
<td>27.2 (18.4-32.5)</td>
<td>0.949</td>
</tr>
<tr>
<td>Treatment experienced</td>
<td>32 (65%)</td>
<td>7 (64%)</td>
<td>0.916</td>
</tr>
<tr>
<td>Liver transplanted</td>
<td>7 (14%)</td>
<td>5 (46%)</td>
<td>0.020</td>
</tr>
<tr>
<td>Genotype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>28 (57%)</td>
<td>3 (27%)</td>
<td>0.073</td>
</tr>
<tr>
<td>1b</td>
<td>7 (14%)</td>
<td>3 (27%)</td>
<td>0.296</td>
</tr>
<tr>
<td>2</td>
<td>3 (6%)</td>
<td>0</td>
<td>0.400</td>
</tr>
<tr>
<td>3</td>
<td>5 (10%)</td>
<td>4 (36%)</td>
<td>0.028</td>
</tr>
<tr>
<td>4</td>
<td>6 (12%)</td>
<td>1 (9%)</td>
<td>0.768</td>
</tr>
</tbody>
</table>

Data are presented as mean (range) or as n (percentage)
P-values calculated by chi-square and independent-samples t-test
## Treatment selection

<table>
<thead>
<tr>
<th>N=60</th>
<th>GT1a (n=31)</th>
<th>GT1b (n=10)</th>
<th>GT2 (n=3)</th>
<th>GT3 (n=9)</th>
<th>GT4 (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + SIM</td>
<td>0</td>
<td>4 (40%)</td>
<td>0</td>
<td>0</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>SOF + SIM + RBV</td>
<td>17 (55%)</td>
<td>3 (30%)</td>
<td>0</td>
<td>0</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>SOF + DAC</td>
<td>9 (29%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SOF + DAC + RBV</td>
<td>5 (16%)</td>
<td>3 (30%)</td>
<td>0</td>
<td>0</td>
<td>2 (29%)</td>
</tr>
<tr>
<td>SOF + RBV</td>
<td>0</td>
<td>0</td>
<td>3 (100%)</td>
<td>9 (100%)</td>
<td>0</td>
</tr>
</tbody>
</table>

RBV n=45 (75%)
SVR rates

<table>
<thead>
<tr>
<th></th>
<th>CP A</th>
<th>CP B+C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SVR 4</strong></td>
<td>90%</td>
<td>73%</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>44/49</td>
<td>19/24</td>
</tr>
<tr>
<td><strong>SVR 12</strong></td>
<td>79%</td>
<td>50%</td>
</tr>
<tr>
<td>Number of Patients</td>
<td>8/11</td>
<td>3/6</td>
</tr>
</tbody>
</table>

p = 0.132

p = 0.148
Failures

- \( n = 8 \) (5 CP A, 3 CP B+C)
Safety CP A vs. CP B+C

• **6 SAE’s (10%)**
  - 1 patient died because of fulminant pneumonia (CPC)
  - 3 hospital admissions: 1 liver related (hepatic encephalopathy)
  - 2 other: portal vein thrombosis, cryoglobulinemia

• CP A: 2, CP B+C: 4 (p=.001)

• **7 blood transfusions (all patients on ribavirin)**

• CP A: 6, CP B+C: 1 (p=.768)
Change in MELD score CP B+C

- Baseline – Follow up week 4
  n=9 (2 missing)

Median: -2.0 (range: -13 – 5)
Treatment for HCV co-infection over time
Rapid uptake of new direct-acting antivirals
Conclusions Hepatitis C in the Netherlands

- All oral AVT HCV available for all patients
- Currently available drugs:
  - Sofosbuvir, daclatasvir, simeprevir
  - Sofosbuvir + ledipasvir
  - Paritaprevir + dasabuvir + ombitasvir
- Main challenge: to treat such that morbidity and mortality will decrease
Thank you!