La coinfezione HIV/HCV
il punto di vista del clinico
nella gestione delle coinfezioni:
L’infettivologo
Dichiaro che negli ultimi due anni ho avuto i seguenti rapporti, anche di finanziamento, con soggetti portatori di interessi commerciali in campo sanitario:

Abbvie, BMS, Beckman Coulter, Gilead Sciences, MSD, Roche, ViiV
HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART

HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART

If HIV RNA <1000 copies/mL: +65% excess risk
If HIV RNA >1000 copies/mL: +82% excess risk

If CD4 < 200/mm²: +203% excess risk
If CD4 > 200/mm²: 56–63% excess risk

ART, antiretroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

High SVR in adult patients with HIV/HCV co-infection treated with DAAs

3. Rockstroh JK, et al. IAS 2016; Abstract # 10333;

- Studies included non-cirrhotic and cirrhotic patients.
- TE: treatment-experienced

### SVR12 (%)

**ALLY-2:**
- GT 1–4, TN & TE
- SOF + DCV

- TN: 98/101 (97%)
- TE: 51/52 (98%)

**ION-4:**
- GT 1 or 4, TE & TN
- LDV/SOF

- 12 weeks: 322/335 (96%)

**TURQUOISE-1, part 2:**
- GT 1 or 4, TN and TE
- OMV/PTV/RTV + DSV ± RBV

- 12 or 24 weeks: 217/223 (97%)

**C-EDGE:**
- GT 1, 4 or 6, TN
- GRZ/EBV

- 12 Weeks: 210/218 (96%)

NOT HEAD-TO-HEAD COMPARISONS
ASTRAL-5: high SVR across all patient types in adult HIV/HCV co-infected patients treated with 12 weeks’ SOF/VEL

**ASTRAL-5: HIV/HCV co-infected**

Treatment-naïve and -experienced, non-cirrhotic and cirrhotic GT 1–4 adults

<table>
<thead>
<tr>
<th>Cirrhosis status</th>
<th>Total</th>
<th>No</th>
<th>Yes</th>
<th>Naïve</th>
<th>Experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>101/106</td>
<td>82/87</td>
<td>19/19</td>
<td>71/75</td>
<td>30/31</td>
</tr>
</tbody>
</table>


Error bars represent 95% confidence intervals.
EXPEDITION-2 Study: efficacy

- One patient with GT3 infection and cirrhosis had on-treatment virologic failure at week 8; the patient was 85% compliant with treatment.

*Patient returned at post-treatment week 24 and had achieved SVR

DAAs were well-tolerated in clinical trials of HIV/HCV co-infected patients

Adverse events common across all DAA regimens in HIV/HCV co-infection trials

<table>
<thead>
<tr>
<th></th>
<th>ALLY-2</th>
<th>ION-4</th>
<th>TURQUOISE-I Part 2</th>
<th>C-EDGE CO-INFECTION</th>
<th>ASTRAL-5</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV + SOF N=203</td>
<td>17%</td>
<td>21%</td>
<td>23%</td>
<td>13%</td>
<td>25%</td>
</tr>
<tr>
<td>LDV/SOF N=335</td>
<td>11%</td>
<td>25%</td>
<td>14%</td>
<td>12%</td>
<td>13%</td>
</tr>
<tr>
<td>OMV/PTV/RTV + DSV ± RBV N=228</td>
<td>7%</td>
<td>11%</td>
<td>14%</td>
<td>7%</td>
<td>8%</td>
</tr>
<tr>
<td>GRZ/EBV N=218</td>
<td>13%</td>
<td>10%</td>
<td>20%</td>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>SOF/VEL N=106</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2 (2%)</td>
</tr>
</tbody>
</table>

Fatigue
Headache
Diarrhoea
Nausea
D/C due to AE


NOT HEAD-TO-HEAD COMPARISONS
This table illustrate adverse events obtained between different regimens from different studies and are therefore not directly comparable as study populations are NOT matched
Treatment outcomes of LDV/SOF 12 weeks

**ITT analysis**

- **Total**: 909
  - SVR12 %: 95.9
  - SVR (95% CI): 872 (85.9), 94.4 - 97.1

- **MoP**: 687
  - SVR12 %: 97.2
  - SVR (95% CI): 668 (97.2), 95.7 - 98.3

- **CoP**: 222
  - SVR12 %: 91.9
  - SVR (95% CI): 204 (91.9), 87.5 - 95.1

**m-ITT analysis**

- **Total**: 883
  - SVR12 %: 97.6
  - SVR (95% CI): 872 (97.6), 96.4 - 98.5

- **MoP**: 668
  - SVR12 %: 98.7
  - SVR (95% CI): 688 (98.7), 97.5 - 99.4

- **CoP**: 219
  - SVR12 %: 94.4
  - SVR (95% CI): 204 (94.4), 90.5 - 97.1

MoP = HCV monoinfected patients
CoP = HIV/HCV coinfected patients

Berenguer J et al CROI 2018;#607
Rates of SVR12 according to the presence of cirrhosis, decompensated cirrhosis, history of previous interferon treatment and HCV genotype in 5464 HCV infected patients treated in Lombardy stratified according to HIV co-infection

<table>
<thead>
<tr>
<th>Study Group</th>
<th>ALL</th>
<th>Cirrhotics</th>
<th>Decompensated</th>
<th>PEGIFN Experienced</th>
<th>Genotype 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>4444/4564</td>
<td>2512/2588</td>
<td>71/75</td>
<td>1434/1472</td>
<td>413/435</td>
</tr>
<tr>
<td></td>
<td>(97.4%)</td>
<td>(97.1%)</td>
<td>(94.7%)</td>
<td>(97.4%)</td>
<td>(94.9%)</td>
</tr>
<tr>
<td>HIV-</td>
<td>872/900</td>
<td>557/576</td>
<td>46/50</td>
<td>150/157</td>
<td>213/225</td>
</tr>
<tr>
<td></td>
<td>(96.9%)</td>
<td>(96.7%)</td>
<td>(92%)</td>
<td>(95.5%)</td>
<td>(94.7%)</td>
</tr>
</tbody>
</table>

Multivariate logistic regression identified two predictors of lack of SVR12 HCV G3 infection (OR 2.25 95% CI 1.5-3.66 p<0.00001) and decompensation at baseline (OR 2.48 95% CI 1.16-5.3 p=0.0187). HIV coinfection was not associated with an increased risk of lack of SVR12 (OR 0.95 95% CI 0.61-1.47)

Spinetti A. et al on Behalf of RETE LOMBARDIA HCV – NAVIGATORE. AASLD 2018 submitted
Treatment indication

1. Every person with HCV/HIV co-infection should be considered for IFN-free anti-HCV treatment regardless of liver fibrosis stage.
2. Due to similar HCV cure rates and tolerability in HCV/HIV co-infected persons as in HCV mono-infected persons under DAA therapy, treatment indication and regimens are to be the same as in HCV mono-infection.
3. Re-test for GT and sub-type should be performed in persons with tests carried out before second-generation tests were available (second-generation line-probe assay or real-time PCR assay) or in persons at risk of ‘super-infection’ for whom the GT/sub-type should be performed on the most recent available specimen.
All (HCV) patients should be tested for human immunodeficiency virus (HIV).

Drug-drug interactions are a key consideration in treating HIV-HCV coinfectected patients, and close attention must be paid to anti-HIV drugs that are contraindicated, not recommended or require dose adjustment with particular DAA regimens (A1).

The same IFN-free, ribavirin-free treatment regimens should be used in HIV-coinfected patients as in patients without HIV infection, as the virological results of therapy are identical. Treatment alterations or dose adjustments should be performed in case of interactions with antiretroviral drugs (A1).
Check for DDIs between HCV and HIV drugs!

• **Drug interactions**
  - http://drugchecker.aol.com
  - http://hcvdruginfo.ca

• **List of CYP substrates, inhibitors, inducers**
  - http://medicine.iupui.edu/clinpharm/ddIs

• **HIV drug interactions**
  - http://www.hiv-druginteractions.org
  - http://www.hep-druginteractions.org

Khoo S. 15th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy, May 2014 [oral presentation].

CYP, cytochrome
Principles: 2018 anti HCV Tx should be (when possible): RBV free, RASs free, less drug treatment.

European Association for the Study of the Liver

Table 7. Treatment recommendations for HCV-monoinfected or HCV/HIV-coinfected patients with chronic hepatitis C without cirrhosis, including treatment-naïve patients (defined as patients who have never been treated for their HCV infection) and treatment-experienced patients (defined as patients who were previously treated with pegylated IFN-α and ribavirin; pegylated IFN-α, ribavirin and sofosbuvir; or sofosbuvir and ribavirin).

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Prior treatment experience</th>
<th>SOF/VEL</th>
<th>GLE/PIB</th>
<th>SOF/VEL/VOX</th>
<th>SOF/LDV</th>
<th>GZR/EBR</th>
<th>OBV/PTV/r + DSV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>8-12 wk</td>
<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
</tr>
<tr>
<td>1b</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>8-12 wk</td>
<td>8 wk (F0-F2) 12 wk (F3)</td>
<td>8 wk (F0-F2) 12 wk (F3)</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
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<td>12 wk</td>
<td>8 wk</td>
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<td>No</td>
<td>No</td>
<td>No</td>
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<td>4</td>
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<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>12 wk</td>
<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
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<tr>
<td></td>
<td>Treatment-experienced</td>
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<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>8 wk</td>
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<td>6</td>
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<td>No</td>
<td>12 wk</td>
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<tr>
<td></td>
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<td>12 wk</td>
<td>8 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX, voxilaprevir.
**Principles:** &lt;2018 anti HCV Tx should be (when possible): RBV free, RASs free, less drug treatment

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**Table 8. Treatment recommendations for HCV-monoinfected or HCV/HIV-coinfected patients with chronic hepatitis C with compensated (Child-Pugh A) cirrhosis, including treatment-naïve patients (defined as patients who have never been treated for their HCV infection) and treatment-experienced patients (defined as patients who were previously treated with pegylated IFN-α and ribavirin; pegylated IFN-α, ribavirin and sofosbuvir; or sofosbuvir and ribavirin).**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Prior treatment experience</th>
<th>SOF/VEL</th>
<th>GLE/PIB</th>
<th>SOF/VEL/Vox</th>
<th>SOF/LDV</th>
<th>GZr/EBR</th>
<th>OBV/PTV/r + DSV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>12 wk</td>
<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
</tr>
<tr>
<td>Genotype 1b</td>
<td>Treatment-naïve</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
<td>12 wk</td>
<td>12 wk</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
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<td>No</td>
<td>12 wk</td>
<td>12 wk</td>
</tr>
<tr>
<td>Genotype 2</td>
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<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>Treatment-naïve</td>
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<td>12 wk</td>
<td>No</td>
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<td>No</td>
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<tr>
<td></td>
<td>Treatment-experienced</td>
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<td>16 wk</td>
<td>12 wk</td>
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<td>No</td>
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<td>12 wk (HCV RNA ≤800,000 IU/ml)</td>
<td>No</td>
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<tr>
<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
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</tr>
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</tr>
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<td></td>
<td>Treatment-experienced</td>
<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Genotype 6</td>
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<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>12 wk</td>
<td>No</td>
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</tr>
<tr>
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<td>12 wk</td>
<td>12 wk</td>
<td>No</td>
<td>No</td>
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</tr>
</tbody>
</table>

DAA, direct-acting antiviral; DSV, dasabuvir; EBR, elbasvir; GLE, glecaprevir; GZR, grazoprevir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; LDV, ledipasvir; OBV, ombitasvir; PIB, pibrentasvir; PTV, paritaprevir; r, ritonavir; SOF, sofosbuvir; VEL, velpatasvir; VOX: voxilaprevir.
Simplified Treatment

• Pretreatment assessment:
  • Proof of HCV replication
  • APRI or FIB-4 for liver disease severity (if treatment for HCC available)
  • Assessment of drug-drug interactions

• Treatment
  • Sofosbuvir/velpatasvir for 12 weeks
  • Glecaprevir/pibrentasvir
    – For 8 weeks in patients without cirrhosis
    – For 12 weeks in patients with cirrhosis
  • Generic drugs possible if quality controls met and guaranteed

• Follow-up:
  • Assessment of SVR dispensable
  • HCC surveillance (if treatment for HCC available)
## Drug-drug Interactions between DAAs and ARVs

<table>
<thead>
<tr>
<th>HCV drugs</th>
<th>ATW/c</th>
<th>ATV/r</th>
<th>DRV/c</th>
<th>DRV/r</th>
<th>LPV/r</th>
<th>EFV</th>
<th>ETV</th>
<th>NVP</th>
<th>RPV</th>
<th>MVC</th>
<th>DTG</th>
<th>EVG/c</th>
<th>RAL</th>
<th>ABC</th>
<th>FTC</th>
<th>3TC</th>
<th>TAF</th>
<th>TDF</th>
<th>ZDV</th>
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<tbody>
<tr>
<td>daclatasvir</td>
<td>↑</td>
<td>↓110%</td>
<td>↑</td>
<td>↑11%</td>
<td>↑15%</td>
<td>↓32%</td>
<td>↓</td>
<td>↓</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>E33%</td>
<td>↑</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>↑10%</td>
<td>E10%</td>
</tr>
<tr>
<td>elbasvir/</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑54/83%</td>
<td>↓</td>
<td>↓</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>↑</td>
<td>E43%</td>
<td>↑</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>↑7/14%</td>
<td>E34%</td>
</tr>
<tr>
<td>grazoprevir/</td>
<td>↑</td>
<td>↑53/64%</td>
<td>↑</td>
<td>↑397%/↑338/148%</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>E84%</td>
<td>E</td>
<td>←</td>
<td>E</td>
<td>1205/57%/E47%</td>
<td>E47%</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>E</td>
<td>←←</td>
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<tr>
<td>pibrentasvir</td>
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<td>↑94%</td>
<td>↑</td>
<td>↑</td>
<td>D↑</td>
<td>vi</td>
<td>↓E</td>
<td>↓E</td>
<td>E</td>
<td>E</td>
<td>E</td>
<td>E134%</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
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<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>E</td>
<td>E</td>
<td>E</td>
<td>E20%</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>E</td>
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<td>↓</td>
<td>E</td>
<td>E</td>
<td>E</td>
<td>E134%</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>E</td>
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<tr>
<td>paritaprevir/</td>
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<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
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<td>E</td>
<td>E</td>
<td>E</td>
<td>E134%</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>←←</td>
<td>E</td>
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<tr>
<td>ombitasvir</td>
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<td>↑171%</td>
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</tbody>
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### Legend
- ↑: potential elevated exposure of DAA
- ↓: potential decreased exposure of DAA
- ←←: no significant effect
- ↑↓: potential decreased exposure of ARV drug
- ↑↑: potential elevated exposure of ARV drug

### Colour legend
- Light blue: no clinically significant interaction expected.
- Green: these drugs should not be co-administered.
- Light red: potential interaction which may require a dosage adjustment or close monitoring.
- Red: potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment is unlikely to be required.
Acute outbreaks of HCV have been reported in HIV+ MSM across the world

**USA** 44 cases

**Canada** 51 cases

**UK** 589 cases

**Germany** 157 cases

**France** 29 cases

**Belgium** 69 cases

**Switzerland** 14 cases

**Denmark** 13 cases

**The Netherlands** 127 cases

**Belgium** 69 cases

**Switzerland** 14 cases

**Denmark** 13 cases

**The Netherlands** 127 cases

**Total number of cases reported in the literature from these countries**

High efficacy of IFN-free DAA therapy for acute HCV infection in HIV+ patients

D. CHROMY1,3, M. MANDORFER1,3, T. BUCSICS1,3, P. SCHWABL1,3, B. SCHEINER1,3, C. SCHMIDBAUER1,3, M.C. AICHELBURG1,3, P. FERENCI1, M. TRAUNER1, M. PECK-RADOŠAVLJEVIĆ1, T. REIBERGER1,3
1 Division of Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University of Vienna, Vienna, Austria
2 Division of Immunology, Allergy and Infectious Diseases, Department of Dermatology, Medical University of Vienna, Vienna, Austria
3 Vienna HIV & Liver Study Group

N=62 HIV+ patients presenting with confirmed AHC between 01/2015 – 01/2018

N=7 (11.3%) spontaneous clearance of AHC

N=55 candidates for IFN-free DAA treatment

N=16 were not eligible for treatment: reimbursement during acute phase

N=1 excluded due to diagnosis of advanced multiple myeloma

N=38 IFN-free DAA treatment initiated

N=6 SOF/LDV
N=15 3D
N=2 2D
N=2 GZV/EBV
N=2 SOF/VEL
N=11 G/P

N=33 completed treatment, n=5 still on treatment, n=0 lost to follow-up

N=33 achieved SVR4 (per protocol SVR4: 33/33, 100%)

SVR4 100%
95%-CI: 88%-100%

Abbreviations: 2D, ritonavir-boosted ombitasvir + paritaprevir; 3D, ritonavir-boosted ombitasvir + paritaprevir + dasabuvir; AHC, acute hepatitis C; CI, confidence interval; DAA, direct-acting antiviral agent; EBV, elbasvir; G/P, glecaprevir + pibrentasvir; GZV, grazoprevir; LDV, ledipasvir; SOF, sofosbuvir; SVR4, sustained virologic response 4 weeks after the end of treatment; VEL, velpatasvir
Acute HCV-epidemic in msm: DAA therapy can make a difference!

Boerekamps A et al, CID 2017
MSM Have Highest HCV Reinfection Risk

- German multi-center cohort (GECCO Cohort)
- 2074 HCV patients
- 66% GT1, 24% GT3
- 37% IVDU, 12% MSM
- 23% HIV coinfected
- Median 63 weeks until HCV reinfection
  (n=41, 36 in MSM)

HCV Reinfection Prevalence

<table>
<thead>
<tr>
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<th>% with Reinfection</th>
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<tbody>
<tr>
<td>Overall</td>
<td>1.9</td>
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<tr>
<td>IVDU</td>
<td>0.7</td>
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<tr>
<td>MSM</td>
<td>14.1</td>
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</table>

NoCo Study Flowchart

Network ICONA patients

6-months screening program

Test yearly

HCV ab-negative

HCV ab-negative

HCV ab-positive (new infection)

HCV RNA negative

HCV RNA yearly

HCV RNA positive (re-infection)

HCV RNA negative

HCV RNA positive (re-infection)

HCV RNA positive

Staging\(^2\)

Start DAA

SVR12

HCV RNA yearly

Cure

3 years

1 If tested in the previous 3 months, not to re-test
2 Blood tests, transient elastography, HCV genotype (if not available in the past year)
ASST GOM NIGUARDA TOTALE RICOVERI SC MALATTIE INFETTIVE PAZIENTI CON FRAGILITÀ SOCIALE HIV+ 2015-2016 59

• Quale fragilità
  – pazienti psichiatrici: 18 (29 ricoveri)
  – pazienti stranieri irregolari: 15 (21 ricoveri)
  – deterioramento cognitivo severo: 2 pazienti (2 ricoveri)
  – disagio socio/economico (TD, SFD, prostituzione): 6 pazienti (7 ricoveri)

2016
23 pazienti 31 ricoveri così divisi:
  – 11 psichiatrici 17 ricoveri
  – 9 stranieri 11 ricoveri
  – 3 disagio socio-economico 3 ricoveri

2015
22 pazienti 28 ricoveri così divisi
  – 9 psichiatrici 12 ricoveri
  – 8 stranieri 10 ricoveri
  – 2 deterioramento cognitivo severo 2 ricoveri
  – 3 disagio socio-economico 4 ricoveri
<table>
<thead>
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<th>Anno</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Ricoveri tot</td>
<td>Valorizzazione (Euro)</td>
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<tr>
<td>MDC 489</td>
<td>32</td>
<td>266.994</td>
</tr>
<tr>
<td>MDC 490</td>
<td>21</td>
<td>65.833</td>
</tr>
<tr>
<td>MDC 488</td>
<td>3</td>
<td>31.731</td>
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<tr>
<td><strong>Totale</strong></td>
<td><strong>56</strong></td>
<td><strong>364.558</strong></td>
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<tr>
<td>Ricoveri pazienti fragili N (%)</td>
<td>28 (50%)</td>
<td>182.279</td>
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</tbody>
</table>
Dati anagrafici
RG, genere maschile, nato nel 1961

• Anamnesi familiare
  – Padre alcolista deceduto per cirrosi a 53 anni
  – Madre di 82 anni cardiopatica
  – Un fratello HIV+

• Anamnesi fisiologica
  – Fumatore (dichiara 10 sigarette al giorno)
  – Storia di abuso alcolico fino al 2010

• Anamnesi patologica remota
  – 1986 - Frattura tibia e perone
  – dal 1979 - Tossicodipendenza in terapia sostitutiva con metadone e poi con buprenorfina fino al 2012
  – dal 1978 - Psicosi di tipo schizofrenico in terapia con diversi schemi terapeutici (benzodiazepinici e neurolettici) seguito da specialisti
  – Epilessia in terapia farmacologica con carbamazepina
  – Diabete in terapia con metformina → insulina 4+6+6+8 dal 2010
  – Ipertensione in terapia con amlodipina 10 mg/die
  – BPCO in terapia con tiotropio bromuro
Anamnesi patologica prossima

- HIV+ noto dal 1985 CD4 all’esordio 506/mm³
- Toxo IgG positive
- VZV IgG positivo
- HSV1-2 IgG negativo
- TPAb, HHV8, HPV negativo
- PPD Quantiferon negativi

- HLA B5701 negativo
- Ricoveri
  - 2005 pleuropolmonite destra
  - 2007 cellulite piede dx HIV correlata
  - 2007 Encefalopatia HIV correlata
  - 2007 Psicosi
  - 2007 Polmonite pneumococcica massiva con grave IR
  - 2009 Psicosi
  - 2010 Ustioni I e II grado gamba sx

Iter terapeutico

- In cART dal 1997 (AZT, ddI, D4T, 3TC, SQV, NFV, ID, ATZ/r fAP/r → dal 2011 tenofovir+ darunavir/r + raltegravir

- Progressivo calo CD4 → 155/mm³ nel 2011 (scarsa aderenza); mai HIV-RNA non dosabile per più di 6 mesi; profilassi con trimetoprim/sulfametossazolo dal gennaio 2011

- Osteoporosi TB score 3,3; BMD 0,872 TC deformazione a cuneo soma di D7
Anamnesi patologica prossima

– All’esordio (1985) ipertransaminasemia
  Child Pugh A MELD 7
    • HBsAg negativo
    • HBcAb positivo
    • HBsAb positivo
    • HBeAb positivo
    • HDVAb negativo
    • HAVAb IgG positivo
– → diagnosi epatite cronica NANB
– 21/6/90 HCVAb+ HCVRNA + HCV
  Genotipo 1a

– Dicembre 2011 - ricovero per anemizzazione.
  EGDS Varici esofagee F2 e gastriche; diagnosi di
  cirrosi in classe A secondo CTP con MELD 7 (non
  ascite nè EE)

– 1/2012 sclerosi emorroidi
– 2/2013 Ricovero per sanguinamento
  da varici esofagee → legatura varici
  e profilassi secondaria con beta-bloccante
– 4/2013 candidosi esofagea
– 5/2013 ascite con buona risposta
  ai diuretici; cirrosi in classe B secondo
  CTP MELD 13
– 12/2013 Recidiva di sanguinamento
  da varici esofagee
– Paziente vive con la madre di 80 anni
  assentandosi da casa per lunghi periodi
  con scarsa aderenza alle terapie e recidive di abuso
  alcolico

Valutazione congiunta infettivologica epatologica dicembre 2013
Anamnesi patologica prossima

– Dicembre 2013
  • HIV-RNA 1553 copie/ml
  • CD4 155 (34,3%)
  • PLT 67000; INR 1,4 Bilirubina 1,4 mg/dL AST 88UI/L ALT 80 UI/L GGT 98 UI/L creatinina 1,1 mg/dL
– Test delle resistenze
  • Mutazioni:
    – NNRTI K101Q
    – PI L101I L33FM46I A71V L76V I84V
  • Referto:
    – NRTI: resistenza a lamivudina emtricitabina, AZT stavudina, possibile resistenza a didanosina e abacavir, non resistenza a tenofovir
    – NNRTI: nessuna resistenza
    – PI: possibile resistenza a SQV, LPV, darunavir, atazanavir
    – INI: non resistenza
Iter terapeutico (2014)

– Il paziente viene collocato in casa alloggio e inizia terapia con risperidone
– Inizia terapia antiretrovirale con emtricitabina+rilpivirina cloridrato+tenofovir disoproxil fumarato + raltegravir 400 bid (non eleggibile per dolutegravir in compassionevole)
– Previa esecuzione di EEG ed ecocardo viene posizionata TIPS
Follow-up (dicembre 2014)

- EO non ascite semeiologicamente rilevabile, non segni EPS, non edemi arti inferiori, ginecomastia dolente a sinistra
- CD4 181/mm3 (24%) HIVRNA TND
- AST 62 U/L
- creatinina 0,89 mg/dl
- glicemia 79 mg/dl
- Bilirubina totale 0,75 mg/dl
- AFP 3,6 UI/ml
- INR 1,33
- Hb 16,6 g/L
- PLT 42 103/µl
- N 1820
- albumina 3,32 g/dl
- MELD 10 CTP B7 (ascite in terapia diuretica; albumina < 3,5 g/dL)

ECOGRAFIA non lesioni focali, TIPS funzionante, milza diametro 14,8 cm, minimo versamento ascitico

- Fibroscan 16,8 Kpa IQR 3,4 SR 77%
Andamento esami durante e dopo terapia con DAC (compassioevole) + SOF x 24 settimane

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<th>Dato</th>
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<td>Bil t/dir</td>
<td>2,25/1,03</td>
<td>1,3/0,94</td>
<td>2,09/0,88</td>
<td>1,15/0,54</td>
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<td>66</td>
<td>NR</td>
<td>NR</td>
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<td>CD4 (%)</td>
<td>181 (26%)</td>
<td>219 (28%)</td>
<td>176 (30%)</td>
<td>196 (29%)</td>
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Ultimo controllo 20 maggio 2018

- CTP A6 (ascite in controllo con terapia diuretica)
- MELD 10
- HIVRNA NR
- CD4 678
- ALT 12 AST 15
- In ottimo compenso psichiatrico vive presso una casa alloggio
- N ricoveri 2007-2013 13
- N ricoveri 2014-2016 : 1 nel nov 2014 (caduta accidentale)