Treatment Around the World
Patients in Poland

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Disclosures

Advisor and/or speaker for

AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Merck, Novartis, Roche
Patient history

55 years old female

History of possible HCV exposure:
• tracheostomy and trephination because of meningitis in 1966,
• appendectomy complicated with bowel obstruction in 1995,
• ovariectomy in 2004,
• physician performing cardiac catheterization 1985-1990.

Diagnosis of HCV infection:
• anti-HCV (routine examin. for health care workers) - Dec 1998,
• HCV RNA(+) and genotype 1b identification - May 1999,
• F3 in liver biopsy - Jun 1999,
• F4 in liver biopsy - Jun 2012,
• Elastography (fibroscan) – 18 kPa – Jun 2012
**History of HCV treatment:**

- 1999-2000: IFNa + RBV $\rightarrow$ no response
- 2007-2008: PegIFNa2a + RBV $\rightarrow$ no response
- 2008-2009: PegIFNa2b low dose monotherapy $\rightarrow$ no response
- 2012-2013: BOC + PegIFNa2a + RBV $\rightarrow$ relapse

**Safety on the BOC + PegIFNa2a + RBV treatment:**

- Anaemia from the beginning (the lowest Hb=8.0 g/dL),
  - RBV dose reduction to 400 mg between weeks 8 and 48,
  - 4 RCC transfusions at week 10, 24, 28 and 46.
- Neutropenia (the lowest neutrophils $0.48 \times 10^3$/mL),
  - PegIFN$\alpha$2a dose reduction to 90-135mg from week 20.
- Severe fatigue, weight loss (15%), recurrent fever, abdominal pain, sleepness.
Genetics (12 Nov 2013 – follow-up week 24):

- IL28B (rs12979860) - CT
- HCV RNA sequencing* → P58S resistance mutation

* Secondary resistance substitution, enhancing the resistance of primary mutations (L31F/V, P32L, and Y93H/N), but themselves not conferring resistance.

- Laparoscopic cholecystectomy (Jan 2014)
- Somach varices obliteration (Apr 2014)
- MELD: 9
- Child-Pugh: 5 (A)
- SWE (Aixplorer): F4 (12,7kPa)
Ombitasvir/Paritaprevir/Ritonavir + Dasabuvir + Ribavirin
12 weeks

IU/mL

day 0 day 1 day 7 week 4 week 12 FU

TND <15 IU/mL

Dec 2014 Sep 2015
HCV management in Poland - January 2015

1) Elastography is not allowed by National Health Fund (NFZ) for enrollment to reimbursed treatment of genotype 1 infected patients (liver biopsy necessary)

2) Genetic selection for triple therapy (BOC or TVR) (reimbursed for 20% HCV population only)

3) No reimbursement of
   - IFN based treatment with SOF, SMV or DCV
   - IFN-free regimen
     - 3D (PRV/OBV/DSV) - ongoing managed access program
     - DCV/ASV - access expected
     - SOF/LDV - not offered
     - combination of SOF with SMV or DCV not allowed ...

4) Long lasting reimbursement approval procedures by regulatory authorities.
   - for BOC and TVR it took >20 months (approved in mid 2013)
HCV medication reimbursement calendar

- GRA+ELB
- DCV+ASV
- OBV/PTV/r±DSV
- SOF+LDV
- SMV+PR
- SOF+PR
- TVR+PR
- BOC+PR

- 3 phase studies
- FDA/EMA
- UE access
- acces in Poland
HCV medication „early access” in Poland

- **DCV+ASV**: 1 Sep 2015
- **OBV/PTV/r±DSV**: 1 Jul 2015
- **SOF+LDV**: 1 Nov 2015
- **SMV+PR**: 1 May 2015
- **SOF+PR**: 1 Nov 2015
- **TVR+PR**:
- **BOC+PR**:

### Efficacy of ongoing therapies in „early access” programs

**SVR [%]**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>1 + 4</th>
<th>1 + 4</th>
<th>1</th>
<th>1</th>
<th>3</th>
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<tbody>
<tr>
<td>available FU12</td>
<td>153 + 6</td>
<td>28 + 2</td>
<td>33</td>
<td>18</td>
<td>27</td>
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<tr>
<td>target FU12</td>
<td>200 + 9</td>
<td>82 + 4</td>
<td>52</td>
<td>28</td>
<td>27</td>
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Data on file; Flisiak R and Tomasiewicz K
Criteria of entry to IFN-free therapeutic program reimbursed by National Health Fund (NFZ) in Poland
Available from 1 July 2015

1. Adults >18 with chronic hepatitis C
2. Anti-HCV in serum
3. HCV RNA in serum or liver tissue
4. Determined genotype 1-6.
5. Any hepatic fibrosis demonstrated with either:
   a) quantitative elastography expressed in kPa
   b) liver biopsy
   \textit{in case of hepatic comorbidity or discordance between clinical and non-invasive evaluation decision should be made based on liver biopsy.}
6. IFN-free regimen should be provided irrespective of hepatic fibrosis in patients with either:
   a) intolerance to IFN
   b) contraindication to IFN
   c) extrahepatic manifestations of HCV infection
### Regimens by genotypes reimbursed by National Health Fund (NFZ) in Poland

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Year</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>G5</th>
<th>G6</th>
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<tbody>
<tr>
<td>PegIFN + RBV</td>
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<td>X</td>
<td>X</td>
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<tr>
<td>BOC + PegIFN + RBV</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>TVR + PegIFN + RBV</td>
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<tr>
<td>SMV + PegIFN + RBV</td>
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<td>X</td>
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<tr>
<td>OBV/PTV/r ± DSV ± RBV</td>
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<tr>
<td>ASV + DCV</td>
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<td>SOF/LDV</td>
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<td>X</td>
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<tr>
<td>SOF + PegIFN + RBV</td>
<td>11-2015</td>
<td>X</td>
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<tr>
<td>SOF + RBV</td>
<td>11-2015</td>
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<td>X</td>
<td>X</td>
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<td>X</td>
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</table>

Regimens marked with a red X are the ones reimbursed by the National Health Fund (NFZ) in Poland.
Sales of IFN-free medication

OBV/PTV/r ± DSV ± RBV
by 9 Nov 2015

already sold
4 week packs – 1100
327 patients*

in tender
180 mln PLN (42 mln EUR)
4 week packs – 9000
2679 patients*

* 88% patients receive 12 weeks regimen based on AMBER proportions
1. Wide access to highly effective IFN-free therapeutic options.

2. Testing of populations identified as a high risk for HCV infection:
   - recipients of blood transfusion before 1992,
   - intravenous drug users (ongoing and past),
   - hospitalized for more than 3 times during the life,
   - history of imprisonment,
   - tested for HIV infection,
   - elevated ALT,
   - diagnosis or suspicion of any hepatic disorder
Conclusions for Poland

1. Reimbursed IFN-free therapeutic program without „fibrosis” or „treatment history” restrictions started in July 2015.

2. More than 400 patients started IFN-free treatment before July 2015 within early access or named patients program.

3. About 3000 patients are expected to start IFN-free therapy by the end of 2015.

4. To improve diagnosis, treatment and screening a high risk populations „National plan for HCV elimination” was created and submitted to Health Ministry in June 2015.