Why do I include peg-IFN in Hepatitis C treatment - genotype 1

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Karolinska Institute
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Sweden
My disclosures

Participated in Advisory boards, served as principal investigator and in the speakers bureau for BMS, Gilead, AbbVie, Merck, Novartis, Janssen, Medivir, and Roche
Development of HCV gt1 treatment

IFN: interferon; RBV: ribavirin
Peg-IFN: peginterferon
DAA: direct-acting antiviral
SVR: sustained virologic response

Multiple Direct Acting Antivirals

5'UTR → Core E1 E2 NS2 NS3 NS4B NS5A NS5B 3'UTR

Protease

HCV PIs

Viral enzyme Active site
Telaprevir Bocaprevir Simeprevir Paltiprevir Asunaprevir ABT-450 MK-5172 Sovaprevir ACH-2684

NS5A Inhibitors

Non-enzyme Replication complex
Daclatasvir Ledipasvir ABT-267 GS-5816 ACH-3102 PPI-668 GSK2336805 Samatasvir MK-8742

Viral enzyme Active site
NS5B Nucs
Sofosbuvir VX-157 IDX20963 ACH-3422

Viral enzyme Allosteric site
NS5B Non-nucs
ABT-333 Deleobuvir BMS-791325 PPI-383 GS-9669 TMC647055
Case no 1: Why do I include peg-IFN in my treatment of genotype 1?

- Gt 1b, HVL
- IL28B CT
- Fibrosis stage 4
- NASH + DM
- Relapse after Peg + RBV 48 weeks
Hepatitis C: Case gt 1b cirrhosis

- Treat immediately with 1st gen PI
- Re-treat immediately with peg-IFN + RBV
- Wait for IFN-free regimen
- Wait for IFN –sparing regimen
- None of the previous
Hepatitis C: Case gt 1b cirrhosis

- Treat immediately with 1st gen PI
- Re-treat immediately with peg-IFN + RBV
- Wait for IFN-free regimen
- Wait for IFN–sparing regimen
- None of the previous
Hepatitis C: gt 1b cirrhosis

- Treat immediately with 1\textsuperscript{st} gen PIs
- Not the best option due to potential many AEs and long treatment
- Deal with his Metabolic sd
- Postpone treatment for shorter more effective Rxs with less AEs and shorter courses
Hepatitis C: Case no 1 gt 1b cirrhosis

- IFN eligible Peg + RBV + Sofosbuvir (Sof) 12 ws

- IFN ineligible Sof + Simeprevir or Daclatasvir 12-24 ws
Hepatitis C: Case no 1 gt 1b cirrhosis

- IFN eligible Peg + RBV + Sofosbuvir (Sof) 12 ws
  Cost: Sof 360,000 SKR + P/R 35,000 SKR
  Total cost 395,000 SKR = 40,000 €
Hepatitis C: Case no 1 gt 1b cirrhosis

- **IFN eligible** Peg + RBV + Sofosbuvir (Sof) 12 ws
  
  Cost: Sof 36.000 €+ P/R 3.500 €
  
  Total cost 40.000 €

- **IFN ineligible** Sof + Simeprevir (Sim) or Daclatasvir (Dac) 12 - 24 ws
  
  Cost: Sof 36.000 €+ Simeprevir 26.000 €
  
  Total cost 12 weeks 62.000 € 24 weeks 124.000 €
Treatment With Sofosbuvir + Peginterferon + Ribavirin for 12 Weeks Achieves 90% SVR12 in Treatment-Naïve Genotype 1, 4, 5, and 6 HCV-Infected Patients: The NEUTRINO Study

Eric Lawitz¹, David Wyles², Mitchell Davis³, Maribel Rodriguez-Torres⁴, K. Rajender Reddy⁵, Ira Jacobson⁶, Kris V. Kowdley⁷, Evguenia Svarovskaia⁸, Deyuan Jiang⁸, John McNally⁸, Diana M. Brainard⁸, William T. Symonds⁸, John G. McHutchison⁸, Lisa Nyberg⁹, Zobair Younossi¹⁰

¹Texas Liver Institute, University of Texas Health Science Center, San Antonio, TX, USA; ²University of California, San Diego, School of Medicine, La Jolla, CA, USA; ³DigestiveCARE-South Florida Center of Gastroenterology, Wellington, FL, USA; ⁴Fundacion de Investigacion, San Juan, Puerto Rico; ⁵University of Pennsylvania, Philadelphia, PA, USA; ⁶Weill Cornell Medical College, New York, NY, USA; ⁷Digestive Diseases Institute, Virginia Mason Medical Center, Seattle, WA, USA; ⁸Gilead Sciences, Inc., Foster City, CA; USA; ⁹Kaiser Permanente, San Diego, CA, USA; ¹⁰Inova Fairfax Hospital, Falls Church, VA, USA
Study Design

- Open label
  - SOF 400 mg QD + Peg-IFN-alfa-2a 180 µg/week + RBV 1000–1200 mg/day for 12 weeks (no response-guided therapy)

- Treatment-naïve, genotype 1, 4, 5, and 6 HCV-infected patients
  - Targeted 20% enrollment of patients with cirrhosis

- Broad inclusion criteria
  - No upper limit to age or BMI
  - Opiate replacement therapy permitted
  - Platelets ≥90,000/mm³, neutrophils ≥1500/mm³ or 1000/mm³ (blacks)

Week 0 12 24

SOF + Peg-IFN + RBV, n=327

SVR12
Results: Virologic Response

- Study met primary endpoint of superiority over historic control rate of 60% (p <0.001)
- Relapse accounted for all virologic failures

Error bars represent 95% confidence intervals.
Results: SVR12 by HCV Genotype

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Patients with HCV RNA &lt;LLOQ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>90/327</td>
</tr>
<tr>
<td>GT 1</td>
<td>89/292</td>
</tr>
<tr>
<td>GT 4</td>
<td>96/28</td>
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<tr>
<td>GT 5,6</td>
<td>100/7</td>
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</table>

Error bars represent 95% confidence intervals.
Results: Virologic Response by Cirrhosis Status

Error bars represent 95% confidence intervals.
Results: SVR12 by Prespecified Subgroups

<table>
<thead>
<tr>
<th>HCV GT</th>
<th>Overall</th>
<th>1 (1a, 1b, 1a/b)</th>
<th>1a</th>
<th>1b</th>
<th>4, 5, 6</th>
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<tbody>
<tr>
<td>Cirrhosis</td>
<td>No</td>
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<tr>
<td></td>
<td>Yes</td>
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<tr>
<td>Race</td>
<td>Black</td>
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<tr>
<td></td>
<td>Non-black</td>
<td></td>
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<tr>
<td>HCV RNA level</td>
<td>&lt;6 log_{10} IU/mL</td>
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<td></td>
<td>≥6 log_{10} IU/mL</td>
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<td>IL28B</td>
<td>CC</td>
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<tr>
<td></td>
<td>Non-CC</td>
<td></td>
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</table>

SOF + Peg-IFN + RBV
Simeprevir plus sofosbuvir with/without ribavirin in HCV genotype-1 prior null-responder / treatment-naïve patients (COSMOS study): primary endpoint (SVR12) results in patients with METAVIR F3-4 (Cohort 2)

Eric Lawitz,1 Reem Ghalib,2 Maribel Rodriguez-Torres,3 Zobair M Younossi,4 Ana Corregidor,5 Mark S Sulkowski,6 Edwin DeJesus,7 Brian Pearlman,8 Mordechai Rabinovitz,9 Norman Gitlin,10 Joseph K Lim,11 Paul J Pockros,12 Bart Fevery,13 Tom Lambrecht,14 Sivi Ouwerkerk-Mahadevan,13 Kathleen Callewaert,13 William T Symonds,15 Gaston Picchio,16 Karen Lindsay,17 Maria Beumont-Mauviel,13 Ira M Jacobson18

1The Texas Liver Institute, University of Texas Health Science Center, San Antonio, TX, USA; 2Medicine and Gastroenterology and Hepatology, The Liver Institute, Dallas, TX, USA; 3Fundación de Investigación, San Juan, Puerto Rico, USA; 4Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, USA; 5Borland-Groover Clinic, Jacksonville, FL, USA; 6Johns Hopkins University School of Medicine, Baltimore, MD, USA; 7Orlando Immunology Center, Orlando, FL, USA; 8Atlanta Medical Center, Atlanta, GA, USA; 9University of Pittsburgh Medical Center, Pittsburgh, PA, USA; 10Atlanta Gastroenterology Association, Atlanta, GA, USA; 11Yale School of Medicine, New Haven, CT, USA; 12Scripps Clinic, La Jolla, CA, USA; 13Janssen Research & Development, Beerse, Belgium; 14Novellas Healthcare, Zellik, Belgium; 15Gilead Sciences Inc, Foster City, CA, USA; 16Janssen Research & Development LLC, Titusville, NJ, USA; 17Formerly of Janssen Research & Development LLC, Titusville, NJ, USA; 18Weill Cornell Medical College, New York, NY, USA
COSMOS study design: Randomised, multicentre, open-label trial

- **Cohort 1**: METAVIR F0-F2, prior null responders
- **Cohort 2**: METAVIR F3-F4, prior null responders or treatment-naïve
  - Stratified by treatment history, HCV GT 1a/1b
- **Primary endpoint**: SVR12
- **Secondary endpoints**: RVR, on-treatment failure, relapse rate, safety and tolerability

<table>
<thead>
<tr>
<th>Week</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
<th>Arm 4</th>
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<tbody>
<tr>
<td>0</td>
<td>SMV + SOF + RBV</td>
<td>SMV + SOF</td>
<td>SMV + SOF + RBV</td>
<td>SMV + SOF</td>
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<tr>
<td>4</td>
<td>Post-treatment follow-up</td>
<td>Post-treatment follow-up</td>
<td>Post-treatment follow-up</td>
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<td>12</td>
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<td>24</td>
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<td>36</td>
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<td>48</td>
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</tbody>
</table>

SMV 150 mg QD + SOF 400 mg QD±RBV 1000/1200 mg/day (BID)

- **Randomised 2:1:2:1**

BID, twice daily; GT, genotype; QD, once daily; RBV, ribavirin; RVR, rapid virologic response; SMV, simeprevir; SOF, sofosbuvir; SVR12, sustained virologic response 12 weeks after end of treatment
COSMOS Cohort 2: SVR12 by HCV GT 1 subtype and baseline NS3 Q80K polymorphism (excluding non-VF*)

*Excluding patients who discontinued for non-virologic reasons

GT, genotype; non-VF, non-virologic failure; RBV, ribavirin
SMV, simeprevir; SOF, sofosbuvir; SVR12, sustained virologic response 12 weeks after planned treatment end
COSMOS Cohort 2: SVR12 by treatment history – METAVIR F4 patients (excluding non-VF*)

*Excluding patients who discontinued for non-virologic reasons

Non-VF, non-virologic failure; RBV, ribavirin; SMV, simeprevir; SOF, sofosbuvir; SVR12, sustained virologic response 12 weeks after planned treatment end
Why do I include peg-IFN in Hepatitis C treatment: Case no 1 gt 1b cirrhosis

• IFN eligible
  – It is much cheaper
Why do I include peg-IFN in Hepatitis C treatment: Case no 1

- IFN eligible
  - It is much cheaper
  - It is very effective
Why do I include peg-IFN in Hepatitis C treatment: Case no 1

• IFN eligible
  – It is much cheaper
  – It is very effective
  – A large subgroup tolerates IFN well
Why do I include peg-IFN in Hepatitis C treatment: if IFN ineligible

• I do not
• Wait for IFN-free regimen
  – Best option, short effective Rx, but expensive
Hepatitis C: Case no 1 gt 1b with cirrhosis

• Possible IFN –sparing regimens
  – Possible as PI + NS5A inh (Asunaprevir + Daclatasvir (in Japan only 1b and IL28B CC)) or
  – Sofosbuvir + RBV, however - 24 ws needed
  – Sofosbuvir + Simeprevir 12 weeks ?
  – Sofosbuvir + Daclatasvir ?
  – Sofosbuvir + Ledipasvir ?
  – Abbvie trippel kombination (PI/r + NS5A inh + NNUC +/- ribavirin)
Lady born 1953 with gt 1b chronic HCV

- Relapse after 72 weeks peg-IFN + ribavirin rx
- Many AE:s during treatment
- IL28B TT
- Fibrosis stage 3
Why do I include peg-IFN in Hepatitis C treatment - genotype 3
Hepatitis C: Why do I include peg-IFN in the treatment

- **Case no 2 - 49 year old male**
- Gt 3a, HVL
- IL28B CT
- Liver stiffness 14.5 kPa = Fibrosis stage 4?
- Plt 120,000 mm$^3$
- Stopped drugs and alcohol
- Treatment experienced without SVR
Case no 2  genotype 3a - can this patient wait without treatment?

• No - transient elastography and PLT indicates cirrhosis

• Treatment options
  – IFN included - Sofosbuvir + P/R
  – IFN-free - Sofosbuvir + R
Current treatment options – Which regimen can benefit this patient most?

• Peg-IFN + RBV longer than 24 ws?
• IFN-free regimen with Sofosbuvir and weight-based RBV?
• Sofosbuvir + Peg-IFN + RBV?
• None of the above?
Male with gt 2b chronic HCV – relapser x 2 on P/R 24 – 48 weeks
Sofosbuvir and Ribavirin in HCV Genotypes 2 and 3

Stefan Zeuzem, M.D., Geoffrey M. Dusheiko, M.D., Riina Salupere, M.D., Ph.D., Alessandra Mangia, M.D., Robert Flisiak, M.D., Ph.D., Robert H. Hyland, D.Phil., Ari Illeperuma, M.S., Evguenia Svarovskaia, Ph.D., Diana M. Brainard, M.D., William T. Symonds, Pharm.D., G. Mani Subramanian, M.D., Ph.D., John G. McHutchison, M.D., Ola Weiland, M.D., Hendrik W. Reesink, M.D., Ph.D., Peter Ferenci, M.D., Christophe Hézode, M.D., and Rafael Esteban, M.D., for the VALENCE Investigators
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

- This patient has gt 3a, DM and cirrhosis
- Has failed earlier peg-IFN + RBV treatment

**IFN free treatment**

- Sofosbuvir + RBV offers only some 60% SVR with 24 weeks rx

*NEJM VALEANCE STUDY 2014*
SVR12 in GT 3 Patients Treated for 24 Weeks

- Experienced, Cirrhotic: 60/45
- Experienced, Noncirrhotic: 87/100
- Naive, Cirrhotic: 12/13
- Naive, Noncirrhotic: 94/92

SVR12 (%)
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

• This patient has gt 3a, DM and cirrhosis
• Has failed earlier peg-IFN + RBV treatment
• Sofosbuvir + RBV offers only some 60 % SVR with 24 weeks rx

**IFN included:**

• Sof + peg-IFN + RBV offers some **80 % SVR** with 12 weeks rx
Successful Retreatment With Sofosbuvir-containing Regimens for HCV Genotype 2 or 3 Infected Patients who Failed Prior Sofosbuvir Plus Ribavirin Therapy

Rafael Esteban¹, Lisa Nyberg², Jay Lalezari³, Liyun Ni⁴, Brian Doehle⁴, Bittoo Kanwar⁴, Diana Brainard⁴, GM Subramanian⁴, William T. Symonds⁴, John G. McHutchison⁴, Maribel Rodriguez-Torres⁵, Stefan Zeuzem⁶

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International Liver Congress 2013, Amsterdam
Methods

- Open-label study offered to all GT 2 or 3 treatment failures from FISSION, POSITRON and FUSION

- Patients offered 2 possible treatment options
  - Choice based on patient’s eligibility for IFN and patient/investigator recommendation

- Included patients with compensated cirrhosis
# Results: Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>12 weeks SOF + PEG/RBV n=34</th>
<th>24 weeks SOF + RBV n=73</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (range)</td>
<td>53 (31–70)</td>
<td>53 (38-63)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>26 (77)</td>
<td>63 (86)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Mean BMI, kg/m² (range)</td>
<td>29 (22–39)</td>
<td>28 (20-41)</td>
</tr>
<tr>
<td>Cirrhosis* n (%)</td>
<td>14 (41)</td>
<td>25 (34)</td>
</tr>
<tr>
<td>IL28B CC, n (%)</td>
<td>11 (32)</td>
<td>27 (37)</td>
</tr>
<tr>
<td>Mean ALT, U/L (range)</td>
<td>96 (14-325)</td>
<td>89 (18-310)</td>
</tr>
<tr>
<td>Genotype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6 (18)</td>
<td>5 (7)</td>
</tr>
<tr>
<td>3</td>
<td>28 (82)</td>
<td>68 (93)</td>
</tr>
<tr>
<td>Mean baseline HCV RNA, log$_{10}$ IU/mL (range)</td>
<td>6.3 (4.8-7.8)</td>
<td>6.6 (4.4–7.6)</td>
</tr>
</tbody>
</table>

*Cirrhosis status determined in parent protocol.
Results: On Treatment Viral Response and SVR 12

12 weeks SOF+PEG/RBV  
24 weeks SOF+RBV

<table>
<thead>
<tr>
<th>Week</th>
<th>Patients with &lt; LLOQ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>28/28 50/50</td>
</tr>
<tr>
<td>End of Treatment</td>
<td>28/28 50/50</td>
</tr>
<tr>
<td>SVR 12</td>
<td>24/26 25/40</td>
</tr>
</tbody>
</table>

♦ Relapse accounted for all virologic failures

Error bars represent 95% confidence intervals.
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

IFN free treatment

• Sofosbuvir + RBV offers only some
  60 % SVR with 24 weeks rx

IFN included:

• Sof + peg-IFN + RBV offers some
  80 % SVR with 12 weeks rx
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

IFN free treatment

• Sofosbuvir + RBV offers only some
  60 % SVR with 24 weeks rx
• Cost: Sof 72.000 €+ ribavirin now cheap

IFN included:

• Sof + peg-IFN + RBV offers some
  80 % SVR with 12 weeks rx
• Cost: Sof 36.000 €+ P/R 3.500 €
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

- **SOF + R**: 70,000 €
- **SOF + P/R**: 40,000 €
Review article: 2014 UK consensus guidelines – hepatitis C management and direct-acting anti-viral therapy


Recommendation: Patients with cirrhosis or severe fibrosis HCV genotype 3 could be offered 24 weeks of sofosbuvir and ribavirin or 12 weeks with sofosbuvir and ribavirin and Interferon alpha, with similar efficacy.

Aliment Pharmacol Ther 2014; 39: 1363-1375
Our case gt 3a cirrhosis non-responder to earlier IFN based regimen – options

• This patient has 3a, DM and cirrhosis
• Has failed earlier peg-IFN + RBV treatment
• Sofosbuvir + RBV offers only some 60 % SVR with 24 weeks rx
• Sof + peg-IFN + RBV offers some 80 % SVR with 12 weeks rx
• Future off label Sof + Dac +/- RBV may offer even higher SVR rates but is expensive
Why do I still include peg-IFN for treatment of HCV?

- For *IFN tolerant patients* it is less expensive
- For *gt 3a* experienced cirrhotics it offers a shorter treatment course and higher SVR rates
- For *gt 1* experienced with well compensated cirrhosis it offers shorter treatment and high SVR rates
Should we await IFN-free regimens to treat HCV genotype 1 treatment-naive patients? A cost-effectiveness analysis (ANRS 95141)

Sylvie Deuffic-Burban, Michaël Schwarzinger, Dorothée Obach, Vincent Mallet, Stanislas Poil, Georges-Philippe Pageaux, Valérie Canva, Pierre Deltenre, Françoise Roudot-Thoraval, Dominique Larrey, Daniel Dhumeaux, Philippe Mathurin, Yazdan Yazdanpanah

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Fig. 1. Model of HCV progression.
Table 1. Probability of virological response according to time and therapeutic options.

<table>
<thead>
<tr>
<th></th>
<th>RVR</th>
<th>EVR if RVR</th>
<th>EVR if no RVR</th>
<th>ETR if EVR</th>
<th>SVR if ETR</th>
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</thead>
<tbody>
<tr>
<td><strong>Triple therapy with telaprevir</strong> [4, 13, 18]: baseline analysis</td>
<td></td>
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<tr>
<td>IL28B/CC</td>
<td>84%</td>
<td>93%</td>
<td>-</td>
<td>100%</td>
<td>95%</td>
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<tr>
<td>IL28B/none-CC</td>
<td>60%</td>
<td>91%</td>
<td>-</td>
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<td>IL28B/CC</td>
<td>86%</td>
<td>94%</td>
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<td>96%</td>
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<tr>
<td>IL28B/none-CC</td>
<td>49%</td>
<td>93%</td>
<td>-</td>
<td>100%</td>
<td>97%</td>
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<td><strong>Dual therapy</strong>† [17, 27, 28]</td>
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<td>IL28B/CC</td>
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<tr>
<td>F0-2</td>
<td>-</td>
<td>-</td>
<td>98.6%</td>
<td>92.7%</td>
<td>87.0%</td>
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<tr>
<td>F3-4</td>
<td>-</td>
<td>-</td>
<td>84.6%</td>
<td>89.2%</td>
<td>79.1%</td>
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<td>F0-2</td>
<td>-</td>
<td>-</td>
<td>74.7%</td>
<td>55.5%</td>
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<tr>
<td>F3-4</td>
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<td>45.3%</td>
<td>49.8%</td>
<td>58.9%</td>
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<td><strong>IFN-based new DAAs</strong> [15]</td>
<td>100%</td>
<td>89%</td>
<td>-</td>
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<td>100%</td>
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<td><strong>IFN-free regimens</strong> [16]</td>
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</tr>
<tr>
<td>F0 2</td>
<td>100%</td>
<td>95%</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>F3-4</td>
<td>100%</td>
<td>85%</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*For TVR/BOC-based triple therapy and IFN-based new DAAs, virological responses corresponded to those for patients at F0–2; for patients at F3–4, a 20% reduction was applied to their responses.
†If HCV RNA was detectable at week 4 of triple therapy, then telaprevir/boceprevir was discontinued; as a result, EVR, ETR and SVR corresponded to that achieved with dual therapy.
RVR, rapid virologic response; EVR, extended virologic response; ETR, end-of-treatment response; SVR, sustained virologic response.
Table 4. Incremental cost-effectiveness analysis: Baseline analysis.

<table>
<thead>
<tr>
<th>Strategies</th>
<th>Lifetime cost (€)</th>
<th>Life expectancy (years)</th>
<th>QALY (years)</th>
<th>ICER (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F0-1 at diagnosis (49 yr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treat with TVR/BOC-based triple therapy when ≥F2</td>
<td>25,700</td>
<td>20.80</td>
<td>19.32</td>
<td></td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when ≥F2</td>
<td>40,500</td>
<td>21.10</td>
<td>19.71</td>
<td>37,900</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs regardless of fibrosis</td>
<td>64,300</td>
<td>21.13</td>
<td>19.94</td>
<td>103,500</td>
</tr>
<tr>
<td>Treat when ≥F2 (IFN-based new DAAAs before 2015, IFN-free regimens from 2015 on)*</td>
<td>69,100</td>
<td>21.22</td>
<td>19.84</td>
<td>Dominated*</td>
</tr>
<tr>
<td>Await IFN-free regimens; then treat when ≥F2*</td>
<td>69,100</td>
<td>21.22</td>
<td>19.84</td>
<td>Dominated*</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when ≥F3; otherwise, await IFN-free regimens and then treat when ≥F2*</td>
<td>69,100</td>
<td>21.22</td>
<td>19.84</td>
<td>Dominated*</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when F4; otherwise, await IFN-free regimens and then treat when ≥F2*</td>
<td>69,100</td>
<td>21.22</td>
<td>19.84</td>
<td>Dominated*</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when ≥F2; otherwise, await IFN-free regimens and then treat regardless of fibrosis**</td>
<td>112,500</td>
<td>21.25</td>
<td>20.09</td>
<td>321,300</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when ≥F3; otherwise, await IFN-free regimens and then treat regardless of fibrosis**</td>
<td>112,500</td>
<td>21.25</td>
<td>20.09</td>
<td>321,300</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when F4; otherwise, await IFN-free regimens and then treat regardless of fibrosis**</td>
<td>112,500</td>
<td>21.25</td>
<td>20.09</td>
<td>321,300</td>
</tr>
<tr>
<td>Await IFN-free regimens; then treat regardless of fibrosis**</td>
<td>112,500</td>
<td>21.25</td>
<td>20.09</td>
<td>321,300</td>
</tr>
<tr>
<td><strong>F2 at diagnosis (54 yr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treat with TVR/BOC-based triple therapy</td>
<td>38,900</td>
<td>18.53</td>
<td>17.22</td>
<td></td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs</td>
<td>65,100</td>
<td>19.12</td>
<td>17.97</td>
<td>34,900</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when ≥F3; otherwise, await IFN-free regimens*</td>
<td>112,900</td>
<td>19.26</td>
<td>18.12</td>
<td>318,700</td>
</tr>
<tr>
<td>Await IFN-free regimens*</td>
<td>112,900</td>
<td>19.26</td>
<td>18.12</td>
<td>318,700</td>
</tr>
<tr>
<td><strong>F3 at diagnosis (56 yr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treat with TVR/BOC-based triple therapy</td>
<td>50,000</td>
<td>16.05</td>
<td>14.60</td>
<td></td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs</td>
<td>71,800</td>
<td>16.99</td>
<td>15.72</td>
<td>19,500</td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs when F4; otherwise, await IFN-free regimens*</td>
<td>120,000</td>
<td>17.36</td>
<td>16.07</td>
<td>137,700</td>
</tr>
<tr>
<td>Await IFN-free regimens*</td>
<td>120,000</td>
<td>17.36</td>
<td>16.02</td>
<td>137,700</td>
</tr>
<tr>
<td><strong>F4 at diagnosis (59 yr)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treat with TVR/BOC-based triple therapy</td>
<td>71,700</td>
<td>11.92</td>
<td>10.32</td>
<td></td>
</tr>
<tr>
<td>Treat with IFN-based new DAAAs</td>
<td>96,800</td>
<td>12.76</td>
<td>11.15</td>
<td>30,200</td>
</tr>
<tr>
<td>Await IFN-free regimens</td>
<td>130,400</td>
<td>12.63</td>
<td>11.04</td>
<td>Dominated†</td>
</tr>
</tbody>
</table>

*These strategies lead to the same results at a given stage of fibrosis at diagnosis, since no patient will progress before the arrival of IFN-free regimens, i.e., within one year.

†Strongly dominated strategies: more expensive and less effective.
Why do I still include peg-IFN for treatment of HCV?

- For *IFN tolerant patients* it is less expensive
- For IFN based new DAA Rxs with fibrosis stage F2 or higher it is cost-effective better than TVR/BOC triple for gt1
- For all *IFN free treatment* the cost-effectiveness is highly dependent on cost
Fig. 2. Impact of varying cost of IFN-free regimens vs. IFN-based new DAAs on the incremental cost-effectiveness (ICER) ratio of the strategy “Await IFN-free regimens; then treat regardless of fibrosis”. In the baseline analysis IFN-free regimens were considered to be 2 times higher than IFN-based new DAAs (multiplier = 2): (A) For patients diagnosed at F0 and F1, the comparison strategy would be “Await IFN-free regimens; then treat when ≥F2” until the multiplier applied to the cost of IFN-based new DAAs is 1.4; then the comparator strategy would be “Treat with IFN-based new DAAs regardless of fibrosis”; (B) for patients diagnosed at F2, the comparison strategy would be “Treat with TVR/BOC triple strategy” until the multiplier is 1.2; then “Treat with IFN-based new DAAs”; (C) for patients diagnosed at F3, the comparison strategy would be “Treat with TVR/BOC triple strategy when ≥F2” until the multiplier applied is 1.2; then the strategy “Await IFN-free regimens” will be dominated by “Treat with IFN-based new DAAs”.