The Changing Face of Hepatitis C Treatment

Nezam H. Afdhal M.D
Professor of Medicine,
Harvard Medical School,
Chief of Hepatology,
Beth Israel Deaconess Medical Center, Boston
<table>
<thead>
<tr>
<th>In the past 2 years I have been an employee of:</th>
<th>BIDMC, HMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the past 2 years I have been a consultant of:</td>
<td>Gilead, Merck, Echosens, GSK, Vertex, Novartis, Boehringer Ingelheim, Ligand, Springbank, Medgenics, Kadmon, Quest</td>
</tr>
<tr>
<td>In the past 2 years I have held investments in the following pharmaceutical organizations, medical devices companies or communications firms:</td>
<td>Springbank, Medgenics</td>
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<td>In the past 2 years I have been a speaker for:</td>
<td>N/A</td>
</tr>
<tr>
<td>In the past 2 years I have received research support (grants) from:</td>
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</tr>
<tr>
<td>In the past 2 years I have received honoraria from:</td>
<td>Gilead, Merck, Echosens, GSK, Vertex, Novartis, Boehringer Ingelheim, Ligand, Springbank, Medgenics, Kadmon, Quest</td>
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<tr>
<td>I agree to disclose approved and non-approved indications for medications in this presentation:</td>
<td>YES</td>
</tr>
<tr>
<td>I agree to use generic names of medications in this presentation:</td>
<td>YES</td>
</tr>
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</table>
The Goal of Combination Regimens

- Different drugs can contribute variably to each goal. Not all components must be direct-acting antivirals (DAAs).
Milestones in Therapy of CHC:
Average SVR Rates from Clinical Trials

- IFN 6m: 6%
- IFN 12m: 16%
- IFN/RBV 6m: 34%
- IFN/RBV 12m: 42%
- Peg-IFN 12m: 39%
- Peg-IFN/RBV 12m: 55%
- Peg-IFN/RBV/DAA: 70+% SVR

History:
- Standard Interferon: 1991
- Ribavirin: 1998
- Peginterferon: 2001
- Direct Acting Antivirals: 2011

Adapted from US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring MD.
Predictors of Response

• **Viral Factors**
  – HCV genotype
  – HCV RNA

• **Patient Factors**
  – Race/ethnicity
  – Metabolic
  – Obesity
  – Age
  – Advanced disease

• **Genetic Contributions**
  – *IL28B* polymorphism

• **On treatment Factors**
  – Selection of regimen
  – Duration of regimen
  – Expected cumulative dose exposure / adherence
  – Viral response
SVR Rates With BOC or TVR in Genotype 1 Treatment-Naive Patients

# BOC + PR: Adverse Events

Significantly higher rates of anemia, neutropenia and dysgeusia in BOC arms vs control

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>BOC + PR RGT/48 n = 1225</th>
<th>PR48 n = 467</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia*</td>
<td>50%</td>
<td>30%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>35%</td>
<td>16%</td>
</tr>
</tbody>
</table>

*Anemia was managed with RBV reduction and/or epoetin alfa (43% of BOC + PR and 24% PR)

What’s In Our Near Future? More Triple Therapy

• Single DAA plus IFN backbone plus ribavirin (RBV)
  – Second-generation PIs
  – Nucleoside polymerase inhibitors
  – Nonstructural protein (NS)5A inhibitors

• Considerations
  – RVR > 90%
  – Sustained virologic response (SVR): 80%
  – Tolerability and side effects
  – RGT
  – 12–16 weeks of therapy for *IL-28B* CC genotype
PILLAR Study: TMC435 + Peg-IFN + RBV in treatment-naïve G1 patients

- Phase IIb, randomized, double-blind study in treatment-naïve, HCV G1, TMC435 (QD oral HCV NS3/4A PI) + Peg-IFNα-2a/RBV (PR)

<table>
<thead>
<tr>
<th>Response, n/N (%)</th>
<th>TMC435 12W PR RGT</th>
<th>TMC435 24W PR RGT</th>
<th>TMC435 12W PR RGT</th>
<th>TMC435 24W PR RGT</th>
<th>Placebo/PR 48W</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>75 mg N=78</td>
<td>150 mg N=77</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVR</td>
<td>59/78 (75.6)</td>
<td>51/75 (68.0)</td>
<td>58/77 (75.3)</td>
<td>59/79 (74.7)</td>
<td>4/77 (5.2)</td>
</tr>
<tr>
<td>EOT</td>
<td>72/78 (92.3)</td>
<td>73/75 (97.3)</td>
<td>71/77 (92.2)</td>
<td>74/79 (93.7)</td>
<td>61/77 (79.2)</td>
</tr>
<tr>
<td>SVR24</td>
<td>64/78 (82.1)*</td>
<td>56/75 (74.7)</td>
<td>62/77 (80.5)*</td>
<td>68/79 (86.1)**</td>
<td>50/77 (64.9)</td>
</tr>
<tr>
<td>SVR W72</td>
<td>63/78 (80.8)*</td>
<td>53/75 (70.7)</td>
<td>60/77 (77.9)*</td>
<td>67/79 (84.8)**</td>
<td>50/77 (64.9)</td>
</tr>
<tr>
<td>Viral relapse</td>
<td>8/72 (11.1)</td>
<td>14/72 (19.4)</td>
<td>6/69 (8.7)</td>
<td>6/75 (8.0)</td>
<td>11/62 (17.7)</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.005, significant difference vs control

- Very high SVR in PR group, European study, low BMI
- For PR: Very poor RVR in CC patients, very high SVR in CT and TT >50%
- Hyperbilirubinemia noted especially in 150 mg group
- High RVR rate in TMC 435 groups, appropriate to move to Phase III
- Needs combination information

Fried M et al. AASLD 2011, San Francisco, #LB-5
Sofosbuvir + PEG/RBV: GT 1,4,5,6

NEUTRINO:
Treatment-naïve patients, multicenter, open-label study

N=327
Sofosbuvir 400 mg QD + PEG 180 µg/week + RBV

Study Weeks
12
24
SVR 12
NEUTRINO SVR12 Results

- No on-treatment virologic failure (all relapses)
- Most common AEs occurring in ≥20% subjects were fatigue, headache, nausea, insomnia, and anemia
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Efficacy</th>
<th>Genotype indep.</th>
<th>Barrier to resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS3/4A (protease inhibitors)</td>
<td>+++</td>
<td>+ - ++</td>
<td>+ - ++</td>
</tr>
<tr>
<td>NS5A</td>
<td>+++</td>
<td>+ - ++</td>
<td>+ - ++</td>
</tr>
<tr>
<td>NS5B (nucleosides)</td>
<td>+ - +++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>NS5B (non-nucleosides)</td>
<td>+ - ++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cyclophilin Inhibitors</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
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</table>
## All Oral Therapies: The Drug classes – 2013 - 16

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Efficacy</th>
<th>Genotype independency</th>
<th>Barrier to resistance</th>
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<tbody>
<tr>
<td>NS3/4A (protease inhibitors)</td>
<td>+++</td>
<td>++ - +++</td>
<td>++ - +++</td>
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<tr>
<td>NS5A</td>
<td>+++</td>
<td>++ - +++</td>
<td>++ - +++</td>
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<tr>
<td>NS5B (nucleosides)</td>
<td>+ - ++++</td>
<td>+++</td>
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<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cyclophilin Inhibitors</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>
All Oral Combinations - Timelines

- **2013/14**
  - NI + RBV (GT 2,3)

- **2014/15**
  - PI + NNI + RBV (GT 1b)
  - PI + NS5A-I + NNI ± RBV (GT 1)
  - PI + NS5A-I (GT 1b; off-label ?)
  - NI + NS5A-I (pan-GT; off-label)
  - NI + PI (GT 1,2,4-6; off-label)

- **2015/16**
  - NI + NS5A-I (FDC, pan-GT)
  - NI + NS5A-I + X
DAA Combination Therapy

- Ribavirin
- Protease-Inh.
- NNI
**SOUND-C2: SVR according to IL28B and HCV subtype: All groups (ITT)**

**Bl 207127 dosing**
- **Duration (weeks):** 16, 28, 40
- **RBV +/-:** +

### SVR (%)

<table>
<thead>
<tr>
<th>Duration (weeks)</th>
<th>TID</th>
<th>1a non-CC</th>
<th>All 1b and 1a-CC</th>
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</thead>
<tbody>
<tr>
<td>16</td>
<td>32</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>38</td>
<td>68</td>
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<tr>
<td>40</td>
<td>38</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>32</td>
<td>84</td>
<td></td>
</tr>
</tbody>
</table>

All groups received faldaprevir 120 mg QD for the same duration as Bl 207127 (16, 28 or 40 weeks)
ABT-450/r + ABT-333 + RBV for 12 weeks in GT1-infected patients

Virologic response rates (%)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Tx-naive (n=19)</th>
<th>Tx-naive (n=14)</th>
<th>Tx-exp. (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250/100 mg</td>
<td>90/90/95</td>
<td>79/79/93</td>
<td>77/59/47</td>
</tr>
<tr>
<td>150/100 mg</td>
<td>90/90/95</td>
<td>79/79/93</td>
<td>77/59/47</td>
</tr>
</tbody>
</table>

Treatment regimen with ABT-450/r, ABT-267, ABT-333 and RBV: Study design

- **448 patients**
  - 358 naive
    - G1a: 66–70%
    - Viral load 6.5 log
    - IL28B CC: 27–34%
    - No cirrhosis
  - 90 null responders
    - G1a: 59–62%
    - Viral load 6.5 log
    - IL28B CC: 2–4%
    - No cirrhosis

<table>
<thead>
<tr>
<th>ABT-450/r Dose (QD)</th>
<th>Wk 0</th>
<th>Wk 8</th>
<th>Wk 12</th>
<th>Wk 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>150/100</td>
<td>80</td>
<td>450</td>
<td>267</td>
<td>333</td>
</tr>
<tr>
<td>150/100</td>
<td>41</td>
<td>450</td>
<td>333</td>
<td></td>
</tr>
<tr>
<td>100/100,200/100</td>
<td>79</td>
<td>450</td>
<td>267</td>
<td></td>
</tr>
<tr>
<td>150/100</td>
<td>79</td>
<td>450</td>
<td>267</td>
<td>333</td>
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<tr>
<td>100/100,150/100</td>
<td>79</td>
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<td>333</td>
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<td>100/100,150/100</td>
<td>45</td>
<td>450</td>
<td>267</td>
<td>333</td>
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<tr>
<td>100/100,150/100</td>
<td>43</td>
<td>450</td>
<td>267</td>
<td>333</td>
</tr>
</tbody>
</table>

ABT-267 25 mg QD; ABT-333 400 mg BID; RBV weight-based 1000–1200 mg daily dose
All subjects to be followed through 48 weeks post-treatment

Kowdley KV, et al. AASLD 2012, Boston, #LB-1
12-Week IFN-free treatment regimen with ABT-450/r, ABT-267, ABT-333 and RBV results

Kowdley KV, et al. AASLD 2012, Boston #LB-1
DAA Combination Therapy

NS5A-I

Protease-Inh.
Daclatasvir + Asunaprevir in GT1b pts with IFN intolerance/null response

- 24 wks of daclatasvir 60 mg QD + asunaprevir 200 mg BID (N = 43)
  - 10 pts received asunaprevir 600 mg BID

- Among pts with virologic breakthrough (7.0%) or relapse (9.3%), almost all had trough daclatasvir and asunaprevir plasma concentrations below median

Suzuki, et al., EASL 2012, A14
DAA Combination Therapy

- NS5A-I
- Protease-Inh.
- NNI
An IFN-free, RBV-free 12-week regimen of daclatasvir (DCV), asunaprevir (ASV), and BMS-791325

- **AEs**: Headache (31%) and diarrhea (25%) most common
- **Resistance**: No data, no virologic failure to date
- **Patients achieving endpoint (%)**
  - 24-week, Group 1, n=16
  - 12-week, Group 2, n=16

- **HCV RNA < LLOQ**
  - 24-week (Group 1)
    - TD or TND
  - 12-week (Group 2)
    - TD or TND

- **Addition of a non-nuc. to a NS3 and NS5A adds incremental benefit in G1a**
- **Regimen should be evaluated with larger numbers and more advanced fibrosis**

Everson GT, et al. AASLD 2012, Boston, #LB-3
DAA Combination Therapy

- Ribavirin
- Protease-Inh.
- NI
COSMOS study: Sofosbuvir + Simeprevir ± RBV in GT1 Null-Responders

Week 12 Group

Sofosbuvir 400 mg QD + Simeprevir 150 mg QD ± RBV x 12 wks

Lawitz et al., CROI 2013, Abstract 155LB
DAA Combination Therapy

Ribavirin

NI
High efficacy of GS-7977 in combination with low- or full-dose RBV for 24 weeks in difficult-to-treat G1 patients: SPARE trial

- In treatment-naive HCV G1, SVR4 in 72% (mITT 75%) who received SOF + full-dose RBV but only in 56% (mITT 64%) in those who received low-dose RBV
- No safety signals or drug-related discontinuations

Osinusi A, et al. AASLD 2012, Boston, #LB-4
Sofosbuvir Phase 3 Programs: GT2/3

Study Weeks

<table>
<thead>
<tr>
<th>FISSION Genotype 2/3 (naïve)</th>
<th>12</th>
<th>16</th>
<th>24</th>
<th>28</th>
<th>36</th>
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<tbody>
<tr>
<td>N=256 Sofosbuvir 400mg QD + RBV</td>
<td>SVR12</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>N=243 Peg-IFN + RBV</td>
<td>SVR12</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>POSITRON Genotype 2/3 (IFN ineligible/intolerant)</th>
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<th>16</th>
<th>24</th>
<th>28</th>
<th>36</th>
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<tbody>
<tr>
<td>N=207 Sofosbuvir 400mg QD + RBV</td>
<td>SVR12</td>
<td></td>
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<tr>
<td>N=71 Sofosbuvir placebo + RBV placebo</td>
<td>SVR12</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>FUSION Genotype 2/3 (treatment-experienced)</th>
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<th>16</th>
<th>24</th>
<th>28</th>
<th>36</th>
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<tbody>
<tr>
<td>N=103 Sofosbuvir 400mg QD + RBV</td>
<td>SVR12</td>
<td></td>
<td></td>
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<tr>
<td>N=98 Sofosbuvir 400mg QD + RBV</td>
<td>SVR12</td>
<td></td>
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</table>
POSITRON SVR12 Results

- SVR12 rate in placebo recipients was 0%
- No on-treatment virologic failure in SOF+RBV arm (all relapses)
- Most common AEs occurring in ≥10% subjects were fatigue, nausea, headache, insomnia, pruritus, and anemia
1 on-treatment virologic failure in SOF+RBV arm due to nonadherence
Most common AEs occurring in ≥20% subjects were fatigue, headache, nausea, and insomnia (all more common in PEG+RBV arm)
FUSION SVR12 Results

- No on-treatment virologic failure (all relapses)
- Most common AEs occurring in ≥15% subjects were fatigue, headache, insomnia, and nausea
DAA Combination Therapy

NS5A-I

NI
All-oral combination of daclatasvir plus sofosbuvir

### Adverse events
- Fatigue 29–50%
- Headache 16–38%
- Nausea 16–32%

### Virologic failures
- G1: Reinfection
- G3: 1 relapse (baseline A30K); 1 started IFN for LLQ-TD

### Results

#### Genotype 2/3 results

<table>
<thead>
<tr>
<th></th>
<th>Week 4</th>
<th>EOT</th>
<th>SVR4</th>
<th>SVR12</th>
<th>SVR24</th>
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<tbody>
<tr>
<td>B</td>
<td>94</td>
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<tr>
<td>D</td>
<td>88</td>
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#### Genotype 1 results

<table>
<thead>
<tr>
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<th>Week 4</th>
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<th>SVR4</th>
<th>SVR12</th>
<th>SVR24</th>
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<tbody>
<tr>
<td>A</td>
<td>93</td>
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</tbody>
</table>

- Ribavirin adds no benefit to SOF+DCV
- No safety signals
- Regimen needs evaluation in cirrhosis
- New bar for other regimens to be compared

Sułkowski MS, et al. AASLD 2012, Boston #LB-2
HIV / HCV Co-infection: Virologic Response Over Time† on Bocepravir

† Three patients undetectable at FW4 have not yet reached FW12 and were not included in SVR12 analysis.
Simeprevir: C212 study design

• **Primary endpoint:** SVR12, safety, and tolerability
• **Secondary endpoints:** virologic response at other time points, on-treatment failure, and relapse rates
• **Interim analysis:**
  - All patients included in the analysis had completed 24 weeks of treatment or had discontinued prior to that point
  - **No. of patients:**
    - Week 24: N=100
    - Week 28: N=71
    - Week 36: N=27

*Response-guided therapy criteria: HCV RNA <25 IU/mL (detectable or undetectable) at Week 4 and undetectable at Week 12

PR, pegIFN-α2a + ribavirin; SMV, simeprevir
C212 interim analysis summary

- Simeprevir 150 mg QD + pegIFN/RBV led to high virologic response rates in co-infected patients, regardless of prior response
  - SVR12
    - Naïve and relapse 77%
  - RVR
    - Naïve 71%
    - Relapse 93%
    - Partial response 80%
- Patients who met RGT criteria 88%
  - achieved SVR12 75%
- At Week 24, 64% of null responders had not experienced treatment failure
- HIV virologic failure not observed over the study period
- Simeprevir was well tolerated, with a safety profile similar to HCV mono-infected patients
The Future of All Oral Regimen
All Oral Therapies – How They Differentiate?

1. Genotype dependency
2. Efficacy
   - Standard population
   - Special populations
3. Treatment duration
   - Standard population
   - Special populations
4. Resistance
5. Drug-Drug-Interactions
6. Safety and Tolerability
7. Posology, Pill Burden
All Oral Therapies – How They Differentiate?

1. Genotype dependency
2. Efficacy
   - Standard population
   - Special populations
3. Treatment duration
   - Standard population
   - Special populations
4. Resistance
5. Drug-Drug-Interactions
6. Safety and Tolerability
7. Compliance, Pill Burden
2 DAAs ± RBV vs 3 DAAs ± RBV

Assuming
- similar efficacy of individual DAA
- no selection of resistant variants

<table>
<thead>
<tr>
<th></th>
<th>2 DAAs</th>
<th>2 DAAs + RBV</th>
<th>3 DAAs</th>
<th>3 DAAs + RBV</th>
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<tbody>
<tr>
<td>„Lag“-phase</td>
<td>Similar</td>
<td>&gt;&gt;</td>
<td>Similar</td>
<td></td>
</tr>
<tr>
<td>Slope</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Efficacy</td>
<td>++</td>
<td>++(+)</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

3 vs. 2 DAAs may allow to shorten therapy and improve SVR rates (at least in more difficult-to-cure patients)
Little if any role of ribavirin in 3 DAAs regimen
## 2 DAAs vs 3 DAAs in patients with cirrhosis

Assuming
- similar efficacy of individual DAA
- no selection of resistant variants

<table>
<thead>
<tr>
<th></th>
<th>F0-3 (2 DAAs)</th>
<th>F4 (2 DAAs)</th>
<th>F4 (3 DAAs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slope</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Efficacy</td>
<td>+++</td>
<td>++</td>
<td>++(+)</td>
</tr>
<tr>
<td>Duration</td>
<td>12 wks</td>
<td>24 wks</td>
<td>12-24 wks</td>
</tr>
</tbody>
</table>
All Oral Therapies: The Combinations

- **2013/14**
  - NI + RBV (GT 2,3)

- **2014/15**
  - PI + NNI + RBV (GT 1b)
  - PI + NS5A-I + NNI ± RBV (GT 1)
  - PI + NS5A-I (GT 1b; off-label ?)
  - NI + NS5A-I (pan-GT; off-label)
  - NI + PI (GT 1,2,4-6; off-label)

- **2015/16**
  - NI + NS5A-I (FDC, pan-GT)
  - NI + NS5A-I + X
The future of HCV therapy

Statements and predictions

- Ribavirin will disappear
- 3 DAAs (vs 2 DAAs) may
  - further shorten therapy
  - lead to higher SVR rates (in particular in cirrhosis)
- Response to previous (IFN-based) therapy will be less relevant
- Cirrhosis (more granular differentiated) is expected to become the key baseline predictor for SVR
- Some patients may relapse with any DAA combination and require maintenance therapy
- Peg-IFN may remain a pan-genotypic compound for some (rare) rescue options
The future of HCV therapy

Potential strategies

Option 1
- Simple (e.g. FDC) regimen for every patient
- Rescue for Relapsers

Option 2
- Highly individualized therapy according to
  - Geno/subtype
  - Fibrosis stage
  - Comorbidity and co-medication (DDI)
  - Previous drug exposure, potential baseline RAVs
## Future of HCV therapy

### Individualized Approaches and Rescue options

<table>
<thead>
<tr>
<th>Genotype</th>
<th>F0-3</th>
<th>F4</th>
<th>F4 + portal hypertension</th>
<th>Post-Ltx</th>
<th>HIV-HCV coinfection</th>
<th>Rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV-1a</td>
<td>NI+NS5 x 12 3 DAA x 12</td>
<td>NI+NS5 x 12-24 3 DAA x 12-16</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
</tr>
<tr>
<td></td>
<td>NI+NS5 x 12 2 DAA x 12</td>
<td>NI+NS5 x 12-24 3 DAA x 12-16</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
</tr>
<tr>
<td>HCV-2</td>
<td>NI+RBV x 12 NI+P Ix 12 3 DAA x 6</td>
<td>NI+NS5 x 12-16 3 DAA x 12</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
</tr>
<tr>
<td>HCV-3</td>
<td>NI+NS5 x 12 CYPI + NS5 x 12</td>
<td>NI+NS5 x 12-24 CYPI + NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
</tr>
<tr>
<td>HCV-4</td>
<td>NI+NS5 x 12 NI+PI x 12 3 DAA x 8</td>
<td>NI+NS5 x 12 3 DAA x 12-16</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
</tr>
<tr>
<td>HCV-5</td>
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<td>NI+NS5 x 12 3 DAA x 12-16</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
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<tr>
<td>HCV-6</td>
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<td>NI+NS5 x 12 3 DAA x 12-16</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>NI+NS5 x 24</td>
<td>4 DAA x 24 2 DAA+PR x 24 3DAA+P x 24</td>
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