Clinical case presentation: HIV/ HCV

15th International Workshop on Clinical Pharmacology of HIV & Hepatitis Therapy,
Washington DC, 20th May 2014

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Department of Medicine I, University of Bonn, Bonn, Germany
Patient 1: Björn
When to treat HCV?

- 39-year old MSM; works as an invasive cardiologist
- HIV first diagnosed in 2008
  - PCP
  - ART history
    - 2008 start with TDF/FTC/efavirenz, subsequently rapid virological treatment failure with development of multiple mutations (M184V, M41L, T215Y, K103N)
    - Switch of ART to darunavir/r, Etraverine, Raltegravir, TDF/FTC
  - Current HIV-RNA <50 copies/ml, CD4 cell count 563 cells/mm³, relativ 27%
    - CD4-nadir 76 cells/mm³
- 11/2010 acute HCV infection
  - Genotype 4
  - HCV viral load $6.7 \log_{10}$
  - IL28B CT genotype
  - Grade 2 ALT elevation
  - Fibroscan 11.1 kpa (F3 fibrosis)

Would you treat HCV and if yes with what?
Acute hepatitis C in HIV-infected individuals: recommendations from the European AIDS Treatment Network (NEAT) consensus conference

The European AIDS Treatment Network (NEAT) Acute Hepatitis C Infection Consensus Panel

AIDS 2011, 25:399–409
Monitoring and initiation antiviral therapy

Testing of retrospective samples may be useful to assess duration of viral infection. In case of HCV infection durations greater than 12 weeks treatment initiation should occur if viable.
Antiviral therapy of AHC in HIV

- **Week 4**
  - HCV-RNA negative*
  - peg-IFN + RBV (AII)

- **Week 12**
  - HCV-RNA positive*
  - Drop HCV-RNA $\geq 2 \log_{10}$
  - 24 weeks All
  - < 2 log$_{10}$
  - Stop Therapy BIII

48 weeks BIII

*evidence based on using a 615 IU/ml cutoff to define negative HCV-RNA*
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    - Switch of ART to darunavir/r, Etraverine, Raltegravir, TDF/FTC
    - Current HIV-RNA <50 copies/ml, CD4 cell count 563 cells/mm³, relativ 27%
      - CD4-nadir 76 cells/mm³
- After 4 weeks HCV viral load remains unchanged with 6log
- Treatment with PEG-IFN/RBV is started
- After 12 weeks of HCV therapy HCV viral load has dropped to 860,000 copies/ml

What would you do now?
Patient 1: Björn
When to treat HCV?

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- 2014 chronic HCV Infection
  - Genotype 4
  - HCV viral load 3.700.587 IU/ml
  - IL28B CT genotype
  - Grade 1 ALT elevation
  - Fibroscan 8.1 kpa (F2 fibrosis)

Would you treat HCV and if yes with what?
# Drug-Drug Interactions

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**Legends:**
- Green: No clinically relevant interaction
- Yellow: No data or risk of potential interaction
- Red: Concomitant use contraindicated or not recommended

**Notes:**
- DCV: Descovy
- SOF: Symiptome Osteo-rénal
- SMV: Simeprevir
- Lamivudine
- Emtricitabine
- Abacavir
- Tenofovir
- Nevirapine
- Efavirenz
- Etravirine
- Rilpivirine
- Lopinavir/r
- Fosamprenavir/r
- Atazanavir/r
- Atazanavir
- Darunavir/r
- Raltegravir
- Dolutegravir
- Elvitegravir/C
- Maraviroc
- No clinically significant DDIs have been observed between SOF and EFV, RPV, DRV + RTV, RAL or the NRTI-Backbone of FTC / TDF.
Sofosbuvir + PEG-IFN / RBV bei HIV / HCV-Koinfektion
SVR12 nach HCV-Genotyp und HIV-ARV-Regime

NNRTI, nicht-nukleosidischer Reverse-Transkriptase-Hemmer

Rodriguez-Torres et al. IDWeek 2013; San Francisco, CA. Poster #714
PHOTON-1 Study:
Virologic Response - Genotype 1, 2, and 3

COSMOS Study Design: Randomized, Multicenter, 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

COSMOS Cohort 2: SVR12 – Primary Endpoint (ITT population)

<table>
<thead>
<tr>
<th></th>
<th>SMV/SOF + RBV 24 weeks</th>
<th>SMV/SOF 12 weeks</th>
<th>SMV/SOF + RBV 12 weeks</th>
<th>SMV/SOF Overall</th>
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<tr>
<td>Proportion of Patients (Percentage)</td>
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<td>SVR12</td>
<td>93%</td>
<td>100%</td>
<td>93%</td>
<td>93%</td>
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<tr>
<td>Non-VF</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
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<td>Relapse</td>
<td>7%</td>
<td>7%</td>
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COSMOS Cohort 2: SVR12 by HCV GT 1 Subtype and Baseline NS3 Q80K Polymorphism (excluding non-VF*)

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<tr>
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<th>GT 1b</th>
<th>GT 1a without Q80K</th>
<th>GT 1a with Q80K</th>
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<tr>
<td>SMV/SOF + RBV 24w</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td>SMV/SOF</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td>SMV/SOF + RBV 12w</td>
<td>93</td>
<td>88</td>
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<tr>
<td>SMV/SOF</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td>SMV/SOF ± RBV</td>
<td>100</td>
<td>95</td>
<td>96</td>
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AASLD and IDSA: Recommendations for Testing, Managing, and Treating Hepatitis C Co-infection

<table>
<thead>
<tr>
<th>GT 1 naïve + relapser</th>
<th>SOF, pegIFN, RBV for 12 weeks or</th>
<th>SOF + RBV for 24 weeks or</th>
<th>SOF, SMV ± RBV for 12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>GT 1 pegIFN/RBV non-responder</td>
<td>SOF, SMV ± RBV for 12 weeks</td>
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<tr>
<td>GT 1 pegIFN/RBV + TPV/BOC non-responder</td>
<td>SOF for 12 and pegIFN, RBV for 12-24 weeks</td>
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</table>
AASLD and IDSA: Recommendations for Testing, Managing, and Treating Hepatitis C Co-infection

- **GT 2 naïve + treatment-experienced**
  - SOF, RBV for 12 weeks
    (16 weeks in cirrhotics and non-responders)

- **GT 3 naïve + treatment-experienced**
  - SOF, RBV for 24 weeks

- **GT 4**
  - naïve: SOF, pegIFN, RBV for 12 weeks (without pegIFN 24 weeks) or: SMV for 12 weeks and pegIFN, RBV for 24-48 weeks
  - Treatment-experienced: SOF, pegIFN, RBV for 12 weeks (without pegIFN 24 weeks)
Genotype 4, Option 5

Recommendations

- Patients infected with HCV genotype 4 can be treated with an interferon-free combination of daily sofosbuvir (400 mg) and daily simeprevir (150 mg) 12 weeks (Recommendation B2)

- There is no data on the impact of adding ribavirin to this regimen. However, adding daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively) should be considered in patients with predictors of poor response to anti-HCV therapy, especially prior non-responders and/or patients with cirrhosis (Recommendation B2)

Comments: There is no data with this combination in patients infected with HCV genotype 4. Nevertheless, given the antiviral effectiveness of both sofosbuvir and simeprevir against this genotype, it is likely that the results of the COSMOS trial in patients infected with genotype 1 can be extrapolated [28].
Genotype 4, Option 6

Recommendations

- Patients infected with HCV genotype 4 can be treated with an interferon-free combination of daily sofosbuvir (400 mg) and daily daclatasvir (60 mg) 12 weeks in treatment-naive patients or 24 weeks in treatment-experienced patients (pending data with 12 weeks of therapy in treatment-experienced patients) (Recommendation B2)

- There is no data on the impact of adding ribavirin to this regimen. However, adding daily weight-based ribavirin (1000 or 1200 mg in patients <75 kg or ≥75 kg, respectively) should be considered in patients with predictors of poor response to anti-HCV therapy, especially prior non-responders and/or patients with cirrhosis (Recommendation B2)

Comments: There is no data with this combination in patients infected with HCV genotype 4. Nevertheless, given the antiviral effectiveness of both sofosbuvir and daclatasvir against this genotype, it is likely that the results in patients infected with genotype 1 can be extrapolated.
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- 39-year old MSM; works as an invasive cardiologist
- HIV first diagnosed in 2008
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  - ART history
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    - CD4-nadir 76 cells/mm³
- 2014 chronic HCV
  - Genotype 4
  - HCV viral load 3.700.587 copies/ml
  - IL28B CT genotype
  - Grade 1 ALT elevation
  - Fibroscan 8.1 kpa (F2 fibrosis)
  - 02/14 Start with PEG-IFN/RBV + Sofosbuvir
    - Day 10 HCV VL 256 IU/ml
    - Day 28 51 IU/ml

What would you do?
Patient 1: Björn
When and how to treat HCV?

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- 2014 chronic HCV
  - Genotype 4
  - HCV viral load 3,700,587 copies /ml
  - IL28B CT genotype
  - Grad 1 ALT elevation
  - Fibroscan 8.1 kpa (F2 fibrosis)
  - 02/14 Start with PEG-IFN/RBV + Sofosbuvir
    - Week 6 and 8 HCV VL <12 IU/ml but positive
    - Week 12 <12 IU/ml negative

What to do now?
Patient 2: Rosalie
When and how to treat HCV?

- 44-year old female, former IVDU
- HIV first diagnosed in 2000
  - ART history
    - Since 2004 TDF/FTC/fosamprenavir/r (1400/100 mg/d)
    - Current HIV-RNA <40 copies/mL, CD4 cell count 377 cells/mm³
      - CD4-nadir 190 cells/mm³
      - No HIV primary resistance
- HCV co-infection
  - Genotyp 1a
  - HCV viral load 2.041.211 IU/mL
  - IL28B TT genotype
  - Grade 1 ALT elevation
  - Transient elastography 43.7 kPa (F4 Fibrosis)
  - Patient showed partial response under previous HCV dual therapy (decrease of HCV RNA >2 log but never below LLQ)

Would you treat HCV? If yes with what?
Patient 2: Rosalie
When and how to treat HCV?

- 44-year old female, former IVDU
- HIV first diagnosed in 2000
  - ART history
    - Since 2004 TDF/FTC/fosamprenavir/r
    - Current HIV-RNA <40 copies/mL, CD4 cell count 377 cells/mm³
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  - No HIV primary resistance

- HCV co-infection
  - 02/2014 Request to company for daclatasvir within patient named program
  - 21 days later approval
  - Since 03/2014 Sofosbuvir + Daclatasvir for 24 Weeks

Which daclatasvir dose would you select?
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**Drug-Drug Interactions**

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  - No HIV primary resistance
- HCV co-infection
  - 02/2014 Request to company for daclatasvir within patient named program
  - 21 days later approval
  - Since 03/2014 Sofosbuvir + Daclatasvir for 24 Weeks
  - HCV RNA Week (1) 1816 IU/ml
  - HCV RNA Week (2) 405 IU/ml
  - HCV RNA Week (4) 76 IU/ml