EUROPEAN HIV NURSING CONFERENCE

19-20 October 2014 • Barcelona, Spain
Viral hepatitis C in HIV infected patient - case study -

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19-20 October 2014 Barcelona, Spain
Liver-related death is a frequent cause of non-AIDS death in HIV+ patients

Pathogenesis of HCV / HIV co-infection

- Immune system
  - CD4+ cell depletion
  - Decreased HCV-specific immune responses
  - Increased HCV replication
  - Hepatocyte apoptosis
  - Increased fibrosis

- Liver

- Gastrointestinal tract
  - Mucosal CD4+ T cell depletion
  - Increased microbial translocation
Faster progression of liver disease in HIV / HCV patients

Figure 3. Liver fibrosis and age among persons coinfect ed with HIV and HCV (dashed line) and those with only HCV (solid line)
HCV Coinfection vs Monoinfection: Cumulative Incidence of Decompensation

- 10-year hepatic decompensation risk 83% higher in coinfected patients
  - Adjusted HR 1.83 (95% CI: 1.54-2.18)

Case scenario

- Female, 31 years old
  - HIV+ since 1998 (at age of 15 years)
  - Lowest CD4 105 cells/mm$^3$
  - Highest HIV-RNA 496000 copies/mL
  - HCV and HBV negative at the beginning
  - Highly treatment-experienced patient with multiple drug resistance
cART history

- 1998 – 2001 IDV + AZT + DDC
- 2001 – 2003 EFV + 3TC + D4T
  • nightmares
- 2003 – 2004 NFV + D4T + DDI
  • Lipoatrophy, peripheral neuropathy
- 2004 – 2005 LPV/r + NFV + 3TC
  • Diarrhea
- 2005 – 2006 LPV/r + SQV + 3TC
  • Diarrhea and vomiting
- 2006 – 2007 TPV/r + 3TC + T20
- 2008 – 2009 RGV + DRV/r + 3TC + T20
  • Nodules at injection site
HCV coinfection

– 2009 – HCV positive (IVDU in the last 10 months)
  • HCV-RNA 6.32 log UI/mL
  • No liver biopsy

– CD4 cell count 312/mm³

– HIV-RNA 430 c/mL
Changes in HIV transmission route in Romania
HIV in IVDU…… a new epidemic?

Change in drug use

2009 → 97% heroin
2010 → 1/3 amphetamine-type stimulants

More frequent injections
More likely to share needles

- Access to sterile needles

- HIV cases in IVDU
- Total number of new HIV cases

97.5% HIV+HCV 13.8% HIV+HBV 9.6% HIV+HCV+HBV 2.5% HIV+HCV+HBV+HDV

[www.cnias.ro; Oprea & al EACS 2013]
HCV coinfection

- 2009 – HCV positive (IVDU in the last 10 months)
  - HCV-RNA 6.32 log UI/mL
  - No liver biopsy

- CD4 cell count 312/mm³

- HIV-RNA 430 c/mL

WHAT NEXT?
Substitutive therapy

– RGV + DRV/r + ETR + 3TC + Methadone

  • After 2 months – withdrawal symptoms – Methadone dose was increased

  • Drug interaction between DRV/r and Methadone
Drug-drug interactions

**INDUCER**

Drug X

Drug X + Drug Y

LIVER ENZYME SYSTEMS

60% of Drug X

20% of Drug X

**INHIBITOR**

Drug X

Drug X + Drug Y

LIVER ENZYME SYSTEMS

60% of Drug X

90% of Drug X

**Inducer drugs ↓↓↓ concentration of other drugs**

**Inhibitor drugs ↑↑↑ concentration of other drugs**
Drug-drug interaction between Analgesics and ARVs

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<thead>
<tr>
<th>Analgesics</th>
<th>ATV/r</th>
<th>DRV/r</th>
<th>FPV/r</th>
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SVR rates with PegIFN/RBV in HIV/HCV
Rare adverse events of PegIFN/RBV

• 2010 – CD4 572/mm³, HIV-RNA undetectable
  – Started on PegIFN +RBV
  – At week 12 HCV-RNA decreased > 2 log UI/mL
  – discontinued therapy after 5 months due to adverse events – fever, dyspnea, cough, CD4 cell count 167/mm³
HCV life cycle and potential therapeutic targets

SVR rates with DAAs

![Bar chart showing SVR rates with different DAAs.](chart_image)
Back to the case

• March 2011
  – 8.6 kPa (F2), HCV-RNA 6.2 log UI/mL

• June 2013
  – 10.4 kPa (F3), HCV-RNA 6.8 log UI/mL
  – IL 28B CT, genotype 1a
  – CD4 913/mm³, HIV-RNA undetectable

WHAT NEXT?

– RGV + ETR + MVC
## Telaprevir drug interactions

### Drug-drug Interactions between ARVs and Non-ARVs

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<th>non-ARV drugs</th>
<th>ATV/r</th>
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EACS Guideline version 7.02 June 2014
Proposed optimal duration of HCV therapy in HCV/HIV coinfected patients

- **HCV-RNA neg**
  - W4
  - W12
  - W24
  - 24 weeks therapy

- **HCV-RNA pos**
  - > 2 log₁₀ drop in HCV-RNA
    - W4
    - W12
    - W24
    - 48 weeks therapy
  - < 2 log₁₀ drop in HCV-RNA
    - Stop

- G2/3
  - 24 weeks therapy
  - 48 weeks therapy

- G1/4
  - 48 weeks therapy
  - 72 weeks therapy

EACS Guideline version 7.02 June 2014
Immuno-virological status undergoing TLV / PegIFN / RBV
Second generation DAAs + PEG-IFN/RBV in HIV/HCV coinfected patients


SMV / PEG / RBV (C212 study)

Pacienți (%) cu SVR12

- GT1b: 16/18 (89%)
- GT1a: 62/88 (71%)
- GT1a cu Q80K: 20/30 (67%)
- GT1a fara Q80K: 42/58 (72%)
• Similar tolerability as in monoinfected patients

• Increased SVR rates in cirrhotic and non-cirrhotic patients
  – Cirrhosis: 76%
  – Without cirrhosis: 74%

• SVR rates according to IL28B genotype
  – CC: 89%; CT: 67%; TT: 67%

SOF / PegIFN / RBV in HIV / HCV coinfection
SVR 12 according to HCV genotype and ARV regimen
IFN-free DAA regimens in HIV/HCV coinfectected patients

**PHOTON-1 study**
Naggie S, et al.
CROI 2014. Oral #26

- GT 1 TN: SOF + RBV, n=114
- GT 2/3 TN: SOF + RBV, n=68
- GT 2/3 TE: SOF + RBV, n=41

**C-WORTHY study**
Sulkowski M, et al.
EASL 2014. Oral #63

- N = 29: MK-5172 + MK-8742 + RBV
- N = 30: MK-5172 + MK-8742 (No RBV)

**LDV/SOF STR ERADICATE study**
Osinusi A, et al.
EASL 2014. Oral #14

- ARV Untreated (n=13):
  - CD4 count stable + HIV RNA < 500 copies OR
  - CD4 count > 500 cells/mm³
- ARV Treated (n=37):
  - CD4 count > 100 cells/mm³
  - HIV RNA < 40 copies
  - Current ARVs ≥ 8 weeks

*ARVs: tenofovir, emtricitabine, efavirenz, rilpivirine, and raltegravir*
PHOTON 1: SOF / RBV in HIV / HCV coinfection

All-oral therapy of SOF / RBV

Comparison of HCV monoinfected to HIV / HCV coinfecteda

**GT 1**
SOF + RBV
24 weeks

**GT 2**
SOF + RBV
12 weeks

**GT 3**
SOF + RBV
12 weeks

**GT 3**
SOF + RBV
24 weeks

Similar response rates observed in HIV/HCV coinfecteda patients
compared with HCV monoinfected patients

All co-infected and mono-infected patients had an HCV RNA <25 IU/mL independent of RBV by week 4 of therapy.
ERADICATE – treatment response

The IFN and RBV free regimen of LDV/SOF in HCV/HIV co-infected patients resulted in SVR12 of 100% in ARV untreated patients and SVR4 of 100% in ARV treated patients.

LDV/SOF STR was generally well tolerated with no discontinuations.

Osinusi A, EASL, 2014, Abstract O14
New online EASL HCV recommendations

Same treatment regimens can be used in HIV/HCV patients as in patients without HIV infection, as the virological results of therapy are identical (A1).
Take home messages

• HIV worsens the prognosis of HCV infection, progression of liver fibrosis being accelerated.

• Response rates to new HCV therapies are similar in HIV+ and HIV- patients.

• IFN-free therapies are now a reality.

• Always keep in mind possible drug-drug interactions.
Thank You