Differential benefits of DAAs in special populations

Hepatitis C and HIV

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Treatment of chronic hepatitis C

• Why to treat?

• The impact of HIV and cART

• How to treat?
Treatment of chronic hepatitis C

- Why to treat?
- The impact of HIV and cART
- How to treat?
Why to treat chronic HCV?

• Hepatic manifestations

• Extra-hepatic manifestations, 2 examples
  o Cardio-vascular disease
  o Renal dysfunction

• Benefits of SVR in HIV patients
HCV increases mortality from hepatic and non-hepatic diseases in mono-infected patients

The REVEAL HCV Cohort Study

23,820 adults, Taiwan

1,095 anti-HCV positive; 69.4% with detectable HCV RNA

Lee M-H et al, J Infect Dis 2012;206:469–477
Prognosis of coinfected patients after the 1st decompensation

- ANRS HP25 – PRETHEVIC prospective study
- 68 patients from 32 centers between 2009 and 2013
- Decompensation: ascites 28, hemorrhagea 3, jaundice 6, combined 31

69 %, 53 % & 43 % at 1, 2 & 3 years, respectively

→ Baseline MELD score is predictive of mortality (one year survival = 84 % MELD 6-11; 83 % MELD 12-15; 48 % MELD ≥ 16) like the MELD-Na & Child-Pugh

Gelu-Simeon M, France, AASLD 2014, Abs. 1521 actualisé
HCV and extra-hepatic over-mortality in mono-infected patients

Significant association between HCV and:
- diabetes (OR = 1.8)
- cardio-vascular morbidity (OR=2.37)
- cerebro-vascular mortality (OR= 2.7)
- renal disease (HR for ESRD < 59 y= 7.8 vs. 3.2)
- extra-hepatic (breast: OR=2) cancers

Lee M-H et al. Stroke 2010;41:2894–2900
Su F-H et al. BMC Cancer 2011;11:495

Lee M-H et al, J Infect Dis 2012;206:469–477
Relative cardio-vascular risk in HIV, HCV mono-infected and HIV-HCV co-infected patients

\[
\begin{align*}
&\beta \text{ coefficient for CVD risk vs NHANES} \\
&HCV \quad 2.37 \quad p<0.001 \\
&HIV \quad 0.88 \quad p=0.24 \\
&HIV+HCV \quad 2.04 \quad p=0.03
\end{align*}
\]

HCV (n=668)  
HIV (n=956)  
HIV+HCV (n=728)

\textit{p values vs general NHANES population}  
HIV, human immunodeficiency virus  
NHANES, National Health and Nutrition Examination Survey

Risk of chronic kidney disease in relation with HCV replication in HIV

NA-ACCORD : 52 602 HIV+/HCV-; 9508 HIV+/HCV viremic, 913 HIV+/HCV aviremic

Lucas GM. J Infect Dis 2013
Impact of HIV on liver fibrosis severity according to age

From: HIV, Age, and the Severity of Hepatitis C Virus–Related Liver Disease: A Cohort Study

Figure Legend:
Liver fibrosis and age among persons coinfected with HIV and HCV and those with only HCV.
For each age, predicted liver fibrosis scores were calculated using a regression equation that included the race, sex, alcohol use, body mass index, hepatitis B virus surface antigen level status, and HCV RNA level values for a representative participant (black overweight male who has no regular alcohol use, is hepatitis B virus surface antigen–negative, and has high HCV viral load) for persons coinfected with HIV and HCV (dashed line) and for persons with only HCV (solid line). For example, a 40-year-old HIV and HCV coinfected person with these characteristics was calculated to have a predicted FibroScan score of 9.04 kPa. For this same degree of fibrosis, the predicted age in a similar person but with only HCV was 49.2 years. Over the entire age range, the average difference in estimated age between persons coinfected with HIV and HCV and those with only HCV was 9.2 years (90% coverage limit, 5.2 to 14.3 years). HCV = hepatitis C virus.
Benefits associated with SVR (1)

Impact on all cause-death

<table>
<thead>
<tr>
<th></th>
<th>Monoinfection</th>
<th>Cirrhosis monoinfection</th>
<th>HIV/HCV Coinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>10 studies</td>
<td>3 studies</td>
<td>2 studies</td>
</tr>
<tr>
<td>Reduction in risk of death</td>
<td>-71%</td>
<td>-73%</td>
<td>-75% -73%</td>
</tr>
<tr>
<td></td>
<td>-62%</td>
<td>-84%</td>
<td></td>
</tr>
</tbody>
</table>

Impact on risk of HCC after 5 years

<table>
<thead>
<tr>
<th></th>
<th>Monoinfection</th>
<th>Cirrhosis monoinfection</th>
<th>HIV/HCV Coinfection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients after 5 years</td>
<td>n = 12,496 Mean F/U 6.1 years</td>
<td>n = 4,987 Mean F/U 6.6 years</td>
<td>n = 2,085 Mean F/U 4.7 years</td>
</tr>
<tr>
<td>SVR</td>
<td>2.9%</td>
<td>9.3%</td>
<td>13.9%</td>
</tr>
<tr>
<td>Non SVR</td>
<td>5.3%</td>
<td>10%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

Hill et al. AASLD 2014, Abs. 44
Risk of liver transplantation after 5 years

**Monoinfection**
- n = 108
- Median F/U 4.2 years

**Cirrhotics Monoinfected**
- n = 1046
- Median F/U 7.7 years

**Coinfected**
- n = 2039
- Median F/U 4.9 years

- Benefits associated with SVR (1)
  - Hill et al. AASLD 2014, Abs. 44
Impact of SVR stratified by level of fibrosis

Incidence of hepatic decompensation or death

![Graph showing impact of SVR stratified by level of fibrosis.](image)

1Berenguer, JAIDS 2014. 2Labarga, HIV Med 2014
HCV cure decreases mortality from both hepatic and non-hepatic diseases

All cause of mortality

Hepatic mortality

Extra-hepatic mortality

Extra-hepatic and non-HIV mortality

Berenguer M et al. CID 2012
CLINICAL CASE: M. Luc, 55 years old (1)

- Man, 55 years
- No co-morbidity except HIV infection
- BMI=23; alcohol=0, tabacco=0
- Ex-IVDU (1982)
- Stable HIV: HIV RNA < 20 copies/mL; CD4: 35% under Reyataz/r + Truvada
- « Simple follow-up» between 1990 and 2004
CLINICAL CASE: M. Luc, 55 years old (2)

- ALT=123 UI/l, AST=98 UI/l in 2004
- HCV-RNA =6.2 logUI/ml
- Genotype 1a
- Full blood count, PT, renal function, TSH: normal
- Liver Biosy: 20 mm, A2F2

Would you have treated this patient in 2004?
CLINICAL CASE: M. Luc, 55 years old (3)

- Treatment with Peg/Riba
- Fair tolerance
- HCV-RNA at W12 = 5.4 log (null responder)

- Discontinuation of therapy
- «Simple follow-up» but discontinuation of hepatology follow up
Four pivotal Peg-IFN/RBV studies in HIV/HCV co-infected patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>APRICOT(^1)</th>
<th>ACTG 5071(^2)</th>
<th>RIBAVIC(^3)</th>
<th>Barcelona(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number enrolled</td>
<td>868</td>
<td>133</td>
<td>412</td>
<td>95</td>
</tr>
<tr>
<td>Peg-IFN</td>
<td>2a</td>
<td>2a</td>
<td>2b</td>
<td>2b</td>
</tr>
<tr>
<td>RBV</td>
<td>800 mg</td>
<td>600 mg up to 1 g</td>
<td>800 mg</td>
<td>800 mg up to 1.2 g</td>
</tr>
<tr>
<td>HIV and CD4 status</td>
<td>&gt;200 cells/mm(^3) or 100–200 cells/mm(^3) if HIV-RNA &lt;5000 copies/mL</td>
<td>&gt;100 cells/mm(^3) + HIV-RNA &lt;10,000 copies/mL or &gt;300 cells/mm(^3), tx naïve + not starting ART during trial</td>
<td>&gt;200 cells/mm(^3)</td>
<td>&gt;250 cells/mm(^3) and HIV-RNA &lt;10,000 copies/mL</td>
</tr>
<tr>
<td>ALT</td>
<td>“elevated”</td>
<td>NA</td>
<td>NA</td>
<td>&gt;1.5x ULN</td>
</tr>
<tr>
<td>Genotype 1, %</td>
<td>60–61</td>
<td>77–78</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>Bridging fibrosis or cirrhosis, %</td>
<td>15–16</td>
<td>9–11 (cirrhosis)</td>
<td>39</td>
<td>30</td>
</tr>
<tr>
<td>Genotype 1 Peg-IFN/RBV SVR rate, n/N (%)</td>
<td>51/176 (29)</td>
<td>7/51 (14)</td>
<td>21/123 (17)*</td>
<td>22/59 (38)*</td>
</tr>
</tbody>
</table>

*Genotype 1 or 4

ART: ARV therapy; Peg-IFN: peginterferon; RBV: ribavirin
SVR: sustained virologic response; tx: treatment; ULN: upper limit of normal

CLINICAL CASE: M. Luc, 55 years old (4)

Back to hepatology unit in 2011

Genotype 1a

VL = 6.2 log UI/ml

BMI = 28 kg/m²

Hypertension

FT: 0.76

AT: 0.56

FS = 16.6 kPa*

ALAT = 145 UI/mL

Hb = 12.5 g/dL

Platelets = 90000/mm³
What do you do?

1. A liver biopsy
2. Other evaluation
3. I see the patient in one year
4. I do consider a new treatment
1. A liver biopsy
2. Other evaluations
3. I see the patient in one year
4. I do consider a new treatment
CLINICAL CASE: M. Luc, 55 years old (6)

- TP = 65%, albuminemia = 36g/l, Total/conjugated bilirubine = 5419 micromol/l, αFP = 3 ng/ml

- Abdominal US:
  Dyssmorphism
  No nodule nor portal thrombosis

- Upper endoscopy: grade 1 oesophageal varices

Would you have treated this patient in 2011?
Treatment of chronic hepatitis C

- Why to treat?
- The impact of HIV and cART
- How to treat?
Potential harmful impact of cART

Meta-analysis of 26 studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Type</th>
<th>Effect Size</th>
<th>CI</th>
<th>Study</th>
<th>Year</th>
<th>Type</th>
<th>Effect Size</th>
<th>CI</th>
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<tbody>
<tr>
<td>Allory, 2000</td>
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<td></td>
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<td>Bierhoff, 1997</td>
<td></td>
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<td>Di Martino, 2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eyster, 1993</td>
<td></td>
<td></td>
<td></td>
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<td>Grabczewska, 2005</td>
<td></td>
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<td></td>
<td></td>
<td>Lesens, 1999</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Makris, 1996</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pol, 1998a</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pol, 1998b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Romeo, 2000</td>
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<tr>
<td>Serfaty, 2001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Soto, 1997</td>
<td></td>
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<tr>
<td>Telfer, 1994</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Fixed effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Random effects</td>
<td></td>
<td></td>
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<td>Fixed effects</td>
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<tr>
<th>Study</th>
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<th>Study</th>
<th>Year</th>
<th>Type</th>
<th>Effect Size</th>
<th>CI</th>
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<tbody>
<tr>
<td>Benhamou, 1999</td>
<td></td>
<td></td>
<td></td>
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<td>Brau, 2006</td>
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<tr>
<td>Marine-Barjoan, 2004</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Martinez-Sierra, 2003</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Macias, 2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Monto, 2005</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Valle Tovo, 2007</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Verma, 2006</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HAART: highly active antiretroviral therapy

Evolution of mortality over 15 years

10-year trends in HCV-related mortality and morbidity in the USA

Ioannou R. Hepatology, 2014
Impact of HCV on HIV-related morbi-mortality

Kaplan-Meier estimates of the probability of remaining AIDS-free and of not dying of AIDS by hepatitis C virus (HCV) status at baseline.

Kovacs A and al. J Infect Dis 2010
HCV infection and global mortality in France

Mortality of 69,913 French PLWHIV (2008-2012)

Adjusted on age, gender, alcohol, decompensated cirrhosis, AIDS

Mallet V et al. CROI 2014

Survival Probability

Logrank p < .0001

0 HCV-/HBV-
1 HCV-/HBV+
2 HCV+

59476 58378 56395 53544 50194 46299 41648 35511 28344 17905 3604
2154 2139 2091 2024 1925 1785 1645 1455 1214 783 174
8283 8206 8030 7706 7331 6897 6342 5593 4650 3061 733

Adjusted on age, gender, alcohol, decompensated cirrhosis, AIDS

Mallet V et al. CROI 2014
The dark side of cART

• Response to cART in HIV-HCV patients
  – Pooled analysis of 4 CTG trials
    • Worse immune reconstitution
    • Shorter time to HIV virological failure (43% excess risk)
    • Earlier occurrence of grade 3-4 side effects (+51% excess risk)
    • Increased AIDS mortality (RR=2.1)

• cART tolerance in HIV-HCV patients
  – Longitudinal cohort study (EUROSIDA, 9535 patients studies for incidence and reasons for cART discontituation
    • Adj. Incidence rate ratio in HCV viremic: 1.44 [1.22 – 1.56]
    • Higher rate in patients on NNRTI (+59%)
    • Higher in patients with high level of hyaluronic acid (surrogate marker of advanced liver disease)

Hua, AIDS 2013. Grint, AIDS 2014
... And the bright side of the moon (1)

- Cohort study on 10,090 HIV/HCV-coinfected patients in the Veterans Aging Cohort Study Virtual Cohort (VACS-VC)
- No cART at inclusion
- Incidence of liver decompensation between 1996 and 2010

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Table 5. Hazard Ratios for Hepatic Decompensation by Antiretroviral Therapy Initiation Status and Time Since Initiation From Marginal Structural Models, Among Patients With Baseline HIV RNA >400 copies/mL (N = 8214)

<table>
<thead>
<tr>
<th>Treatment Status</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No initiation</td>
<td>Referent</td>
</tr>
<tr>
<td>ART initiation</td>
<td>0.59 (.43-.82)</td>
</tr>
<tr>
<td>No initiation</td>
<td>Referent</td>
</tr>
<tr>
<td>&lt;2 y since initiation</td>
<td>0.60 (.42-.84)</td>
</tr>
<tr>
<td>2 to &lt;4 y since initiation</td>
<td>0.60 (.37-.96)</td>
</tr>
<tr>
<td>≥4 y since initiation</td>
<td>0.53 (.31-.91)</td>
</tr>
</tbody>
</table>

Anderson, Clin Infect Dis 2014
... And the bright side of the moon (2)

Longitudinal cohort of 638 HIV-HCV patient from the John Hopkins HIV clinic from 1996 to 2010

Incidence RR of ESLD, HCC and all-cause death

Fibrosis stage 0-1
Fibrosis stage 2
Fibrosis stage 3
Fibrosis stage 4
Active cART

0.27
2.34
3.18
3.57

Limketkai, JAMA 2012
CLINICAL CASE: M. Luc, 55 years old (6)

- TP = 65%, albuminemia = 36g/l, Total/conjugated bilirubine = 54/19 micromol/l, αFP = 3 ng/ml
- Abdominal US:
  - Dyssmorphism
  - No nodule nor portal thrombosis
- Upper endoscopy: grade 1 oesophagocal varices

YES OF COURSE!
Treatment of chronic hepatitis C

• Why to treat?

• The impact of HIV and cART

• How to treat?
Increase in efficacy over time in HIV-HCV co-patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>2003</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>PegIFN alone</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>PegIFN/RBV</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>BOC + P/R</td>
<td></td>
<td>63</td>
</tr>
<tr>
<td>TVR + P/R</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>SMV + P/R</td>
<td></td>
<td>74</td>
</tr>
<tr>
<td>SOF + P/R</td>
<td></td>
<td>89</td>
</tr>
<tr>
<td>SOF + RBV</td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>X-DAA</td>
<td></td>
<td>95</td>
</tr>
</tbody>
</table>
Treatment of chronic hepatitis C in 2011

2011-2014

Combination PEG-IFN – RBV

« 2011 » DAAs

Treatments with IFN

SVR in GT1

45%

75%
TVR or BOC + PR in naïve HCV GT 1 HIV-co-infected patients

- Triple therapy increased SVR but increased adverse events\(^1,2\)
- SVR rates comparable to HCV GT 1 mono-infection (75% and 68%)\(^3,4\)

SVR: sustained virological response; TN: treatment-naïve

Efficacy of TVR in PR-experienced HIV-infected patients

ANRS TélapreVIH trial in (n=69) PR experienced patients

Cotte et al. CID 2014
CLINICAL CASE: M. Luc, 55 years old (7)

- Evaluation of cirrhosis: oesophageal varices stage 2, introduction of β-blockers
- PegINF/Ribavirine/Telaprevir begun in 2012, according to the patient request
CLINICAL CASE: M. Luc, 55 years old (8)

PEG + Riba+ tela

Hb=10.2 g/dL

Platelets = 40,000/mm³

Undetectable HCV RNA
Treatment has been continued for 48 weeks (12 TPR and 36 PR)

A virological relapse occurred 2 months after discontinuation
CLINICAL CASE: M. Luc (10)

- Cirrhosis
- Non responder to PR
- Non responder to TPR
- On RAL + TDF + FTC in 2014

YES OF COURSE!
Understanding of HCV life cycle revealed several potential innovative drug targets

**Viral targets**

<table>
<thead>
<tr>
<th>NS3</th>
<th>NS5A</th>
<th>NS5B</th>
<th>Cyclophilin A</th>
</tr>
</thead>
<tbody>
<tr>
<td>The NS3/4A serine protease is essential for post-translational processing of HCV polyproteins¹</td>
<td>Multifunctional membrane-associated phosphoprotein essential component of the HCV-RNA replication complex²,³</td>
<td>NS5B is an HCV-specific, RNA-dependent RNA polymerase¹</td>
<td>Host protein involved in HCV replication through interaction with NS5A and the HCV polymerase⁴</td>
</tr>
</tbody>
</table>

**Host targets**

- Boceprevir
  - ABT-450/r, ACH-1625
  - Asunaprevir, TMC-435 (Simeprevir), BI-201335
  - Danoprevir/r, GS-9451 MK-5172
- Telaprevir
- NS5A
- Daclatasvir
  - GS-5885
  - ABT-267
  - PPI-668
- NS5B
  - Nucleos(t)ide analogue
    - GS-7977, Mericitabine, IDX-184*
  - Non-nucleoside analogue
    - BI-207127, ABT-333
    - ABT-072, BMS-791325
    - Tegobuvir, Setrobuvir
    - VX-222, Filibuvir
- Cyclophilin A
  - Host protein involved in HCV replication through interaction with NS5A and the HCV polymerase⁴

Treatment of chronic hepatitis C in 2014

2011-2013

2011 DAAs

Combination PEG-IFN – RBV

Treatments with IFN

SVR in GT1

45%

75%

75-95%

New DAAs

Combination PEG-IFN – RBV

- Better efficacy (pan-genotypic)
- Better tolerability
- Reduction of duration
- Easier dosing schedule
- Reduced pill burden

Sofosbuvir 1Q14
Simeprevir 2Q13
Daclatasvir 3Q14
Efficacy of SMV-PR in HCV-GT1 HIV- infected patients

Dieterich D, et al. CROI 2014; Abstract 24

<table>
<thead>
<tr>
<th>Group</th>
<th>SVR12 (%)</th>
<th>SMV/P/R</th>
<th>Historical P/R-only control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>74/106</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Treatment naïve</td>
<td>42/53</td>
<td>29/51</td>
<td>51/176</td>
</tr>
<tr>
<td>Relapsers</td>
<td>13/15</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Partial responders</td>
<td>7/10</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Null responders</td>
<td>16/28</td>
<td>5/57</td>
<td>2/37</td>
</tr>
</tbody>
</table>

P < 0.001
Efficacy of SOF + PR in naïve diverse GT HCV-HIV infected patients

- SVR12 was similar by HCV GT and by HIV ART regimen
- There was no on-treatment HCV or HIV virologic breakthrough
- Relapse occurred in 1 patient and accounted for all virologic failures
- 2 patients discontinued treatment early due to adverse events
  - One patient at Week 6 due to anemia and was lost to follow-up
  - One patient at Week 8 and achieved SVR12

Treatment of chronic hepatitis C > 2014

- **2012**: PEG-IFN – RBV Combination
- **2017**: DAAs
- **2020**: DAAs Combinations (PI/Pol I/NS5A Inh) +/_ RBV...
- **> 2020**: Cyclophyllin inhibitors
- **> 2020**: Dual, Triple, Quad therapy

**IFN-containing regimens vs. IFN-free regimens**

90-95% SVR
Efficacy of SOF + RBV in diverse GT HIV-infected patients (1)

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>SVR12 (%)</td>
<td>81</td>
<td>89</td>
<td>90</td>
<td>84</td>
</tr>
<tr>
<td>Relapse</td>
<td>39 (17)</td>
<td>1 (2)</td>
<td>2 (7)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>Breakthrough</td>
<td>1 (&lt; 1)</td>
<td>1 (2)</td>
<td>0</td>
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<td>1 (2)</td>
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<td>2 (4)</td>
<td>1 (3)</td>
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</tbody>
</table>

Rockstroh J et al. AASLD 2014, Abs. 195
Efficacy of SOF + RBV in diverse GT HIV-infected patients (2)

SVR12 according to fibrosis

- G1: 82% (168/204) - Naïf de traitement
  - Non cirrhosis: 74% (14/22)
  - Cirrhosis: 97% (154/22)

- G1a: 85% (147/173)
  - Non cirrhosis: 75% (11/17)
  - Cirrhosis: 96% (136/173)

- G1b: 67% (20/30)
  - Non cirrhosis: 67% (3/5)
  - Cirrhosis: 83% (17/20)

- G4: 83% (19/23)
  - Non cirrhosis: 78% (7/8)
  - Cirrhosis: 95% (12/23)

Rockstroh J et al. AASLD 2014, Abs. 195
Towards an universal virologic cure

**SOF + RBV:** Comparison HCV mono- vs HCV/HIV coinfected

- **GT 1**
  - SOF + RBV
  - 24 weeks

- **GT 2**
  - SOF + RBV
  - 12 weeks

- **GT 3**
  - SOF + RBV
  - 12 weeks

**SVR12 (%)**

- **SPARE**
  - 68

- **PHOTON-1**
  - 76

- **VALENCE**
  - 93

- **PHOTON-1**
  - 88

- **FISSION**
  - 56

- **PHOTON-1**
  - 67

- **VALENCE**
  - 85

The concept of difficult-to-treat population Has been removed by the antiviral potency of DAAs

PEG-IFNα-free regimens in GT1-HCV HIV infected patients

CLINICAL CASE: M. Luc, HOPE! (11)

- Cirrhosis/Non responder to PR and TPR

- The patient received Sofosbuvir 400mg+Daclatasvir 60 mg+RBV 1200 mg for 12 weeks and achieved SVR 12

- ARV did not need to be changed because no DDI with RAL

Don’t forget the US each 6 months For the early screening of HCC
# Drug-Drug Interactions in HIV: the last issue?

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>DCV</th>
<th>SOF</th>
<th>SMV</th>
<th>LDV</th>
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</thead>
<tbody>
<tr>
<td>Lamivudine</td>
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<td>Emtricitabine</td>
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<td>Abacavir</td>
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<td>Etravirine</td>
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<td>Rilpivirine</td>
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<tr>
<th>HIV Protease Inhibitors</th>
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<tbody>
<tr>
<td>Lopinavir/r 30</td>
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<tr>
<td>Fosamprenavir/r 30</td>
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<tr>
<td>Atazanavir/r 30</td>
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<tr>
<td>Atazanavir 60</td>
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<tr>
<td>Darunavir/r 30</td>
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<tr>
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<tr>
<td>Dolutegravir/ir</td>
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<td>Elvitegravir/r/C</td>
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<th>Entry Inhibitors</th>
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<tr>
<td>Maraviroc</td>
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</table>

- **Yellow** represents no data or risk of potential interaction.
- **Green** represents no clinically relevant interaction.
- **Red** represents concomitant use contraindicated or not recommended.