Case study: Therapeutic options in acute and chronic HCV in HIV coinfection

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Patient A

- 41-year-old male patient, msm with multiple sexual partners
- HIV diagnosis 1999, CDC A2
- Since 01/2008 cART: Atripla (before Combivir + Sustiva since 2000)
- 03.02.2009:
  - HIV-RNA <40 copies/ml, CD4 T-cell count 772/µl (46%)
  - ALT 167 U/l (41 U/l in 10/08)
  - Syphilis negativ

What is your presumed diagnosis?

Patient A

- Acute HCV (GT 4a):
  - HCV-RNA 717.000 IU/ml
  - Anti-HCV positive (last negative 1 year prior)

Acute HCV Definition

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

(1) Positive anti-HCV immunoglobulin G (IgG) in the presence or absence of a positive HCV-RNA and a documented negative anti-HCV IgG in the previous 12 months.

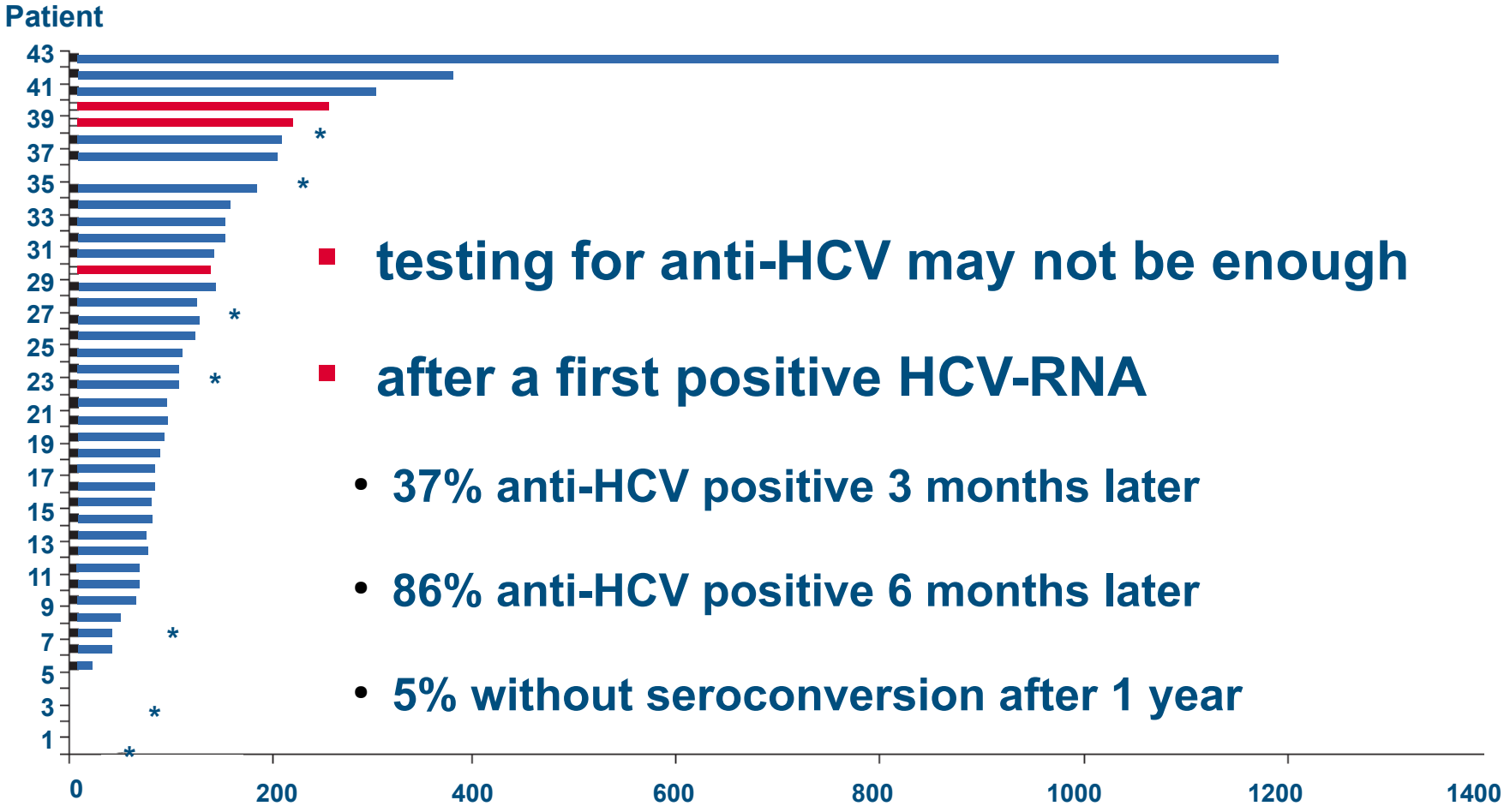
(2) Positive HCV-RNA and a documented negative HCV-RNA and negative anti-HCV IgG in the previous 12 months.

Initial presentation acute HCV HIV- vs. HIV+ patients

	HIV-positive n=157	HIV-negative n=259
Age (years)	39 (35 - 44)	37 (27 - 48)
Sex (male)	99%	58%
BMI > 30	0%	13%
Transmission risk		
MSM	97%	2%
heterosexual	1%	20%
IVDA	1%	17%
HCV Status		
HCV-GT		
1/4	84%	69%
2/3	15%	29%
anti-HCV positive	83%	79%
HCV-RNA (log10)	5.8 (5.4 - 6.4)	5.0 (4.0 - 5.8)
Laboratory presentation		
Maximum ALT (IU/l)	261 (92 - 499)	660 (363 - 1213)
ALT > 20 x ULN	7%	37%
Bilirubin > 2 mg/dl	10%	58%
Clinical presentation		
Days transm. - sympt.	62 (42 - 101)	48 (30 - 63)
	32%	59%

Vogel, Deterding et al. CID 2009

Caveat diagnostics: anti-HCV in HIV+ individuals



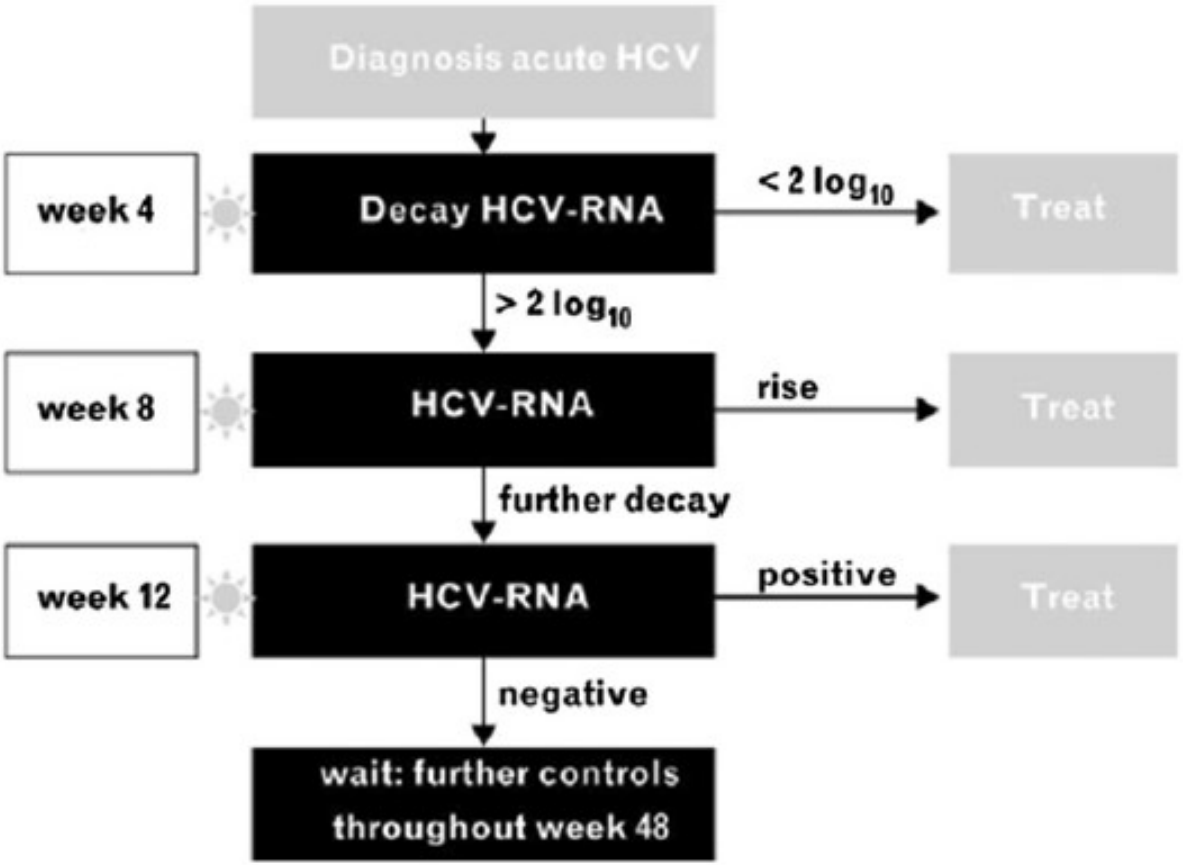
- testing for anti-HCV may not be enough
- after a first positive HCV-RNA
  - 37% anti-HCV positive 3 months later
  - 86% anti-HCV positive 6 months later
  - 5% without seroconversion after 1 year

Thomson et al. AIDS 2009, 23:89–93

Question?

Would you treat acute HCv and if yes how?

Timing of Treatment



Boesecke et al, Infect Dis Clin N Am 2012

Course I

4 weeks after diagnosis:

HCV-RNA 2.560.415 IU/ml

Course II

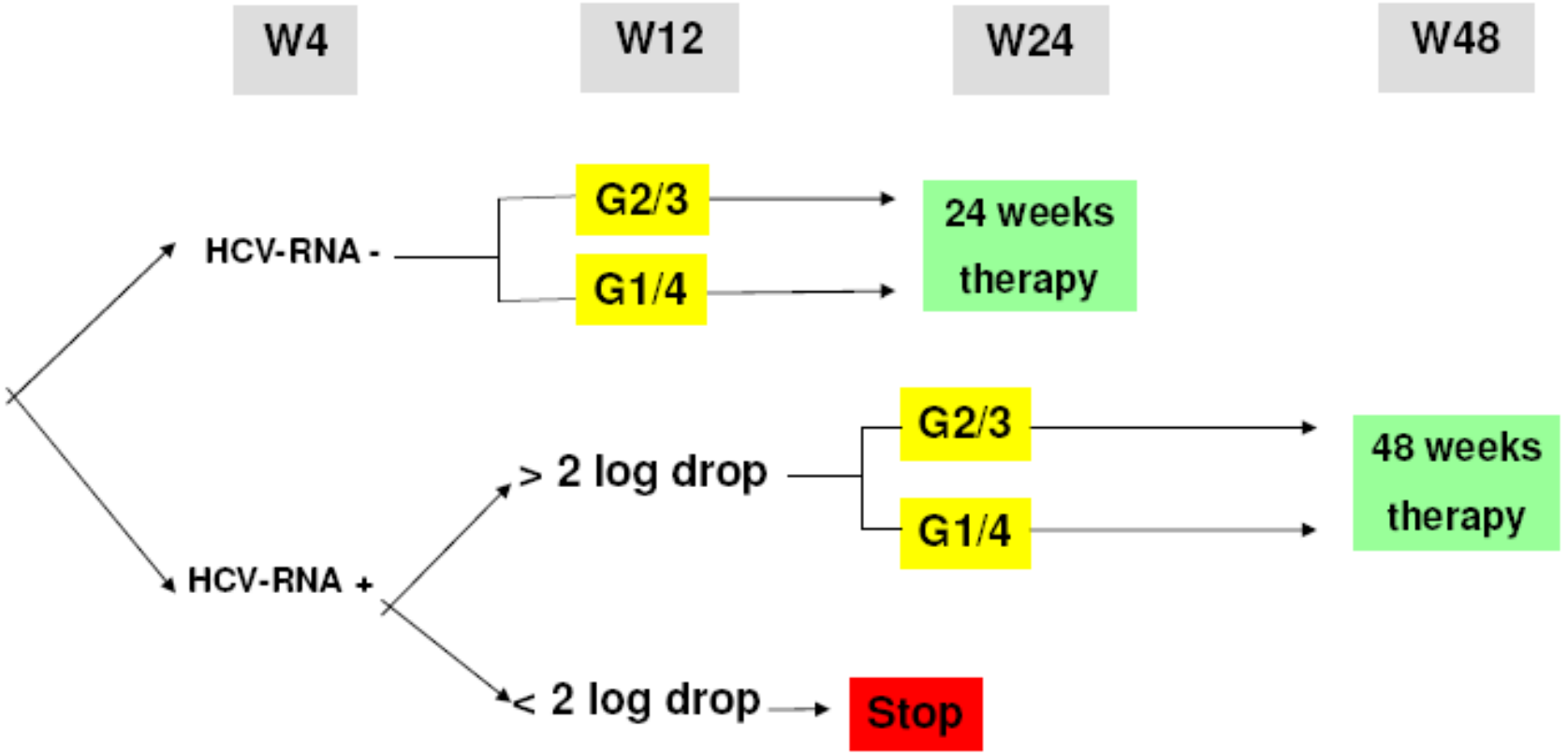
- 9.3.09: Pegasys 180µg s.c./week + Copegus 1200mg/d (>75kg)

- HCV-RNA week 4: 3.923 IU/ml
- From week 4: Fatigue, headache

- HCV-RNA week 12: <12 IU/ml

How long would you treat?

Duration of therapy



Rockstroh, Hepatology 2nd edition 2010

Course III

- HCV-RNA week 24: <12 IU/ml

- HCV-RNA week 48: <12 IU/ml

  -> End of therapy 16.02.2010

- HCV-RNA week 72: <12 IU/ml

  -> SVR

Patient 1: Thomas
When to Treat HCV

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- HIV infection first diagnosed in 2001
  - ART history
    - Since 2004 TDF/FTC/efavirenz
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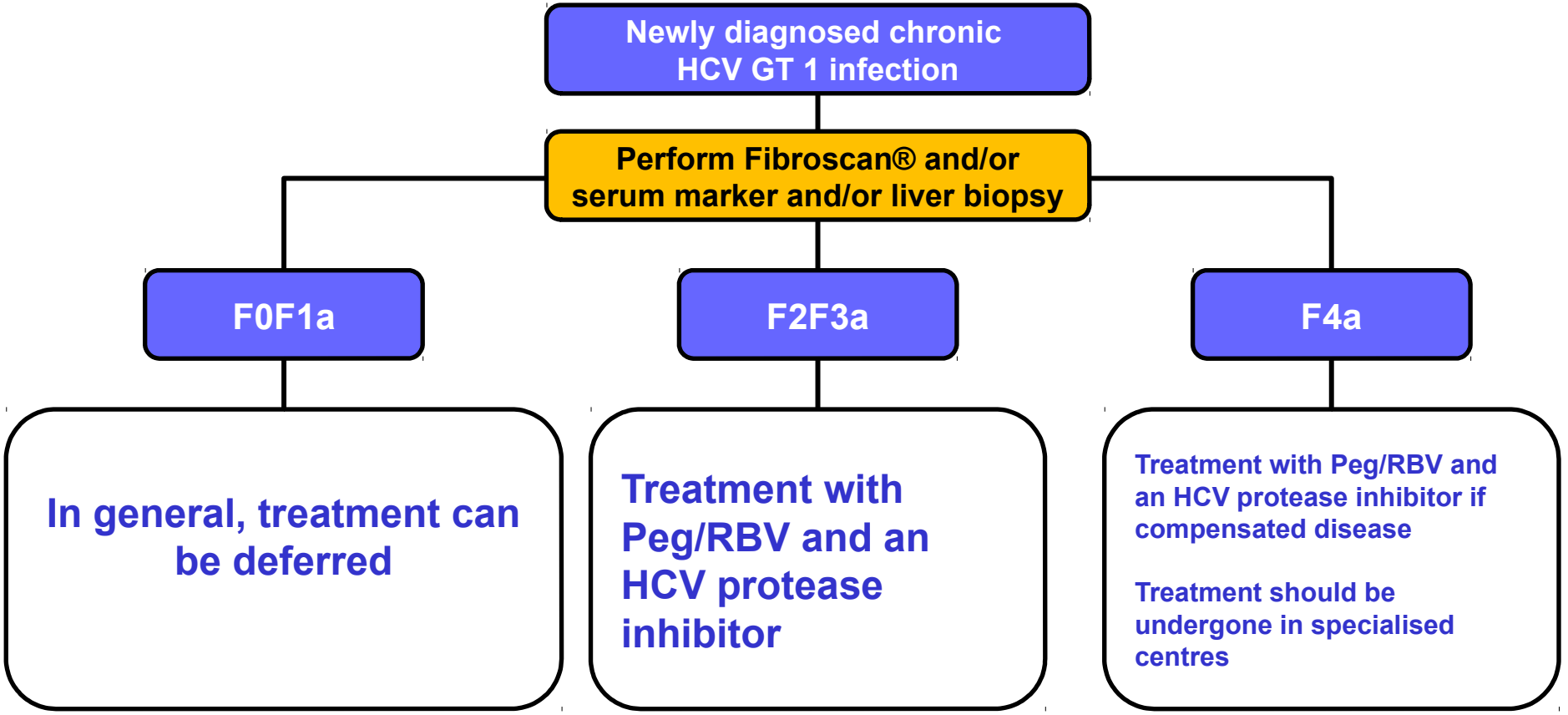
- HCV co-infection
  - Genotype 1a
  - HCV viral load 6.7 log10
  - ILB28 CT
  - Grade 1 ALT elevation
  - Transient elastography 5.4 kpa (F0 fibrosis)

Would you treat HCV? If so, with what?

Management of newly diagnosed HIV-HCV co-infected genotype-1 patients

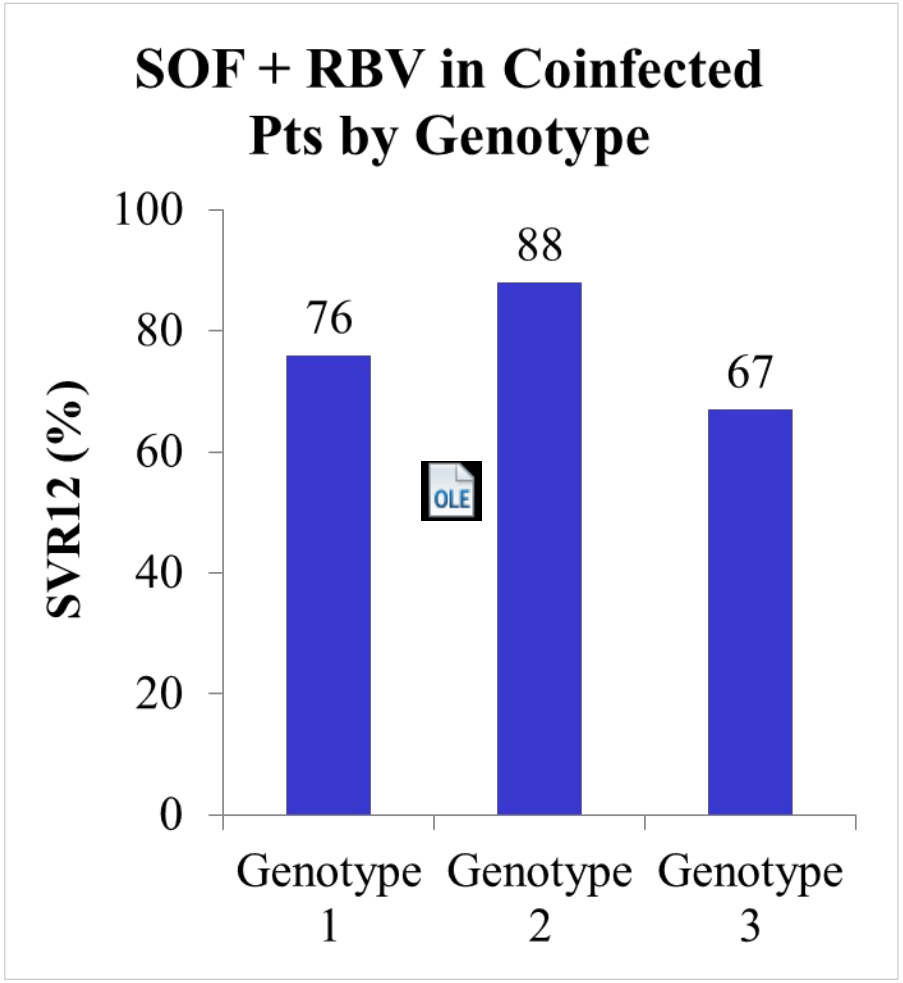


aMetavir fibrosis score: F0=no fibrosis; F1= portal fibrosis, no septae; F2= portal fibrosis, few septae; F3=bridging fibrosis; F4=cirrhosis; Peg, pegylated interferon; RBV, ribavirin

Ingiliz Rockstroh J. Liver International 2012;32:1194–9; EACS treatment guidelines, Version 7.0, Nov 2013. Available at: http://www.europeanaidsclinicalsociety.org/images/stories/EACS-Pdf/EacsGuidelines-v6.1-2edition.pdf. Accessed November 2013

PHOTON-1: SOF + RBV in G1,2,3 HCV Tx-Naive HIV/HCV Coinfected Pts

- Phase III, open-label, study
  - 12 or 24 wks of all-oral SOF 400 mg qd + wt-based dose RBV (1000 or 1200 mg/d)
- Viral relapse occurred in almost all pts not achieving SVR12
- Discontinuation rates due to AEs similar regardless of tx duration
- Safety profile consistent with RBV



Sulkowski MS, et al. AASLD 2013. Abstract 212.

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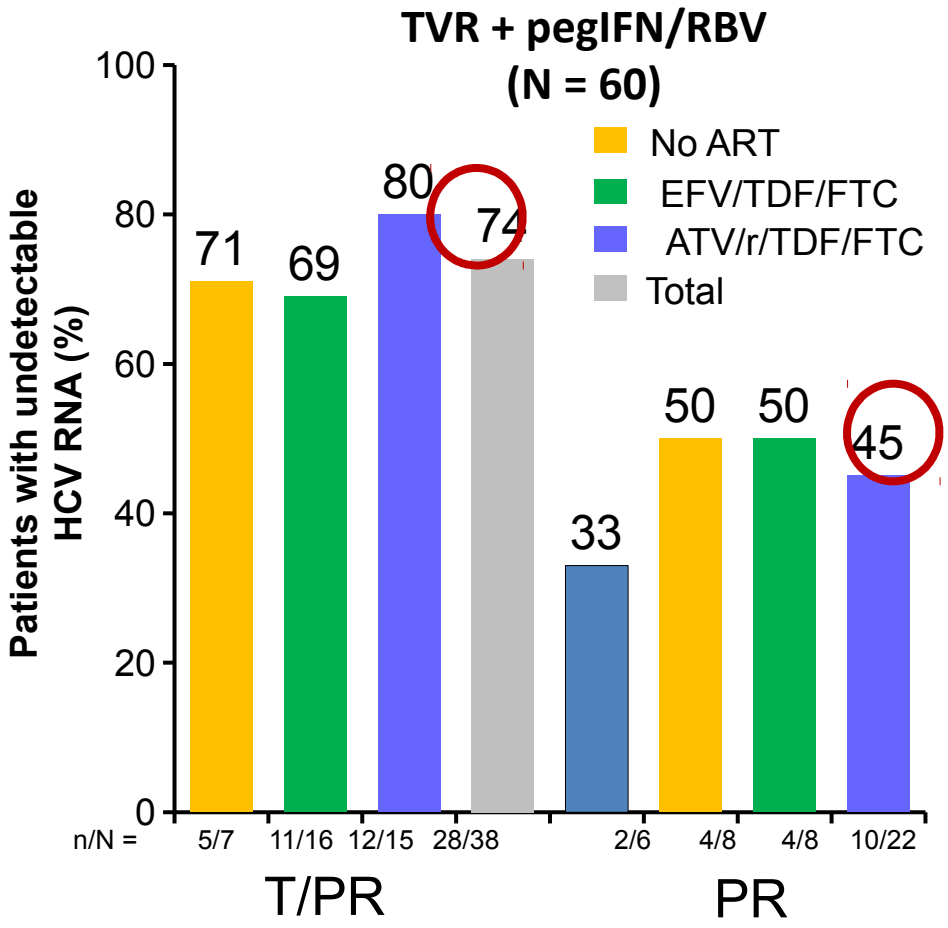
    11.4 kpa (F3 fibrosis)

Would you treat HCV? If so, with what?

Study 110: SVR With TVR + PegIFN/RBV in HIV/HCV Coinfection

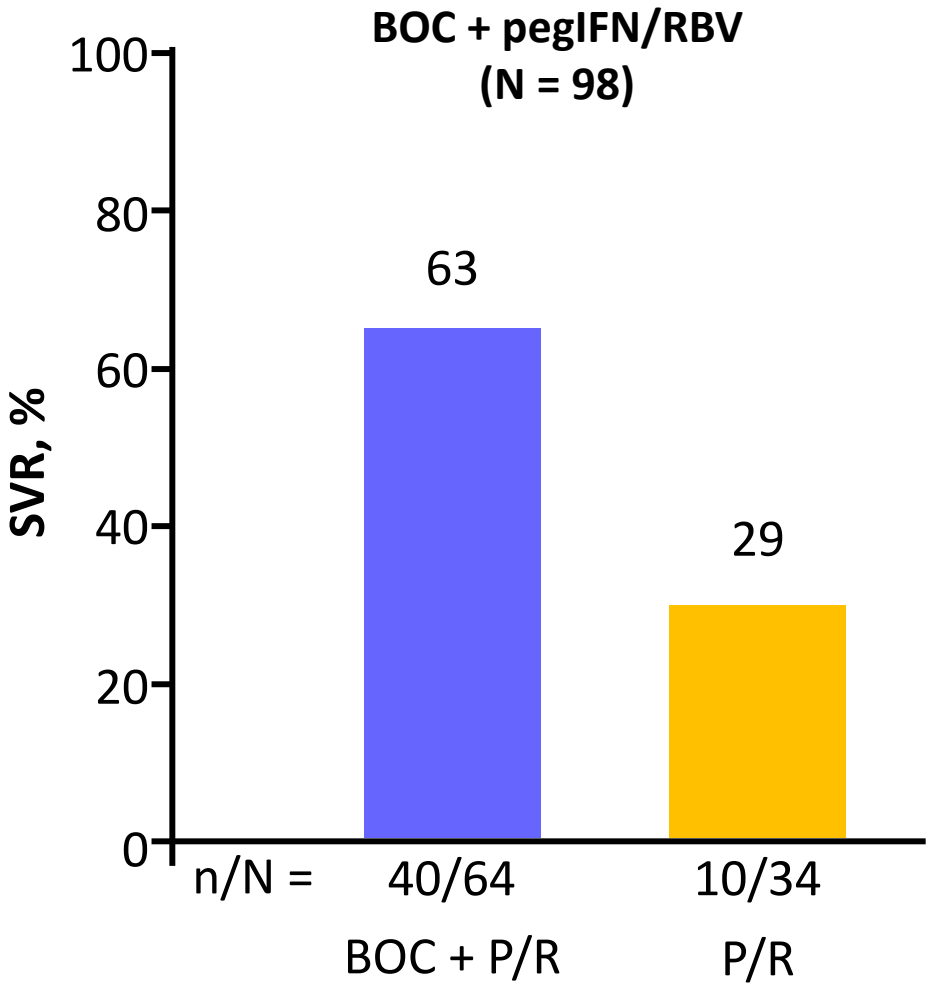
- **HCV tx-naive, HIV-1-infected patients1, treatment duration 48wks**
- **Safety and tolerability1**
  - **Increased pruritus, headache, nausea, rash, and dizziness for telaprevir-based regimens; but no rash associated discontinuations**
- **HCV monoinfected SVR rates G1 comparable (75%)2**



1. Sulkowski MS, et al. Ann Intern Med. 2013;159:86-96. 2. Jacobson IM, et al. N Engl J Med. 2011;364:2405-2416.

Study P05411: SVR With BOC + PegIFN/RBV in HIV/HCV Coinfection

- **2010: double-blind, RCT (2:1), Phase II trial1 , 48 wks treatment duration**
- **HCV treatment-naive1**
- **Safety and tolerability1**
  - **Increased anemia, pyrexia, and decreased appetite for boceprevir-based regimens**
- **HCV monoinfected SVR rates G1 comparable (68%)2**



1. Sulkowski M, et al. Lancet Infect Dis. 2013;13:597-605. 2. Poordad F, et al. N Engl J Med. 2011;364:1195-1206.

New treatment options for HIV/HCV genotype 1 patients: EACS guidelines

With first pilot studies in HIV/HCV-co-infected subjects demonstrating significant higher SVR12 rates with triple therapy compared to dual therapy HCV protease inhibitor based therapy with either boceprevir or telaprevir is now the new standard of treatment in HCV genotype 1 infection in HIV-infected individuals where available

Although shorter treatment durations of triple therapy have been demonstrated to be very efficacious in HCV monoinfected subjects with rapid virological response this data so far is not available for HIV/HCV co-infected subjects

EACS Guidelines, September 2012, Version 7.0. Available at: http://www.viraled.com/modules/info/files/files_50b4f84a4a3ac.pdf. Accessed June 2013

Patient 1: HY
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  - Transient elastography 11.4 kpa (F3 fibrosis)
- Co-medications
  - On stable methadone substitution

Would you treat HCV? If so, with what?

www.hep-druginteractions.org

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Reviews - Nature Outlook, Hepatitis C supplement.

Drug Interactions - Telaprevir and ciclosporin or tacrolimus.

Meeting Report - 6th International Workshop on Hepatitis Clinical Pharmacology

New Drugs - Danoprevir and ritonavir

Drug Interactions - Studies with telaprevir and boceprevir.

FDA News - Telaprevir and Boceprevir

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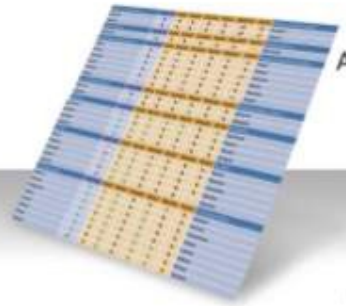
SITE UPDATES

Boceprevir and Telaprevir
Boceprevir and telaprevir have been added as columns to the interaction charts. Where an interaction...

>>more

DRUG INTERACTION CHARTS



Access our comprehensive, user-friendly, free, drug interaction charts

CLICK HERE

Providing clinically useful, reliable, up-to-date, evidence-based information

INTERACTIONS WITH TELAPREVIR AND BOCEPREVIR

Telaprevir & Boceprevir - INTERACTIONS NOW FULLY LISTED

Telaprevir and boceprevir were licensed by the FDA in May and have been added as columns to the interaction charts. To view the interactions, click on the drug interaction chart section above.

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ASSOCIATED SITES

www.hiv-druginteractions.org

A comprehensive HIV drug-drug interaction resource, freely available to healthcare workers, patients and researchers.

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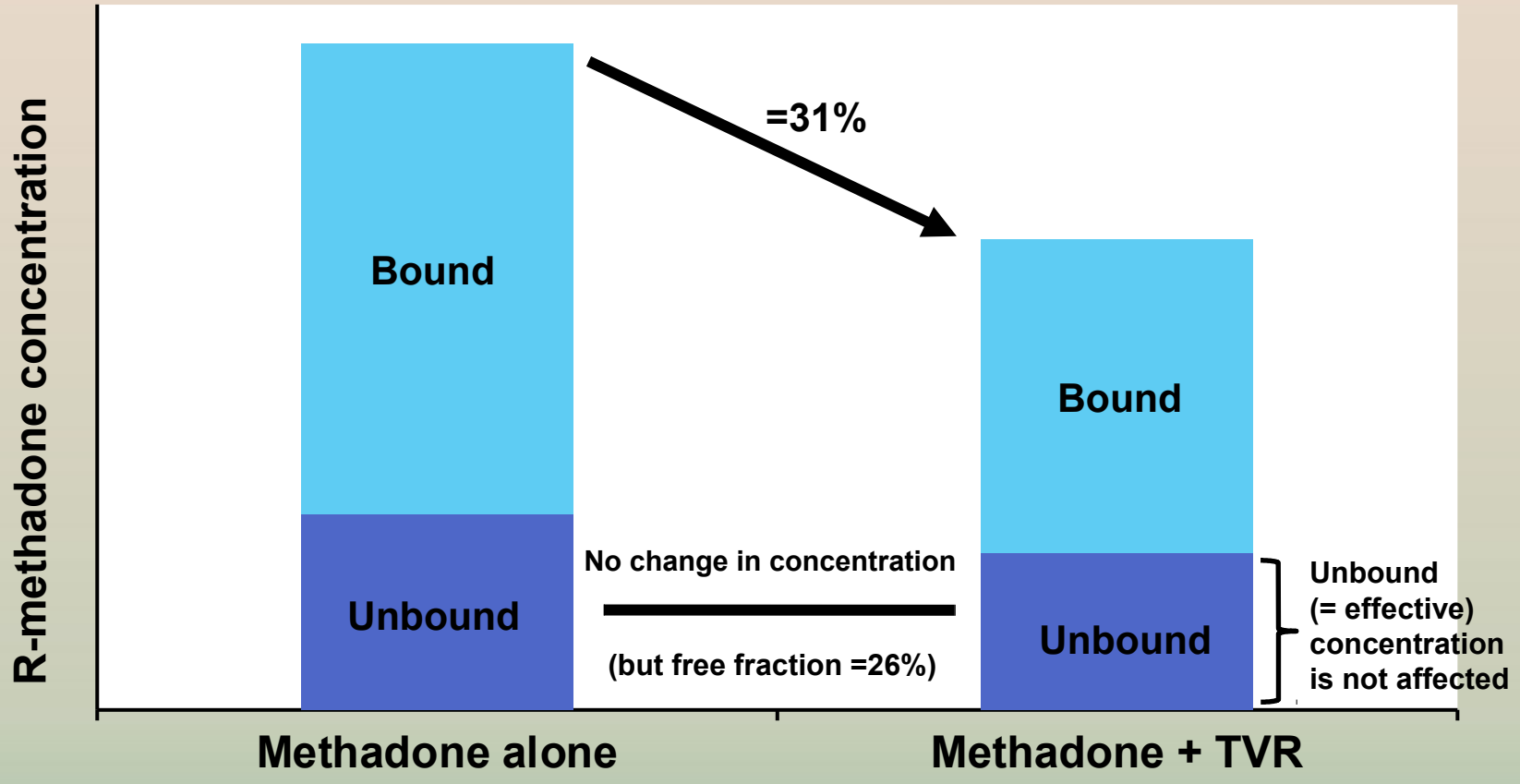
Please add noreply@hep-druginteractions.org and hivgroup@liv.ac.uk to your address book to assist in uninterrupted delivery and check your SPAM or BULK folder to ensure emails are not being lost.

Absolute unbound concentration of R-methadone was not affected by TVR co-administration



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Summary of key DAA and ARV DDI recommendations

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	TVR	BOC
ATV/r	Monitoring for hyperbilirubinemia recommended	Consider on a case by case basis if deemed necessary
DRV/r/, FPV/r LPV/r	Not recommended	Not recommended
EFV	Increase TVR to 1250 mg q8h	Not recommended
ETR	No dose adjustment needed	No dose adjustment needed
RPV	No dose adjustment needed	No dose adjustment needed
RAL	No dose adjustment needed	No dose adjustment needed
Stribild	No dose adjustment needed	Not studied
TDF	Increased monitoring is warranted	No dose adjustment needed

Telaprevir EU SmPC; Boceprevir EU SmPC; Kakuda TN, et al. IWCPHT 2012. Abstract O-18

BOCEPREVIR IN COMBINATION WITH HIV PROTEASE INHIBITORS IN PATIENTS WITH ADVANCED FIBROSIS - ALTERED DRUGDRUG-INTERACTIONS?

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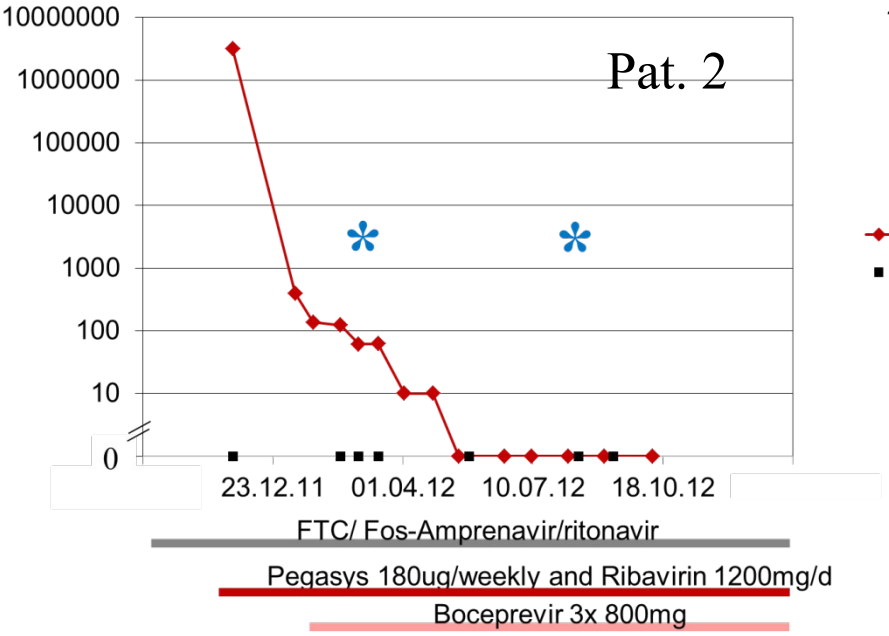
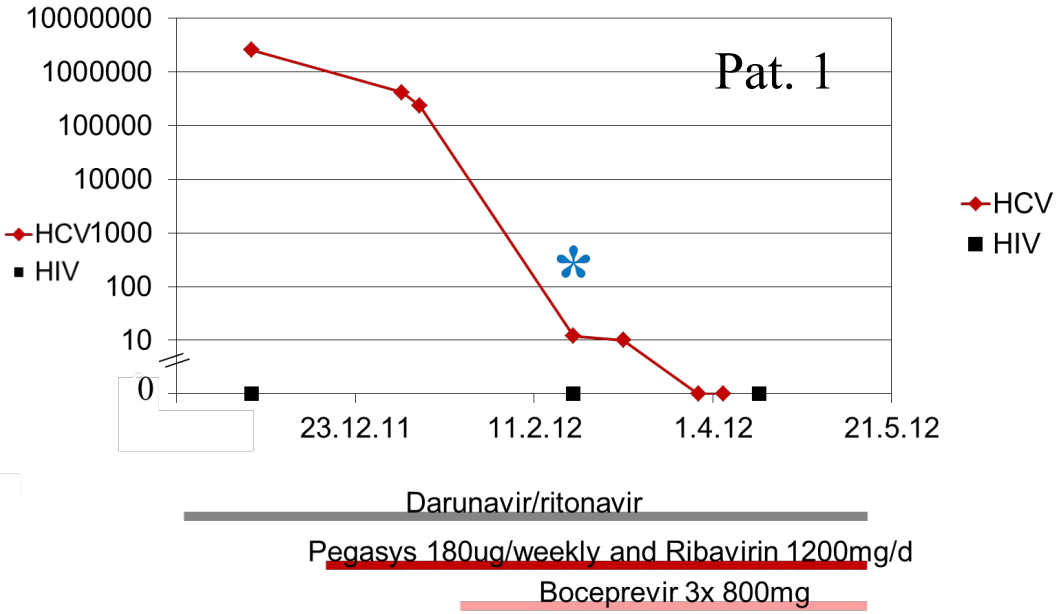
Patient 1 was on darunavir 800mg/ ritonavir 100mg once-daily monotherapy due to extensive N(t)RTI resistance. Liver disease had progressed to liver cirrhosis confirmed in FibroScan with a liver stiffness of 34 kPa.
Patient 2 had previously undergone chemotherapy for NHL and was on a simplified FTC daily and fos-amprenavir 700mg/ ritonavir 100mg twice-daily regimen. Liver stiffness was 32 kPa suggestive of liver cirrhosis.





* Amprenavir trough concentration (reference trough concentration 750–2500 ng/ml)
13.03.2012: 1699 ng/ml
06.08.2012: 1422 ng/ml

* Darunavir trough concentration (reference trough concentration 2400–4600 ng/ml):
3777 ng/ml

Schwarze-Zander C et al., HIV 11; Glasgow 2012, p130

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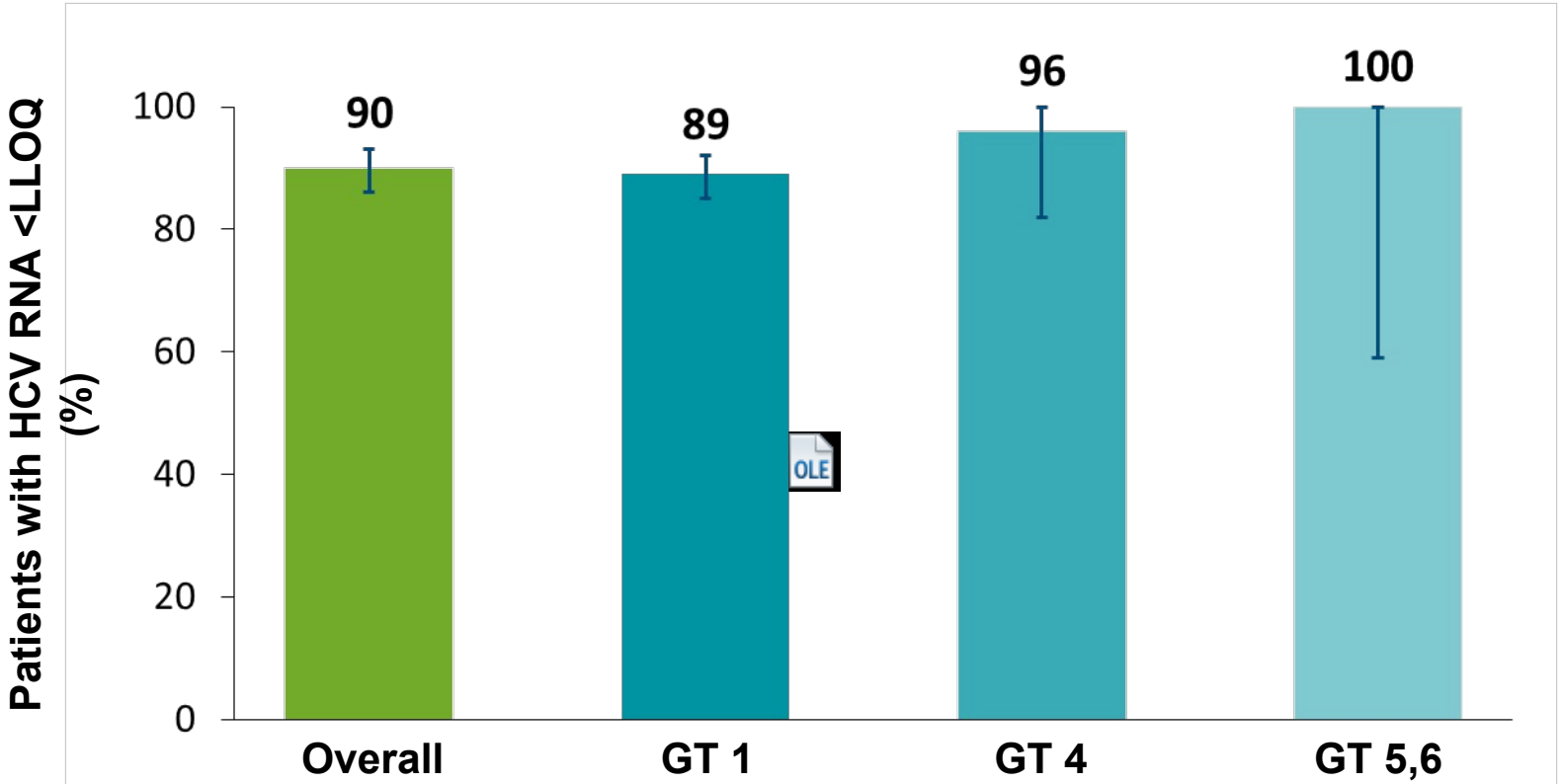
NEUTRINO Study: SVR12 by HCV Genotype



Error bars represent 95% confidence intervals.

Lawitz E, et al. 48th EASL; Amsterdam, Netherlands; April 24-28, 2013. Abst. 1411.