2015 8th Paris Hepatitis Conference
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Palais des Congrès, Paris
Organised by Pr Patrick Marcellin

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Real-life examples: HIV coinfection

Jürgen Rockstroh, Department of Medicine I, University of Bonn, Germany

Conflict of interest

I have received honoraria for speaking at educational events or consulting from:

Abbott, Abbvie, Bionor, BMS, Boehringer, Gilead, Janssen, Merck, Novartis, Pfizer, Roche, Tibotec, Tobira and ViiV

Herbert: 52y old hemophiliac

- **HIV infection 1984**
  - ART history
    - 1993: AZT + DDC
    - 1997: D4T + DDI + Saquinavir
    - 1999: Efavirenz + Indinavir
    - Multiple treatment failures with resistance development
    - 2001: lopinavir/r, TDF/3TC/AZT
    - **since 2005 darunavir/r, TDF/FTC/AZT**
      - HIV-1 RNA <50 c/ml
- **HCV co-infection**
  - Genotype 1a; VL 6.7 log10
  - ILB28 CT
  - Transient elastography 11.6 kpa (F3 fibrosis)
- **Other co-morbidities**
  - Hypertension: irbesartan 300mg
  - Hypercholesterolemia: pravastatin 20mg/d

Herbert: resistance results

RT: 67N, 103N, 184V, 219Q

- **Lamivudine**
- **Abacavir**
- **Zidovudine**
- **Stavudine**
- **Didanosine**
- **Emtricitabine**
- **Tenofovir**

- **Efavirenz**
- **Etravirine**
- **Nevirapine**
- **Rilpivirine**

PRO: 10I, 46I, 90M

- **Atazanavir/r**
- **Fosamprenavir/r**
- **Lopinavir/r**
- **Saquinavir/r**
- **Darunavir/r**
- **Indinavir/r**
- **Nelfinavir**
- **Tipranavir/r**

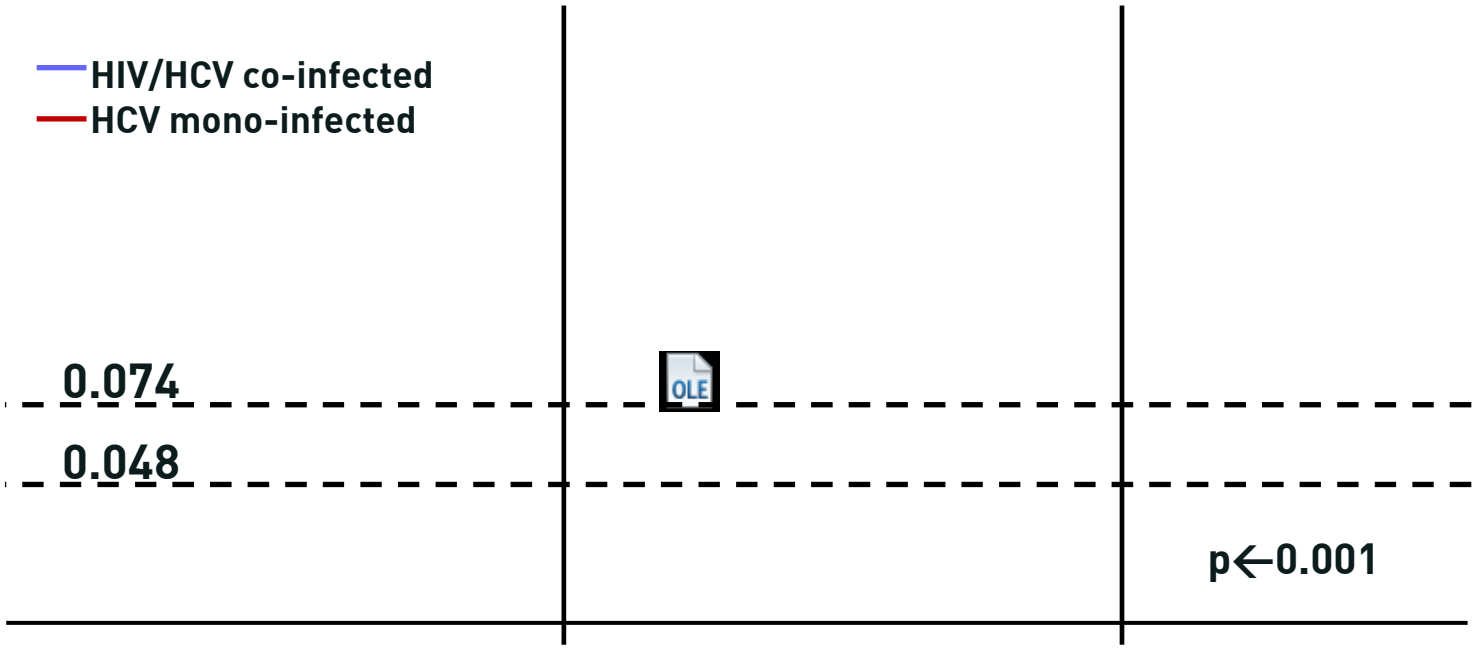
Question

- Should we treat Herberts HCV ?

- ≥ Yes
- ≥ no

Standardised cumulative incidence of hepatic decompensation

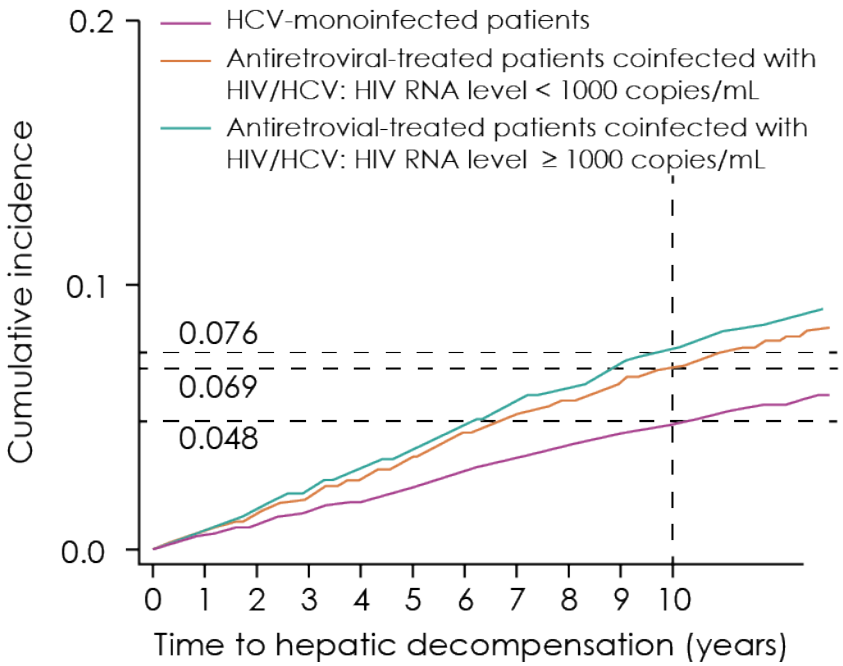
Cohort study, 4,286 cART-treated HIV/HCV-coinfected and 6,639 HCV-monoinfected patients in the Veterans Aging Cohort Study Virtual Cohort (1997-2010)

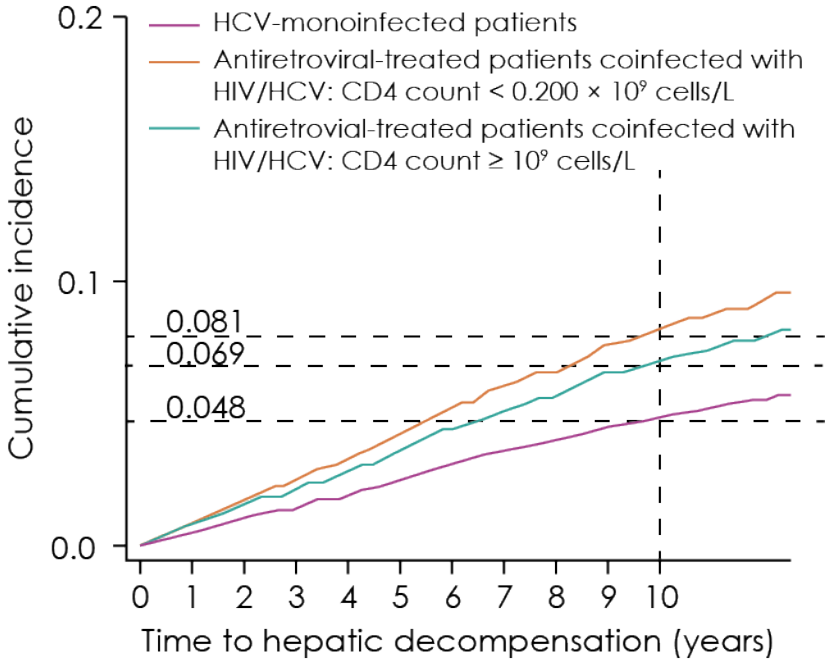


Hepatic decompensation risk 83% higher in the co-infected group (aHR 1.83, 95% confidence interval [CI] 1.54–2.18)

Lo Re V *et al Annals of Internal Medicine 2014*

HCV disease progression remains faster in coinfected patients, despite effective ART





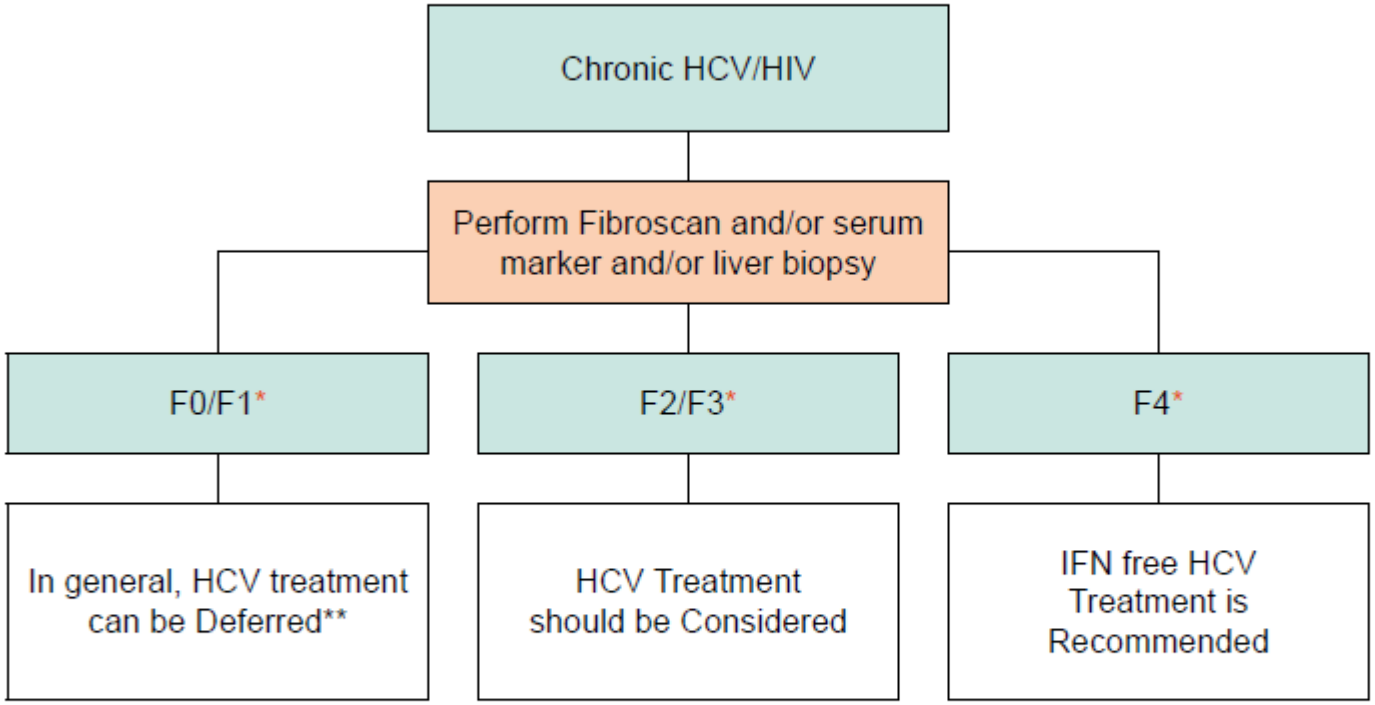
- If HIV RNA **< 1000 copies/mL:** +65% excess risk
- If HIV RNA **> 1000copies/mL:** +82% excess risk

- If CD4 **< 200/mm2:** +203% excess risk
- If CD4 **> 200/mm2:** 56–63% excess risk

ART, antiretroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

Lo Re V 3rd. Ann Intern Med 2014.

Management of Persons with Chronic HCV/HIV Co-infection



* Metavir fibrosis score: F0=no fibrosis; F1= portal fibrosis, no septae; F2= portal fibrosis, few septae, F3=bridging fibrosis, F4=cirrhosis.

** Monitor fibrosis stage annually, preferably with two established methods. Consider Treatment, if rapid progression.

New online EASL HCV recommendations

Indications for HCV treatment in HIV/HCV co-infected patients are identical to those in HCV mono-infection (A1)

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)

EASL recommendations April 2014 http://files.easl.eu/easl-recommendations-on-treatment-of-hepatitis-c-summary.pdf

Question

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» Which HCV therapy would you suggest ?

» ≥ Sofosbuvir and ribavirin
» ≥ Sofosbuvir/Ledipasvir ± ribavirin
» ≥ Sofosbuvir + simeprevir ± ribavirin
» ≥ Sofosbuvir + daclatasvir ± ribavirin
» ≥ Ombitasvir/Paritaprevir/Ritonavir +
» Dasabuvir + ribavirin

IFN free HCV treatment options

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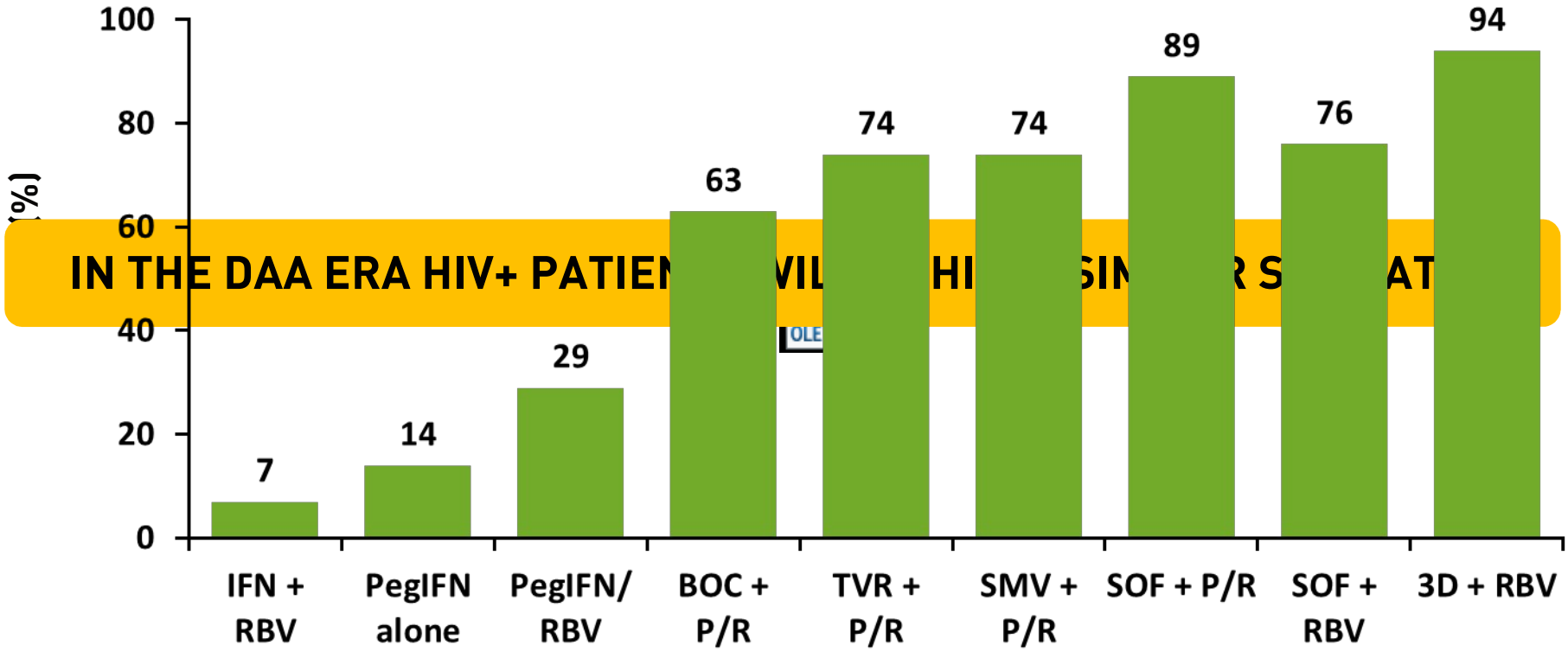
HCV genotype	Treatment	Treatment duration in treatment-naive patients	Treatment duration in treatment-experienced patients
1 & 4	SOF + RBV	24 weeks	24 weeks
	SOF + SMP	12 weeks (possible extension up to 24 weeks and/or addition of RBV)	12 weeks (possible extension up to 24 weeks and/or addition of RBV)
	SOF + DCV	12 weeks in non-cirrhotics, 24 weeks in compensated cirrhotics +/- RBV	12 weeks in non-cirrhotics, 24 weeks in compensated cirrhotics +/- RBV
	SOF/Ledipasvir	8-12 weeks in non-cirrhotics, 12-24 weeks in cirrhotics +/- ribavirin	24 weeks +/- ribavirin
	Ombitasvir/ Paritaprevir/Ritonavir + Dasabuvir + /- RBV (only for GT 1)	12 weeks in non-cirrhotics; RBV for GT1a but not GT 1b; 24 weeks in cirrhotics + RBV for GT1a and 12 weeks + RBV in GT1b	12 weeks in non-cirrhotics; RBV for GT1a but not GT 1b; 24 weeks in cirrhotics + RBV for GT1a and 12 weeks + RBV in GT1b

RBV: Ribavirin, SOF: Sofosbuvir, SMP: Simeprevir, DCV: Daclatasvir

Improved SVR12/24 rates over time in HCV GT1 patients co-infected with HIV

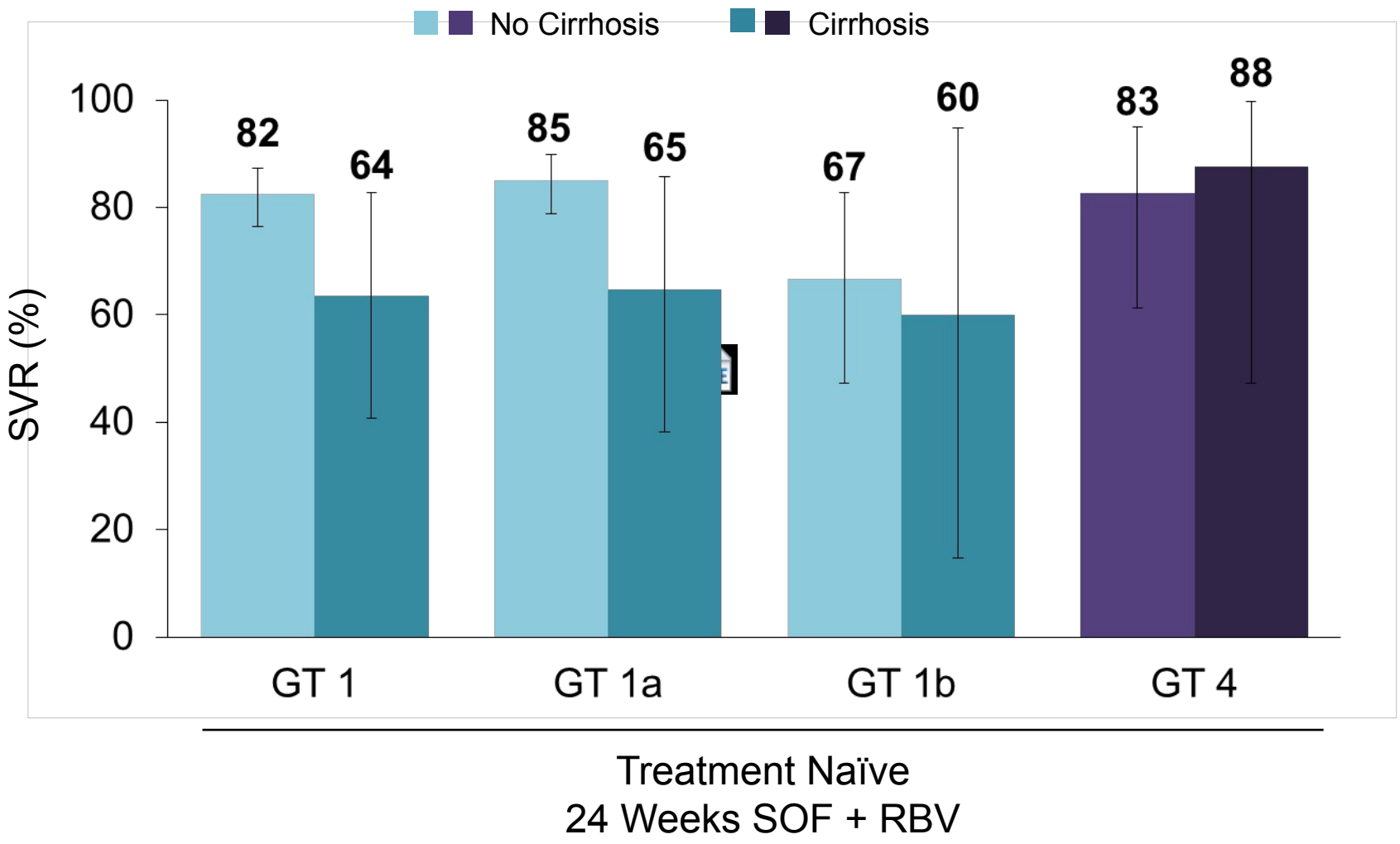


» Torriani FJ, *et al. N Engl J Med* 2004; 351:438–450;
Sulkowski M, *et al. Lancet Infect Dis 2013*; 13:597–605;
Sulkowski M, *et al. Ann Intern Med 2013*; 159:86–96;
Dieterich D, *et al*. EACS 2013. Abstract LBPS9/5;
Sulkowski M, *et al. Hepatology* 2013; 58 (Suppl):313–314A;
Dieterich D, *et al*. DDW 2014. Oral presentation 240;
» Sulkowski M, *et al*. AIDS 2014. Late breaker abstract 104 LB

3D = ABT-450/r/ombitasvir + dasabuvir P/R = PegIFN/RBV.

Results: SVR12 in GT 1 and GT 4

Cirrhosis vs No Cirrhosis (PHOTON-1 and 2)



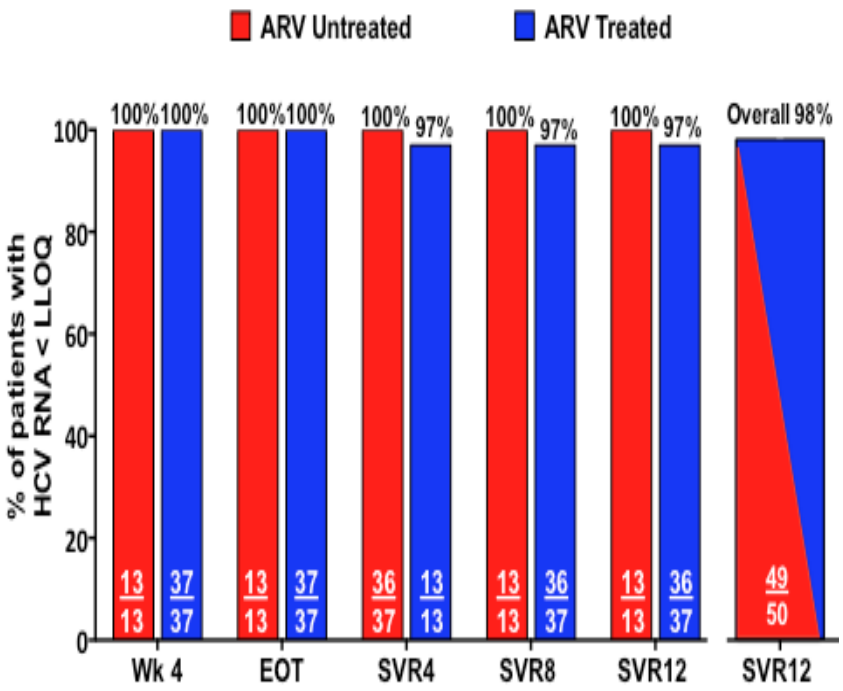
Rockstroh J et al., AASLD 2014

*1 patient could not be subtyped.

NIAID ERADICATE: SOF/LDV in TN GT 1 HIV/HCV co-infected patients

In this Phase 3 study, 50 GT 1 TN (n=13) or TE (n=37) patients were treated with SOF/LDV for 12 weeks

Treatment Response:



Safety data:

Event, n (%)	SOF/LDV ART naïve (n=13)	SOF/LDV ART experienced (n=37)
D/C due to AEs	0	0
Grade 4 AEs	0	0
Death	0	0
Grade ≥2 lab abnormality in >5% of population		
Hypophosphataemia	1 (8)	7 (19)
Decreased ANC	2 (15)	4 (11)
Elevated ALT	1 (8)	3 (8)
Elevated AST	1 (8)	3 (8)

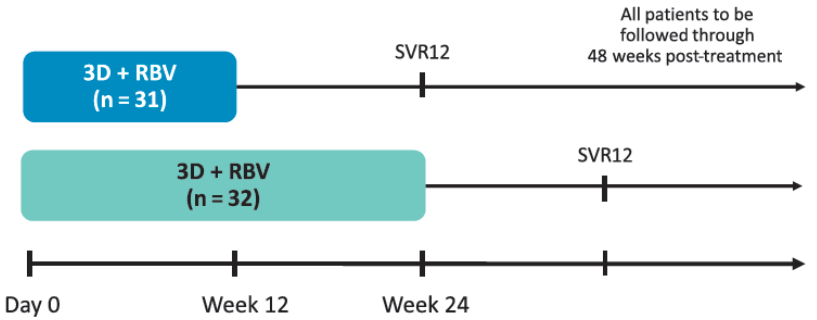
ANC, absolute neutrophil count; AST, aspartate aminotransferase

Osinusi A et al. J Hepatol 2014;60(Suppl):S7 and Osinusi A, et al. 65th AASLD; Boston, MA; November 7-11, 2014. Abst. 84

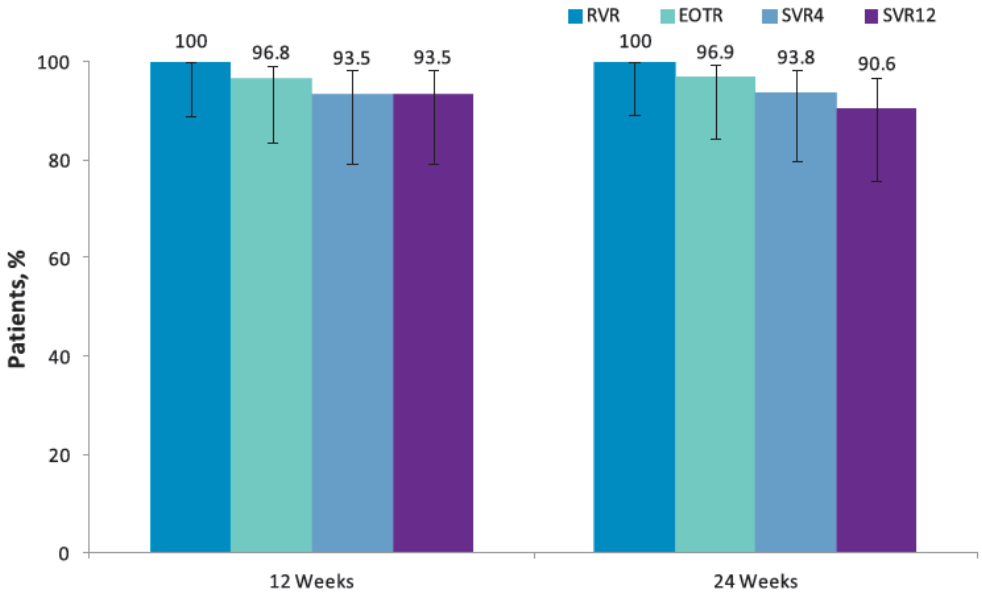
HIV-HCV Coinfection study: TURQUOISE-I: 3 DAAs + RBV

Characteristic	3D + RBV	
	12-Week Group (n = 31)	24-Week Group (n = 32)
Male, n (%)	29 (93.5)	29 (90.6)
Race, n (%)		
White	24 (77.4)	24 (75.0)
Black	7 (22.6)	8 (25.0)
Age, y (mean ± SD)	50.9 ± 6.0	50.9 ± 8.3
BMI, kg/m^2 (mean ± SD)	26.4 ± 3.9	27.2 ± 4.3
HCV RNA level, $\log_{10}$ IU/mL (mean ± SD)	6.54 ± 0.57	6.6 ± 0.78
CD4+ T-cell count/mm^3 (mean ± SD)	633 ± 236	625 ± 296
IL28B genotype, n (%)		
CC	5 (16.1)	7 (21.9)
Non-CC	26 (83.9)	25 (78.1)
HCV GT/subtype, n (%)		
1a	27 (97.1)	29 (90.6)
1b	4 (12.9)	3 (9.4)
Cirrhosis present, n (%)	6 (19.4)	6 (18.8)
Prior HCV treatment history		
Treatment-naïve, n (%)	20 (64.5)	22 (68.8)
Treatment-experienced	11 (35.5)	10 (31.3)
Prior pegIFN/RBV response, n (%)		
Relapser	1 (3.2)	3 (9.4)
Partial responder	5 (16.1)	2 (6.3)
Null responder	5 (16.1)	5 (15.6)
HIV-1 ART regimen, n (%)		
Atazanavir	16 (51.6)	12 (37.5)
Raltegravir	15 (48.4)	20 (62.5)

3D, ABT-450/r/ombitasvir and dasabuvir; ART, antiretroviral therapy; BMI, body mass index; HCV, hepatitis C virus; IL, interleukin; pegIFN/RBV, pegylated interferon plus ribavirin; r, ritonavir; RBV, ribavirin.



3D, co-formulated ABT-450/r/ombitasvir (150/100/25 mg) administered once daily; dasabuvir 250 mg administered twice daily. RBV, ribavarin, weight-based dosing (1000 or 1200 mg), administered twice daily. SVR12, sustained virologic response 12 weeks after the last dose of study drug.



EOTR, end of treatment response; RBV, ribavirin; RVR, rapid virologic response (week 4); SVR4, sustained virologic response at 4 weeks after the end of treatment; SVR12, sustained virologic response at 12 weeks after the end of treatment.

Wyles, AASLD 2014 #1939

Question

- How many clinically relevant drug-drug-interactions do you need to work on before starting DAA based HCV therapy in this patient ?

- 1) only HCV drugs and HIV PI (darunavir/r)
- 2) only HCV drugs and HIV PI and pravastatin
- 3) HCV drugs and HIV PI and all comedications

ARV Interaction Score Card

	Simeprevir	Sofosbuvir	Ledipasvir	Daclatasvir	AbbVie 3D
ATV/r	No data	ATV ↔ SOF ↔	No data	DCV ↑*	ATV ↔; ABT450 ↑
DRV/r	SIM ↑; DRV ↔	SOF ↑; DRV ↔	No data	DCV (↑)	DRV ↓; 3D ↓
LPV/r	No data	No data	No data	DCV↔	LPV ↔; ABT450 ↑
TPV/r	No data	No data	No data	No data	No data
EFV	SIM ↓; EFV ↔	SOF ↔; EFV ↔	LDV ↓; EFV ↓	DCV ↓*	No PK data**
RPV	SIM ↔; RPV ↔	SOF ↔; RPV ↔	LDV ↔; RPV ↔	No data	ABT450 ↑; RPV ↑
ETV	No data	No data	No data	No data	No data
RAL	SIM ↔; RAL ↔	SOF ↔; RAL ↔	LDV ↔; RAL ↔	No data	3D ↔; ↑ RAL
ELV/cobi	No data	No data	No data	No data	No data
DLG	No data	No data	No data	No data	No data
MVC	No data	No data	No data	No data	No data
TDF	SIM ↔; TDF ↔	SOF ↔; TDF ↔	LDV ↔; ↑TDF	DCV ↔; TDF ↔	3D ↔; TDF ↔

* Decrease DCV dose to 30mg QD, Increase DCV dose to 90mg QD, ** 3D + EFV led to premature study discontinuation due to toxicities

Personal communication Jennifer Kiser, University of Colorado, Denver, USA

Drug Interaction Charts

Printable Charts | View All | View all HCV DAAs | View all Interferons | View all Nucleoside/tide Analogues | Back to start

Step 1	Searching by: **Daclatasvir, Ledipasvir/Sofosbuvir, OBV/PTV/r + DSV, Simeprevir, Sofosbuvir**	Amend Selection
Step 2	Searching by: **Hepatitis C Directly Acting Antivirals (DAAs), Hypertension/Heart Failure Agents, Lipid Lowering Agents**	Amend Selection
Step 3	Searching by: **Daclatasvir, Ledipasvir/Sofosbuvir, OBV/PTV/r + DSV, Simeprevir, Sofosbuvir, Candesartan, Eprosartan, Irbesartan, Losartan, Atorvastatin, Fluvastatin, Lovastatin, Pravastatin, Rosuvastatin, Simvastatin**	Amend Selection
Step 4	View results	

Key to symbols:

Clicking on a solid symbol within a table will give further information on the interaction.
Empty symbols indicate that the combination has not been assessed (either by study or within the product label) and an interaction has been predicted based on the metabolic profiles of the drugs.

- These drugs should not be coadministered
- Potential interaction – may require close monitoring, alteration of drug dosage or timing of administration
- No clinically significant interaction expected
- This interaction has not been assessed
- n/a — Data not available

If a drug is not listed it cannot automatically be assumed it is safe to coadminister.

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Hepatitis C Directly Acting Antivirals (DAAs)	Daclatasvir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Daclatasvir	n/a	◇	⊖	◇	◇
Ledipasvir/Sofosbuvir	◇	n/a	⊖	⊖	⊖
OBV/PTV/r + DSV	⊖	⊖	n/a	⊖	⊖
Simeprevir	◇	⊖	⊖	n/a	□
Sofosbuvir	◇	⊖	⊖	□	n/a

Hypertension/Heart Failure Agents	Daclatasvir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Candesartan	□	□	□	□	□
Eprosartan	◇	◇	◇	◇	◇
Irbesartan	◇	□	□	◇	◇
Losartan	◇	◇	◇	◇	◇

Lipid Lowering Agents	Daclatasvir	Ledipasvir/Sofosbuvir	OBV/PTV/r + DSV	Simeprevir	Sofosbuvir
Atorvastatin	□	□	□	□	◇
Fluvastatin	□	□	□	◇	□
Lovastatin	□	□	⊖	□	◇
Pravastatin	□	□	□	□	◇
Rosuvastatin	□	⊖	□	□	◇
Simvastatin	□	□	⊖	□	◇

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NOTE: The Report ID is used to generate the pdf file and can be no more than 10 alphanumeric characters with no spaces. However, the pdf can be saved with a different file name which does not have these character restrictions, but the file name will not show on the report.

Report ID:

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ass:	Drug:	HEP Drug:
pertension/Heart Failure Agents	Irbesartan	OBV/PTV/r + DSV

Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration

Quality of Evidence:

Summary

oadministration has not been studied. Irbesartan is a substrate of UGT, CYP2C9 and OATP1B1. Ombitasvir/paritaprevir/ritonavir + dasabuvir increased exposure of raltegravir (a GT substrate) by up to 2-fold and a similar interaction is possible with other UGT substrates. Paritaprevir is an inhibitor of OATP1B1 and may increase irbesartan exposure. Conside besartan dose reduction and monitor blood pressure and heart rate.

Description

See Summary)

View all known interactions with OBV/PTV/r + DSV

Back


HIV-Druginteractions.org - Windows Internet Explorer
http://www.hiv-druginteractions.org/InteractionDetail.aspx?CombinationId=3126&F
HIV-Druginteractions.org
www.hiv-druginteractions.org
Interaction Charts
News & Archive
About Us
Pharmacology Resources
Links
Meetings
Feedback
Home
Drug Interaction Details
Class:
Lipid Lowering Agents
Drug:
Pravastatin
HIV Drug:
Darunavir
Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration
Quality of Evidence: Moderate
Summary
Coadministration of pravastatin (40 mg single dose) and darunavir/ritonavir (600/100 mg twice daily) increased pravastatin AUC on average by 81%, but up to a 5-fold increase was seen in a limited subset of subjects. When coadministration is required, it is recommended to start with the lowest possible dose of pravastatin and titrate it up to the desired clinical effect while monitoring for safety.
Description
Coadministration of pravastatin (40 mg single dose) and darunavir/ritonavir increased pravastatin Cmax by 63%; AUC increased by 81%, but an up to 5-fold increase was seen in a limited subset of subjects. When administration of pravastatin and darunavir coadministered with low dose ritonavir is required, it is recommended to start with the lowest possible dose of pravastatin and titrate it up to the desired clinical effect while monitoring for safety.
Prezista Summary of Product Characteristics, Janssen-Cilag Ltd, June 2012.
Coadministration of pravastatin (40 mg single dose) and darunavir/ritonavir (600/100 mg twice daily) was studied in 14 subjects. Pravastatin Cmax increased by 63%. The mean increase in pravastatin AUC was 81%; however, pravastatin AUC increased by up to 5-fold in some subjects. Titrate pravastatin dose carefully and use the lowest necessary dose while monitoring for safety.
Prezista Prescribing Information, Tibotec Inc, June 2012.
The effect of darunavir/ritonavir (600/100 mg twice daily) on the pharmacokinetics of a single dose of pravastatin (40 mg) was investigated in 14 HIV- subjects. Pravastatin Cmax and AUC increased by 63% and 81% respectively. However, substantial interindividual variability in pravastatin exposure was observed (treatment ratios from 0.57 to 6.79) and in 4/14 subjects, pravastatin exposure was increased by over 200%. Coadministration was generally well tolerated but, due to the variation in response, it is recommended to start with the lowest possible dose of pravastatin and titrate as necessary whilst monitoring safety.
Pharmacokinetic drug-drug interaction between the new HIV protease inhibitor darunavir (TMC114) and the lipid-lowering agent pravastatin. Sekar VJ, et al. 8th International Workshop on Clinical Pharmacology of HIV Therapy, Budapest, April 2007, abstract 54

Herbert

- **Patient is switched from his antiretroviral therapy to Darunavir/r and raltegravir and screened for the BI coinfection study where darunavir/r and raltegravir are both allowed as ART**

Herbert: 52y old hemophiliac

- **HIV infection 1984**
  - ART history
    - 1993: AZT + DDC
    - 1997: D4T + DDI + Saquinavir
    - 1999: Efavirenz + Indinavir
    - 2001: TDF + AZT + 3TC + lopinavir/r
    - 2005: TDF + FTC + AZT + darunavir/r
    - **2012: raltegravir + darunavir/r**

      HIV-1 RNA ↓50 c/mL,
- HCV co-infection
  - Genotype 1a; VL 6.7 log10
  - ILB28 CT
  - Transient elastography 17.4 kpa (F4 fibrosis)
  - Patient developed relapse after 24 weeks of feldaprevir + PEG-IFN + RBV followed by 24 weeks of PEG-IFN + RBV
- Other co-morbidities
  - Hypertension: irbesartan 300mg
  - Hypercholesterolemia: pravastatin 20mg/d

Question?

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» **Which HCV therapy would you suggest ?**

» ≥ **Sofosbuvir + Simeprevir**
» ≥ **Sofosbuvir + Daclatasvir + ribavirin**
» ≥ **Sofosbuvir + Ledipasvir +/- ribavirin**
» ≥ **Ombitasvir/Paritaprevir/Ritonavir +**
» **Dasabuvir + ribavirin**

Herbert: 52y old hemophiliac

- **HIV infection 1984**
  - ART history
    - 1993: AZT + DDC
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    - **2012: raltegravir + darunavir/r**

    HIV-1 RNA ↓50 c/mL,

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  - Genotype 1a; VL 6.7 log10
  - Transient elastography 17.4 kpa (F4 fibrosis)
  - Patient developed relapse after 24 weeks of feldaprevir + PEG-IFN + RBV followed by 24 weeks of PEG-IFN + RBV
  - **Patient starts Sofosbuvir and Daclatasvir**
  - **After 4 weeks HCV viral load 89 copies/ml**
  - **After 12 weeks HCV ←LLOQ but positive**

Question

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- **Which Daclatasvir dosis would you suggest ?**

- **≥ Sofosbuvir 400mg + Daclatasvir 60mg**
- **≥ Sofosbuvir + Daclatasvir 30mg**
- **≥ Sofosbuvir + daclatasvir 90mg**

Drug-drug Interactions between DAAs and ARVs

HCV drugs		ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	DTG	EVG/c	RAL	ABC	FTC	3TC	TDF	ZDV
DAAs	Boceprevir	D35%	↓32%D44%	↓45%D34%	↓19%E20%	↑10%D23%	↓E	E	E	↔	↓D	↔	↔	↔	↔	↔	↔[i]
	Daclatasvir	↑110%[ii]	↑[iii]	↑[iii]	↓32%[iv]	↓[iv]	↓[iv]	↔	↔	↔	↑[iii]	↔	↔	↔	↔	↑10%E10%	↔
	Simeprevir	↑	↑	↑	↓71%D10%	↓	↓	↑6%E12%	↔	↔	↑	↓11%E8%	↔	↔	↔	↓14%E18%	↔
	Sofosbuvir	↔	↑34%	↔	↓6%D4%	↔	↔	↑9%E6%	↔	↔	↔	↓13%D27%	↔	↓6%	↔	↓6%	↔
	Telaprevir	↓20%E17%	↓35%D40%	↓54%	↓26%D7%	↓16%	↓?	↓5%E	E	E25%	↑13%D16%	E31%	↔	↔	↔	E30%	↔[i]

Legend

↑ potential elevated exposure of DAA
↓ potential decreased exposure of DAA
↔ no significant effect
D potential decreased exposure of ARV
E potential elevated exposure of ARV

Numbers refer to decreased/increased AUC of DAAs and ARVs as observed in drug interactions studies

i potential haematological toxicity
ii Daclatasvir should be reduced to 30 mg once daily with ATV/r. No dose reduction with unboosted ATV
iii Daclatasvir should be reduced to 30 mg once daily
iv Daclatasvir should be increased to 90 mg once daily.

Colour legend

no clinically significant interaction expected.
these drugs should not be coadministered.
potential interaction which may require a dosage adjustment or close monitoring.

Note: the symbol (green, amber, red) used to rank the clinical significance of the drug interaction is based on www.hep-druginteractions.org.

EACS guidelines 12/2014

ARV Interaction Score Card

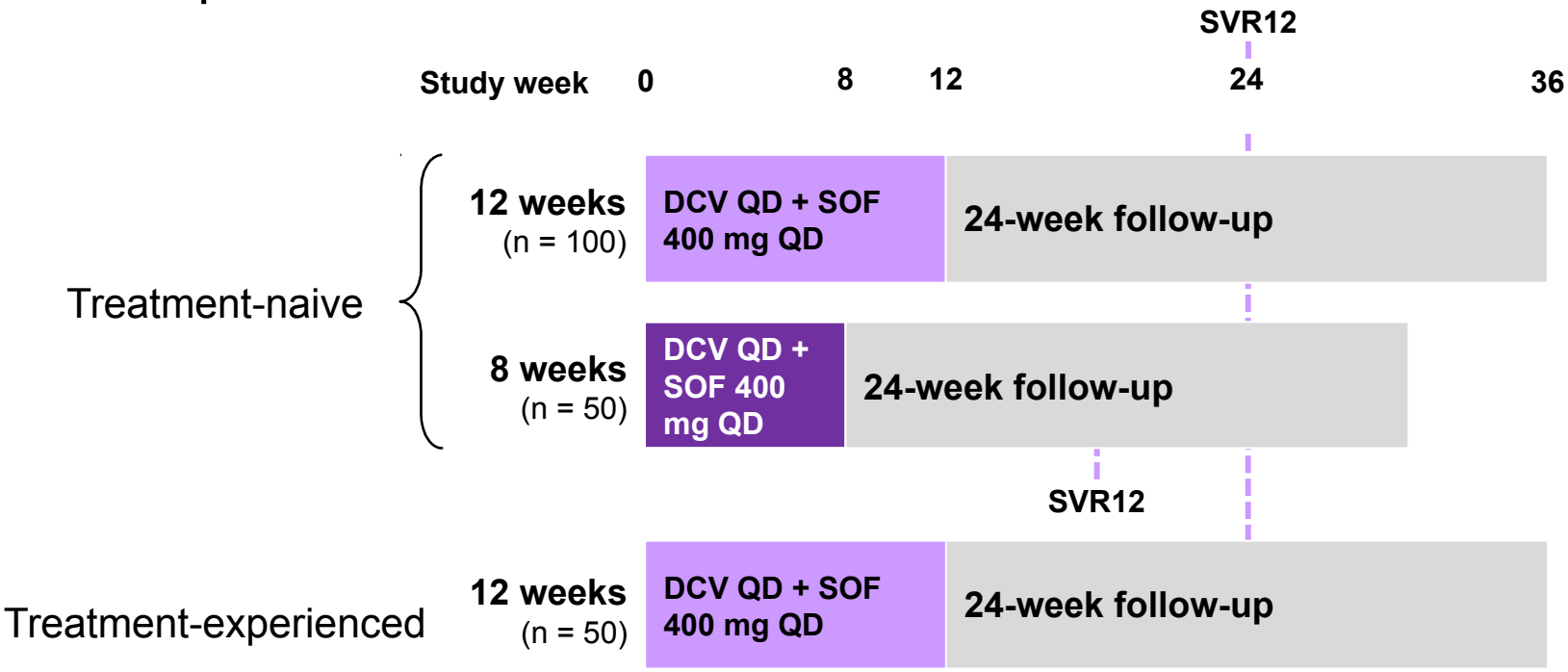
	Simeprevir	Sofosbuvir	Ledipasvir	Daclatasvir	AbbVie 3D
ATV/r	No data	ATV ↔ SOF ↔	No data	DCV ↑*	ATV ↔; ABT450 ↑
DRV/r	SIM ↑; DRV ↔	SOF ↑; DRV ↔	No data	DCV (↑)	DRV ↓; 3D ↓
LPV/r	No data	No data	No data	DCV↔	LPV ↔; ABT450 ↑
TPV/r	No data	No data	No data	No data	No data
EFV	SIM ↓; EFV ↔	SOF ↔; EFV ↔	LDV ↓; EFV ↓	DCV ↓*	No PK data**
RPV	SIM ↔; RPV ↔	SOF ↔; RPV ↔	LDV ↔; RPV ↔	No data	ABT450 ↑; RPV ↑
ETV	No data	No data	No data	No data	No data
RAL	SIM ↔; RAL ↔	SOF ↔; RAL ↔	LDV ↔; RAL ↔	No data	3D ↔; ↑ RAL
ELV/cobi	No data	No data	No data	No data	No data
DLG	No data	No data	No data	No data	No data
MVC	No data	No data	No data	No data	No data
TDF	SIM ↔; TDF ↔	SOF ↔; TDF ↔	LDV ↔; ↑TDF	DCV ↔; TDF ↔	3D ↔; TDF ↔

* Decrease DCV dose to 30mg QD, Increase DCV dose to 90mg QD, ** 3D + EFV led to premature study discontinuation due to toxicities

Personal communication Jennifer Kiser, University of Colorado, Denver, USA

HCV/HIV coinfection: ALLY-2 study design

GT-1–6 patients with HIV/HCV coinfection



DCV dosing was 30, 60 or 90 mg in each arm

DCV, daclatasvir; GT, genotype; HCV, hepatitis C virus; HIV, human immunodeficiency virus; QD, once-daily; SOF, sofosbuvir; SVR, sustained virologic response.

Study AI444-216. Available from: www.ClinicalTrials.gov/ct2/show/NCT02032888. Accessed October 2014.

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 (700/100 mg bid)
  - 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)

Question

- **Should we treat Rosalie`s HCV ?**

- **≥ Yes**
- **≥ no**

Question?

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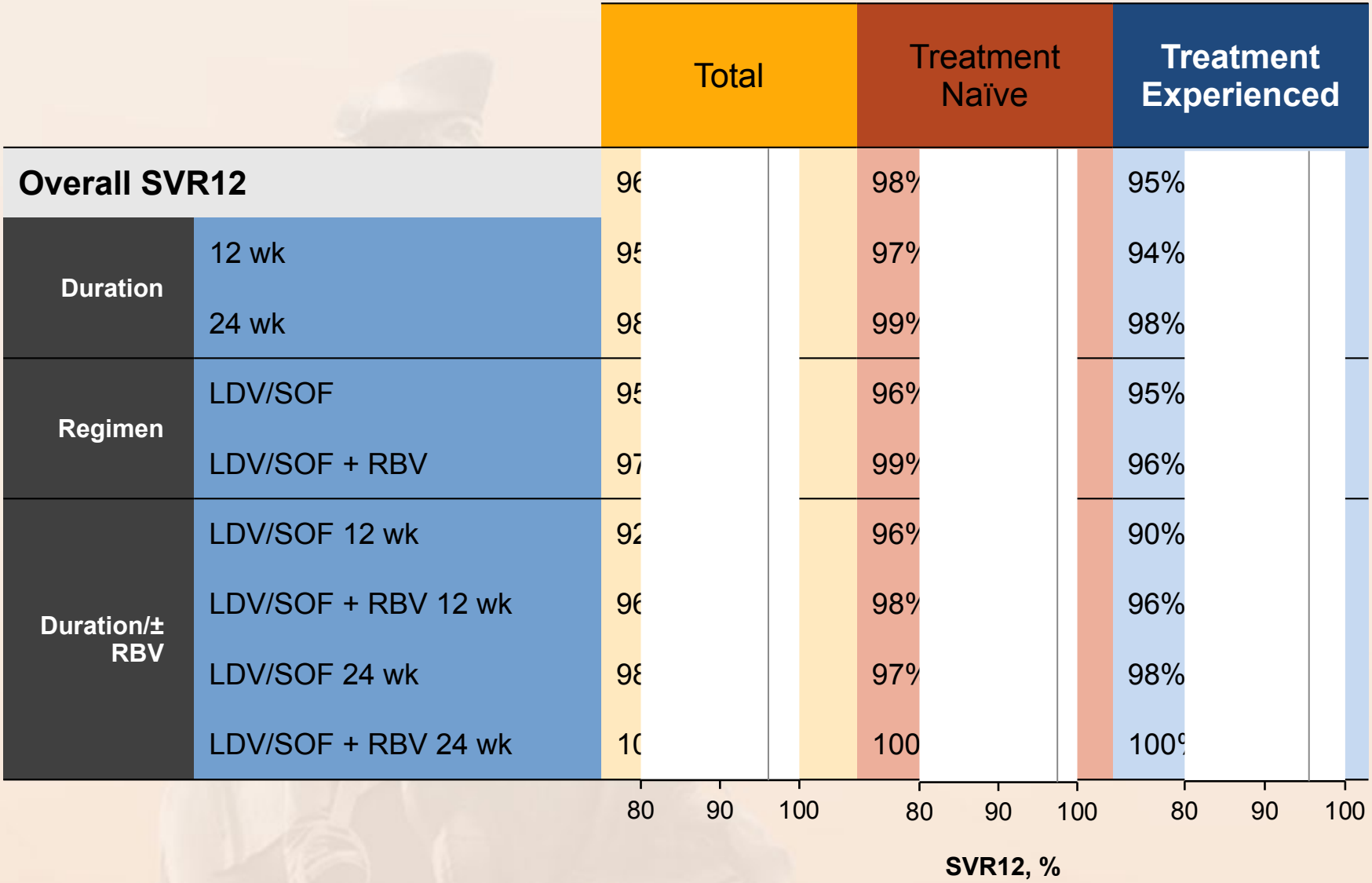
» Which HCV therapy would you suggest ?

» ≥ Sofosbuvir + Simeprevir +/- ribavirin
» ≥ Sofosbuvir + Daclatasvir +/- ribavirin
» ≥ Sofosbuvir + Ledipasvir +/- ribavirin
» ≥ Ombitasvir/Paritaprevir/Ritonavir +
» Dasabuvir + ribavirin

Bourlière:
Results - SVR12 by Treatment Regimen



Bourlière M, et al. 65th AASLD; Boston, MA; November 7-11, 2014. Abst. 82.

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
  - CD4-nadir 190 cells/mm3
  - 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 30mg for 24 Weeks

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
  - CD4-nadir 190 cells/mm3
  - 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

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
  - CD4-nadir 190 cells/mm3
  - No HIV primary resistance

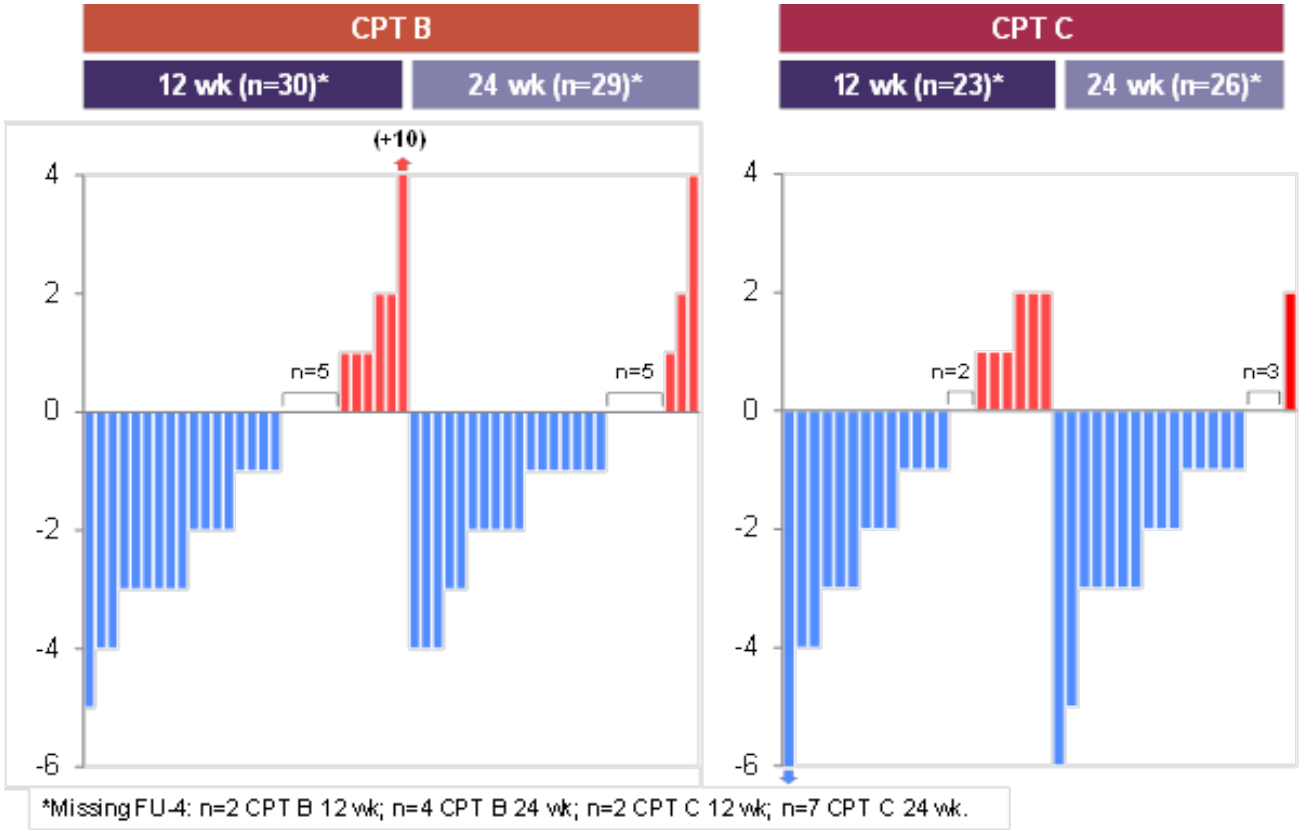
- HCV co-infection
  - 02/2014 Request to company for daclatasvir within patient named program
  - 21 days later approval
  - Since 03/2014 Sofosbuvir + Daclatasvir for 24 Weeks
  - HCV RNA Week (8) 18 IU/ml
  - HCV RNA Week (12) <LLOQ but positive
  - HCV RNA Week (16 and 24) <LLOQ IU/ml

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
  - CD4-nadir 190 cells/mm3
  - 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
  - Patient improves clinically significantly:
    - Liver transaminases normalized
    - INR improved
    - Platelets increase
    - Much less fatique

Laboratory Results: MELD Score. Change From Baseline to Follow-Up Week 4.



Flamm SL et al. 65th Annual Meeting of the American Association for the Study of Liver diseases, November 7-11, 2014, Boston,USA; abstract 239

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
  - CD4-nadir 190 cells/mm3
  - No HIV primary resistance

- HCV co-infection
  - 10/2014 4 weeks after EOT:
    - HCV-RNA 2,3 Mill IU/ml
    - Flare in transaminases
    - INR increase

Question

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- Should we treat Rosalie`s HCV again?

- ≥ Yes
- ≥ no
- ≥ need additional information and diagnostic workup

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
  - CD4-nadir 190 cells/mm3
  - No HIV primary resistance

- HCV co-infection
  - 10/2014 4 weeks after EOT:
    - HCV-RNA 5 Mill IU/ml
    - Flare in transaminases
    - INR increases
- HCV genotypic resistance testing
  - Q80K (Simeprevir)
  - Q30H (DCV/OMB/LDV)
  - H58H/D (DCV/OMB/LDV)

Question?

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» Which HCV therapy would you suggest ?

» ≥ Sofosbuvir + Simeprevir +/- ribavirin
» ≥ Sofosbuvir + Daclatasvir +/- ribavirin
» ≥ Sofosbuvir + Ledipasvir +/- ribavirin
» ≥ Ombitasvir/Paritaprevir/Ritonavir +
» Dasabuvir + ribavirin

Case #3: What would you do, Dr. ...?

60-year old patient with chronic HIV/HCV coinfection (First diagnosis 1993; former IVDU) presents for possible HCV treatment evaluation as he has heard a lot about new treatment options. He feels well and has no clinical complaints other than joint problems. His current ART is DRV/r and Dolutegravir after some previous virological failures and HIV resistance development (NRTI and NNRTI). CD4 count is stable 36 %, 694/μl abs., and HIV viral load well suppressed ↓40 copies/ml.

HCV: GT 3, Fibroscan 11,8 kPa = F3 Fibrosis
Therapy with PEG-IFN/RBV 2009, relapse after 24 weeks, again dual therapy 2011, relapse after W48

Would you treat the patient and with what?