

19-20 October 2014 • Barcelona, Spain



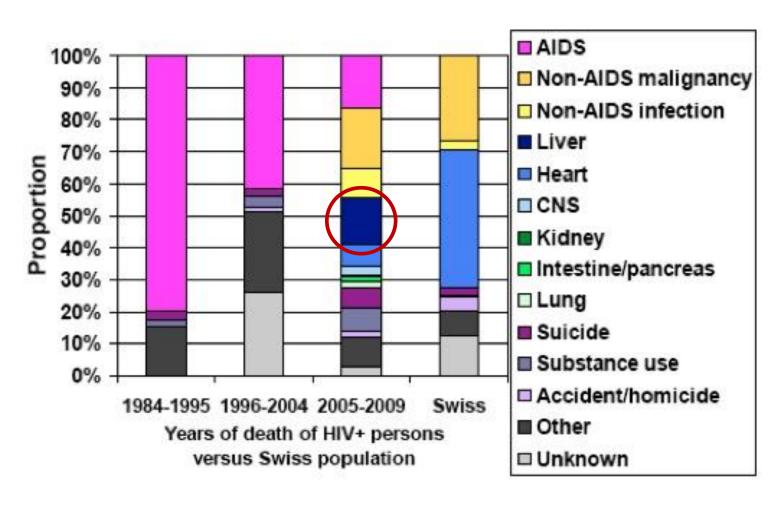
Viral hepatitis C in HIV infected patient - case study -

Daniela Munteanu

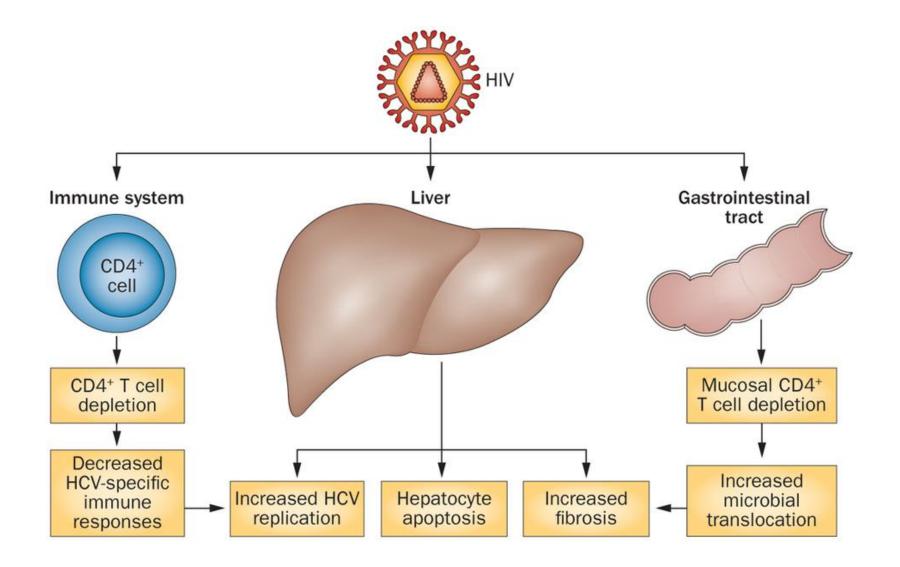
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Liver-related death is a frequent cause of non-AIDS death in HIV+ patients



Pathogenesis of HCV / HIV co-infection



Faster progression of liver disease in HIV / HCV patients

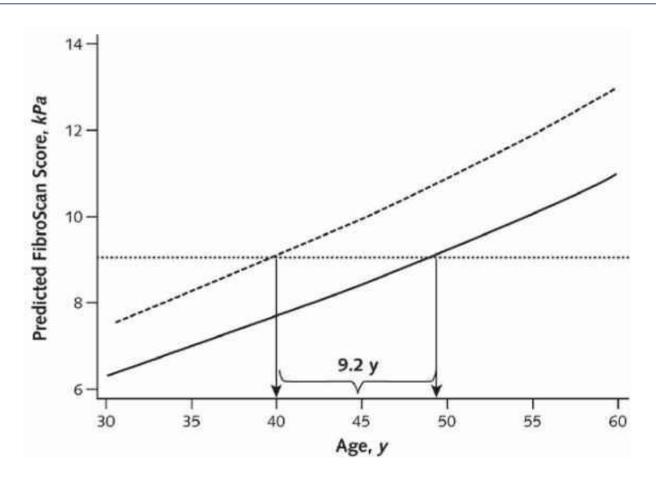
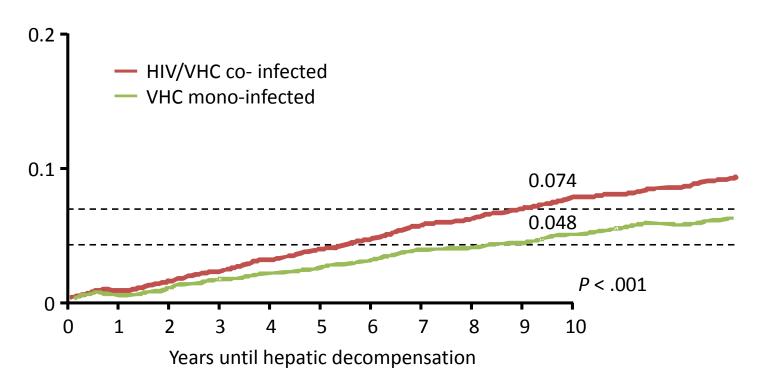


Figure 3. Liver fibrosis and age among persons coinfected with HIV and HCV (dashed line) and those with only HCV (solid line)

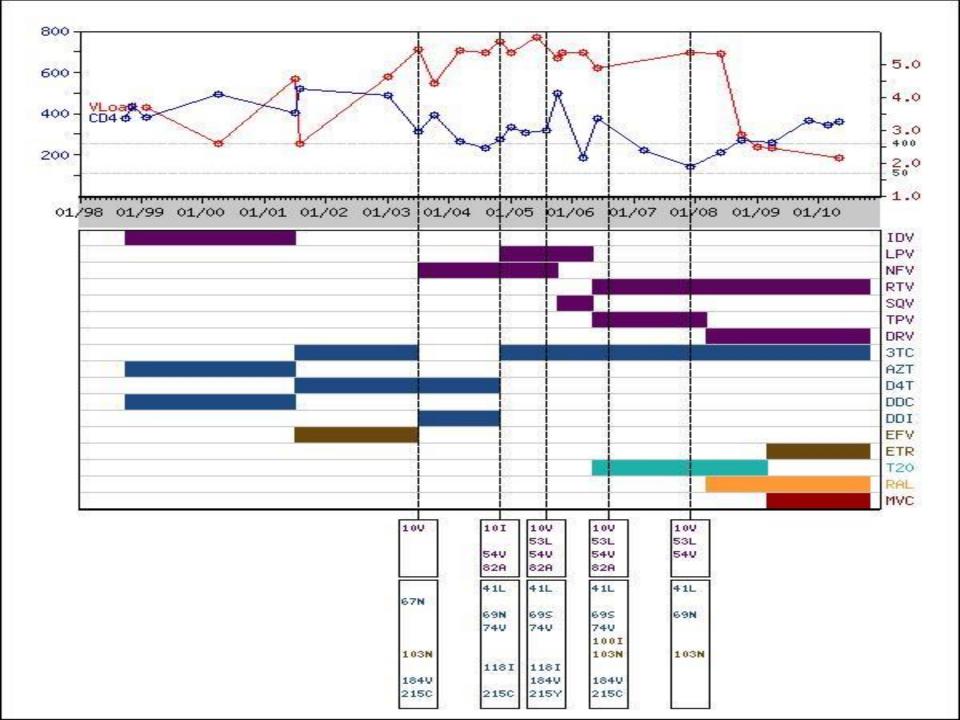
HCV Coinfection vs Monoinfection: Cumulative Incidence of Decompensation

- 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/mm³
 - Highest HIV-RNA 496000 copies/mL
 - HCV and HBV negative at the beginning
 - Highly treatment-experienced patient with multiple drug resistance



cART history

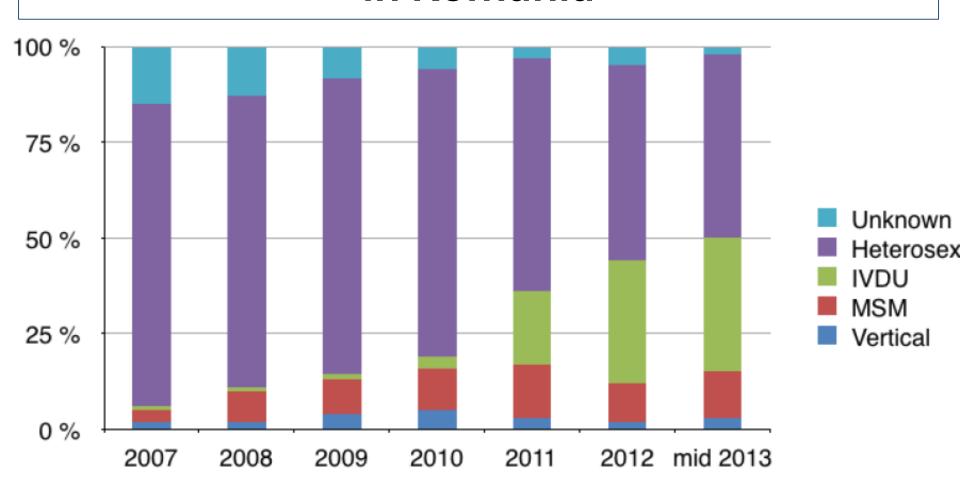
- 1998 2001 IDV + AZT + DDC
- 2001 2003 EFV + 3TC + D4T
 - nightmares
- 2003 2004 NFV + D4T +DDI
 - Lipoatrophy, peripheral neuropathy
- 2004 2005 LPV/r + NFV + 3TC
 - Diarrhea
- 2005 2006 LPV/r + SQV + 3TC
 - Diarrhea and vomiting
- 2006 2007 TPV/r + 3TC + T20
- 2008 2009 RGV + DRV/r + 3TC + T20
 -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

HCV coinfection

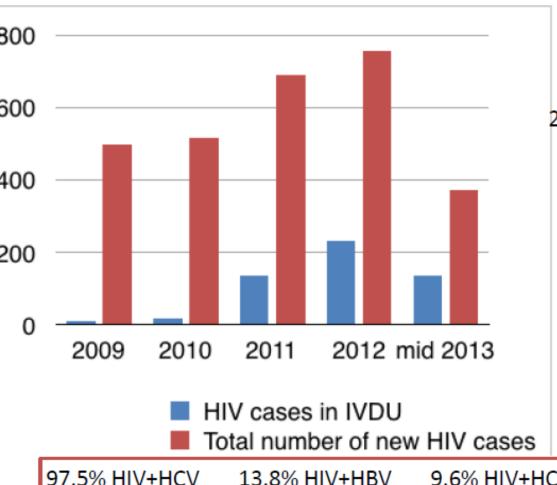
- 2009 HCV positive (IVDU in the last 10 months)
 - HCV-RNA 6.32 log UI/mL
 - No liver biopsy
- CD4 cell count 312/mm3

– 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

97.5% HIV+HCV

9.6% HIV+HCV+HBV

2.5% HIV+HCV+HBV+HDV

HCV coinfection

- 2009 HCV positive (IVDU in the last 10 months)
 - HCV-RNA 6.32 log UI/mL
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- CD4 cell count 312/mm3

– HIV-RNA 430 c/mL

WHAT NEXT?

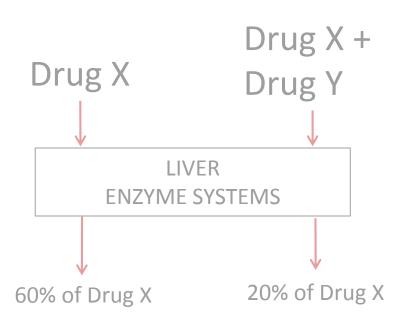
Substitutive therapy

 After 2 months – withdrawal symptoms – Methadone dose was increased

Drug interaction between DRV/r and Methadone

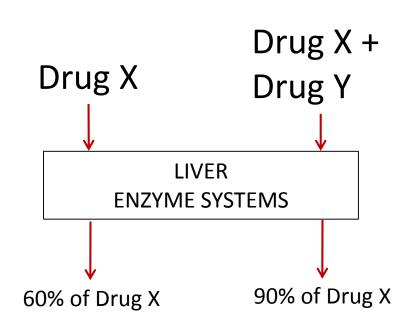
Drug-drug interactions

INDUCER



Inducer drugs ↓↓↓ concentration of other drugs

INHIBITOR

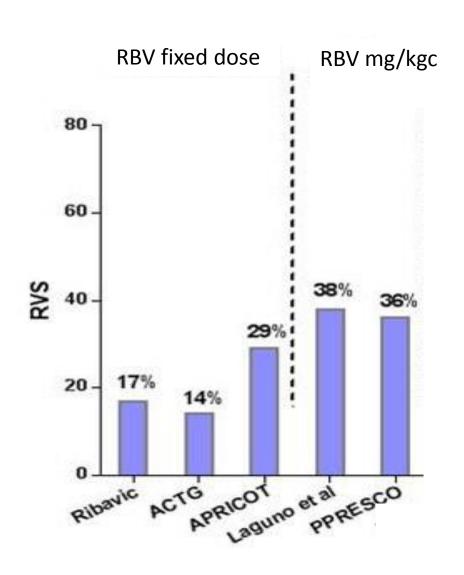


Inhibitor drugs ↑↑↑ concentration of other drugs

Drug-drug interaction between Analgesics and ARVs

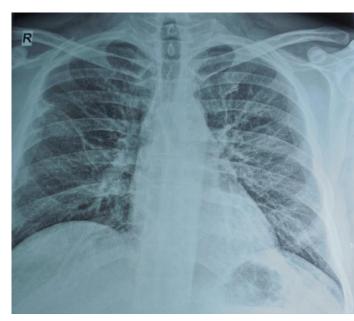
ana	analgesics		DRV/r	FPV/r	IDV/r	LPV/r	SQV/r	EFV	ETV	NVP	RPV	MVC	RAL
	alfentanil	†	†	1	1	†	1	Ţ	ļ	ļ	\leftrightarrow	\leftrightarrow	+ +
	buprenorphine	†67%	1 ^d	+	†	↔	1	150%	↓25%	+ +	+ +	\leftrightarrow	↔
o	codeine	†9	†9	†9	†9	†9	†9	Ţ9	19	Ţ9	\leftrightarrow	\leftrightarrow	\leftrightarrow
<u>s</u>	dihydrocodeine	J†	J†	J†	J†	Į†	Į†	Į†	ļ	ļ	\leftrightarrow	\leftrightarrow	↔
<u>a</u>	fentanyl	†	†	†	†	†	†	ļ	ļ	ļ	↔	\leftrightarrow	↔
analgesics	methadone	1e	↓16%	↓18%	Ţ	↓53%e	↓19% ^{ef}	↓52%	†6%	↓≈50%	↓16%e	\leftrightarrow	+
	morphine	ļ	ļ	ļ	ļ	ļ	ļ	†	↔	↔	↔	↔	+ +
opioid	oxycodone	†	†	†	†	†	†	ļ	Ţ	Ţ	↔	\leftrightarrow	↔
0	pethidine	1 _p	1 _p	1 _p	İch	1 _p	1p	1 _p	\leftrightarrow	Ţħ.	\leftrightarrow	\leftrightarrow	\leftrightarrow
	sufentanil	†	†	1	1	1	1	Ţ	Ţ	Ţ	+	\leftrightarrow	↔
	tramadol	†9	†9	†9	†9	†9	†9	Į ⁱ	↔	↔	\leftrightarrow	\leftrightarrow	↔

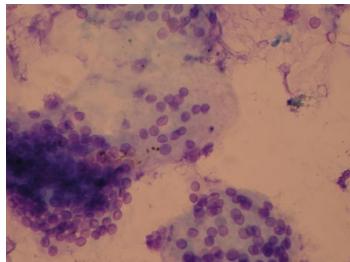
SVR rates with PegIFN/RBV in HIV/HCV



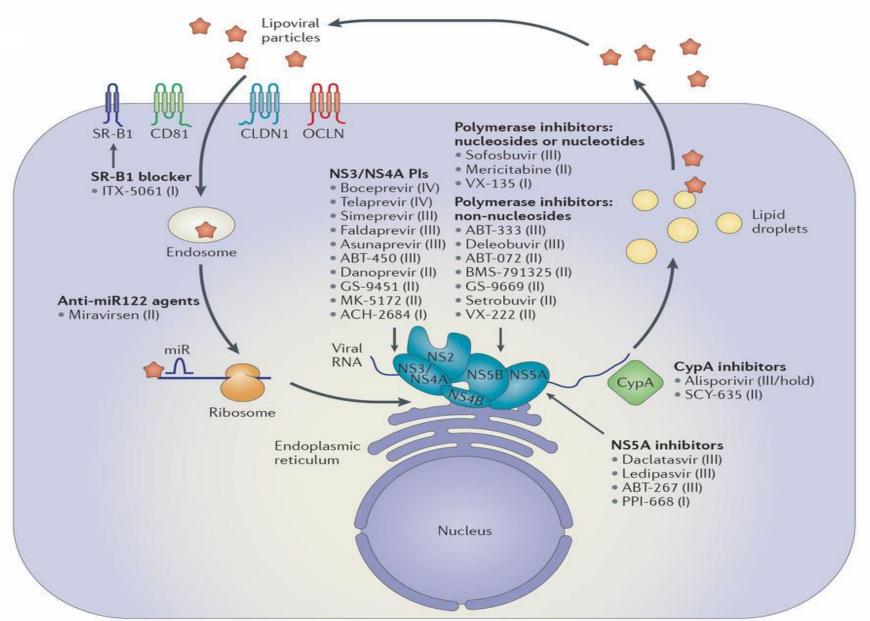
Rare adverse events of PegIFN/RBV

- 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

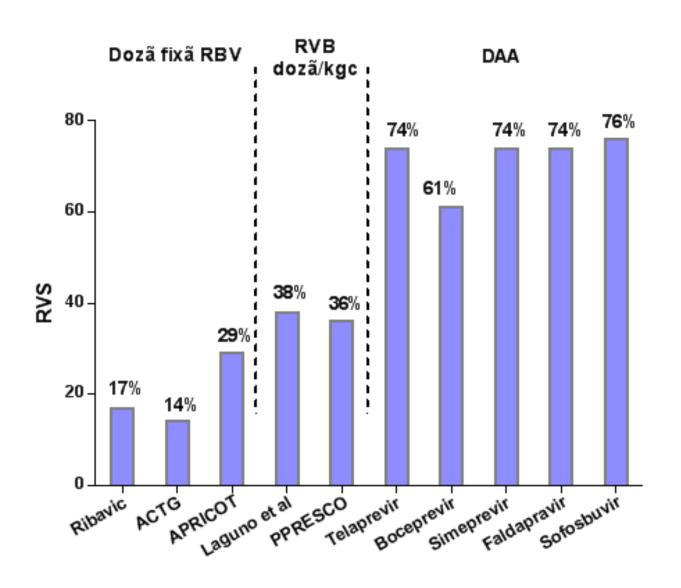




HCV life cycle and potential therapeutic targets



SVR rates with DAAs



Back to the case

- March 2011
 - 8.6 kPa (F2), HCV-RNA 6.2 log UI/MI
- 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

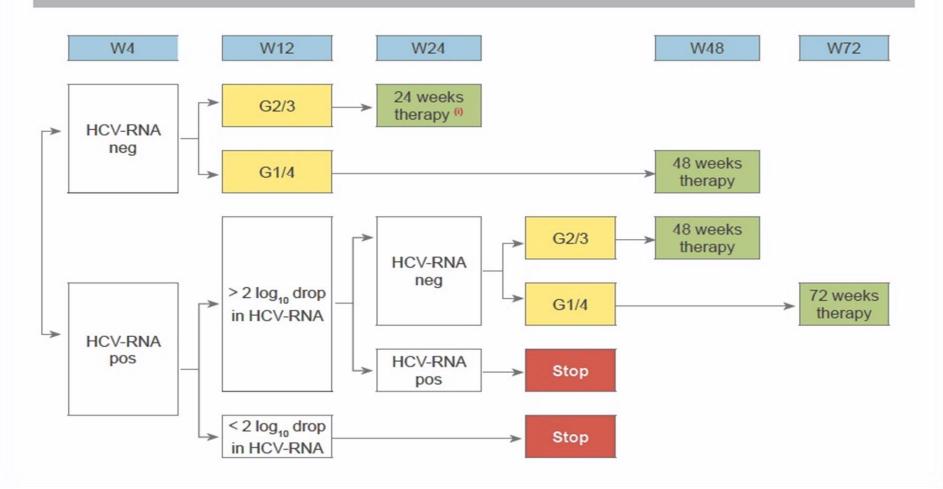
Drug-drug Interactions between ARVs and Non-ARVs⁽¹⁾

no	n-ARV drugs	ATV/r	DRV/r	LPV/r	EFV	ETV	NVP	RPV	MVC	RAL	ABC	FTC	3TC	TDF	ZDV
П	boceprevir	D35%	132%D44%	145%D34%	119%E20%	†10%D23%	↓E	E	E	++	++	++	++	++	↔ix
	clarithromycin	† ⁱⁱⁱ	1	111	1	1E	1	E	E	++	++	++	++	↔	D
Z.	fluconazole	++		↔	++	E86%	E100%	E	++	++	++	++	++	++	E74%
ect	itraconazole	↑E	†Ε	†Ε	1	ŢΕ	161%	E	E	++	++	++	++	++	++
nti-inf	rifabutin	1	†E50%	†	1	D37%	↑17%	D		++	++	++	++	++	++
	rifampicin	D72%	D	D	D26%	D	D58%	D80%	D	D40%	D	++	++	++	D47%
92	telaprevir	↓20%E17%	135%D40%	154%	126%D7%	↓16%	1?	↓5%E	E	E31%	++	++	++	E30%	↔ix
	voriconazole		1	1	ţΕ	↑E	ŢΕ	Е	Е		++	++	++	++	0
	antacids	D	++	++	++	++	++	D		D	++	↔	++	++	++
	PPIs	D	++		+ +	++	++	D	++	E	++	++	++	++	++

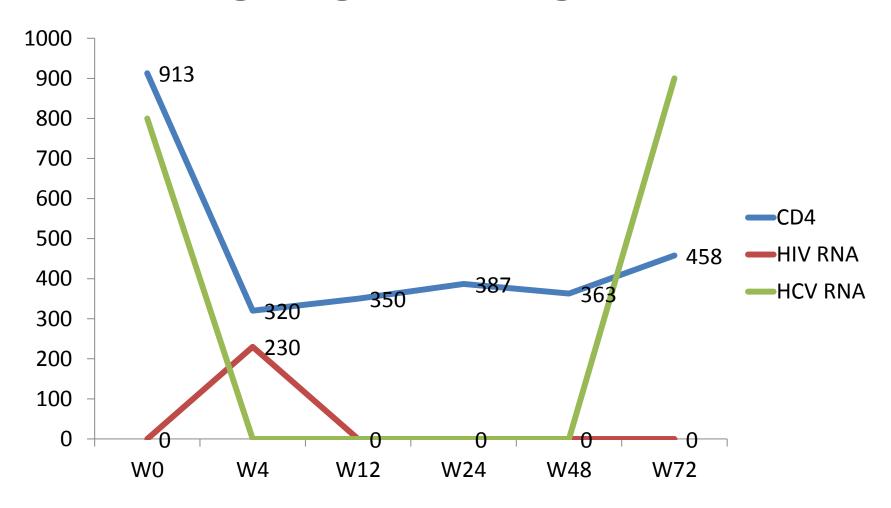
EACS



Proposed optimal duration of HCV therapy in HCV/HIV coinfected patients

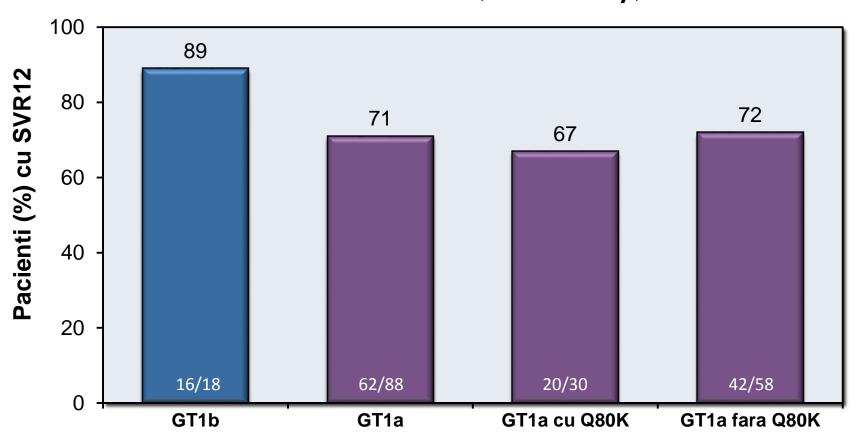


Immuno-virological status undergoing TLV / PegIFN / RBV



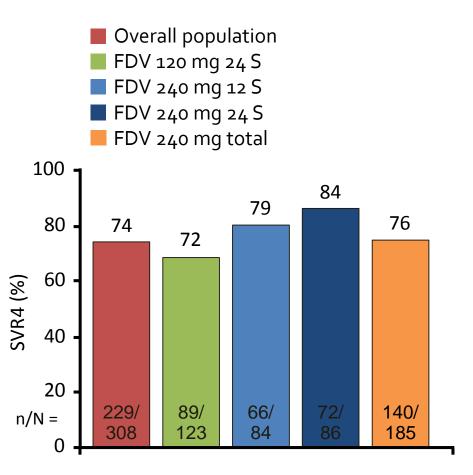
Second generation DAAs + PEG-IFN/RBV in HIV/HCV coinfected patients

SMV / PEG / RBV (C212 study)



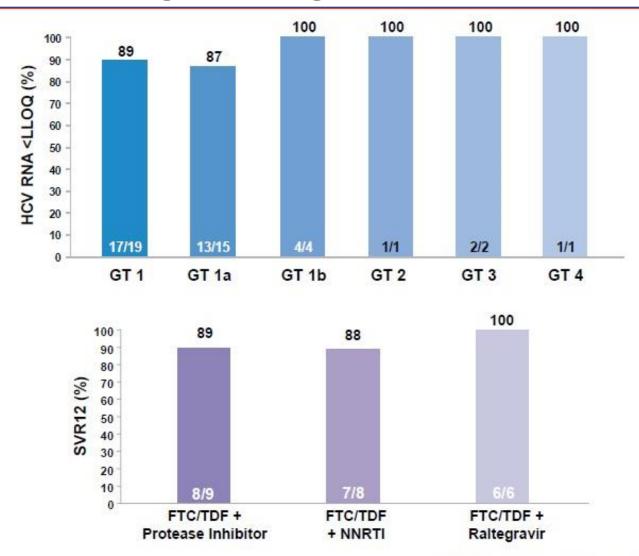
STARTVERSO 4 STUDY

FDV / PEGIFN / RBV

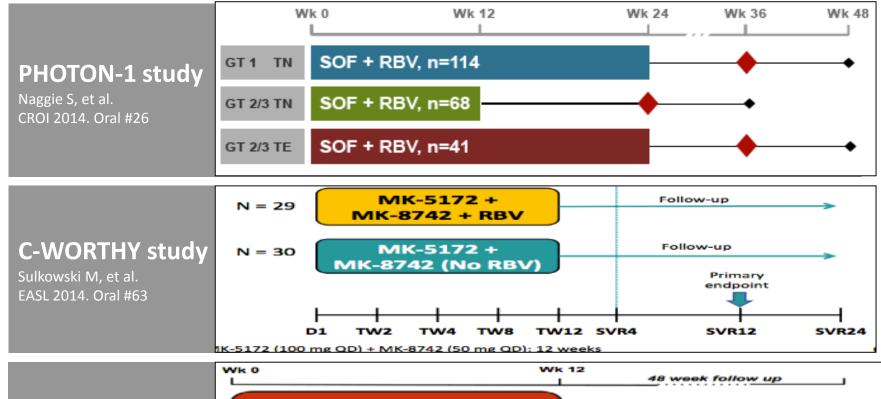


- Similar tolerability as in monoinfected patients
- Increasd SVR rates in cirrhotin and non-cirrhotic patients
 - Cirrhosis: 76%
 - Without cirrhosis: 74%
- SVR rates according to IL28B genotype
 - CC: 89%; CT: 67%;
 - TT: 67%

SOF / PegIFN / RBV in HIV / HCV coinfection SVR 12 according to HCV genotype and ARV regimen



IFN-free DAA regimens in HIV/HCV coinfected patients



LDV/SOF STR ERADICATE study

Osinusi A, et al. EASL 2014. Oral #14 ARV Untreated (n=13)

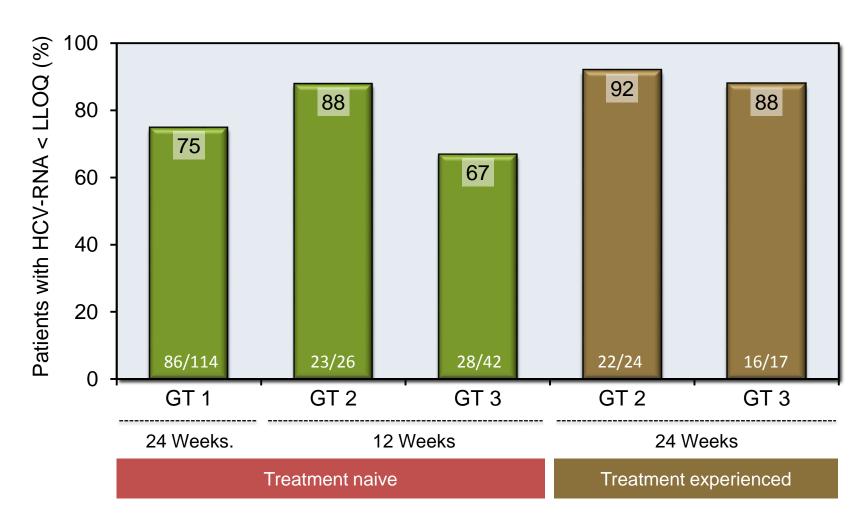
CD4 count stable + HIV RNA <500 copies
OR
- CD4 count > 500 cells/mm²

SOF/LDV (400/90mg)

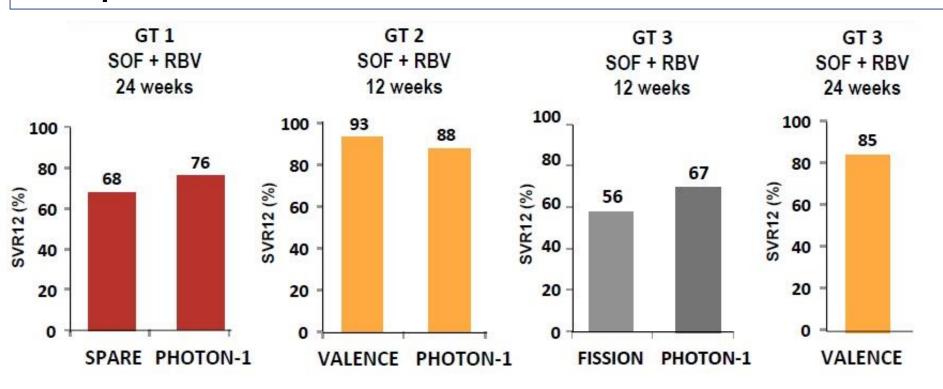
ARV Treated (n=37)
- CD4 count > 100 cells/mm²
- HIV RNA < 40 copies
- Current ARVs ≥ 8 weeks

ARVs: tenefovir, emtricitabline, efavirenz, rilpivirine and raitegravir

PHOTON 1: SOF / RBV in HIV / HCV coinfection

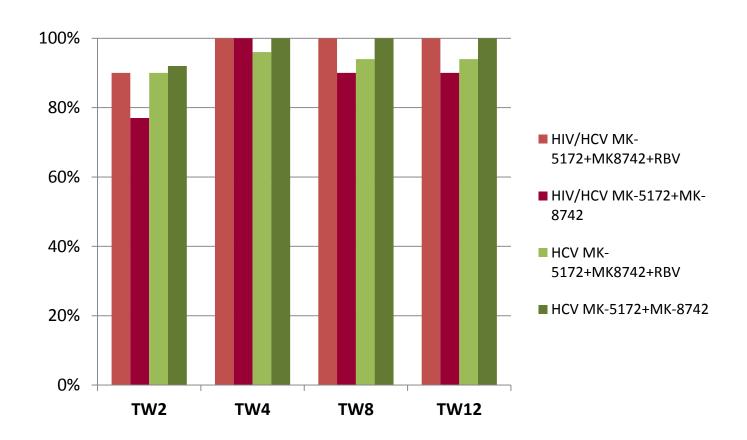


All- oral therapy of SOF / RBV Comparison of HCV monoinfected to HIV / HCV coinfected



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

C-Worthy virologic response



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

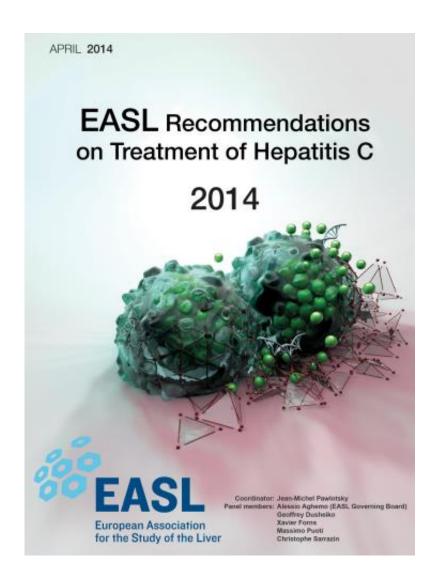
ERADICATE – treatment response



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

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