Is HIV a Special Patient Population for Managing Hepatitis B or C ?

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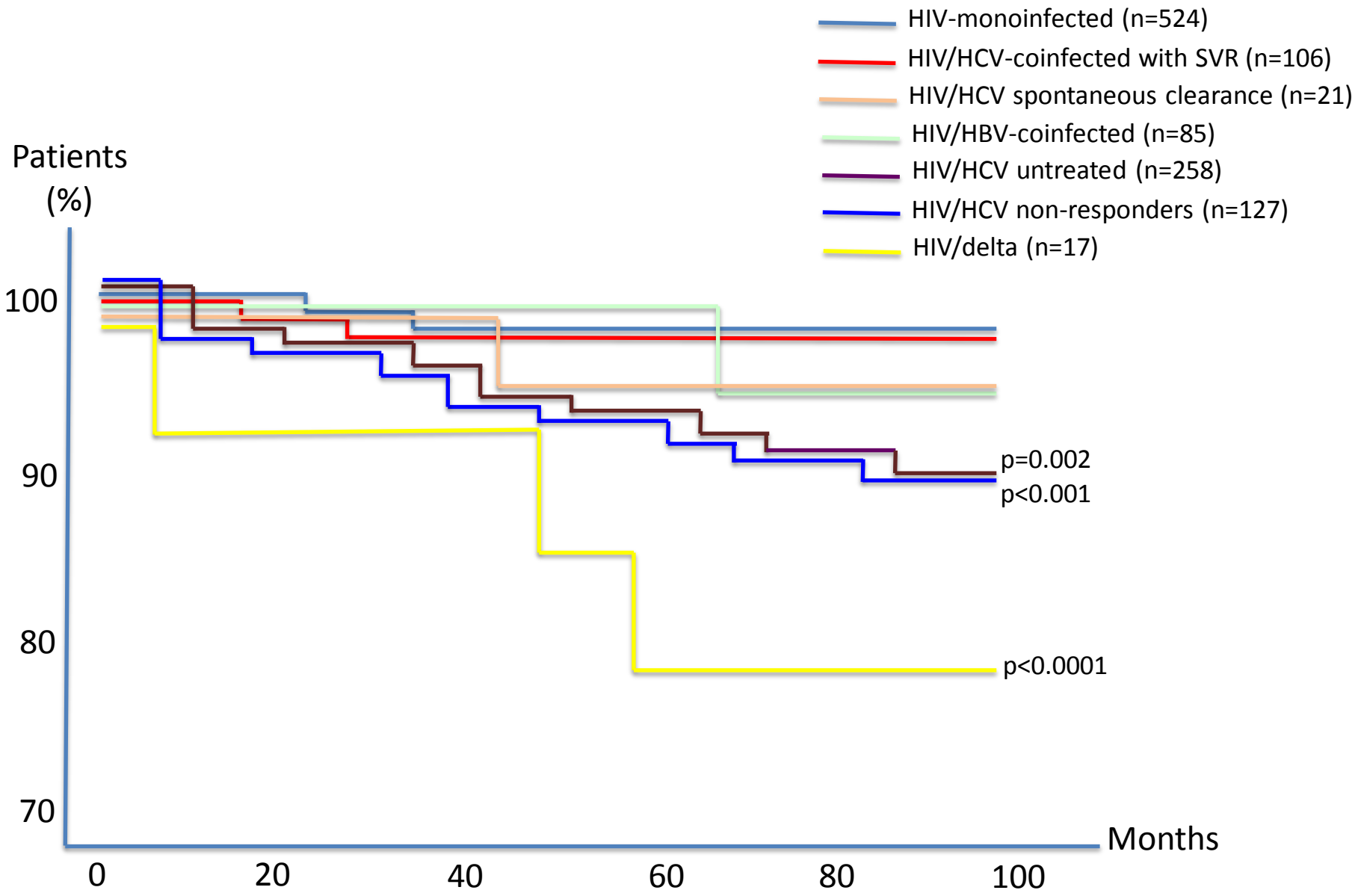
Time free from liver decompensation events or death in HIV+ patients

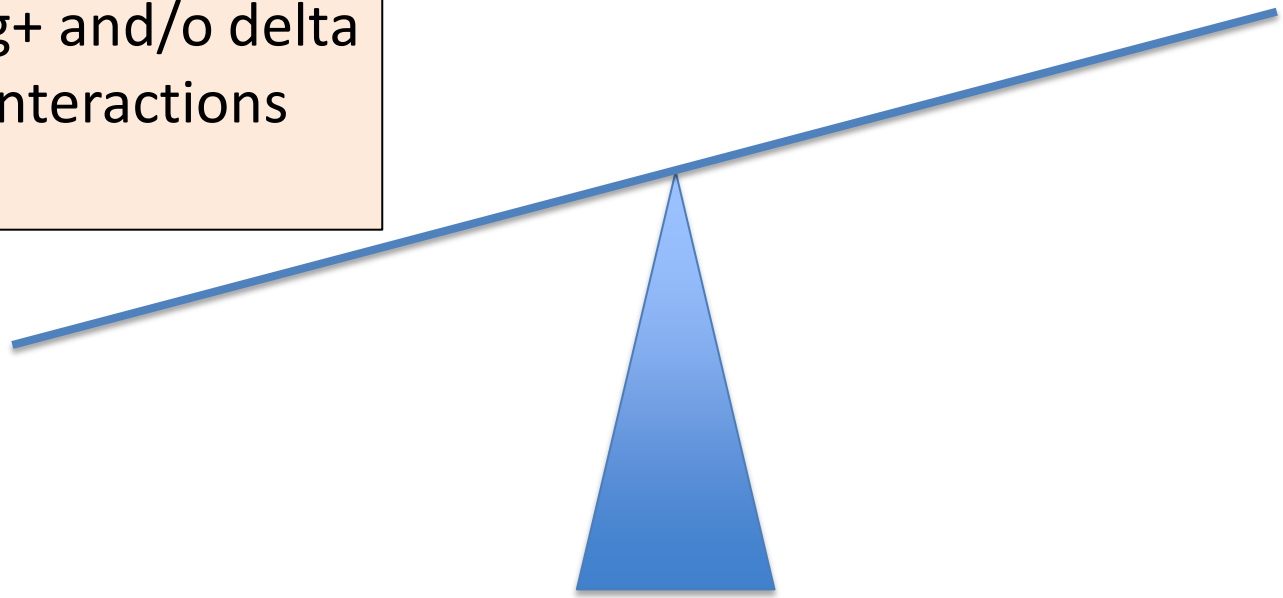


Fernandez-Montero et al. Clin Infect Dis 2014;58:1549-53.

Hepatitis C therapy in HIV - equal or not?

- ↑ HCV G3 and G1a
- ↑ HCV-RNA
- ↑ liver fibrosis
- ↑ HBsAg+ and/o delta
- ↑ drug interactions
- ↑ male

- ↑ drug adherence



DAA real world experience

	TRIO (n=1685)	Madrid (n=363)
Male	58%	75%
Advanced liver fibrosis	30% (cirrhosis)	48%
Elevated ALT	?	83%
Baseline HCV-RNA > 6 log	21% (>6 million)	59%
HCV genotype 4	0 (67% G1a)	15%
HIV coinfection	7%	31%
Ribavirin added	5%	38%
Prior interferon failure	?	49%
SOF+LDV	88%	80%
SVR	96	97

Afdhal et al. AASLD 2015
Arias et al. ICVH 2016

Main characteristics of the study population according to treatment outcome.

	Sustained virological response (n=352)	Treatment failure (n=11)	p
Male gender, n (%)	255 (73.1)	9 (81.8)	0.7
Elevated ALT, n (%)	311 (81.2)	10 (90.9)	0.8
IL28B-CC, n (%)	97 (27.1)	2 (18.2)	0.9
Advanced liver fibrosis, n (%)	146 (42.8)	10 (90.9)	0.003
Baseline HCV-RNA >6 log IU/mL, n (%)	225 (62.4)	6 (54.5)	0.7
Prior interferon exposure, n (%)	164 (47.2)	6 (54.5)	0.7
HIV coinfection, n (%)	91 (27.2)	7 (63.6)	0.04
HCV genotype 4, n (%)	46 (13.1)	4 (36.4)	0.05
Ribavirin added, n (%)	120 (34)	5 (45.4)	0.4

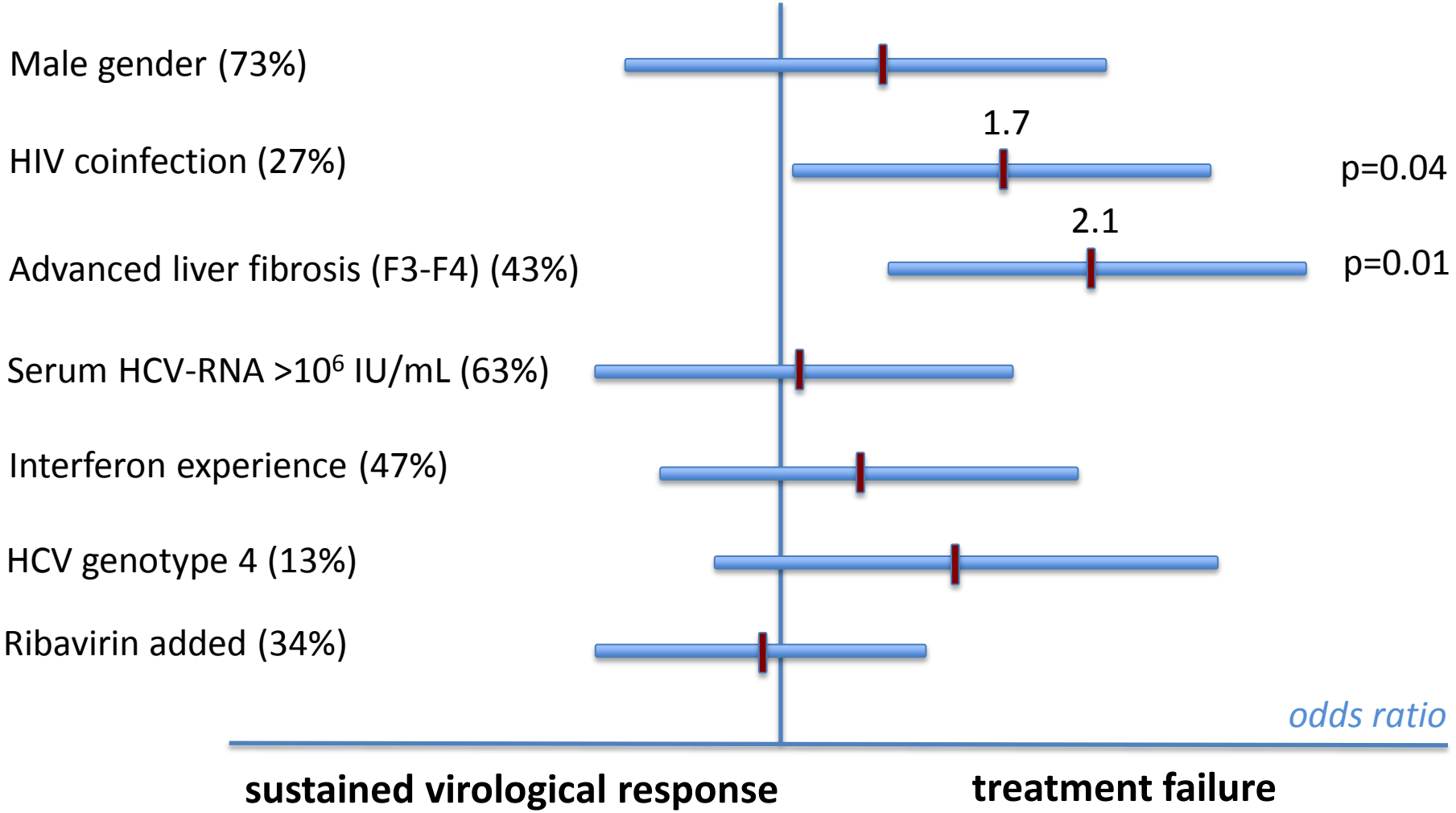
Arias et al. ICVH 2016

Main baseline characteristics of chronic hepatitis C patients that experienced DAA treatment failure.

	1	2	3	4	5	6	7	8	9	10	11
Age (years)	52	55	78	54	50	50	57	49	49	45	52
Gender	male	male	male	male	male	male	male	female	male	male	female
ALT (IU/L)	39	87	53	64	45	30	73	70	55	69	83
Serum HCV-RNA (log IU/mL)	6.5	5.8	6.3	6.5	5.8	6.9	5.8	6.7	4.8	7.1	4.6
HCV genotype	1a	4	1b	1a	4	1a	1b	4	3	4	1b
Liver fibrosis stage (Metavir)	F4	F4	F4	F1	F4	F3	F4	F4	F4	F3	F3
IL28B polymorphisms	CC	CT	CT	CT	CT	CT	CC	CT	CT	TT	CT
Prior interferon exposure	no	no	no	no	yes	yes	yes	no	yes	yes	yes
HIV coinfection	yes	yes	no	yes	yes	no	yes	yes	no	no	yes
DAA regimen	SOF/LDV/RBV	SOF/LDV/RBV	SOF/LDV/RBV	SOF/LDV	SOF/LDV/RBV	SOF/LDV	SOF/SMV	SOF/SMV	SOF/RBV	SOF/LDV	SOF/LDV

Arias et al. ICVH 2016

Predictors of DAA treatment failure in the study population. Multivariate analysis.



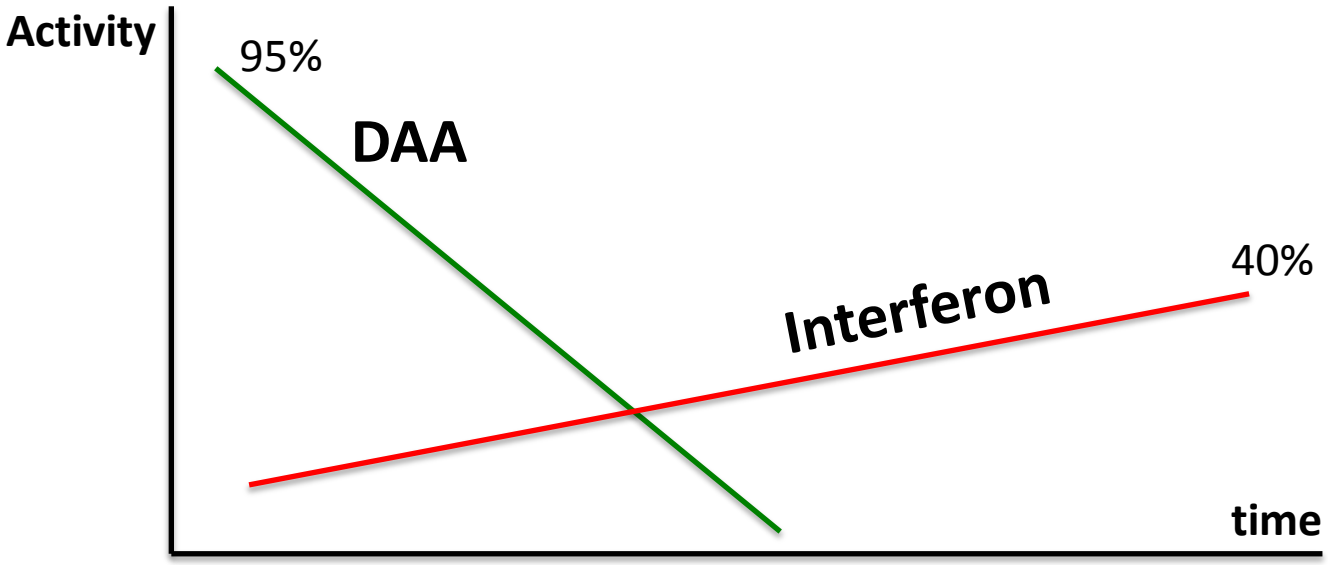
Arias et al. ICVH 2016

Why DAAs may work less well in HIV?

- **Impaired Immunity**
  - immunosuppression, role of innate immunity
- **Lower antiviral activity**
  - Cumulative poor phenotype - Drug interactions, higher HCV-RNA, drug adherence, advanced liver fibrosis

The HCV cure equation

$$\text{SVR} = \left[\text{Viral replication suppression} + \text{Immune response trigger}\right] \times \text{Time length}$$



Predictors of DAA failure

Baseline	On-treatment
• Cirrhosis • Genotype 3 • RAVs • Prior Interferon failure • Elevated serum HCV-RNA • IFNL4 unfavorable • AA ethnicity	• Drug adherence • Side effects • Drug interactions

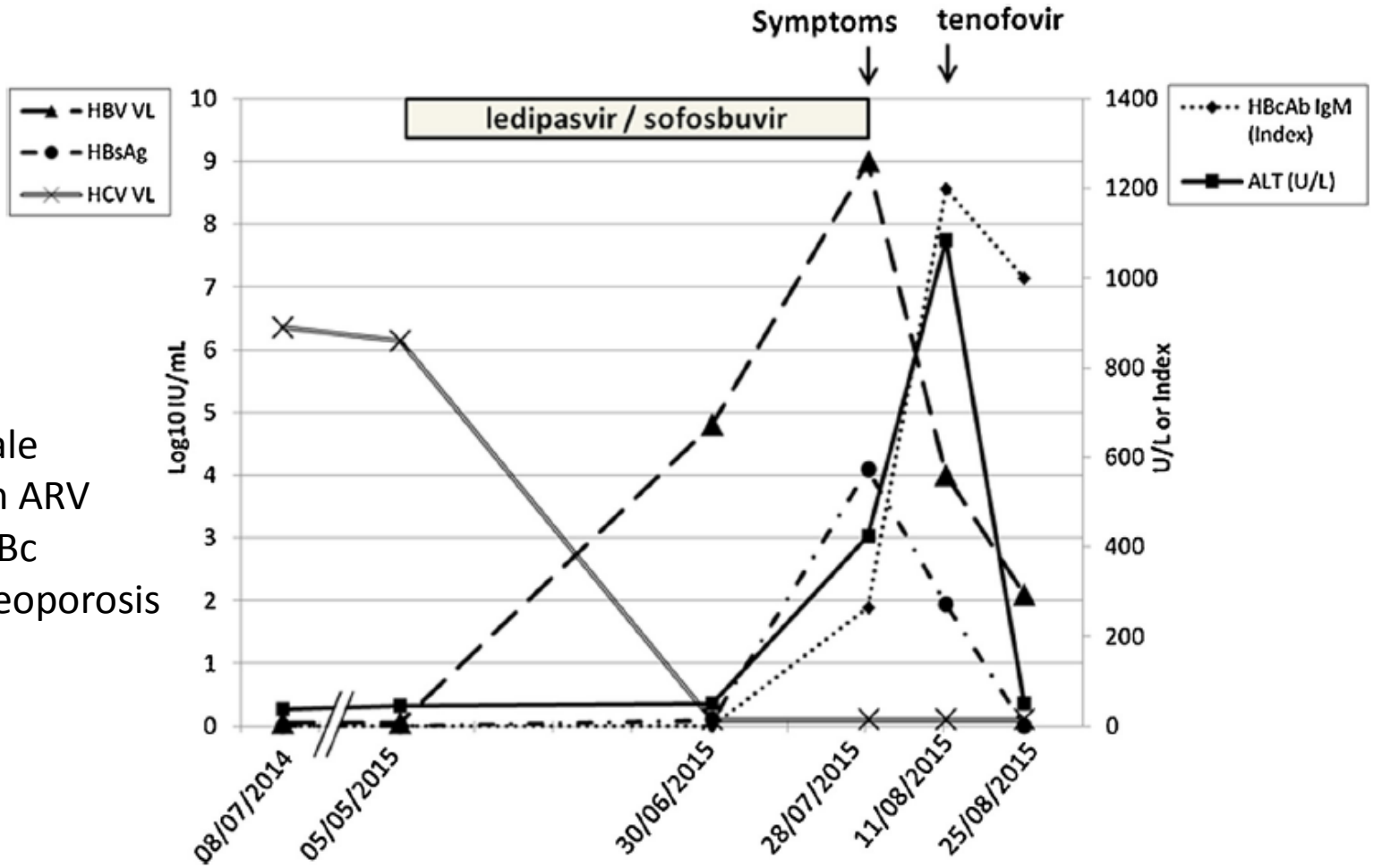
Considerations for HCV re-treatment

- **Virologic challenges:**
  - Presence of RAVs (prior DAA failure)
  - Exclude HCV genotype shift (misinterpretation)
  - Exclude HCV re-infection (risk behaviors)
- **Strategic management:**
  - Adding ribavirin
  - Extent the length of therapy
- **Maximize drug benefit:**
  - Avoid drug interactions (co-morbidities)
  - Prevent and manage side effects
  - Ensure drug adherence

Direct-acting antiviral treatment in adults infected with hepatitis C virus: Reactivation of hepatitis B virus coinfection as a further challenge

Anne De Monte[a], Johan Courjon[b], Rodolphe Anty[c,d,e], Eric Cua[b], Alissa Naqvi[b], Véronique Mondain[b], Jacqueline Cottalorda[a], Laurence Ollier[a,*], Valérie Giordanengo[a,e,f]

Journal of Clinical Virology 78 (2016) 27–30

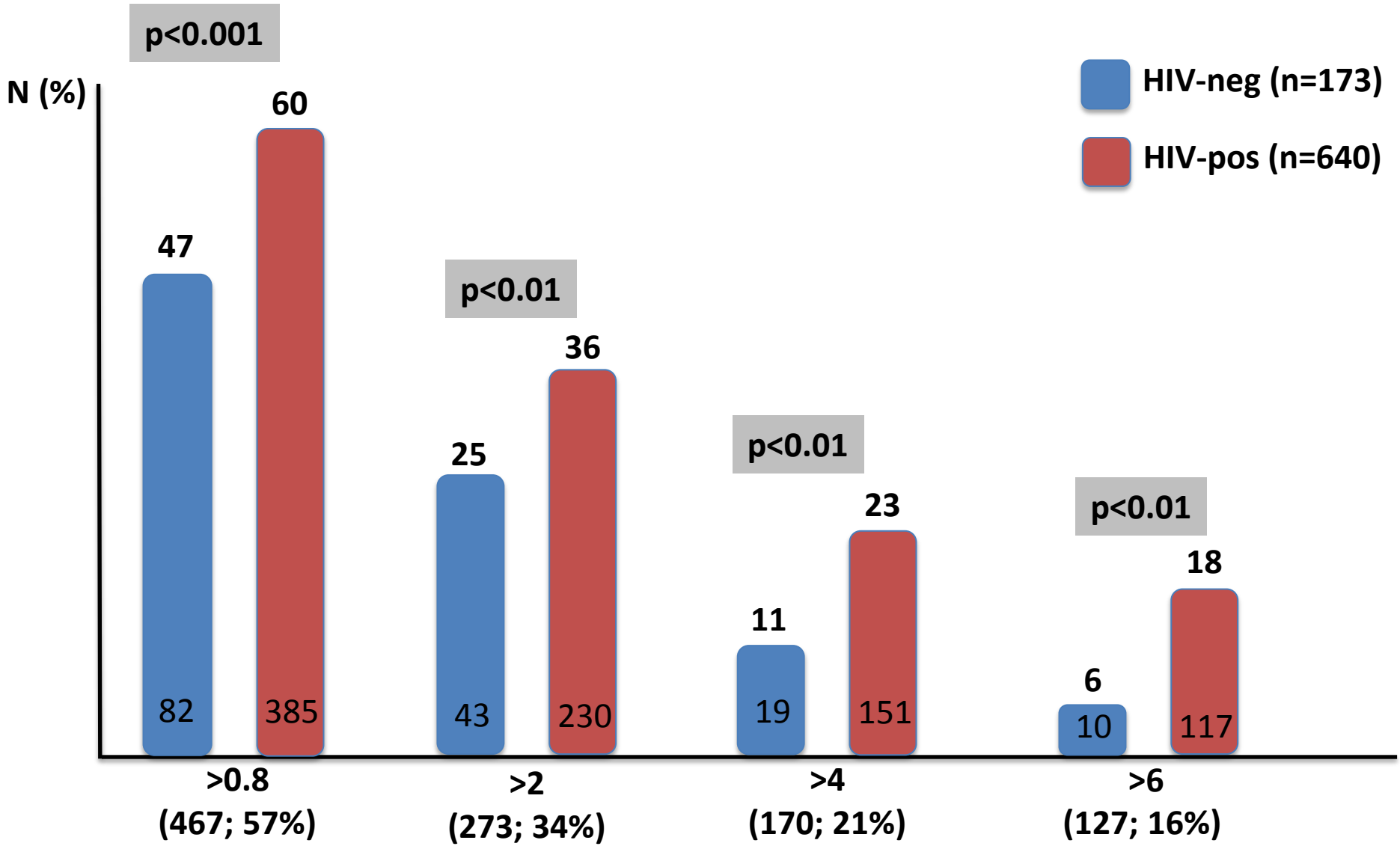


53-year-old male
HIV-positive on ARV
Isolated anti-HBc
No TDF for osteoporosis

Frequent meds other than ARV in HIV+ pts

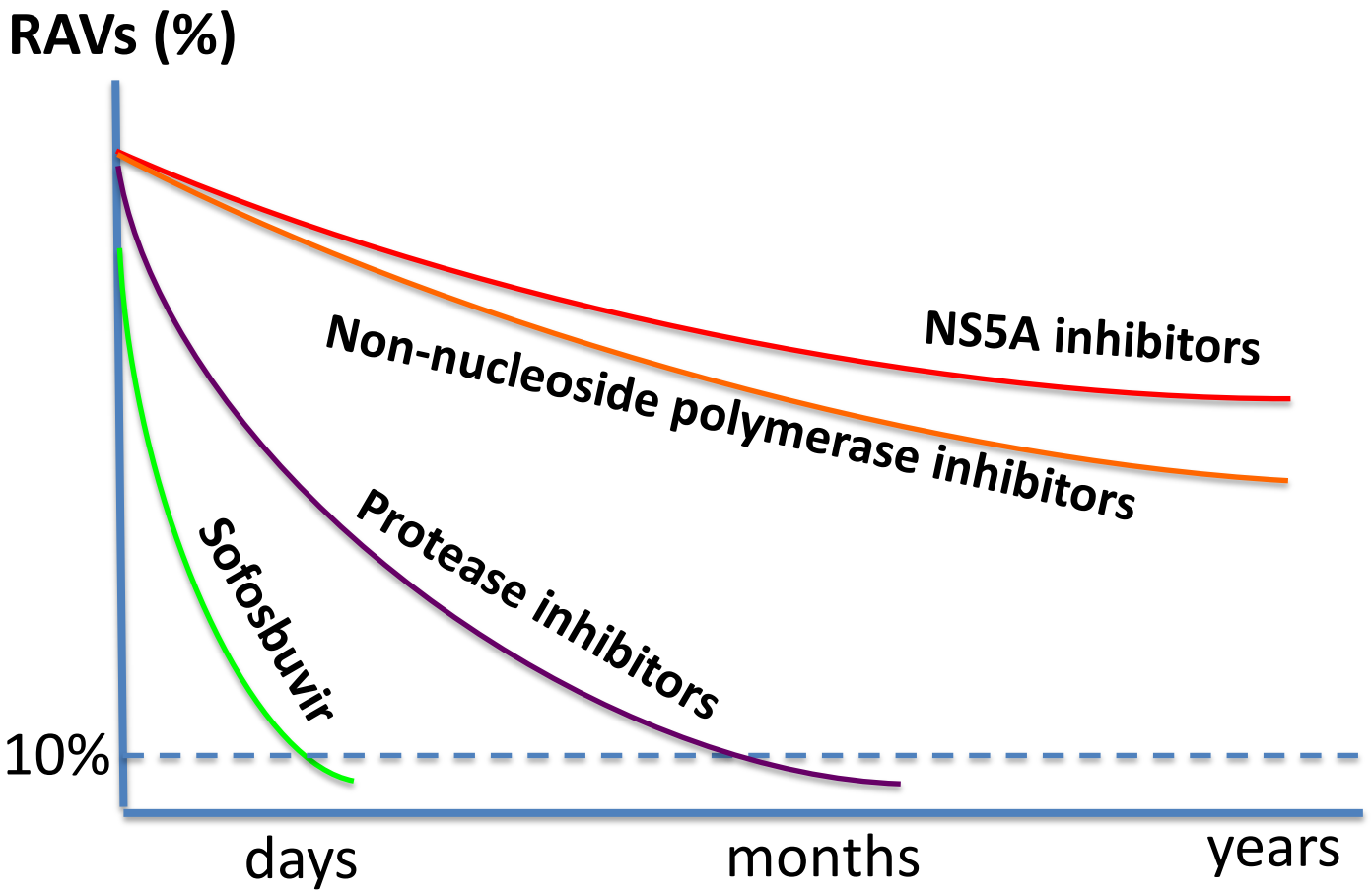
- Methadone/buprenorphine
- Proton pump inhibitors
- Antidepressants
- Hipnotics
- Statins
- Cothrimoxazole

Serum HCV-RNA values in chronic hepatitis C patients according to HIV status



Barreiro et al. Antivir Ther 2016

Estimated clearance time for RAVs selected upon treatment failure



Caveats

- Enthusiasm unabated, DAA treatment of HCV in HIV-pos should provide good results, overall as good as in HIV-neg. However, unique features should be taken into account, including DDI, reinfections, adherence, etc.

- Transmission of NS5A RAVs should be assessed periodically in acute hepatitis C patients, most of whom are coinfected with HIV.

- New drug interactions and side effects should be checked accurately in coinfected patients on DAA and antiretrovirals.

- The efficacy of DAA in HIV-HCV coinfected patients with low CD4 counts must be examined properly. It will provide further insights into the role of immunity on HCV clearance.