Patient M

- Aged 65
  - Chronic hepatitis C
  - Genotype 1a
- Liver biopsy
  - 2012 – mild fibrosis
  - 2005 progressive fibrosis stage 3 grade 3

- 2006 Fibroscan 14.8 1QR 1.7

- Treatment:
- 2006 consented to participate in PROVE 2
  - Randomised controlled trial of Telaprevir, PEG IFN and RBV
  - Received placebo; follow on study received Telaprevir PEG IFN and RBV
- **Stopped treatment July 2009 failed to respond**

Patient M course post treatment (non responder PI)

- Third liver biopsy 2010
  - Developing cirrhosis, steatosis moderate inflammatory activity moderate steatosis
- Hepatic wedge pressure measurement: 8
- Endoscopy upper GIT December 2010 did not show oesophageal varices

Subsequent course 2011

- October 2011: GP referred to a hematologist
  - Enlarged lymph nodes posterior trial neck and groin
  - Chest CT paratracheal and subcarinal lymphadenopathy
  - Reviewed frequently: lymphadenopathy resolved spontaneously
  - No fever or sweating
  - Some weight loss
- Not biopsied
- Desquamating skin rash:
  - discoid eczema; ruled out lymphoma
- Bone marrow June 2012: normal
- Developed consolidation in lung
- Follow up endoscopy March 2013
- Portal hypertensive gastropathy – no varices

Course 2013

- April 2013:
  - Dizziness and loss of balance
  - Slow mentation
  - Dyspraxia
  - Parkinsonism
  - Ataxia
- Accident and emergency 15 April 2013
- Diagnostic tests done

Questions

- **What is your diagnosis?**
- **What tests would you do?**

Diagnostic tests:

- MRI scan
  - subcortical white matter T2 hyper-intense foci
  - No mass or haemorrhage
  - Mild cerebral and cerebellar involutional change

Diagnostic tests

- Anti-HIV positive
  - Illness in 2011-2012 ? HIV seroconversion illness
  - Previous syphilis (latent)
  - CSF negative
- HBsAg negative, anti-HBs anti-HBc positive

HIV treatment

- Admission CD4 0.039 x 109/ml
- HIV 1 6.7 log copies/ml 5,542,968 copies/ml
- Treatment
  - (tenofovir emtricibine efavirenz) Atripla May 2013
  - Grand mal seizure (efavirenz)
  - Subsequent treatment:
    - Ritonavir 100 mg daily
    - Truvada 1 daily
    - Atazanavir 300 mg daily

Discussion

- Diagnosis of HIV missed
  - (by several disciplines)
  - Inadequate sexual history
  - Tested negative for anti-HIV
  - PROVE 2 in 2006 and follow up 2009
- Seroconverted almost certainly after 2009
- Focus was on ruling out a lymphoma and his liver disease; Castlemans disease

Treatment of his hepatitis C Genotype 1a

- Start treatment
  - 15 August 2014 AST 106 ALT 86 albumin 42 Haemoglobin 15.4, WCC 2.7 platelets 85
  - sofosbuvir 400 mg ledipsasvir 90 mg mg and ribavirin 1000 mg

Week	Date	HCV RNA (iu/ml)	HIV (c/ml)
Start	15 August 2014	3,285,993	114
TW2	28 August 2014	708	
TW4	8 September 2014	570	< 40
TW8	9 October 2014	269	
TW12	6 November 2014	86	< 40
TW 16	4 December 2014	14	
TW 20	29 December 2014	Detected < 12	
TW 24	29 January 2015	Detected < 12	
Post TW 4	26 February 2015	UD	
Post TW12	26 April 2015	UD	< 40

Discussion

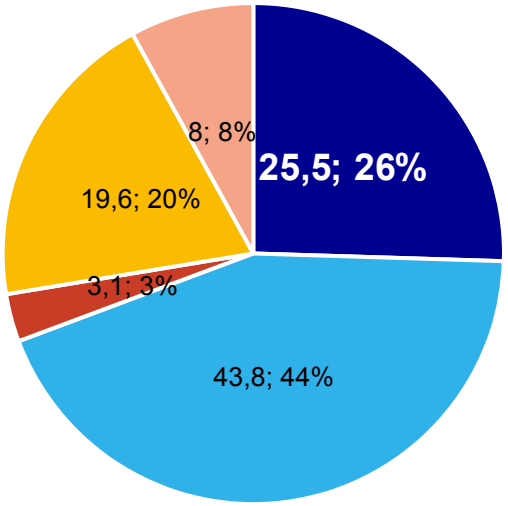
- Summary: HIV HCV cirrhosis; 1a
- Non responder (PI failure)
- Treatment within expanded access program
- Questions:
  - Duration of treatment (viral kinetics)
  - Interpreting detectable HCV RNA during treatment
  - Decision making
    - Extending treatment HIV cirrhosis slow decline
  - ? Explanation: defective non infectious virus?
  - Preventing reactivation of HBV

Patients WITH HIV/HCV co-infection

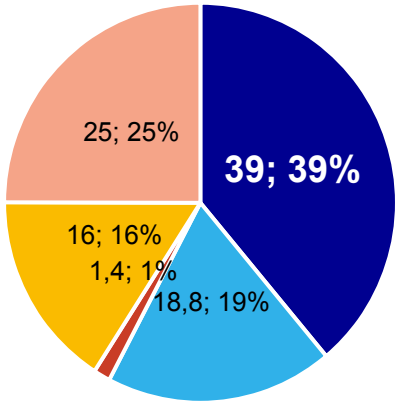
Genotype distribution differs between general HCV population and HIV/HCV co-infected population

Genotype distribution among general population in Spain[1] **Genotype distribution among HIV/HCV co-infected**

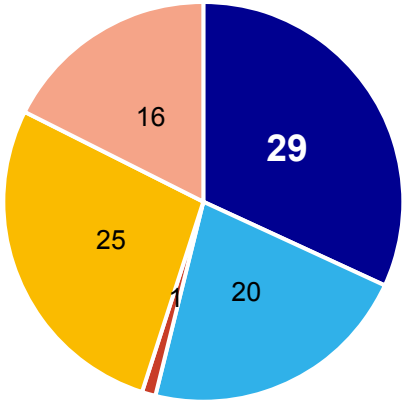
Systematic literature review



Multicentre study across Spain (n=367)



HIV/HCV co-infected cohort in Madrid (n=672)



GT 1a GT 1b GT 2 GT 3 GT 4

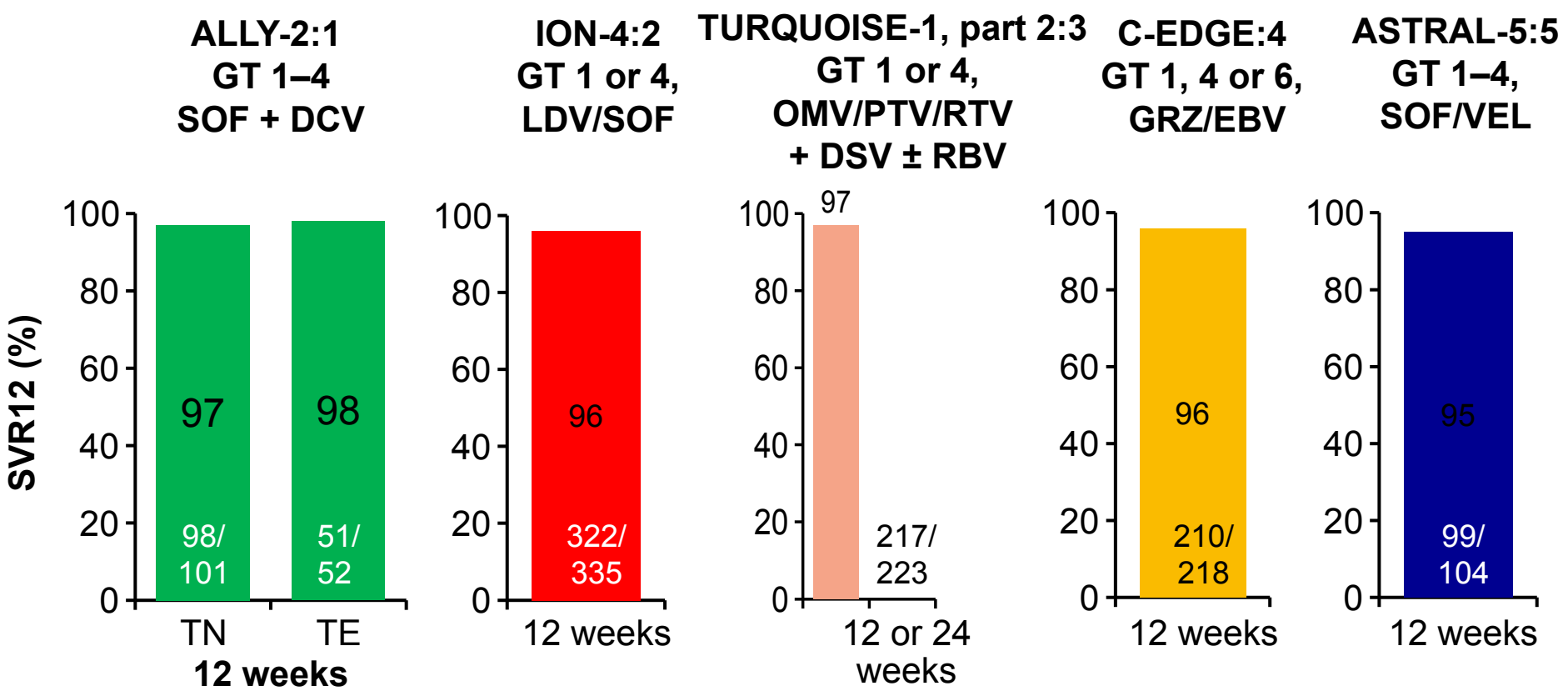
- Proportion of GT 1 (especially GT 1b subtype) is lower and GT 4 is higher among co-infected population compared with general population

1. Gower E, et al. J Hepatol 2014;61:S45–S57;
2. Berenguer J, et al. Open Forum Infect Dis 2016;3:ofw059;
3. Medrano J, et al. J Viral Hepat 2011;18:325–30

Efficacy of DAAs in patients with HIV/HCV co-infection

‡

Virological response



1. Wyles D, et al. N Engl J Med 2015;373:714–25;
2. Naggie S, et al. N Engl J Med 2015;373:705–13;
3. Rockstroh JK, et al. IAS 2016; Oral # WEAB0304LB
4. Rockstroh JK, et al. Lancet HIV 2015;2:e319–27;
5. Wyles D, et al. EASL 2016; Oral #PS104

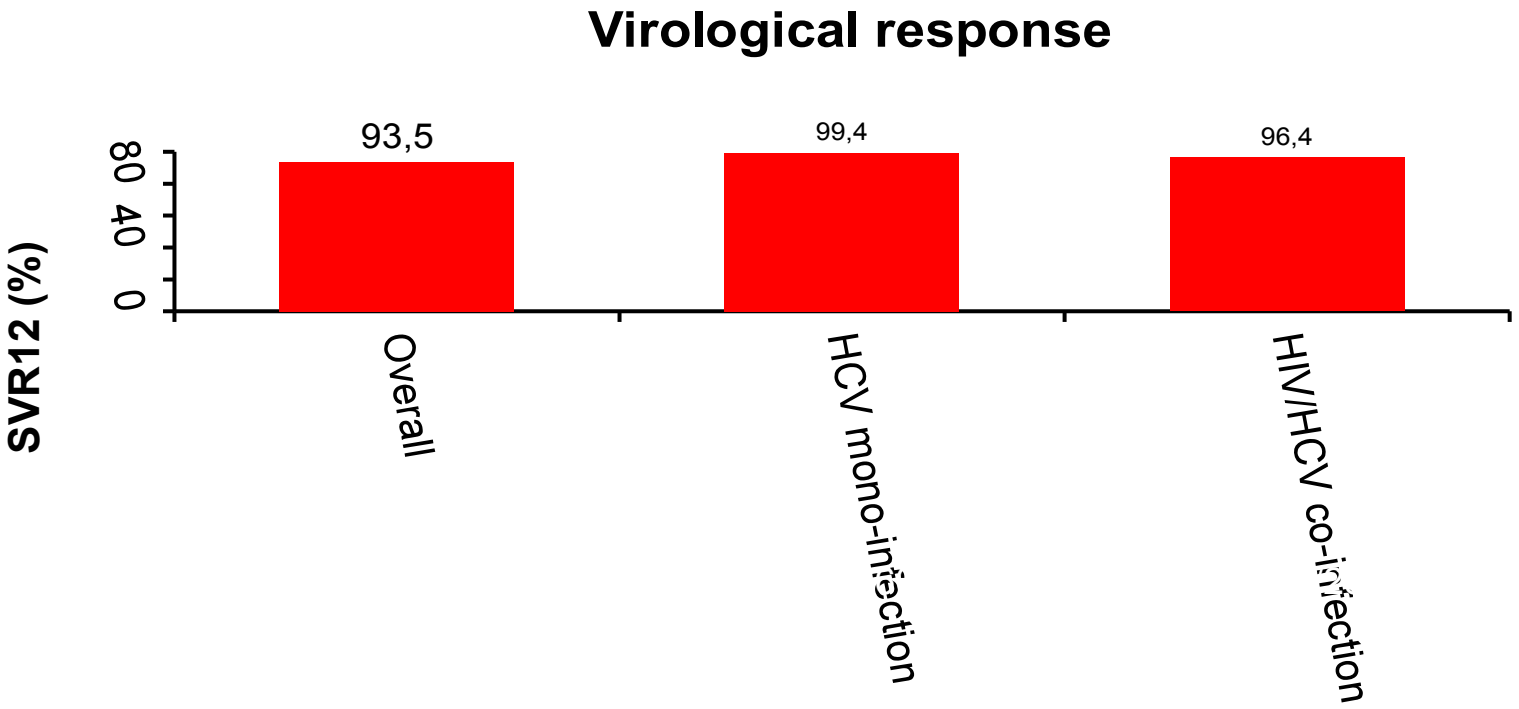
NOT HEAD-TO-HEAD COMPARISONS

These graphics serve to illustrate SVRs obtained between different regimens from different studies and are therefore not directly comparable as study populations are NOT matched.

GRZ/EBV is not approved in the EU for GT 6 patients

GECCO Cohort: Efficacy of 8-week LDV/SOF in HCV GT 1 mono-infected and HIV/HCV GT 1 co-infected patients

- Interim results from an ongoing prospective, multicentre cohort of 9 treatment centres in Germany



Ingiliz P, et al. Clin Infect Dis 2016;63:1320–4

*10 patients were lost to follow-up

Drug–drug interactions with HIV ARTs

HEP Drug Interactions

		SOF	LDV/ SOF	SOF/ VEL	OMV/PTV/RTV + DSV	GRZ/EBV	DCV	SMV
NRTIs	Abacavir	◆	◆	◆	◆	◆	◆	◆
	Emtricitabine	◆	◆	◆	◆	◆	◆	◆
	Lamivudine	◆	◆	◆	◆	◆	◆	◆
	TDF	◆	■	■	◆	◆	◆	◆
NNRTIs	Efavirenz	◆	■	●	●	●	■	●
	Etravirine	◆	◆	●	●	●	■	●
	Nevirapine	◆	◆	●	●	●	■	●
	Rilpivirine	◆	◆	◆	■	◆	◆	◆

◆ No clinically significant interaction expected

■ Potential interaction which may require a dosage adjustment, altered timing of administration or additional monitoring

● These drugs should not be co-administered.

Most frequently prescribed ARTs in Europe

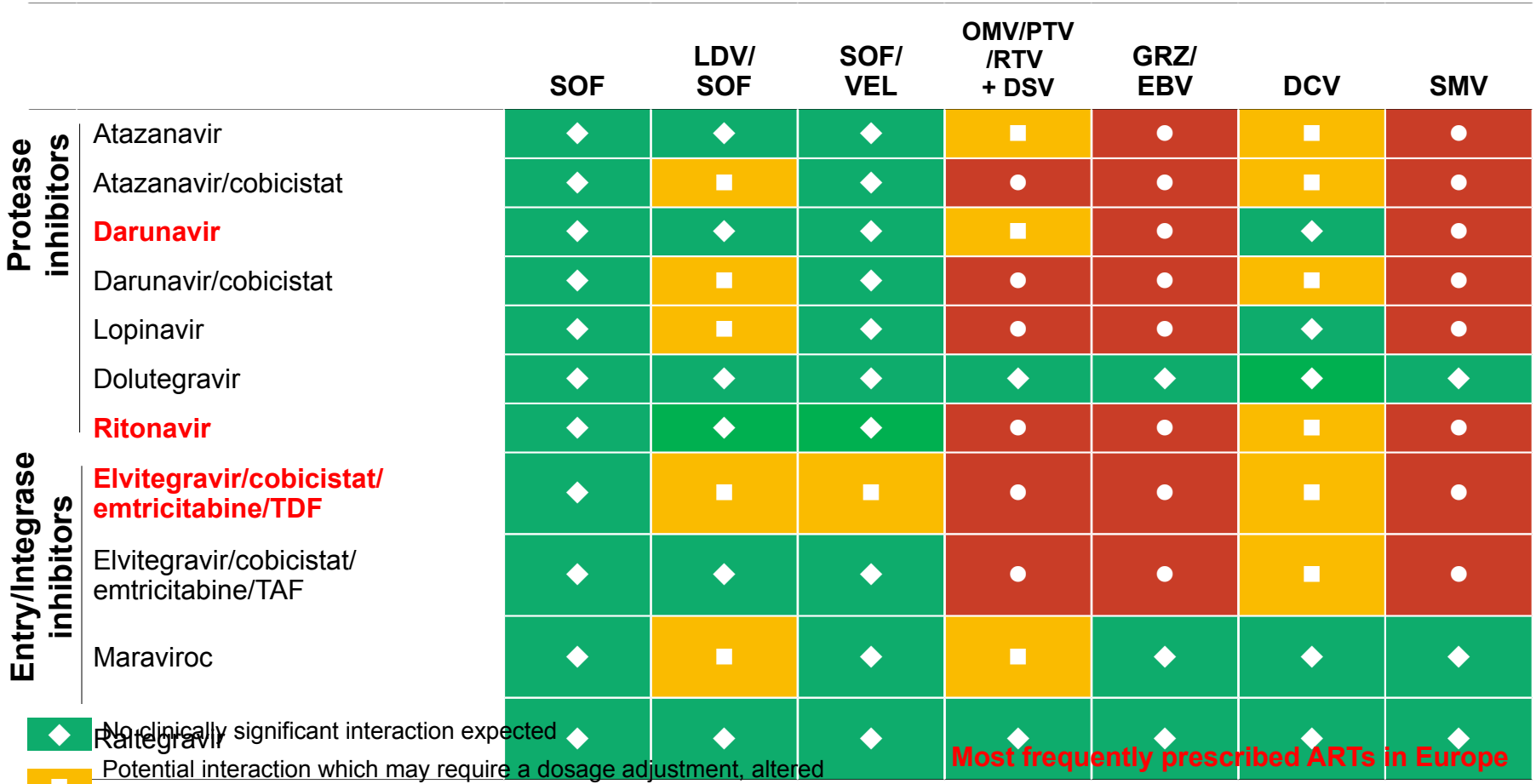
1. Abacavir, dolutegravir and lamivudine
2. Emtricitabine, rilpivirine and TDF
3. Efavirenz/emtricitabine/TDF
4. Elvitegravir, emtricitabine and TDF
5. Emtricitabine/TDF/darunavir/ritonavir

ART: antiretroviral therapy;
NNRTI: non-nucleoside reverse-transcriptase inhibitor;
NRTI: nucleoside reverse-transcriptase inhibitor;
TDF: tenofovir disoproxil fumarate

University of Liverpool HEP drug interactions. Available at: http://www.hep druginteractions.org (accessed January 2017)

Drug–drug interactions with HIV ARTs

HEP Drug Interactions



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University of Liverpool HEP drug interactions. Available at: http://www.hep-druginteractions.org (accessed January 2017)

TAF: tenofovir alafenamide