Poster No. 13/20

15th European AIDS Conference 2015

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HCV RNA profiles among HIV/HCV coinfected individuals in ESPRIT; spontaneous HCV RNA clearance observed in 9 individuals

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Objectives: Studies have shown that HCV RNA levels remains stable over time in HIV/HCV coinfected individuals taking cART, while spontaneous clearance of HCV RNA during chronic infection has been documented in rare cases among those with the CC IL28B genotype. This study aimed to describe HCV RNA profiles and factors associated with changes over time in HCV RNA levels in the ESPRIT study.

Methods: HIV/HCV coinfected individuals positive for HCV RNA were included. Follow-up was counted from first HCV RNA positive test and censored at the initiation of interferon-based treatment. HCV RNA and IL-28B measurements were measured in the same reference laboratory. Random effects mixed models were used to analyse changes over time in HCV RNA.

Results: Three hundred and twelve HIV/HCV coinfected individuals from ESPRIT were included (151 from the IL-2 arm and 161 from the control arm). Follow-up was counted from May 2000 and ended in January 2009 with a median follow-up per individual of 5 years (IQR 3 - 6; Range 1 - 9). A median of 5 (IQR 2 - 6) HCV RNA measurements per individual were included. The randomisation groups were well-matched at baseline (Table 1).

The majority of individuals included were male (IL-2 arm: 78.2% vs. control arm: 73.9%), of white race (88.1% vs. 90.1%) and aged less than 40. A large proportion were infected with HIV via IDU (76.2% vs. 66.5%), but few individuals were also coinfected with HBV (2.9% vs. 0.7%). The most common HCV genotypes were G1 (58.9% vs. 57.1%) and G3 (19.9% vs. 19.9%). The majority of individuals were taking cART (96.0% vs. 95.0%) and consequently few had detectible HIV RNA (5.3% vs. 8.7%) and median CD4 cell counts were high (434 vs. 435 cells/mm^3).

Factors associated with HCV RNA levels

Overall HCV RNA levels decreased 12.8% per year over the study period (95% CI 7.6 - 17.8%; *P*<0.0001), while 9 individuals spontaneously cleared HCV RNA. Omitting the 9 individuals who cleared HCV RNA during follow-up HCV RNA levels decreased 11.7% per year (95% CI 6.4 – 16.7%; *P*<0.0001). Baseline levels of HCV RNA were significantly associated with HCV genotype and HIV RNA. HCV genotype 3 was associated with 64.7% lower HCV RNA than HCV genotype 1 (95% CI 43.5 – 77.9%; *P*<0.0001), while undetectable HIV RNA was associated with 20.4% lower HCV RNA compared with HIV viral load above the limit of detection (95% CI 3.7 – 34.2%; *P*=0.019). Older age was also associated with higher HCV RNA with borderline statistical significance (13.8% higher per 5 years older (95% CI -1.3% to 31.4%; *P*=0.075)).

An interaction term between randomisation arm and time from baseline was added to the model to see whether the rate of HCV RNA decline over time was affected by the addition of IL-2. Baseline levels of HCV RNA appeared to be somewhat higher among those in the IL-2 randomisation arm and the rate of decline in HCV RNA over time somewhat faster (Figure 1). However, neither effect approached statistical significance and there was no evidence to suggest that randomisation arm was associated with baseline HCV RNA levels or the rate of decline in HCV RNA over time (*P*=0.16 and *P*=0.56, respectively).

Spontaneous HCV RNA clearance and IL-28B genotype

There were 9 cases of spontaneous HCV RNA clearance during the chronic phase of HCV infection over the course of the study. The IL-28B genotypes of these individuals were CC: 5/9 (55.6%) and CT: 4 (44.4%), none of them had the TT genotype. Further characteristics are summarized in table 2.

Conclusions: HCV RNA levels decreased over time in this population with well-controlled HIV infection. Spontaneous clearance of HCV RNA was documented in 5 individuals with IL28B genotype CC and 4 with the CT genotype.

Baseline characteristics % / Median (IQR)		IL-2 Arm (N=151)	Control Arm (N=161)	P-value
Male		78.2	73.9	0.38
Age		38 (34 – 41)	39 (34 – 43)	0.21
Race	White	88.1	90.1	0.57
	Non-white	11.9	9.9	
HIV transmission via IDU		76.2	66.5	0.059
HBsAg +		2.9	0.7	0.15
HCV genotype	1	58.9	57.1	0.78
	2	1.3	1.9	
	3	19.9	19.9	
	4	13.3	16.8	
	5	0.7	0	
	Unknown	6.0	4.4	
CD4 cell count		434 (370 - 540)	435 (365 - 553)	0.92
CD4 cell count nadir		163 (70 - 262)	150 (70 - 258)	0.93
Taking cART		96.0	95.0	0.67
Detectible HIV-RNA (>50 copies/ml)		5.3	8.7	0.24
Hyaluronic acid (ng/ml)		35.4 (16.6 – 57.9)	32.1 (18.9 – 65.2)	0.86
Randomisation date		AUG/01 (FEB/02 – OCT/02)	AUG/01 (FEB/02 – SEP/02)	0.94

Table 1 Baseline characteristics of HIV/HCV coinfected individuals in ESPRIT stratified by randomisation arm

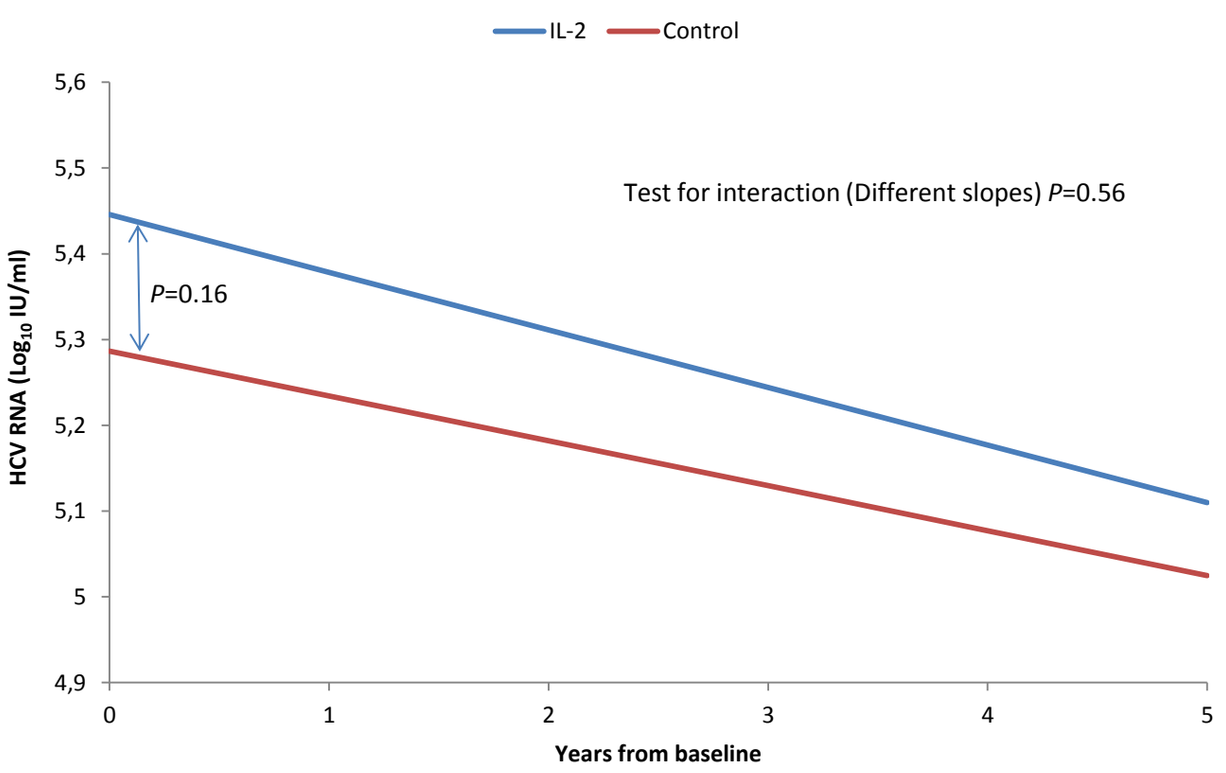

Figure 1 The effect of ESPRIT randomisation arm on the course of HCV RNA levels

Characteristics N (%) / Median (IQR)		Spontaneous clearance (N=9)
Male		5 (55.6)
Age		38 (36 – 42)
Race	Asian	1 (11.1)
	White	8 (88.9)
Mode of infection	IDU	5 (55.6)
	MSM	1 (11.1)
	Heterosexual	3 (33.3)
	Blood products	0
HBsAg	Negative	8 (88.9)
	Unknown	1 (11.1)
HCV genotype	1a	2 (22.2)
	1b	1 (11.1)
	2b	1 (11.1)
	3a	5 (55.6)
	4c	0
	Unknown	0
CD4 cell count (IQR)	Cells/mm^3	435 (400 - 702)
CD4 nadir (IQR)		199 (155 - 352)
IL28B genotype	CC	5 (55.6)
	CT	4 (44.4)
	TT	0
Baseline HCV RNA	Log_{10} IU/ml	6.01 (4.60 – 6.13)
Detectible HIV-RNA		4 (44.4)
Hyaluronic acid	Ng/ml	15.0 (13.4 – 115.2)

Table 2 Characteristics of cases and controls at HCV RNA clearance or last visit

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