CAN'T BUY ME LOVE? OBSTACLES TO MICRO-ELIMINATION OF ACUTE HCV COINFECTION IN EUROPE

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Background

Several trials have shown high sustained viral response (SVR) rates with shortened direct acting antivirals (DAA) containing therapy in acute hepatitis C (AHC) coinfection. In addition, data from modelling and real life cohorts have shown a reduced AHC incidence with early DAA therapy. However, with no DAA currently being licensed for the treatment of AHC and with the high drug prices low DAA treatment uptake poses the biggest obstacle to HCV micro-elimination in a high-risk population. Here we evaluate rates of DAA treatment initiation of AHC coinfection in a large European cohort.

Methods

The PROBE-C study is an observational cohort on AHC in HIV coinfection. Between 2007 and 2017 464 AHC episodes were documented in HIV-infected patients with at least 12 months of follow-up from Austria, Denmark, France, Germany, Great Britain and Spain. Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.

Conclusions

IFN-containing therapy was no longer used for the early treatment of AHC coinfection in our pan-European cohort after 2015. Although available and recommended by guidelines during the early acute phase, DAA-based therapy was mostly deferred to post six-months after first presentation of HCV infection (traditional definition of chronic HCV). However, the lack of a 2log drop in HCV RNA four weeks after presentation identified almost 90% of patients going on to develop chronic HCV infection. With more patients remaining viremic longer now than in the interferon-era, we urge funding authorities to allow use of early DAA-based therapy based on demonstrating lack of a 2log drop in HCV RNA post initial presentation.

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Results

457/464 (98%) patients were male, median age was 41 years (IQR 38-46). Main risk groups for HCV transmission were MSM (98.9%) and injecting drug use (IDU) (1.1%). 78.3% of patients were infected with HCV genotype (GT) 1, 2.6% with GT3 and 18.6% with GT4. Median baseline HCV-RNA was 230,000 IU/mL (135,000-474,432), median CD4+ T cell count 574 cells/µl (547-604). 92% of all patients received cART, 91% had baseline suppressed HIV-RNA (<200 copies/mL). Median maximum ALT was 445 U/l (402-522, see table 1).

Table 1: Baseline characteristics

	All n=464
Median age [years] (IQR)	41 (40-42)
Male gender [%]	98.3
Transmission risk [%]	
MSM	98.8
Hetero	0.5
IVDU	0.7
Median CD4-cells [/µl] (IQR)	574 (547-604)
[%] (IQR)	29 (29-31)
HIV-RNA <200 copies/mL [%]	90.8
cART [%]	91.5
Median HCV-RNA [IU/mL] (IQR)	682,646 (518,000-1,149,828)
Median maximum ALT [U/l] (IQR)	445 (402-522)
HCV genotype [%]	
1 (94% GT 1a, 6% GT 1b)	78.5
2	0.5
3	2.4
4	18.6
>2log decline in HCV RNA @ week 4 [%]	13.6

Figure 1. Virologic outcome

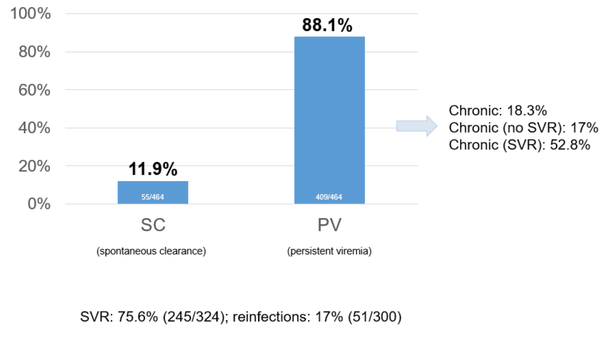


Table 2: Baseline characteristics per group

	All n=464	PV n=409	SC n=55	p-value
Median age [years] (IQR)	41 (40-42)	41 (40-42)	42 (40-46)	0.997
Male gender [%]	98.3	98.5	96.4	0.243
Transmission risk [%]				0.474
MSM	98.8	98.9	97.9	
Hetero	0.5	0.5	0	
IVDU	0.7	0.5	2.1	
Median CD4-cells [/µl] (IQR)	574 (547-604)	580 (550-607)	544 (459-666)	0.696
[%] (IQR)	29 (29-31)	29 (28-31)	27 (24-31)	0.226
HIV-RNA <200 copies/mL in pts on cART [%]	90.8	90.4	94.1	0.604
cART [%]	91.5	92.6	83.6	0.036
Median HCV-RNA [IU/mL] (IQR)	682,646 (518,000-1,149,828)	687,811 (518,000-1,149,994)	677,481 (149,000-2,764,000)	0.389
Median maximum ALT [U/l] (IQR)	445 (402-522)	431 (385-497)	591 (408-907)	0.337
HCV genotype [%]				0.929
1	78.5	78.6	77.5	
2	0.5	0.5	0	
3	2.4	2.4	2.5	
4	18.6	18.5	20	
>2log decline in HCV RNA @ week 4 [%]	13.6	2.5	96.4	≤0.001
Median time to 1st negative HCV RNA [weeks] (IQR)	-	-	13 (12-18)	-
Median time to treatment initiation* [weeks] (IQR)	-	11 (10-13)	-	-

In only 55/464 (11.9%) spontaneous clearance of AHC occurred (see figure 1, table 2 and 3). A >2log decline in HCV RNA 4 weeks after AHC diagnosis was statistically significantly associated with SC (≤0.001, see tables 2 and 3). In 324/464 (70%) HCV treatment was initiated. In 277/324 (85%) treatment was interferon (IFN)-containing, in 47/324 (15%) DAA-based. Overall, median time from AHC diagnosis to treatment initiation was 11 weeks (10-13): 14 weeks in patients receiving IFN-containing treatment versus 44 weeks in patients receiving DAA (≤0.001). 241 of 277 (87%) AHC patients receiving INF were treated within 24 weeks of AHC diagnosis, only 8 of 47 (17%) AHC patients receiving DAA were treated within 24 weeks of AHC diagnosis. Overall rates of treatment uptake within 24 weeks of diagnosis dropped from 75% in 2007 to 14% in 2017 (see table 4).

Table 3: Factors associated with spontaneous clearance

	PV n=409	SC n=55	Univariate p-value**	Multivariate p-value***	Multivariate Odds-Ratio (95% CI)***
Median age [years] (IQR)	41 (40-42)	42 (40-46)	0.997		
Male gender [%]	98.5	96.4	0.243		
Transmission risk [%]			0.474		
Median CD4-cells [/µl] (IQR)	580 (550-607)	544 (59-666)	0.696		
[%] (IQR)	29 (28-31)	27 (24-31)	0.226		
HIV-RNA <200 copies/mL [%]	90.4	94.1	0.604		
cART [%]	92.6	83.6	0.036	0.230	3.9 (0.4-36.4)
Median HCV-RNA [IU/mL] (IQR)	687,811 (518,000-1,149,994)	677,481 (149,000-2,764,000)	0.389		
Median maximum ALT [U/l] (IQR)	431 (385-497)	591 (408-907)	0.337		
HCV genotype [%]			0.929		
>2log decline in HCV RNA @ week 4 [%]	2.5	96.4	≤0.001	≤0.001	1115.3 (225.5-5515.3)
Median time to 1st negative HCV RNA [weeks] (IQR)	-	13 (12-18)	-		
Median time to treatment initiation* [weeks] (IQR)	11 (10-13)	-	-		

Table 4: Annual rates of treatment initiation within 6 months for new AHC diagnoses from 2007 to 2017

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number of treatment initiations within 6 mths/total number of treatment initiations (%)	6/8 (75)	16/17 (94)	27/30 (90)	38/40 (95)	44/47 (94)	50/54 (93)	42/47 (89)	16*/ 23 (70)	4*/ 14 (29)	3**/ 22 (14)	3**/ 22 (14)

*Including 1 DAA-based treatment
**DAA-based treatments only