Abstract THU-309

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Efficacy and safety of IFN-free DAA HCV therapy in HIV/HCV co-infected persons: Results from a pan-European study

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INTRODUCTION

Real-life data on efficacy and safety of direct-acting antiviral (DAA) therapy in HIV/HCV co-infected patients from Europe, especially Eastern Europe, are still scarce[1-3].

The EuroSIDA study is a pan-European prospective observational cohort study that follows more than 3000 HIV positive individuals with chronic HCV co-infection in 35 countries in all geographical regions of Europe[4].

AIM

We aimed to investigate the efficacy of DAAs and the prevalence and reasons for premature discontinuation of DAAs in HIV/HCV co-infected individuals in the EuroSIDA study.

METHODS

Patients

Individuals starting DAA therapy without interferon between 2 June 2014 – 17 March 2017, during prospective follow-up in EuroSIDA. Persons were required to have a CD4 count and a viral load measured before baseline, defined as the date of starting the DAA regimen and be aged >16 at baseline. Persons without 12 weeks follow-up after stopping treatment were excluded from analyses.

Definitions of HCV treatment outcome

1. SVR – undetectable HCV-RNA at 12 weeks or later after stopping treatment
2. Treatment failure – detectable HCV-RNA at end of treatment or later
3. End-of-treatment (EOT) response – undetectable HCV-RNA after treatment stopped but prior to 12 weeks after stopping treatment, and no further HCV-RNA at or after 12 weeks
4. Unknown treatment response – persons with no HCV-RNA data at or after 12 weeks after stopping treatment excluding group 3

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Statistical methods

Logistic regression was used to calculate the odds of having a known response to DAAs, factors significant in univariate analyses (p<0.1) were included in multivariate models. Logistic regression was also used to examine factors associated with SVR.

RESULTS

Patients

Among 632 persons starting DAA, the median age was 51 years and 79% were males. 58% had a history of injecting drug use and 19% were men who have sex with men; 98.6% had HIV-RNA<500 copies/ml and median CD4 cell count was 600/mm^3; 32.4% had cirrhosis.

HCV treatment regimens

The most commonly used regimen was sofosbuvir + ledipasvir +/- ribavirin (n=289, 45.7%), followed by sofosbuvir + daclatasvir +/- ribavirin (n=126, 19.9%) and paritaprevir/ombitasvir + dasabuvir +/- ribavirin (n=84, 13.3%). Ribavirin was used in 272/632 (43%) DAA regimens.

HCV treatment outcome

Among persons with known SVR status, 433/468 (92.5%; 95% CI 90.1 – 94.9%) achieved SVR. The characteristics at time of starting treatment according to treatment outcome among those with known SVR status is shown in the table. 164 persons had unknown SVR status, 82 (50%) of whom were HCV-RNA negative at end of treatment and 82 (50%) with unknown treatment response. Patients with unknown SVR status were generally similar to those with known SVR status, but more likely to be from Central East and Eastern Europe, p=0.059). In an intention to treat analysis, 433/632 (68.5%; 95% CI 64.9-72.1) achieved SVR.

Factors associated with achieving SVR

In adjusted analysis, only white ethnicity vs. non-white ethnicity, fibrosis stage 0-1 vs. 2-4 and treatment duration per one week longer were associated with higher odds of SVR (figure).

Reasons for stopping HCV treatment earlier than scheduled

Thirty-one (4.9%; 95% CI 3.2-6.6%) out of 632 patients stopped one or more HCV drugs earlier than scheduled. The reasons were toxicity (N=11), viral failure (N=1), physician choice (N=3), drug out of stock (N=1), substance abuse (N=1), other (N=7) and unknown (N=7).

The median duration of treatment was 12 weeks for the 20 persons who interrupted treatment for non-toxicity reasons (IQR 8 – 18), 9 weeks for the 11 persons who interrupted treatment for toxicities (IQR 4 – 16) and was 12 weeks for the 601 persons who did not report any interruption (IQR 12-18 weeks), p=0.0011.

Adverse effects of DAA treatment

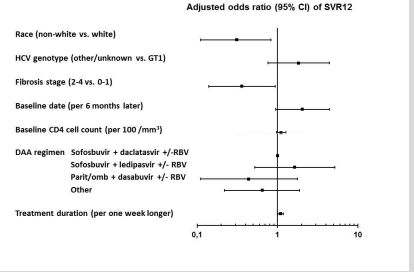
In nine out of 11 treatment stops due to toxicity, ribavirin was the only drug in the regimen that was stopped due to well-known adverse effects (anemia, rash, neuropathy, gastrointestinal symptoms). In only two cases were all drugs stopped early due to toxicity: 1) localized rash (sofosbuvir/ledipasvir) and 2) fatigue, dizziness and anorexia (simeprevir, sofosbuvir/velpatasvir, ribavirin).

Table
Characteristics at time of starting treatment in 468 persons with known SVR status

		SVR	Failure	P*
All (%)		433 (92.5)	35 (7.5)	
Age (median years)		52	51	0.52
Gender (%)	Male	340 (92.9)	26 (7.1)	0.56
	Female	93 (91.2%)	9 (8.8)	
Race (%)	White	401 (93.7)	27 (6.3)	0.0016
	Other	32 (80)	8 (20)	
Region (%)	South/Argentina	196 (92)	17 (8)	0.27
	West	136 (95.8)	6 (4.2)	
	North	69 (89.6)	8 (10.4)	
	East/Central East	32 (88.9)	4 (11.1)	
HIV transmission risk (%)	IDU	256 (93.1)	19 (6.9)	0.58
	Non-IDU	177 (91.7)	16 (8.3)	
HCV genotype (%)	1	234 (94.7)	13 (5.3)	0.26
	2	9 (90.0)	1 (10.0)	
	3	57 (91.9)	5 (8.1)	
	4	59 (86.8)	9 (13.2)	
	Unknown	74 (91.4)	7 (8.6)	
Fibrosis stage (%)	METAVIR 0/1	171 (96.1)	7 (3.9)	0.14
	METAVIR 2	64 (88.9)	8 (11.1)	
	METAVIR 3	72 (93.5)	5 (6.5)	
	METAVIR 4	125 (89.3)	15 (10.7)	
CD4 (median cells/µl)		612	516	0.063
HIV-RNA (% <500 cp/ml)		428 (92.6)	34 (7.4)	0.39

Among 632 persons completing DAA therapy, 164 had unknown SVR status and are excluded from this table.
*The p-value compares the characteristics of persons with SVR vs. failure

Figure
Factors associated with achieving SVR



Model adjusted for factors shown. Gender, age, region of Europe, HIV risk, HCV viral load, prior HCV treatment, HBsAg, nadir CD4 cell count and treatment duration ≤ 12 vs. >12 weeks all had p>0.1 in univariate analysis

CONCLUSIONS

- In a diverse population of HIV/HCV co-infected patients from all regions of Europe, DAA therapy resulted in an overall SVR rates of 92.5% which is similar to what has been shown for national cohorts in Western Europe[1-3].
- There were no significant differences in response across regions, although with limited power in Central East and Eastern Europe, and further follow-up is warranted to confirm these findings.
- Factors associated with higher odds of SVR were white race, fibrosis stage 0/1 and treatment duration per one week longer.
- A quarter of all persons who had completed treatment did not have a follow-up HCV-RNA to determine SVR12.This could either reflect other follow-up schedules than what is seen in clinical trials; treatment outside the HIV clinic, loss to follow-up or data not reported and requires further data to clarify.
- Only 5% stopped one or more HCV drugs earlier than scheduled, and a third of these were due to toxicity mostly related to well-know adverse effects of ribavirin. We saw no new safety signals for DAAs.

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