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Uptake of HCV Treatment in HIV/HCV Co-infected Persons across Europe in the Era of Direct-acting Antivirals

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INTRODUCTION

Due to the high cost of new effective direct-acting antivirals (DAA) against hepatitis C virus (HCV), their use is expected to vary significantly across Europe, and in some European countries and particular patient groups, pegylated interferon (IFN) and ribavirin (RBV) might still be used.

AIMS

- To investigate regional differences in the rate of HCV treatment uptake among HIV/HCV co-infected persons in the pan-European EuroSIDA study after 2011.
- To investigate regional differences in uptake and factors associated with use of DAA treatment

METHODS

The EuroSIDA study is a prospective observational study of HIV-1 infected individuals ≥16 years of age. At the end of 2015, 21880 patients have been enrolled from 107 hospitals in 35 European countries plus Israel and Argentina. In the present study we included all patients positive for HCV-RNA who were followed up after January 2011. Baseline was defined as the latest of a positive HCV antibody test, January 2011 or recruitment to EuroSIDA. Characteristics at starting HCV treatment or at last clinic visit were compared between HCV treated and untreated patients. The incidence per 1000 person-years of follow-up (PYFU) of starting HCV treatment was calculated. Poisson regression was used to determine factors associated with starting the first DAA-based treatment during follow up.

RESULTS

A total of 3083 HCV-RNA+ HIV positive persons were included in the study. Among included persons, 884 (28.7%) were from EuroSIDA region South, while 665 (21.6%), 536 (17.4%), 472 (15.3%), 489 (15.9%) and 37 (1.2%) were recruited from West, North, Central East, East, and Argentina respectively (figure 1). During 5493 PYFU, 470 (15.2%) started any HCV therapy (incidence 85.6/1000 PYFU; 95%CI 77.8-93.3). The incidence remained stable between 2011 (62.0/1000 PYFU; 95% CI 47.6 – 76.4) and 2014 (72.4/1000 PYFU; 95% CI 56.5 – 88.3), but increased sharply in 2015 (248.3/1000 PYFU; 95% CI 212.8 – 283.8)

Patient characteristics at time of starting HCV treatment

Table 1 shows the patient characteristics at time of starting any HCV treatment compared with last clinic visit in those untreated during follow up. The median age of both treated and untreated was 48 years, and around a third of all patients were HCV treatment experienced. Compared with untreated, HCV treated patients were more likely to be from South (34% vs. 28%), to be of white race (94% vs. 86%) to have HCV genotype 1 (49% vs. 42%) and have METAVIR fibrosis stage F4 (34% vs. 15%). Treated and untreated persons had similar HIV-related characteristics.

Figure 1

Recruitment from different EuroSIDA regions

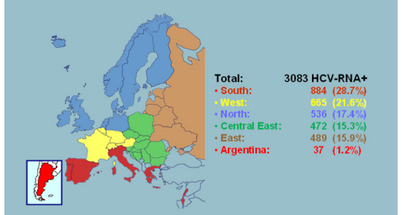


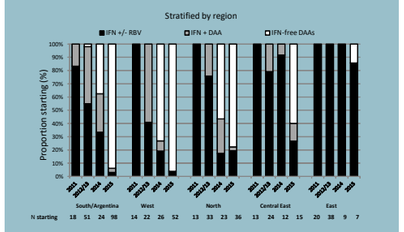
Table 1

Characteristics at starting any HCV treatment

Factor		Total	Untreated	Started treatment
All (%)		3083 (100)	2613 (84.8)	470 (15.2)
Age (median years, IQR)		48 (IQR 40-53)	48 (IQR 40-53)	48 (IQR 40-53)
Male (%)		2200 (71.4)	1844 (70.6)	352 (75.7)
White (%)		2693 (87.4)	2253 (86.2)	440 (93.6)
Region (%)	South	884 (28.7)	723 (27.7)	161 (34.3)
	North	536 (17.4)	463 (17.7)	73 (15.5)
	West	665 (21.6)	563 (21.5)	102 (21.7)
	Central East	472 (15.3)	410 (15.7)	62 (13.2)
	East	489 (15.9)	421 (16.1)	68 (14.5)
	Argentina	37 (1.2)	3 3(1.3)	4 (0.9)
Cirrhosis (%)		538 (17.5)	380 (14.5)	158 (33.6)
HCV genotype 1 (%)		1316 (42.7)	1086 (41.6)	230 (48.9)
HCV treatment experienced		972 (31.5)	814 (31.2)	158 (33.6)
CD4 (median cells/mm^3, IQR)		537 (369 – 750)	537 (365 – 752)	530 (389 – 737)
HIV-Viral Load <400 copies/mL (%)		2677 (88.1)	2254 (87.6)	423 (90.8)

Figure 2

HCV treatment started during prospective follow up



RESULTS (CONTINUED)

Use of different HCV treatment regimens

Among individuals starting HCV treatment in 2014 in Western Europe the majority received an IFN-free regimen. However, in 2015 20% of all treatments in North were still IFN + RBV. In Central East IFN-based treatment was used exclusively until 2015. In East IFN/RBV dominated in the entire study period. Among 186 persons receiving INF-free treatment in 2015 the most commonly used regimen was sofosbuvir/ledipasvir +/- RBV (n=90, 48.4%) followed by sofosbuvir/daclatasvir +/- RBV (n=35, 18.8%) and ombitasvir/paritaprevir/ritonavir +/- dasabuvir +/- RBV (n=30, 16.1%).

Incidence of starting DAA-based HCV treatment

Among 2603 persons with prospective follow up, 282 (10.8%) started 295 DAA regimens during 5770 PYFU (incidence 58.1 /1000 PYFU). The incidence of starting DAA increased from 41.5/1000 PYFU (29.9–53.2) in 2014 to 227.4/1000 PYFU (194.3–260.5) in 2015, and varied significantly across regions (figure 3). The increase was highest in South and West and intermediate in North. In Central East there was a slight increase incidence in 2015, while only a single patient in East received IFN-free treatment in the entire study period.

Factors associated with starting DAA treatment

After adjustment, females, those of non-white race, from Central East or East, HCV genotype non-1 versus genotype 1 and those with detectable HIV viral load were less likely to start DAA-based HCV treatment (figure 4). In contrast, older persons, those with HCV RNA >500.000 IU/ml, with more advanced fibrosis, and those starting IFN/RBV treatment alone during follow-up were more likely to start DAA. After adjustment, there also remained a strong increase in the incidence of starting DAA-based HCV treatment with later calendar year of follow-up. Table 2 shows the interaction between starting DAA and region according to calendar year and fibrosis stage. Central East and Eastern Europe were combined due to small numbers. West and Central Eastern/Eastern Europe were starting DAA-based HCV treatment at lower stages of fibrosis compared to South/Argentina and North, and the relative increase from 2014 to 2015 in uptake of DAA-based HCV treatment was most pronounced in South and Central East and least pronounced in West and North.

CONCLUSIONS

Uptake of DAA therapy among HIV/HCV coinfected persons increased considerably in most regions of Europe since 2014, but remains negligible in East, where use of IFN/RBV is still more common than DAA. Females and non-white persons were less likely than males and whites to start IFN-free treatment. Although persons with cirrhosis were more likely to be prioritized for treatment compared with persons with lower stages of fibrosis, 15% of untreated persons have signs of cirrhosis, and hence are at increased short-term risk of liver-related complications if they do not get access to effective HCV treatment.

LIMITATIONS

Among all anti-HCV positive individuals followed up after 2011, 26.4% have unknown HCV-RNA status (not tested or result not reported) with some variation across different groups of co-infected individuals.

Figure 3

Incidence of starting DAA-based HCV treatment

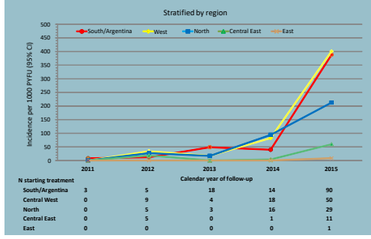


Figure 4

Adjusted incidence rate ratios of starting DAA during follow up

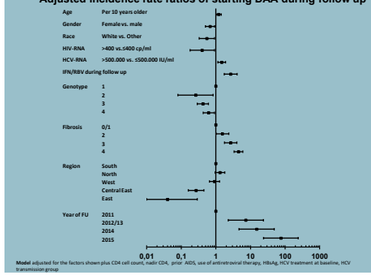


Table 2a: Adjusted incidence rate ratio of starting DAA according to fibrosis stage stratified by region

	South/Argentina		West		North		Central East/East	
Fibrosis	aIRR 95% CI	P-value	aIRR 95% CI	P-value	aIRR 95% CI	P-value	aIRR 95% CI	P-value
F0-F2	1		1		1		1	
F3-F4	4.41 (3.00 – 6.47)	<.0001	2.78 (1.74 – 4.45)	<.0001	3.63 (2.1 – 6.29)	<.0001	2.54 (0.92 -7.01)	0.071

P-value for interaction <0.0001

Table 2b: Adjusted incidence rate ratio of starting DAA according to calendar year stratified by region

	South/Argentina		West		North		Central East/East	
Year	aIRR 95% CI	P-value	aIRR 95% CI	P-value	aIRR 95% CI	P-value	aIRR 95% CI	P-value
<2013	0.55 (0.29 – 1.05)	0.072	0.21 (0.10 – 0.43)	<.0001	0.16 (0.07 – 0.39)	<.0001	1.88 (0.22 -16.14)	0.56
2014	1		1		1		1	
2015	9.54 (5.42-16.76)	<.0001	5.21 (2.99 – 9.06)	<.0001	2.30 (1.25 – 4.24)	0.0078	14.36 (1.85 -111.4)	0.0011

P-value for interaction <0.0001

Model was adjusted for gender, race, HCV RNA as time-updated covariate, genotype (1 versus all others), HIV viral load (time updated) starting IFN/RBV only (time-update), and age

The EuroSIDA study group: http://www.chip.dk/Ongoing-Studies/EuroSIDA/
Download poster at: www.chip.dk