

Background

- Since June 2014, new generation DAA (NG-DAA) are recommended for the treatment of HCV mono-infected (HCVm) and HIV/HCV co-infected (HCVc) persons in Italy with a F3-F4 stage of liver disease
- Starting from January 2015 AIFA officially released DAA drugs as fully refundable for these patients and therapy should be started immediately

Objectives

- To describe the probability of uptake of DAA treatment and to identify predictors of delayed in DAA initiation in HIV/HCV co-infected individuals seen for care in Italy

Methods

All participants of PITER cohort (HCVm), Icona Foundation Study and HepalCONA cohorts (HCVc) who on January 1st 2015 (Jan15) were naive to NG-DAA and with a positive HCV-RNA were included in this analysis.

Study populations on Jan15 were described. Baseline for an analysis for time to NG-DAA initiation was Jan15 or the date of F3-F4 diagnosis, whichever occurred last. In the HCVc group a Fib4>3.25 was used to establish F3-F4 stage of disease.

In the HCVm group, we estimated the probability of NG-DAA initiation by two years from enrolment in PITER using a logistic regression model.

In the HCVc group, time to DAA-NG initiation was estimated using Kaplan-Meier curves. Predictors of delayed initiation was also identified separately in HCVc by mean of multivariable Cox regression models. The same set of potential predictors, commonly recorded in the two cohorts were included in the multivariable logistic and Cox regression models.

Results

We included 2,520 HCVm and 531 HCVc patients with F3-F4.

In the HCVm group, 37% were females, 85% over 50 years old, 11% reported hazardous drinking, 11% had HCV genotype 3, 22% were diagnosed with diabetes and 40% had current AST higher than the upper limit of normal level. HCVc group had similar characteristics: 24% were females, 80% 50+ years, 11% reported hazardous drinking, 3% a BMI>25, 19% had HCV genotype 3, 8% with a diagnosis of diabetes, approximately 50% had ALT/AST/PLT markers 2-fold higher than the upper limit of normal level and 47% were diagnosed with F3-F4 by 6 months or longer (Table 1).

By 2 years of baseline the probability of NG-DAA initiation was 47% (1,173 initiations) in HCVm and 48%; 95% CI:42-54% in HCVc (overall, 172 initiations, Figure 1).

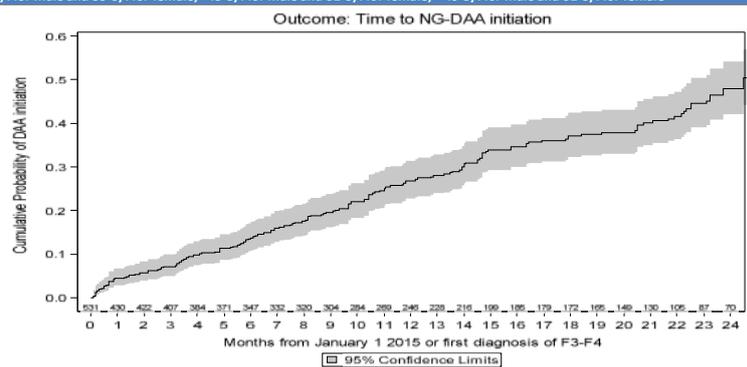
Factors independently associated with the probability of initiation of NG-DAA separately in the HCVm and HCVc cohorts are shown in Table. Both in HCVm and HCVc uptake of NG-DAA appeared to be similar regardless of whether a participant received care through a Hospital or a University clinical centre.

People with more severe disease (measured by Fib4 or Fibroscan) were more likely to be treated but, conversely, people with moderate/high alcohol consumption were less likely to start NG-DAA. Opposite trends for the probability of initiation were observed in HCVm and HCVc participants with diabetes and according to nationality.

Table 1. Characteristics of patients analysed by cohort

Characteristics	HCVm	HCVc
		N= 531
Age, n(%)		
50+		425 (80.0%)
Gender, n(%)		
Female		126 (23.7%)
Alcohol abuse, n(%)		
No		181 (34.1%)
Yes		60 (11.3%)
Unknown		290 (54.6%)
BMI, n(%)		
25+		10 (2.7%)
HCV genotype, n(%)		
1,2,4		188 (35.4%)
3		99 (18.6%)
Other/unknown		244 (46.0%)
Diabetes, n(%)		44 (8.3%)
ALT, n(%)		
>=2-fold upper limit of normal*		273 (51.4%)
AST, n(%)		
>=2-fold upper limit of normal*		259 (48.8%)
Gamma-GT, n(%)		
>=2-fold upper limit of normal**		242 (45.6%)
Platelets, n(%)		
>=150,000		108 (20.3%)
Months from diagnosis of F3-F4, n(%)		
>=6 months		249 (46.9%)
<6 months		35 U/I for male and 55 U/I for female; 45 U/I for male and 51 U/I for female; 49 U/I for male and 52 U/I for female

Figure 1 - KM estimate of the time to access to DAA treatment in the HCVc group



Factors	Adjusted* odds ratio (95% CI)	Adjusted* relative hazards (95% CI)	p-value
Fib-4			
>5.1 vs. 3.25-5.1	1.57 (1.19-2.08) [§]	1.78 (1.29, 2.44)	<.001
Mode of HIV transmission	N/A		
Heterosexual contacts		1.00	
PWID		1.26 (0.72, 2.22)	0.423
MSM		0.36 (0.12, 1.13)	0.081
Other/unknown		0.96 (0.45, 2.07)	0.926
Age, years			
50+ vs. <50	1.03 (0.73-1.47)	1.56 (0.96, 2.52)	0.072
Gender			
Female vs. male	1.16 (0.87-1.55)	0.78 (0.54, 1.14)	0.198
Alcohol consumption			
None	1.00	1.00	
Moderate/Hazardous	0.99 (0.63-1.57)	0.41 (0.20, 0.83)	0.012
Unknown	7.66 (1.93-30.4)	1.26 (0.86, 1.85)	0.239
HCV genotype			
1,2,4	1.00	1.00	
3	0.94 (0.64-1.38)	1.18 (0.76, 1.82)	0.466
Other/unknown	0.49 (0.28-0.86)	0.71 (0.50, 1.03)	0.069
Diabetes			
Yes vs. No	1.36 (0.99-1.88)	0.48 (0.26, 0.90)	0.021
Gamma-GT			
>=2-fold upper limit of normal** vs. lower	1.07 (0.76-1.50)	1.16 (0.84, 1.60)	0.372
Type of clinical site			
Hospital vs. university	0.82 (0.58-1.15)	1.01 (0.67, 1.51)	0.970
Education level			
Primary vs. secondary/university	1.55 (0.65-3.68)	1.17 (0.50, 2.73)	0.713
Nationality			
Italian vs. not	1.38 (0.67-2.82)	0.46 (0.28, 0.78)	0.004

Conclusions

More than a half of patients with advanced fibrosis, with or without HIV co-infection, are still waiting to be cured in Italy, regardless of clinical setting. The severity of liver disease is the main factor leading to prompt DAA initiation

ICONA Foundation Study and PITER study Group (full list shown in the like below)

<https://www.dropbox.com/s/zuinjy7mbyj2ff/Icona%2C%20Hepalcona%20and%20Piter%20Study%20Groups.docx?dl=0>