

## 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 naïve to NG-DAA, with a diagnosis of F3-F4 (or Fib4>3.25 for HCVc) 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.

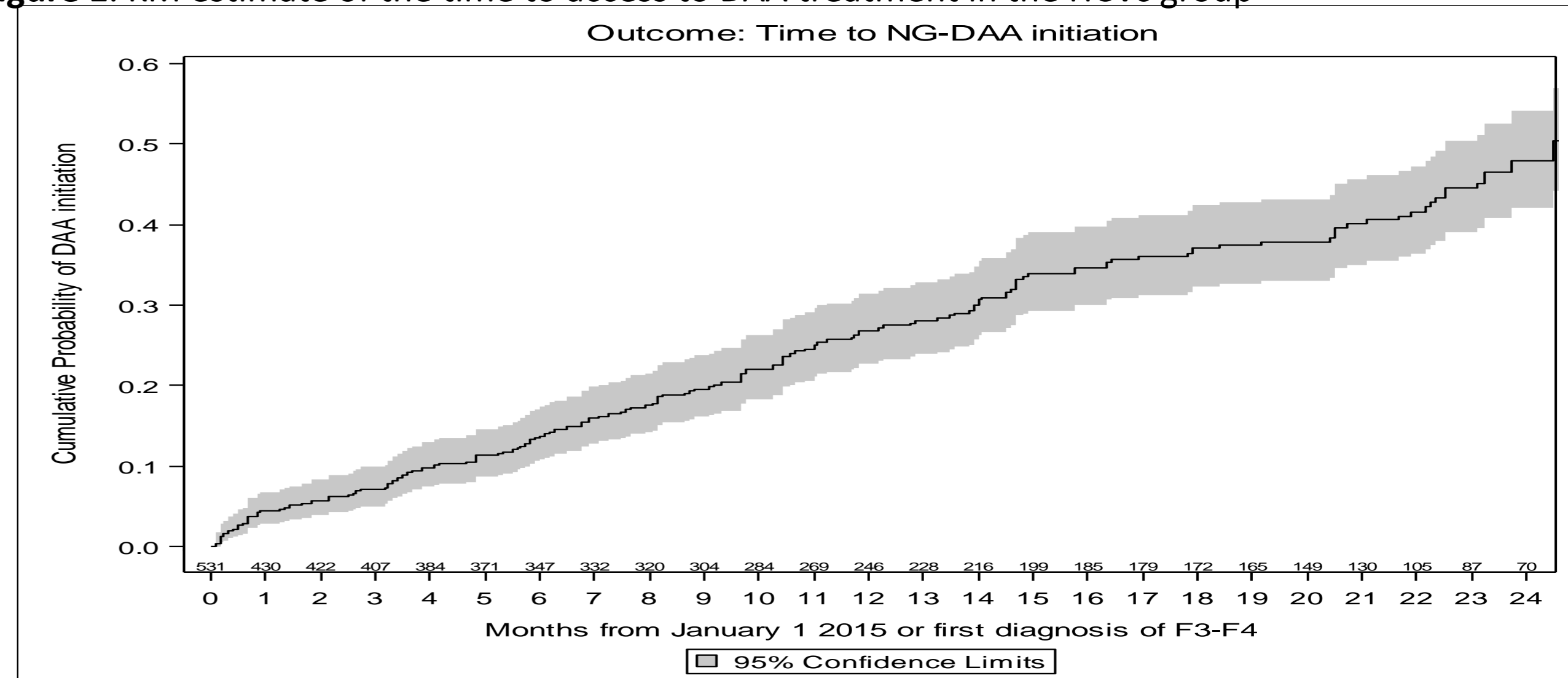
People with more severe disease (measured by Fib4 or Fibroscan) were more likely to be treated but, conversely, people with moderate/high alcohol consumption were less likely to start NG-DAA. Opposite trends for the probability of initiation were observed in HCVm and HCVc participants with diabetes and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

**Table 1.** Characteristics of patients analysed by cohort

| Characteristics                             | HCVm<br>N=2520 | HCVc<br>N= 531 |
|---|----------------|----------------|
| Age, n(%)                                   |                |                |
| 50+   | 2139 (84.8%)   | 425 (80.0%)    |
| Gender, n(%)                                |                |                |
| Female                                      | 924 (36.6%)    | 126 (23.7%)    |
| Alcohol abuse, n(%)                         |                |                |
| No  | 2218 (88%)     | 181 (34.1%)    |
| Yes   | 268 (10.6%)    | 60 (11.3%)     |
| Unknown                                     | 34 (1.4%)      | 290 (54.6%)    |
| BMI, n(%)                                   |                |                |
| 25+   | 1380 (54.8%)   | 10 (2.7%)      |
| HCV genotype, n(%)                          |                |                |
| 1,2,4                                       | 1946 (77.2%)   | 188 (35.4%)    |
| 3   | 284 (11.3%)    | 99 (18.6%)     |
| Other/unknown                               | 290 (11.5%)    | 244 (46.0%)    |
| Diabetes, n(%)                              | 544 (21.6%)    | 44 (8.3%)      |
| ALT, n(%)                                   |                |                |
| >=2-fold upper limit of normal*             | 1151 (45.7%)   | 273 (51.4%)    |
| AST, n(%)                                   |                |                |
| >=2-fold upper limit of normal <sup>§</sup> | 1010 (40.1%)   | 259 (48.8%)    |
| Gamma-GT, n(%)                              |                |                |
| >=2-fold upper limit of normal**            | 681 (27.0%)    | 242 (45.6%)    |
| Platelets, n(%)                             |                |                |
| >=150,000                                   | 606 (24.0%)    | 108 (20.3%)    |
| Months from diagnosis of F3-F4, n(%)        |                |                |
| >=6 months                                  | nd             | 249 (46.9%)    |

\*35 U/l for male and 35 U/l for female; <sup>§</sup>45 U/l for male and 31 U/l for female; \*\*49 U/l for male and 32 U/l 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) <sup>§</sup> | 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   |

\*OR refers to the comparison >13 vs. <=13 kPa in fibroscan  
N/A = not applicable

## 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/zuinjy7mnbj2ff/Icona%2C%20Hepalcona%20and%20Piter%20Study%20Groups.docx?dl=0>