17° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research

POSTER

Hepatitis and Liver Diseases

P 73 Long-term outcomes and incidence of clinically significant events after HCV eradication in people with HIV: data from ICONA/HepaICONA cohorts

Authors
M. Mazzitelli[1], N. Lentini[2], A. Cozzi-Lepri[3], A. Tavelli[4], V. Malagnino[5], A. Giacomelli[6], V. Mazzotta[7], E. Quiros-Roldan[8], A. Siribelli[9], G. Lapadula[10], A. Cingolani[11], R. Pastorino[2,12], M. Puoti[13], A. d'Arminio[4], R. Rossotti[14] on behalf of Icona/HepaIcona Study Group

Affiliation
[1]Infectious and Tropical Diseases Unit, Padua University Hospital, Padua, Italy, [2]Section of Hygiene, University Department of Health Sciences and Public Health, Università Cattolica del Sacro Cuore, Rome, Italy, [3]Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, UCL, London, UK, [4]ICONA Foundation, Milan, Italy, [5]Clinical Infectious Diseases, Department of System Medicine, Tor Vergata University, Policlinico Tor Vergata of Rome, Rome, Italy, [6]III Infectious Diseases Unit, ASST Fatebenefratelli-Sacco, DIBIC Luigi Sacco, Università degli Studi di Milano, Milan, Italy, [7]Clinical Infectious Diseases Department, National Institute for Infectious Diseases Lazzaro Spallanzani IRCCS, Rome, Italy, [8]Department of Clinical and Experimental Sciences, Unit of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili di Brescia, Brescia, Italy, [9]Department of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Milan, Italy, [10]Department of Infectious Diseases, IRCCS San Gerardo dei Tintori, University of Milano-Bicocca, Monza, Italy, [11]UOC Malattie Infettive, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Dipartimento di Sicurezza e Bioetica, Università Cattolica del Sacro Cuore, Rome, Italy, [12]Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, [13]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, University of Milan-Bicocca, Milan, Italy, [14]Department of Infectious Diseases, ASST Grande Ospedale Metropolitano Niguarda, School of Medicine and Surgery, Milan, Italy

ABSTRACT

Background: Direct antiviral agents (DAAs) revolutionized the management of HCV-related liver disease even in presence of advanced fibrosis/cirrhosis. While it is established that people with cirrhosis remain at high risk of liver-related outcomes after sustained virological response (SVR12), long-term data on incidence and relevance of non-liver related clinical significant events (CSE) are lacking.

Methods: We retrospectively assessed the incidence and type of CSE (solid and haematological cancers, cardiovascular diseases, hypertension, diabetes, liver-related events, and death) in PWH after SVR12 with DAA over 2014-2023 in the Icona/HepaIcona cohorts. The "liver-related events" outcome was a composed outcome including liver decompensation, hepatocellular carcinoma, and liver transplantation. Incidence risks (with 95% CI) of events past SVR were calculated as number of events per total number of participants. We used an outcome-wide analysis approach with a single exposure (liver disease stage at SVR), 6 CSE outcomes and the same set of confounders in separate Poisson regression models for all outcomes. Liver disease stage at SVR was classified using the Baveno VII consensus definition.

Results: Overall, 2,034 people who achieved SVR12 were included: they were mostly males (76%), with a median age of 53 (IQR:50-56) years, 95% had an undetectable HIV RNA, and median CD4+ T cell count was 632 (IQR:431-865) cell/mm3. Median follow up was 5.20 (IQR: 3.07-6.29) years.

years (IQR). Participants' main characteristics are shown overall and by liver disease stage in Table 1A. Over follow up, we observed a total of 467 incident CSE, the most frequent ones were diabetes (n=205, incidence risk=12.1%, 95% CI: 10.5-13.7) and death (n=100, incidence risk=4.9%, 95% CI: 4.0-5.9).

The outcome wide analysis (Table 1B) showed that people with compensated advanced chronic liver disease (cACLD) and clinically significant portal hypertension (CSPH) as by Baveno VII had a significantly higher incidence of liver-related events (IRR: 11.7, 95% CI 4.1 -33.5) and diabetes (HR: 1.3, 95% CI 1.0-1.6) while we found null results for all other CSE. Of note, there was no evidence that participants with cACLD "grey zone" (i.e., minimal risk of transitioning to further stages of liver disease) were at higher risk of CSE compared to those with no or low stage liver disease.

Discussion: In our large cohort of HIV/HCV positive individuals who achieved SVR12 we observed a concerningly high incidence of CSE over 5 years after viral eradication. Individuals with cACLD/CSPH showed a significantly higher risk of developing further liver events and diabetes compared to those with lower liver disease stage but, after controlling for confounding there was no evidence that liver disease stage at SVR was predictive of other CSE. These data provide innovative insights on the natural history of liver disease after viral eradication.

Table 1A. Main characteristics of the study population, overall and by liver disease stage.

Median(IQR)/n(%)	Overall	No or low fibrosis	cACLD "grey zone"	cACLD and CSPH	p
n	2034	1230	381	423	
fibr_cat					<0.001
F0-2	1230 (60.5)	1230 (100.0)	0 (0.0)	0 (0.0)	
F3	288 (14.2)	0 (0.0)	288 (75.6)	0 (0.0)	
F4	516 (25.4)	0 (0.0)	93 (24.4)	423 (100.0)	
Age	53.00 (50.00, 56.00)	53.00 (49.00, 56.00)	53.00 (50.00, 56.00)	53.00 (51.00, 57.00)	0.034
Sex, male	1549 (76.2)	912 (74.1)	285 (74.8)	352 (83.2)	0.001
BMI_cat					<0.001
1	81 (4.0)	57 (4.6)	13 (3.4)	11 (2.6)	
2	873 (42.9)	581 (47.2)	139 (36.5)	153 (36.2)	
3	379 (18.6)	206 (16.7)	69 (18.1)	104 (24.6)	
4	76 (3.7)	36 (2.9)	20 (5.2)	20 (4.7)	
missing	625 (30.7)	350 (28.5)	140 (36.7)	135 (31.9)	
Baseline comorbidities					
Diabetes	333 (16.4)	187 (15.2)	60 (15.7)	86 (20.3)	0.046
Hypertension	558 (27.4)	307 (25.0)	105 (27.6)	146 (34.5)	0.001
Cancer hematologic	42 (2.1)	30 (2.4)	2 (0.5)	10 (2.4)	0.064
Cancer solid	83 (4.1)	50 (4.1)	16 (4.2)	17 (4.0)	0.991
AIDS	298 (14.7)	171 (13.9)	59 (15.5)	68 (16.1)	0.484
Cardiovascular event	58 (2.9)	32 (2.6)	9 (2.4)	17 (4.0)	0.261
Liver event	174 (8.6)	41 (3.3)	34 (8.9)	99 (23.4)	<0.001
HIV RNA>50 copies/ml	107 (5.3)	52 (4.2)	31 (8.1)	24 (5.7)	0.011
HBsAG					<0.001
Negative	1370 (67.4)	926 (75.3)	222 (58.3)	222 (52.5)	
Positive	48 (2.4)	20 (1.6)	13 (3.4)	15 (3.5)	
missing	616 (30.3)	284 (23.1)	146 (38.3)	186 (44.0)	
CD4+ T cell count	632.00 (431.00, 865.00)	672.00 (479.25, 894.50)	634.00 (424.00, 859.00)	492.00 (306.00, 734.50)	<0.001
HSI_cat					<0.001
<36	960 (37.2)	643 (16.5)	144 (37.8)	173 (40.9)	
>36	446 (21.9)	235 (19.1)	97 (25.5)	114 (27.0)	
missing	628 (30.9)	352 (28.6)	140 (36.7)	136 (32.2)	
Smoking status					0.584
No	462 (22.7)	284 (23.1)	87 (22.8)	91 (21.5)	
Si	871 (42.8)	539 (43.8)	155 (40.7)	177 (41.8)	
missing	701 (34.5)	407 (33.1)	139 (36.5)	155 (36.6)	
Alcohol consumption					0.282
No	654 (32.2)	379 (30.8)	137 (36.0)	138 (32.6)	
Si	478 (23.5)	286 (23.3)	85 (22.3)	107 (25.3)	
missing	902 (44.3)	565 (45.9)	159 (41.7)	178 (42.1)	
Intravenous drug use	1474 (72.5)	850 (69.1)	285 (74.8)	339 (80.1)	<0.001

Table 1B. Outcome-wide analysis results (incidence risk ratios from fitting separate Poisson regression models).

Disease	No or low fibrosis	cACLD "grey zone" (95% CI)	cACLD and CSPH (95% CI)	Type III pvalue
Cancer solid	ref	IRR: 0.981 (0.5045-1.905), p=0.953	IRR: 1.341 (0.698-2.576), p=0.379	0.657
Cancer hematological	ref	IRR: 0.000 (0.000-inf), p=0.998	IRR: 0.000 (0.000-inf), p=0.999	0.999
Cardiovascular	ref	IRR: 1.253 (0.517-3.035), p=0.617	IRR: 1.092 (0.441-2.700), p=0.850	0.885
Diabetes	ref	IRR: 0.950 (0.745-1.211), p=0.679	IRR: 1.291 (1.041-1.603), p=0.0203	0.0318
Liver	ref	IRR: 0.673 (0.095-4.774), p=0.692	IRR: 11.692 (4.086-33.460), **p<0.0001**	**<0.0001**
Non-liver related death	ref	HR: 0.879 (0.496-1.559), p=0.660	HR: 1.390 (0.849-2.277), p=0.190	0.240

All model adjusted for age, sex, CD4+ T cell count, BMI categories, HBsAg status, drug and alcohol use, smoking status, HIV viral load, and the presence of diabetes, hypertension, hematological or solid cancer, AIDS, cardiovascular diseases, liver diseases at the baseline. cACLD: compensated advanced chronic liver disease; CSPH: clinically significant portal hypertension.