Safety of Cabotegravir + Rilpivirine Long-Acting Regimen Among PLWH With Previous HBV Exposure

532

N.Bana[1,2] (nicholasbrian.bana@ospedaleniguarda.it.), F.Artelli[2,3], G.Lapadula[2,3], P.Bonfanti[2,3], P.Vitiello[4], C.Abeli[4], M.Farinazzo[4], L.Comi[5], D.Ripamonti[5], D.Valenti[5], M.Puoti[1,2], R.Rossotti[1]

[1]*ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy,* [2]*Università degli Studi di Milano Bicocca, Milan, Italy,* [3]*IRCCS San Gerardo dei Tintori, Monza, Italy,* [4]*ASST Valle Olona, Busto Arsizio (VA), Italy,* [5]*ASST Papa Giovanni XXIII, Bergamo, Italy*

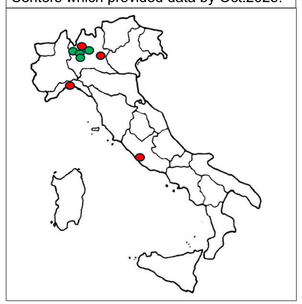
BACKGROUND

- Cabotegravir + Rilpirivirine Long-Acting (CARLA) is the first and only complete long-acting injectable cART regimen.
- People with resolved Hepatitis B (HBcAb+, HBsAb+/-, HBsAg-) can show a cryptic HBV replication in blood or liver, in the context of Occult HBV Infection (OBI).
- OBI can be associated with hepatitis flares, impaired liver function and HBV reactivation in particular conditions.
- CARLA is not recommended among PLWH with active HepB (HBsAg+), since it does not contain any drug with anti-HBV activity.
- No data exist about CARLA hepatic safety among PLWH with resolved HepB.
- Aim of this study is to demonstrate CARLA liver safety among PLWH with resolved HepB, and to describe any possible HBV reactivation over a long follow-up time.

METHODS

- SCRIBE ("Safety of Cabotegravir + Rilpivirine long-acting Injectable regimen among PLWH with previous HBV Exposure") is a multicenter retrospective observational study, including all PLWH switched to CARLA since this regimen availability, with no active HBV infection. Here preliminary data of this study are shown.

Fig.1: Participating Centers; in green dots, Centers which provided data by Oct.2025.



- For any individual, demographic data, information about liver health and CARLA retention in care, HIV related past-medical history and laboratory data were collected.
- Participants were divided into 2 cohorts: people with no exposure to HBV (HBcAb-, HBsAb+/-) and individuals with resolved HepB (HBcAb+, HBsAb+/-).
- CARLA hepatic safety was assessed by describing any significant changes of ALT and FIB-4 trend over time, using a mixed linear model with a random intercept and slope adjustment.
- Hepatitis flares (increase 3X the ALT normal values) incidence rate was reported, and factors associated with hepatitis flares were described using standard survival analyses.
- Results were corrected by confounding variables: hepatic steatosis defined by HSI (Hepatic Steatosis Index), alcohol intake and HCV exposure.

Long-Acting CAB/RPV regimen was associated with liver safety among PLWH with resolved HepB over a long follow-up time.

RESULTS

- 394 PLWH were included: 283 (71.8%) with no HBV exposure, 111 (28.2%) with Resolved HepB. Participants' main features are shown in Tab.1.
- At a descriptive analysis the following factors were associated with Resolved HepB status: older age (p<0.001), use of injectable drugs (p<0.001), longer HIV infection (p<0.001), previous HCV exposure (p=0.001), higher FIB-4 score (p<0.001) and higher ALT values (p=0.015).

Tab.1: Main features of study population.

		Overall (N=394)	HBV unexposed (N=283)	Resolved Hepatitis B (N=111)
Gender: Males, n (%)		323 (82.0)	230 (86.3)	93 (83.8)
Age, years, median (IQR)		48 (40-57)	45 (38-54)	56 (49-61)
Italian born, n (%)		326 (82.7)	230 (81.3)	96 (86.5)
Type of risk exposure, n (%)	GBMSM	219 (55.6)	163 (57.6)	56 (50.5)
	MSW/WSM	121 (30.7)	96 (33.9)	25 (22.5)
	IVDU	39 (9.9)	11 (3.9)	28 (25.2)
	Other	15 (3.8)	13 (4.6)	2 (1.8)
BMI, median (IQR)		24.5 (22.6-27.2)	24.4 (22.5-26.8)	25.0 (22.8-27.9)
Length of infection, years, median (IQR)		11.5 (6.9-18.7)	10.6 (5.8-15.6)	17.8 (10.1-27.0)
CD4 nadir, cell/mmc, median (IQR)		340 (141-514)	360 (157-515)	303 (140-454)
Liver steatosis (HSI>36), n (%)		121 (30.7)	89 (31.5)	32 (28.8)
Alcohol use: Abuse, n (%)		18 (4.6)	13 (4.6)	5 (4.5)
Number of previous therapeutic lines, median (IQR)		3 (2-5)	3 (2-5)	4 (3-6)
Isolated HBcAb+, n (%)		23 (5.8)	--	23 (20.7)
Previous HCV infection, n (%)		45 (11.4)	22 (7.8)	23 (20.7)
FIB-4, median (IQR)		0.90 (0.68-1.24)	0.82 (0.64-1.15)	1.08 (0.85-1.41)
ALT, IU/ml, median (IQR)		21 (16-30)	22 (16-32)	20 (15-27)
Follow up, years, median (IQR)		1.98 (0.99-2.53)	1.98 (0.99-2.53)	1.98 (1.15-2.38)
CARLA Discontinuation, n (%)		68 (17.3)	50 (17.7)	18 (16.2)
Virologic failure, n (%)		10 (2.5)	4 (1.4)	6 (5.4)
Hepatitis flares, n (%)		9 (2.3)	4 (1.4)	5 (4.5)

Legend: GBMSM: Gay, Bisex and other Men who have Sex with Men; MSW/WSM: Men who have Sex with Women/Women who have sex with Women; IVDU: Intravenous Drugs Users; BMI: Body Mass Index; IQR: Interquartile range.

- At a mixed linear model, resolved Hepatitis B status was not associated with any significant effect on ALT trend over time, while liver steatosis defined by HSI seemed to have a significant impact, even with an increase of only 0.88 IU/ml for every point of the HSI score (p<0.001).
- Resolved Hepatitis B status did not have any significant impact on FIB-4 over time. HCV exposure tended to be associated with increased FIB-4 score, but at the limit of statistical significance (coef.0.14, 95%CI -0.03-0.31, p=0.096).

Fig.2. ALT predicted trend over time (IU/ml) in HBV-unexposed individuals and PLWH with resolved HepB.

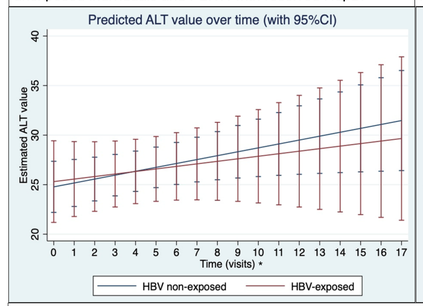
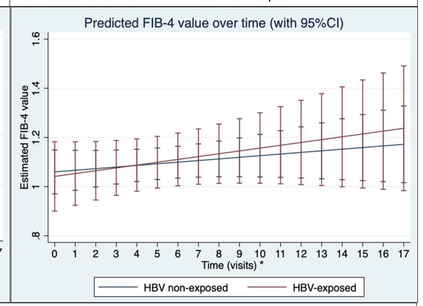


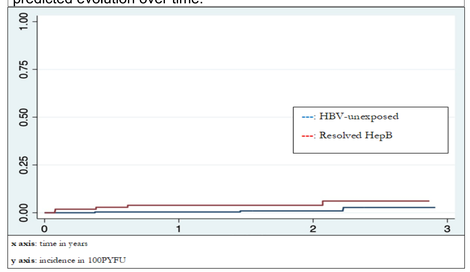
Fig.3. FIB-4 predicted trend over time in HBV-unexposed individuals and PLWH with resolved HepB.



* Visit 1 at day 28, Visit 2 at day 84, then every 56 days, according to CARLA injections schedule.

- 9 hepatitis flares were observed: 4/283 (1.4%) in people not exposed to HBV, 5/111 (4.5%) among individuals with resolved HepB.
- No significant difference in hepatitis flares incidence was seen between the two groups: IRR 0.32 (95%CI 0.08-1.25), p=0.09.

Fig.4. Kaplan-Meyer's curves showing hepatitis flares incidence predicted evolution over time.



- At a Cox's regression analysis, only HSI was associated with higher risk of hepatitis flare (aHR 1.10 for every point of HSI increase, 95%CI 1.00-1.21, p=0.04). No impact was seen for HBV and HCV exposure, nadir CD4+ cell count and alcohol intake.
- Isolated HbcAb+ status was strongly associated with higher risk of hepatitis flare over time (aHR 11.15, 95%CI 1.67-74.28, p=0.013), even if a small number of flares was detected overall.
- No confirmed cases of HBV reactivation were observed. For one person with isolated HBcAb+ a flare was described, with HBsAb seroconversion and HBV DNA 17 IU/ml, followed by spontaneous resolution.

CONCLUSIONS

- PLWH with resolved HepB were older and more ART-experienced, with more prevalence of IVDU.
- CARLA was associated with liver safety profile among people with resolved HepB, with no impact on FIB-4 and ALT trend over time.
- Hepatitis flares seemed to be mainly related to liver steatosis.
- No HBV reactivations on CARLA was seen after a long follow-up time.

PLAIN LANGUAGE SUMMARY: Long-acting injectable regimen based on Cabotegravir + Rilpirivine seems to be safe even among people with previous exposure to Hepatitis B virus, although it does not contain any drug with anti-HBV activity.