Lack of Compliance to Hepatocellular Carcinoma (HCC) Screening Guidelines in Hepatitis B (HBV) or C (HCV) Virus co-infected with HIV Patients with Cirrhosis

C. Smit on behalf of the HCC screening project working group for the collaboration of observational HIV Epidemiological Research Europe (COHERE) In EuroCoord.

Project team S.B. Willemse, C. Smit, P.S. Sogni, M. Sarcletti, C. Uberti-Foppa, D. Barger, D. Raben, F. Dabis, A. d'Arminio-Monforte, L. Wittkop, M. van der Valk.

Executive Committee: Stéphane de Wit (Chair, St. Pierre University Hospital), Jose Mª Miró (PISCIS), Dominique Costagliola (FHDH), Antonella d'Arminio-Monforte (ICONA), Antonella Castagna (San Raffaele), Julia del Amo (CoRIS), Amanda Mocroft (EuroSida), Dorthe Raben (Head, Copenhagen Regional Coordinating Centre), Geneviève Chêne (Head, Bordeaux Regional Coordinating Centre). **Steering Committee:** Robert Zangerle (AHIVCOS), Giota Touloumi (AMACS), Josiane Warszawski (ANRS CO1 EPF/ANRS CO11 OBSERVATOIRE EPF), Laurence Meyer (ANRS CO2 SEROCO), François Dabis (ANRS CO3 AQUITAINE), Murielle Mary Krause (ANRS CO4 FHDH), Jade Ghosn (ANRS CO6 PRIMO), Catherine Leport (ANRS CO8 COPILOTE), Linda Wittkop (ANRS CO13 HEPAVIH), Peter Reiss (ATHENA), Ferdinand Wit (ATHENA), Maria Prins (CASCADE), Heiner Bucher (CASCADE), Caroline Sabin (CHIC), Diana Gibb (CHIPS), Gerd Fätkenheuer (Cologne-Bonn), Julia Del Amo (CoRIS), Niels Obel (Danish HIV Cohort), Claire Thorne (ECS), Amanda Mocroft (EuroSIDA), Ole Kirk (EuroSIDA), Christoph Stephan (Frankfurt), Santiago Pérez-Hoyos (GEMES-Haemo), Osamah Hamouda (German ClinSurv), Barbara Bartmeyer (German ClinSurv), Nikoloz Chkhartishvili (Georgian National HIV/AIDS), Antoni Noguera-Julian (CORISPE-cat), Andrea Antinori (ICC), Antonella d'Arminio Monforte (ICONA), Norbert Brockmeyer (KOMPNET), Luis Prieto (Madrid PMTCT Cohort), Pablo Rojo Conejo (CORISPES-Madrid), Antoni Soriano-Arandes (NENEXP), Manuel Battegay (SHCS), Andri Rauch (SHCS), Cristina Mussini (Modena Cohort), Pat Tookey (NSHPC), Jordi Casabona (PISCIS), Jose M. Miró (PISCIS), Antonella Castagna (San Raffaele), Deborah_Konopnick (St. Pierre Cohort), Tessa Goetghebuer (St Pierre Paediatric Cohort), Anders Sönnerborg (Swedish InfCare), Carlo Torti (Italian Master Cohort), Ramon Teira (VACH), Myriam Garrido (VACH), David Haerry (European AIDS Treatment Group); *Paediatric cohort representatives:* Ali Judd, Pablo Rojo Conejo. **Regional Coordinating Centres:** Bordeaux RCC: Diana Barger, Christine Schwimmer, Monique Termote, Linda Wittkop; Copenhagen RCC: Maria Campbell, Nina Friis-Møller, Jesper Kjaer, Dorthe Raben, Rikke Salbøl Brandt. *European AIDS Treatment Group:* David Haerry. **Funding sources:** The COHERE study group has received unrestricted funding from: Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), France; HIV Monitoring Foundation, the Netherlands; and the Augustinus Foundation, Denmark. The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under EuroCoord grant agreement n° 260694. A list of the funders of the participating cohorts can be found at www.COHERE.org.

Contact

Colette Smit
Stichting HIV Monitoring
E: colette.smit@amc.uva.nl

www.hiv-monitoring.nl

Background

The incidence of hepatocellular carcinoma (HCC) in HBV or HCV HIV-co-infected patients is increasing possibly due to an increase in the prevalence of cirrhosis.[1] Since 2005 guidelines recommend HCC screening by ultrasonography every 6 months in patients with cirrhosis.[2-5]

Aim

We assessed compliance with HCC screening guidelines in HBV and HCV HIV-co-infected patients with cirrhosis.

Methods

Patients with cirrhosis and HCV or HBV HIV-co-infection from 4 cohorts from The Netherlands, France, Austria and Italy participating in the COHERE collaboration (www.Cohere.org) were followed between 1 January 2005 and 1 January 2015.

HBV co-infection was defined as being HBsAg positive and HCV co-infection as HCV antibody-positivity.

Assessment of liver cirrhosis was based on a) clinical diagnosis reported in the chart, b) liver biopsy, c) fibroscan result (>11.8 kPa for HBV and >12.6 kPa for HCV), or d) APRI-score >2.0.

Compliance to HCC screening guidelines was defined as at least one ultrasound every 6.5 months (during follow-up time). Generalized estimating equation (GEE) models adjusted for repeated measurements were fitted to determine the predictors of the lack of compliance to HCC screening guidelines.

Sensitivity analyses were conducted, in which:

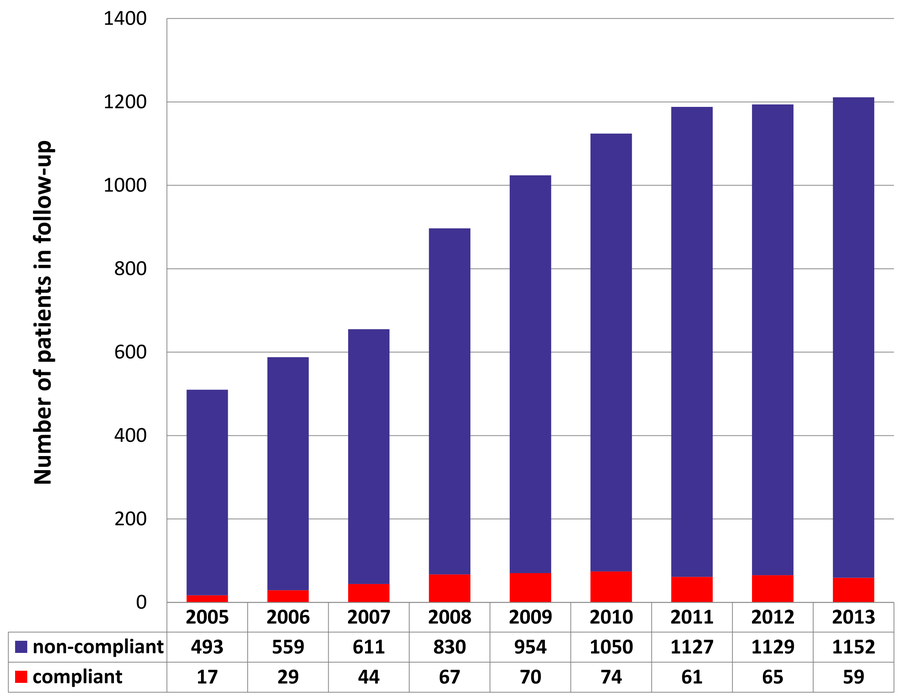
- patients with a cirrhosis assessment using APRI-score were excluded;
- the allowed time in between ultrasounds was extended to 9 and 12 months.

Results

Table 1. Demographic characteristics

Total	N	**1743**
Cohort	AHIVCOS (%)	327 (19)
	ATHENA (%)	763 (44)
	HEPAVIH (%)	337 (19)
	HSR (%)	316 (18)
Age at cirrhosis diagnosis	Years, median (IQR)	43 (36-48)
Gender	Male/Female (%)	1387/356 (80/20)
Region of origin	Western (%)	1451 (83)
	Sub Saharan Africa (%)	131 (8)
	Other (%)	161 (9)
Transmission route of HIV	IDU (%)	772 (44)
	MSM (%)	555 (32)
	Heterosexual (%)	246 (14)
	Other (%)	69 (4)
	Unknown (%)	101 (6)
Hepatitis co-infection	HCV (%)	1306 (75)
	HBV (%)	320 (18)
	HCV&HBV (%)	117 (7)
Use of cART	N (%)	1676 (96)
Follow up time in years	Median (IQR)	6.2 (3.7-9.7)
Cirrhosis diagnosis	Chart / Fibroscan / Liver biopsy (%)	646 (37)
	Chart (%)	*563 (87)*
	Liver biopsy (%)	*12 (2)*
	Fibroscan (%)	*71 (11)*
	Apri-score > 2.0 (%)	1097 (63)

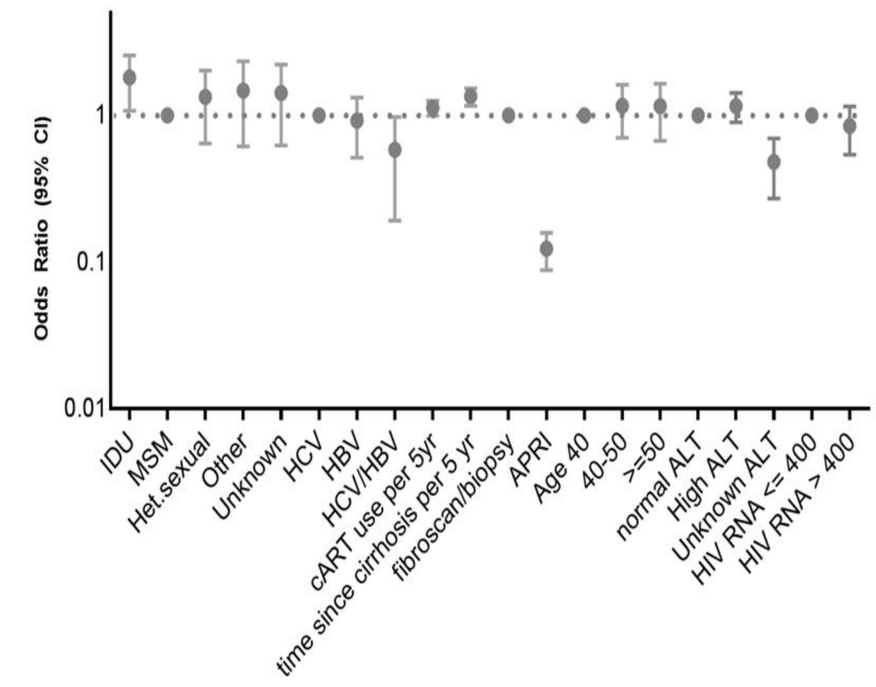
Figure 1. Compliance to HCC screening ≤6.5 months varied between 3% (2005) and 7% (2007-2010).



	2005	2006	2007	2008	2009	2010	2011	2012	2013
non-compliant	493	559	611	830	954	1050	1127	1129	1152
compliant	17	29	44	67	70	74	61	65	59

Figure 2. Adjusted odds ratios for compliance to HCC screening (≤6.5 months between two ultrasounds).

In multivariate analysis, longer cumulative combination antiretroviral therapy (cART) use, longer time since diagnosis of cirrhosis and injecting drug use (IDU) were associated with a higher compliance. Lack of ALT measurements, assessment of cirrhosis by APRI score and HBV+HCV co-infection were associated with a lower compliance.



Sensitivity analyses

If all patients with cirrhosis assessment using APRI-score were excluded, HCC screening compliance increased and varied between 5% in 2005 and 18% in 2008. If screening intervals were increased to 9 and 12 months, compliance varied between 4% and 11% with 9 months interval and between 4% and 15% for the 12 months interval.

Conclusions

Compliance with HCC screening recommendations in at-risk HBV and/or HCV HIV-co-infected patients is low in Europe. In the light of an aging population and subsequently an increasing prevalence of liver cirrhosis this is a situation that needs to be addressed urgently.

References

1. Gjaerde et al. Clin Infect Dis 2016.
2. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. J Hepatol 2012.
3. Bruix J and Sherman M. Management of Hepatocellular Carcinoma. Hepatology 2005.
4. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology 2011. 5. European AIDS Clinical Society (EACS). 2015 Guidelines for the treatment of adult HIV-positive persons. Version 8.0. October 2015.