Does availability of new DAAs influence treatment uptake in acute hepatitis C in HIV coinfection?

Christoph Boesecke[1,2,3], Mark Nelson[4], Patrick Ingiliz[5], Thomas Lutz[6], Stefan Scholten[7], Christoph D. Spinner[8], Michael Rausch[9], Thomas Reiberger[10], Stefan Mauss[11], Jürgen K. Rockstroh[1,2,3], and the PROBE-C study group

1) Bonn University Hospital, Bonn, Germany; 2) German Centre for Infection Research (DZIF), Partner Site Cologne-Bonn, Bonn, Germany; 3) NEAT ID Foundation, London, UK; 4) Chelsea and Westminster Hospital, London, UK; 5) MiB, Berlin, Germany; 6) Infektiologikum, Frankfurt/Main, Germany; 7) Praxis Hohenstaufenring, Cologne, Germany; 8) Interdisciplinary HIV Centre (IZAR), University Hospital Klinikum rechts der Isar, Munich, Germany; 9) Ärztezentrum Nollendorfplatz, Berlin, Germany; 10) Medical University of Vienna, Vienna, Austria; 11) Center for HIV and Hepatogastroenterology, Düsseldorf, Germany

CROI 2015
Abstract #670

Christoph Boesecke MD
Department of Medicine I
University Hospital Bonn
Sigmund-Freud-Str.25
53127 Bonn · Germany
Tel +49 228 287 16558
Fax +49 228 287 15034
christoph.boesecke@ukb.uni-bonn.de

Abstract

Background: With the availability of newer DAAs for treatment of chronic hepatitis C infection (HCV) HCV therapy has become considerably less toxic and even more successful than treatment of acute hepatitis C infection (AHC) with pegylated interferon (pegIFN) and ribavirin (RBV). Current DAA-based regimens are not approved for treatment of AHC and thus, also not reimbursed. Here we evaluate potential changes in the annual rates of treatment initiation in Europe for AHC coinfection in the DAA era.

Methods: The PROBE-C study is an observational European cohort on AHC in HIV coinfection. Between Feb 2007 and Aug 2014 483 AHC episodes were documented in 461 HIV-infected patients from Austria, Denmark, France, Germany, Great Britain and Spain. Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.

Results: All patients were male, median age was 41 years. Main routes of transmission were MSM (97.4%) and IVDU (2.6%). 77.4% of patients were infected with HCV GT1 and 18.9% with GT4. Median baseline HCV-RNA was 2.019.500IU/mL and median CD4+ T cell count 478 cells/µL. 93% of all patients received cART, 86% had baseline suppressed HIV-RNA (<200copies/mL). Median ALT was 388 U/l. In 60/483 (12.4%) episodes AHC resolved spontaneously, in 309/483 (64%) treatment with pegIFN/RBV was initiated within 24 weeks of AHC diagnosis. Median time from diagnosis to treatment initiation was 8 weeks. SVR rate was 70%.
Overall, as shown in table 1 there was an increase in treatment initiation for AHC from 2007-2012. However, since 2012 an annual decline from 76% to 45% was observed. There was no association between treatment initiation and HCV transmission risk, HCV GT, HCV RNA levels nor baseline ALT.

Conclusions: Treatment uptake for AHC has substantially decreased in the last 2 years potentially reflecting patients' and/or physicians' wish for a short, well-tolerated and highly successful DAA-based therapy which to date is only approved and reimbursed for treatment of chronic HCV infection. However, when treatment during AHC is withhold, more patients remain viremic, which then may foster the epidemic of AHC among HIV-infected MSM. Therefore, studies evaluating safety and efficacy of IFN-free DAA regimens for AHC are urgently needed.

Background

With the availability of newer DAAs for treatment of chronic hepatitis C infection (HCV) HCV therapy has become considerably less toxic and even more successful than treatment of acute hepatitis C infection (AHC) with pegylated interferon (pegIFN) and ribavirin (RBV). Current DAA-based regimens are not approved for treatment of AHC and thus, also not reimbursed. Here we evaluate potential changes in the annual rates of treatment initiation in Europe for AHC coinfection in the DAA era.

Methods

The PROBE-C study is an observational European cohort on AHC in HIV coinfection. Between February 2007 and December 2014 591 AHC episodes were documented in 538 HIV-infected patients from Austria, Denmark, France, Germany, Great Britain and Spain. Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.

Results

All patients were male, median age was 41 years. Main routes of transmission were MSM (99.4%) and IVDU (0.6%). 77.2% of patients were infected with HCV GT1 and 18.9% with GT4. Median baseline HCV-RNA was 2.190.460IU/mL and median CD4+ T cell count 466 cells/µL. 74.4% of all patients received cART, of those 86% had baseline suppressed HIV-RNA (<200copies/mL). Median ALT was 349 U/l. In 62/509 (12.2%) episodes AHC resolved spontaneously, in 331/509 (65%) treatment with pegIFN/RBV was initiated within 24 weeks of AHC diagnosis. Median time from diagnosis to treatment initiation was 8 weeks. SVR rate was 70.1% (see table 1 and figure 1).

Median age [years] (IQR)	Transmission risk [%]		Median CD4-cells [/µl] (IQR)	HIV-RNA <200copies /ml [%]	cART [%]	Median HCV-RNA [IU/ml] (IQR)	HCV-RNA >800.000 IU/ml [%]	HCV-Genotype [%]		Median maximum ALT [U/l] (IQR)	Clinical symptoms* [%]	Median time from diagnosis to treatment [weeks] (IQR)	SVR rate [%]
	MSM	IVDU						1	4				
41 (38-46)	99.4	0.6	466 (340-702)	86	74.4	2.190.460 (701.550-6.880.000)	67	77.2	18.9	349 (160-644)	19	8 (7-11)	70.1

Table 1: Baseline characteristics

* Fatigue, abdominal pain, jaundice

Overall, as shown in table 2 there was an increase in treatment initiation for AHC from 2007-2012. However, following the European licensing of two first generation HCV protease inhibitors in 2011 for the treatment of chronic HCV an annual decline from 71% to 55.7% since 2012 could be observed.

Year	2007	2008	2009	2010	2011	2012	2013	2014
# treated per newly diagnosed AHC episodes (%)	10/16 (62.5)	22/45 (48.9)	31/41 (75.6)	42/60 (70)	78/121 (64.5)	88/124 (71)	76/117 (65)	34/61 (55.7)
Relative change in treatment uptake	N/A	-13.6%	+26.7%	-5.6%	-5.5%	+6.5%	-6%	-9.3%

Table 2: Annual rates of treatment initiation for new AHC diagnoses from 2007 to 2014

↖ *Licensing of first HCV PIs in Europe*

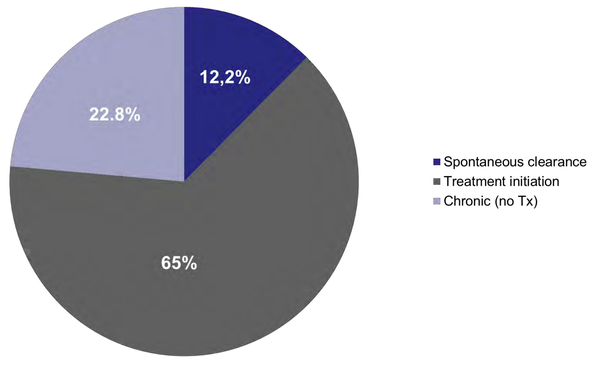

Figure 1. Overall outcome of AHC episodes (n=591)

There was no statistically significant association between treatment initiation and HCV transmission risk, HCV GT, HCV RNA levels nor baseline ALT.

Conclusions

Treatment uptake for AHC has substantially decreased in the last 2 years potentially reflecting patients' and/or physicians' wish for a short, well-tolerated and highly successful DAA-based therapy which to date is only approved and reimbursed for treatment of chronic HCV infection. However, when treatment during AHC is withheld, more patients remain viremic, which then may foster the epidemic of AHC among HIV-infected MSM. Therefore, studies evaluating safety and efficacy of IFN-free DAA regimens for AHC are urgently needed.

Acknowledgements

We extend our grateful thanks to all study participants and contributing investigators: Austria: Mattias Mandorfer; Denmark: Lars Peters; France: Julie Bottero, Karine Lacombe, Marc-Antoine Valantin; Germany: Axel Baumgarten, Christiane Cordes, Gerd Fätkenheuer, Susan-Beatrice Franz, Tobias Glaunsinger, Arne Jessen, Heiko Jessen, Heribert Knechten, Tim Kümmerle, Christoph Mayr, Antonius Mutz, Ramona Pauli, Stephan Schneeweiss, Dietmar Schranz, Carolynne Schwarze-Zander, Miriam Speer, Luca Stein, Andreas Trein, Martin Vogel, Jan-Christian Wasmuth, Christoph Wyen; Netherlands: Bart Rijnders; Spain: Bonaventura Clotet, Jordi Puig, Cristina Segundo, Vincent Soriano, Cristina Tural; UK: Sanjay Bhagani, Martin Fisher, Richard Gilson, Gurmit Jagjit Singh, Emma Page, Daniel Webster.
The PROBE-C study is funded by NEAT ID, German Centre for Infection Research (DZIF) and Deutsche Leberstiftung. The European AIDS Treatment Network (NEAT) was funded by the European Union under the 6th Framework programme number LSHP-CT-2006-037570.