Has increased rollout of DAA therapy decreased the burden of late presentation and advanced liver disease in patients starting HCV therapy in Germany?

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Abstract # PO1/12

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Background

Directly-acting agents (DAA) against HCV have impressively improved treatment outcome of HCV therapy including patients with cirrhosis. To date, it remains unclear if wide-spread DAA usage has already led to a reduction in HCV-positive patients presenting with advanced liver disease. More recently, a consensus definition of advanced liver disease has been developed which defines advanced liver disease due to chronic viral hepatitis as a patient with chronic hepatitis B, C or D who shows significant fibrosis (≥F3 assessed by APRI score >1.5, FIB-4 >3.25, Fibrotest >0.59 or alternatively a transient elastography (FibroScan) >9.5 kPa) with no previous antiviral treatment. Therefore, we assessed the proportion of HCV-positive patients presenting with advanced liver disease at DAA treatment initiation over time in the German hepatitis C cohort (GECCO).

Methods

The GECCO cohort is a multicenter cohort from 9 German sites. All treatment-naïve HCV mono- (n=822) and coinfected (n=197) patients (n=1019) initiating DAA-based treatment since 2014 were analysed. Advanced liver disease was considered a liver stiffness >9.5 kPa in transient elastography (n=718) or APRI score >1.5 (n=301). HCV-RNA PCR testing was done with Roche COBAS® AmpliPrep/COBAS® TaqMan® Version 2.0 HCV Test with a lower limit of quantification (LLQ) of 15 IU/ml or Abbott RealTime HCV assay® with a LLQ of 12 IU/mL. Fisher's exact, chi-square and Mann-Whitney U test were used for statistical analysis.

Results

651/1019 (64%) patients were male, median age was 50 years (IQR:41-57) (see table 1). HCV genotype (GT) distribution was: GT1 60%, GT2 5%, GT3 30%, GT4 5% (see figure 1). 129/416 (31%) had IL28B C/C GT polymorphism. Median baseline HCV RNA was 1.000.000 Mio IU/mL (288.327-2.933.105). Median baseline ALT was 69 U/l (43-121). Liver cirrhosis was present in 219/1019 (22%). Median baseline CD4 was 585/ul (398-768). 254/1019 (25%) were on opiate substitution therapy (OST). Overall SVR rate was 87.9%.

Table 1. Baseline Characteristics

	n=1019
Median age [years] (IQR)	50 (41-57)
Sex male [%] (n)	64 (651)
Median CD4-cells [/µl] (IQR)	585 (398-768)
Median HCV-RNA [IU/ml] (IQR)	1.000.000 (288.327-2.933.105)
IL28B C/C GT [%]	31 (129/416)
Median baseline ALT [U/l] (IQR)	69 (43-121)
Liver cirrhosis [%] (n)	22 (219/1019)
OST [%]	25 (254/1019)

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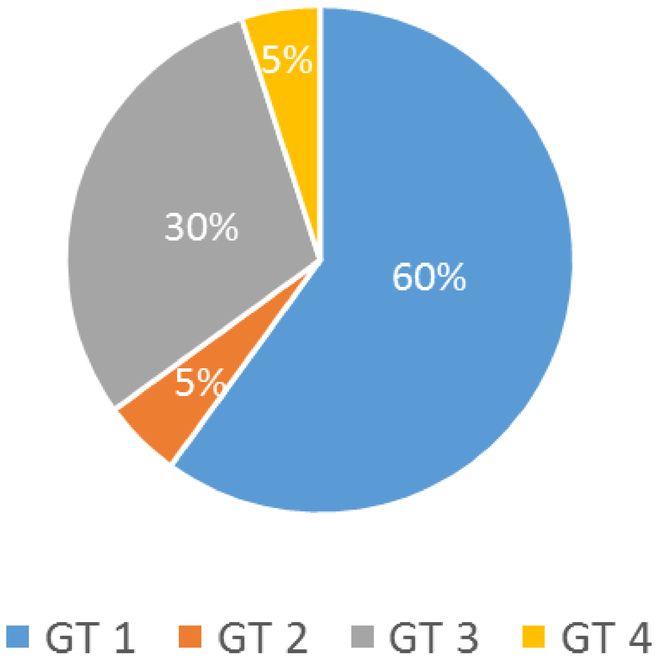
Results

Figure 1. HCV genotype (GT) distribution



In 2014 44% (115/264) of all patients presented with advanced liver disease (see table 2). In the following years that proportion decreased to 25% (147/586) in 2015 and 30% (50/169) in 2016 (p<0.001).

Table 2. Distribution of DAA-treated HCV patients with/without advanced liver disease over time

Year	% no/minimal fibrosis (n)	% advanced fibrosis (n)
2014 (n=264)	56 (149)	44 (115)
2015 (n=586)	75 (439)	25 (147)
2016 (n=169)	70 (119)	30 (50)

Conclusions

In line with recommendations from clinical guidelines our real life data confirm that initially DAA therapy was prioritized to HCV patients with advanced liver disease. As a consequence the proportion of patients initiating DAA-based therapy with no or minimal HCV related liver disease has increased in recent years. The use of a consensus definition for advanced liver disease will contribute to both improving the epidemiological understanding of viral hepatitis and other liver diseases as well as testing policies and linkage to care.

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Press release

New consensus definition of late presentation for viral hepatitis

The number of people living with viral hepatitis in increasing – a better understanding of the testing policies and strategies is needed.

Thursday 22 October 2015, Barcelona: Today, EASL and HIV in Europe announce a consensus definition of late presentation for viral hepatitis. The announcement coincides with the European AIDS Conference in Barcelona and aims to encourage policy makers, health professionals, public health institutions and civil society organisations to implement this definition to improve the European surveillance of and response to the viral hepatitis epidemic.

Over 13 million adults are living with hepatitis B and 15 million with hepatitis C in the WHO European Region and most of the people remain undiagnosed. Effective treatments for both HBV and HCV are available with great impact on the possibility to treat people if they are diagnosed timely. However, it remains unknown whether current testing policies and strategies are successful in reaching the undiagnosed population at the right time. Further, linkage to the health care system and their ability to provide comprehensive care is also unknown.

As a consequence, a large proportion of the chronically infected population enters care only after they have developed clinical symptoms and others after the initiation of treatment would have provided them with an optimal treatment response.

A consensus definition on late presentation for viral hepatitis is essential in order for public health authorities in Europe and elsewhere to be able to understand and respond to the issues around late presentation of viral hepatitis. The consensus definition will contribute in both improving surveillance of viral hepatitis as well as testing policies and strategies.

In early 2015 a group of viral hepatitis experts within the HIV Europe Initiative formed a working group to develop a consensus definition for viral hepatitis. After discussions,

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meetings and several reviews the final two agreed upon definitions were approved by the EASL GB in early October 2015:

Definition 1:

Advanced HBV, HCV or HDV associated liver disease is clinically defined by presence of hepatocellular carcinoma or decompensated cirrhosis (jaundice, hepatic encephalopathy, clinically detectable ascites, variceal bleeding).

Definition 2:

Late presentation of HBV or HCV associated liver disease is defined as a patient with chronic hepatitis B or C and significant fibrosis (≥F3 assessed by APRI score >1.5, FIB-4 >3.25, Fibrotest > 0.59 or alternatively a FibroScan >9.5 kPa) with no previous antiviral treatment.

Stefan Mauss, HIV in Europe Steering Committee Member, says: 'this is an important milestone for the public health response to viral hepatitis. A key step will be to convince policy makers, health authorities and researchers to implement the definition to contribute to understanding the magnitude of the proportion of late presenters and monitor and evaluate changes in these numbers.'

In 2011 a consensus definition for late presentation for HIV was presented and has since then been widely implemented in Europe. It has contributed to shed light on the number of people diagnosed late for HIV and has been used to evaluate current testing policies and strategies.

Jürgen Rockstroh, co-chair of the HIV in Europe Steering Committee, continues: 'the HIV late presentation definition has been a valuable tool in assessing current HIV testing strategies and dealing more effectively with HIV testing. I am excited to see improvements in viral hepatitis surveillance and testing as a result of this new definition and hope that it will be well received and widely implemented in Europe and elsewhere as we have seen with the HIV definition.'