Daten aus dem Deutschen Hepatitis C Register

Poster „The Liver Meeting“ 2016 AASLD
Nov 11-15, Boston, USA

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TREATMENT OUTCOMES FOR HEPATITIS C GENOTYPE 1 INFECTION WITH DIRECT ACTING ANTIVIRALS (DAA): DATA FROM THE GERMAN HEPATITIS C-REGISTRY (DHC-R)

Stefan Mauss1, Peter Buggisch2, Klaus H.W. Böker3, Eckart Schott4, Hartwig Klinker5, Rainer Günther6, Heike Pfeiffer-Vornkahl7, Thomas Berg8, Christoph Sarrazin9, Dietrich Hüppe10, Michael P. Manns11, German Hepatitis C-Registry12

INTRODUCTION

In pivotal studies with modern direct acting antivirals (DAA) SVR rates in HCV genotype 1 (GT1) are >90%. However these data were reported in 76%: cardiovascular 27%, psychiatric 15%, drug abuse 14%, diabetes mellitus 10%, thyroid dysfunction 10% and HIV-coinfection 8% being the most frequent.

For the efficacy analysis patients treated with one of the approved regimens for GT1 were considered. Treatment regimens and SVR12 are shown in figure 1. SVR12 ITT overall was 4,445/4,846 (92%) and in the PP analysis SVR12 was 4425/4609 (96%). In GT1a SVR12 ITT was 91% and in GT1b 93%. There was no statistical difference between SVR rates in both subtypes regardless of regime used (figure 2). HCV-coinfected patients (n=247) had an overall SVR12 of 92% which was the same as for HCV-monoinfected patients.

RESULTS

Between 2/2014 and 6/2016 6,606 patients with GT1 have been enrolled. SVR12 data are available for 4,846 patients at the time of the analysis.

Demographics: 57% male, median age 55 years, 98% Caucasian, 50% treatment experienced, 28% liver cirrhosis, 11% with a HCV-RNA >6 Mio IU/mL. Comorbidities were reported in 76%: cardiovascular 27%, psychiatric 15%, drug abuse 14%, diabetes mellitus 10%, thyroid dysfunction 10% and HIV-coinfection 8% being the most frequent.

For the efficacy analysis patients treated with one of the approved regimens for GT1 were considered. Treatment regimens and SVR12 are shown in figure 1. SVR12 ITT overall was 4,445/4,846 (92%) and in the PP analysis SVR12 was 4425/4609 (96%). In GT1a SVR12 ITT was 91% and in GT1b 93%. There was no statistical difference between SVR rates in both subtypes regardless of regime used (figure 2). HCV-coinfected patients (n=247) had an overall SVR12 of 92% which was the same as for HCV-monoinfected patients.

DISCUSSION

Adverse events were reported by 53% of patients with fatigue (23%), headache (16%), nausea (7%) and insomnia (6%) being the most frequent. Serious adverse event were observed in 240 patients (4%) and 30 patients (0.5%) died, 11/30 due to liver associated complications.

CONCLUSION

• Data from this real life cohort show SVR 12 rates close to those obtained in clinical studies.
• Efficacy of interferon free treatment regimens were superior to interferon containing therapy for GT1.
• Physician tailored therapy according to cirrhosis status achieved high response rates not withstandng a remaining lower SVR in cirrhotic patients.
• Discontinuation rates are low confirming good tolerance of the regimens and good adherence of patients.

ACKNOWLEDGEMENTS

We thank all study nurses and all study investigators. Special thanks to Bianka Wiebner as well as Yvonne Serfert for the management of the German Hepatitis C-Registry.

DISCLOSURES

Details of individual authors’ disclosures can be found in the abstract book.
8 weeks treatment under real life conditions with Ledipasvir/Sofosbuvir in HIV co-infected treatment-naive HCV genotype 1 infected patients: with similar results to mono-infected HCV patients: data from the German Hepatitis C-Registry (DHC-R)

Peter Buggisch1, Klaus Böker2, Rainer Günther3, Gerlinde Teuber4, Hartwig Klinker5, Anita Pathil5, Stefan Christensen7, Heike-Pfeiffer-Vornkahl8, Karl-Georg Simon9, Claus Niederau10, Heiner Wedemeyer11, Stefan Zeuzem12, German Hepatitis C-Registry13

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Introduction
Ledipasvir/Sofosbuvir (LDV/SOF) for 8-24 weeks is approved for the treatment of chronic hepatitis C. In the ION-3 study 8 weeks of LDV/SOF was non-inferior to 12 wks in previously untreated GT1 patients without cirrhosis. Although the number of patients eligible for 8 weeks according to the summary of product characteristics (SmPC) is high, a large proportion of patients still gets a longer treatment duration. One of the reasons might be the uncertainty whether 8 weeks treatment duration is sufficient in so called harder to treat populations as HIV co-infected patients, patients on substitution treatment (OST) or older patients (> 70 yrs.). Aim of this analysis was to evaluate the virologic response rates of 8 wks treatment under real world conditions in these patients.

Methods
The DHC-R (Deutsches Hepatitis C-Register) is a registry for the documentation of the HCV treatment situation in Germany. Data are collected in a centralized database and on-site monitoring is implemented. Data collection is ongoing. In this analysis data of patients with 8 or 12 wks treatment with LDV/SOF and available SVR12 data (until 6/2016) were included. Baseline characteristics, prior treatment history, safety and effectiveness were investigated.

Table 1: Patient characteristics

Table 2: More patients are eligible

Table 3: Regression analysis

Conclusions
• Under real world conditions, 8 weeks LDV/SOF achieves comparable SVR rates to 12 weeks treatment even in coinfected patients or patients on OST at older age. The occurrence of cirrhosis seems to be the major factor for relapse. Even following the strict selection criteria more patients could get a shorter treatment duration.

Acknowledgements
We thank all study nurses and all study investigators. Special thanks to Blanka Wiebner as well as Yvonne Serfort for the management of the German Hepatitis C-Registry.

Conflicts of Interests
Details of individual authors’ disclosures can be found in the abstract book.

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Corresponding author: Dr. Peter Buggisch (buggisch@ifi-medizin.de)
Treatment of HCV genotype 2 with sofosbuvir and ribavirin results in low SVR rates in a real world cohort (German Hepatitis C-Registry, DHC-R)

Stefan Mauss1, Rainer Günter2, Peter Buggisch3, Hartwig Klinker4, Andreas Schober5, Christine John6, Thomas Lutz7, Helke Pfeiffer-Vornkahl8, Claus Niederau9, Markus Cornberg10, Christoph Sarrazin11, Frank Tacke12, German Hepatitis C-Registry13

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INTRODUCTION
HCV genotype 2 (GT2) is generally considered to be easy to treat. The current standard therapy is 12 weeks of sofosbuvir (SOF) and ribavirin (RBV). However, due to low patient numbers, sustained virologic response (SVR) rates varied substantially between studies. Therefore, re-assessing the efficacy of interferon-free therapy in cohorts with larger patient numbers is warranted.

PATIENTS & METHODS
The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,300 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring.

RESULTS
Patient characteristics are given in Table 1.

At the time point of the analysis, SVR 12 (ITT) was achieved with SOF+RBV 12 weeks in 136/164 (83%) patients, with SOF+DCV, LDV/SOF treatments. Table 2. Outcome of therapy (SVR12 ITT) in different subgroups

SVR rates for SOF+RBV 12 weeks (ITT) in patients treated per protocol excluding patients discontinuing therapy or being lost to follow up was 135/151 (89%).

5 patients (2.4%) discontinued therapy prematurely, of whom 1 patient had liver cirrhosis. In 3 patients at least one serious adverse event was reported (anemia, ascites, dysphagia, syncopal episode). No patient died.

CONCLUSION
In this large HCV GT2 cohort, therapy with SOF+RBV for 12 weeks achieved a low SVR rate compared to treatment outcomes expected from phase III trials. Even patients with favorable outcome factors did not achieve SVR rates above 90% in clinical practice.

Table 1. Patient characteristics and therapy

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>patients (n=236)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sex: male</td>
<td>141/236 (60%)</td>
</tr>
<tr>
<td>mean age [years] (IQR)</td>
<td>53.4 (46 – 61)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>230/236 (98%)</td>
</tr>
<tr>
<td>Region of birth</td>
<td>Germany 169/236 (72%)</td>
</tr>
<tr>
<td>Former Soviet Union</td>
<td>55/191 (29%)</td>
</tr>
<tr>
<td>HCV RNA [IU/mL] &gt; 2 Mio IU/mL</td>
<td>66/236 (28%)</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>41/236 (17%)</td>
</tr>
<tr>
<td>Prior HCV treatment</td>
<td>65/236 (28%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18/236 (9%)</td>
</tr>
<tr>
<td>Opioid substitution therapy (OST)</td>
<td>22/236 (9%)</td>
</tr>
</tbody>
</table>

Table 2. Outcome of therapy (SVR12 ITT) in different subgroups

<table>
<thead>
<tr>
<th>Variable subgroup</th>
<th>SVR ITT % (n/total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-cirrhotic</td>
<td>Cirrhotic</td>
</tr>
<tr>
<td>Age ≤70 years</td>
<td>85% (136/151)</td>
</tr>
<tr>
<td>HCV RNA &gt; 2 Mio IU/mL</td>
<td>85% (114/134)</td>
</tr>
<tr>
<td>Non-diabetic</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>HCV RNA &gt; 2 Mio IU/mL</td>
<td>83% (126/152)</td>
</tr>
<tr>
<td>Non opioid substitution</td>
<td>Opioid substitution</td>
</tr>
<tr>
<td>Origin outside former Soviet Union (SU)</td>
<td>Origin from former SU</td>
</tr>
<tr>
<td>83% (122/149)</td>
<td>87% (13/15)</td>
</tr>
<tr>
<td>84% (97/116)</td>
<td>81% (30/38)</td>
</tr>
</tbody>
</table>

*data on initial viral load not available for 2 patients
Treatment of patients with hepatitis C virus (HCV) genotype 3 infection in the era of direct acting antivirals (DAA): Data from the German Hepatitis C-Registry (DHC-R)

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INTRODUCTION

Treatment of HCV genotype 3 (GT3) is still more challenging compared to HCV genotype 1. Sustained virological response (SVR) rates for GT3 with the first approved IFN free regimen sofosbuvir (SOF)+ribavirin (RBV) are not satisfactory in patients with cirrhosis. Further treatment options include pegylated interferon (PegIFN)+SOF+RBV for 12 weeks, SOF+ledipasvir (LDV) or SOF+daclatasvir (DCV)+RBV for 12-24 weeks. Data from large cohorts and the real-world are still limited.

PATIENTS & METHODS

The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a monitoring. This data analysis is based on 8,090 patients who started antiviral treatment on or before 30 Sep 2015.

RESULTS

1322 patients with GT3 have been enrolled. Treatment has been initiated in 1,111 patients (Figure 1A, 1B).

CONCLUSION

- Real-world data can validate the effectiveness and safety for treatment regimens that had previously been approved with limited data in particular for specific subgroups of patients.
- The present study demonstrates how rapid new scientific data, new treatment guidelines, new drug approvals, and label changes are implemented into routine clinical practice today.

ACKNOWLEDGEMENTS

We thank all study nurses and all study investigators. Special thanks to Bianka Wiebner as well as Yvonne Serfert for the management of the German Hepatitis C-Registry.

DISCLOSURES

Details of individual authors’ disclosures can be found in the abstract book.
Effectiveness and Safety of DAA Combination Therapies for Treatment of HCV in Elderly Patients (>70 yrs.): Results from the German Hepatitis C-Register (DHC-R)

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INTRODUCTION

Few pivotal trials reported outcomes of novel direct-acting antiviral (DAA) therapies in elderly patients. We investigated effectiveness and safety of all-oral DAA regimens in patients >70 yrs. of age vs. younger patients (<70 yrs.) in the DHC-R.

PATIENTS & METHODS

The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. This data analysis is based on 8,090 patients who started antiviral treatment on or before 30 Sep 2015.

RESULTS

Of 7,133 patients who started all-oral DAA combination treatments, 686 (9.6%) were >70 years of age. Table 1 summarizes demographic and clinical characteristics of the patient population.

Table 1. Demographic and clinical characteristics by age group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>≤70 years (N = 6,447)</th>
<th>&gt;70 years (N = 788)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>3,634/2,813 (56.1%)</td>
<td>417/371 (52.9%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.9 (37-57)</td>
<td>80.0 (70-90)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9 (21.7-31.4)</td>
<td>25.9 (21.7-31.4)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age</td>
<td>70-75</td>
<td>76-80</td>
</tr>
<tr>
<td>BMI</td>
<td>25.9 (21.7-31.4)</td>
<td>25.9 (21.7-31.4)</td>
</tr>
<tr>
<td>Treatment</td>
<td>First-time treatment</td>
<td>Second-time treatment</td>
</tr>
<tr>
<td>Efficacy</td>
<td>90.5% (90.5%)</td>
<td>88.9% (88.9%)</td>
</tr>
<tr>
<td>Safety</td>
<td>90.5% (90.5%)</td>
<td>88.9% (88.9%)</td>
</tr>
</tbody>
</table>

Despite a higher proportion of SAEs and RBV dose modifications in patients >70 years of age, compared to younger patients, few elderly patients were infected with HCV GT 3-6.

CONCLUSION

- In this large real-world cohort, all-oral DAA treatments were effective and well tolerated in patients >70 years of age.

ACKNOWLEDGEMENTS

We thank all study nurses and all study investigators. Special thanks to Bianka Wiberner as well as Yvonne Serfert for the management of the German Hepatitis C-Register.

DISCLOSURES

Details of individual authors’ disclosures can be found in the abstract book.

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Safety and efficacy of IFN- free antiviral therapies in advanced HCV- associated liver cirrhosis: Results from the German Hepatitis C-Registry (DHC-R)

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Introduction

Direct-acting antiviral (DAA) regimens improved the efficacy of chronic HCV treatment. Phase 3 trials suggested lower response rates in patients with liver cirrhosis. However, there is limited information on the efficacy of DAA therapies in interferon- ineligible patients with advanced cirrhosis. To what extent liver function improves in cirrhotic patients receiving interferon-free therapies is unknown.

Methods

The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,300 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. This data analysis is based on 6034 patients who were observed for at least 40 weeks after initiation of antiviral treatment. Patients with advanced liver cirrhosis, defined by at least one of the following criteria: FibroScan >20kPa, Child-Pugh-Score C, MELD >15, liver transplant waiting list, or ascites were excluded. There were 484 patients with cirrhosis included in the analysis.

Patient flow

A total of 763 patients were enrolled between February 1, 2014 and February 15, 2016. Of these patients, 632 finished antiviral treatment. Details of individual authors’ disclosures can be found in the abstract book.

Patient characteristics

Characteristics n (%)

Male/total 479/763 (63)
Age; mean (range) 58 (range 29-81)
HCV- genotype
1 592 (78)
2 17 (2.2)
3 124 (16.3)
4 28 (3.7)
5 1 (0.1)
6 1 (0.1)
Child Pugh Score
A 550 (72)
B 100 (13)
C 9 (1.2)
Oesophageal varices 265 (35)
Ascites at screening 79 (38)

Treatment regimes

Regimen n %
SOF+RBV 74 9.7
SIM+SOF 119 15.6
SIM+SOF+RBV 19 2.5
DCV+SOF 161 21.1
DCV+SOF+RBV 68 8.9
LDV/SOF 12 W 64 8.4
LDV/SOF 24 W 54 7.1
LDV/SOF+RBV 12 W 106 13.9
LDV/SOF+RBV 24 W 40 5.2
OBV/PTV/r+DSV 12 W 9 1.2
OBV/PTV/r+DSV+RBV 12 W 46 6.0
OBV/PTV/r+DSV+RBV 24 W 7 0.4
Total 763 100.0

Virological response

Regimen SVR ITT n %
SOF+RBV 36 65.5
SIM+SOF 88 85.4
SIM+SOF+RBV 15 88.2
DCV+SOF 126 91.3
DCV+SOF+RBV 48 90.6
LDV/SOF 12 W 51 91.1
LDV/SOF 24 W 34 91.9
LDV/SOF+RBV 12 W 77 86.5
LDV/SOF+RBV 24 W 30 90.9
OBV/PTV/r+DSV 12 W 8 100.0
OBV/PTV/r+DSV+RBV 12 W 41 100.0
OBV/PTV/r+DSV+RBV 24 W 2 100.0
Total 556 88.0

Conclusions

• This real-world cohort confirms that DAA treatment is feasible in patients with advanced liver cirrhosis leading to a partial restoration of liver function.
• A broad spectrum of individual treatment regimens was applied reflecting individualization of treatment in this difficult-to-treat cohort.

• Liver function parameters including albumin, bilirubin and prothrombin time improved in the majority of patients during antiviral therapy/follow-up.
• The median platelet count, as a clinical marker of portal hypertension, increased from 88,000/µl at baseline to 108,000/µl during follow-up (p<0.05). Creatinine levels were stable during antiviral treatment.
• SAEs were reported in 8.1% and 4 patients died from cirrhosis associated complications.

Acknowledgements
We thank all study nurses and all study investigators. Special thanks to Blankia Wiebner as well as Yvonne Serfert for the management of the German Hepatitis C-Registry.

Conflicts of Interests
Details of individual authors’ disclosures can be found in the abstract book.

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Corresponding author: Dr. Katja Deterding (deterding.katja@mh-hannover.de)
SVR12 rates under DAA-based HCV therapy from the National German Cohort Study: Does HIV co-infection impair the response to DAA combination therapy?

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INTRODUCTION
More recently, cohort analyses have claimed that HIV co-infection independently impairs the response to direct-acting antiviral (DAA)-based therapy against chronic hepatitis C (HCV) in real-life cohorts (1). The aim of this study was therefore to compare SVR12 rates between HIV/HCV co-infected and HCV mono-infected subjects from the National German HCV cohort.

PATIENTS & METHODS
The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. The aim of this study was therefore to compare SVR12 rates between HIV/HCV co-infected and HCV mono-infected patients mostly had good CD4-counts at baseline (63% >350 CD4-cells/µl; only 2.6% had a CD4-count below 200/µl).

RESULTS
Overall, 488 HIV/HCV coinfected and 5,657 HCV mono infected subjects were included into this analysis. Baseline characteristics for both groups are shown in Table 1. HCV coinfected patients mostly had good CD4-counts at baseline (63% >350 CD4-cells/µl; only 2.6% had a CD4-count below 200/µl).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV/HCV cohort (n=488)</th>
<th>HCV mono-infected (n=5657)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>57.2</td>
<td>58.7</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>53.8 ± 9.2</td>
<td>46.8 ± 9.8</td>
</tr>
<tr>
<td>Cirrhosis (%)</td>
<td>20.6</td>
<td>17.2</td>
</tr>
<tr>
<td>Genotype (GT 1 (%) / GT 2 (%) / GT 3 (%) / GT 4 (%)</td>
<td>78.4 / 6.9 / 10.3 / 2.4</td>
<td>78.4 / 2.2 / 4.0 / 5.7</td>
</tr>
<tr>
<td>HCV treatment-naive</td>
<td>51.4</td>
<td>53.5</td>
</tr>
<tr>
<td>LDV/SOF + / RBV // or DAC + SOF + / RBV // or SOF + RBV // or DAC + PTV / or SOF + PTV / or SOF + PTV // or SOF + PTV + RBV for GT3 (%)</td>
<td>56.6 / 11.3 / 10.1</td>
<td>67.7 / 8.4 / 9.4</td>
</tr>
<tr>
<td>DSV + RBV // or DSV + PEGIFN + RBV // or DSV + PEGIFN + RBV + RBV for GT3 (%)</td>
<td>30.2 / 28.7 / 21.3</td>
<td>45.8 / 12.5 / 14.7 / 12.5</td>
</tr>
<tr>
<td>DSV + RBV // or DSV + PEGIFN + RBV // or DSV + PEGIFN + RBV + RBV for GT4 (%)</td>
<td>13.2 / 20.3 / 27.3</td>
<td>15.6 / 44.3 / 28.6</td>
</tr>
</tbody>
</table>

RESULTS (continued)
Also no difference in HCV SVR12 rate was observed between cirrhotic patients with and without HIV coinfection (see figure 3). Also in the subset of GT1 patients receiving 8 weeks of LDV/SOF no difference in SVR12 rates was noted between HIV- and HIV+ HCV patients (93.7% (n=792) vs. 93.7% (n=741)). Number of treatment discontinuations was low for both groups with 2.4 and 2.1%, accordingly. SAEs leading to discontinuation were noted in 0.5% and 0.8% of patients, death occurred in 0.2% of patients (10 in the HIV-arm, 1 in the HIV+ arm).

FIGURE 3: SVR12 response in cirrhotics per group (ITT)

CONCLUSION
- This analysis from a large national real-life patient cohort finds no difference in HCV cure rates between HIV/HCV and HCV mono infected patients and therefore supports current HCV guidelines which no longer see a need to consider HIV coinfected individuals a special patient population.
- Also in the subset of GT1 patients receiving 8 weeks of Ledipasvir/sofosbuvir no difference in SVR12 rates was noted between HIV- and HIV+ HCV patients.

REFERENCES
1) Neukam K et al., HIV coinfection impairs response to DAA-based HCV therapy. EASL 2016; Abstract: LBP513

ACKNOWLEDGEMENTS
We thank all study nurses and all study investigators. Special thanks to Bianka Wiebner as well as Yvonne Serfert for the management of the German Hepatitis C-Register.

DISCLOSURES
Details of individual authors’ disclosures can be found in the abstract book.

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Prof. Dr. Jürgen Rockstroh (rockstroh@uni-bonn.de)
DAA-Treatment of HCV-infected patients on Opioid Substitution Therapy (OST): does the clinical setting matter? Data from the German Hepatitis C-Registry (DHC-R)

Stefan Christensen1,2, Andreas Schober2, Stefan Mauss3, Heiner Busch1, Rainer Günter4, Gerlinde Teuber5, Peter Buggisch6, Heike Pfeiffer-Vornkahl7, Bernd Weber8, Jens Reimer9, Klaus Weckbecker10, Heiner Wedemeyer11, German Hepatitis C-Registry12

INTRODUCTION
There is growing evidence from clinical studies and real world cohorts that successful DAA treatment could be implemented in PWIDs on OST. Nevertheless it might be useful to get more information about treatment success in different clinical settings and a possible correlation with different medication used for OST.

PATIENTS & METHODS
The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. At time of analysis n = 8878 were enrolled in the cohort and n = 7747 started second generation DDA therapy before 30th of September 2016. Of those n = 5582/7747 patients without OST (NON-OST population) have institution (SI: n= 232/739) and patients treated for both in different institutions (DI: n = 507/739). N = 528/7747 patients on OST and n = 5582/7747 patients without OST (NON-OST population) had completed therapy and at least one follow up documentation (intention to treat [ITT] population), and n = 462/7747 patients on OST and n = 5315/7747 NON-OST had complete data sets allowing a per-protocol (PP) efficacy analysis.

RESULTS
Baseline demographics of all patient groups are shown in table 1 and distribution of therapy of chronic hepatitis C are shown in table 2. Compared to NON-OST more OST patients were younger (median age 46 vs. 54 years), male (79% vs. 57%), Genotype 3 infected (26% vs. 12%) and had a psychiatric comorbidity (25% vs. 15%) at baseline. Cirrhosis was diagnosed in 28% of both patient groups, with a median MELD score of 8 in both groups. SVR12 or SVR 24 data were available for n=528 OST and n=5,582 NON-OST patients. In ITT analysis SVR 12 / SVR 24 was 85,2% in OST and 91% in NON-OST (p=.000), relapse 1,7% in OST, 3.5% in NON-OST (p=.031) and lost to follow up (LTFU) 10.2% in OST and 4.3% in NON-OST (p=.000). In PP analysis SVR 12 /24 did not differ significantly between OST with 95,9% and NON-OST with 95,1% respectively (p=.464) (figure 1). In ITT SVR12 /24 (p=.251) did not differ significantly between SI (88,2%) and DI (84,2%) population. Relapse rates with 5,1% in SI and 0,5% in DI were significantly different (P=.000) (figure 2).

RESULTS (continued)
Table 1. Baseline demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>NON-OST (ITT)</th>
<th>NON-OST (PP)</th>
<th>OST</th>
<th>SVR 12/24 (ITT)</th>
<th>SVR 12/24 (PP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian, % (n/N)</td>
<td>96.3 (6.746/7.008)</td>
<td>97.8 (723/739)</td>
<td>96.6 (224/232)</td>
<td>98.4 (499/507)</td>
<td>85.2 (616/718)</td>
</tr>
<tr>
<td>Male, % (n/N)</td>
<td>97.8 (723/739)</td>
<td>96.6 (224/232)</td>
<td>98.4 (499/507)</td>
<td>85.2 (616/718)</td>
<td>91.0 (790/867)</td>
</tr>
<tr>
<td>Age (years, mean SD)</td>
<td>57.2 (4.012/7.008)</td>
<td>79.4 (587/739)</td>
<td>79.3 (184/232)</td>
<td>79.5 (403/507)</td>
<td>57.2 (4.012/7.008)</td>
</tr>
<tr>
<td>HCV RNA ≤800.000 IU/ml, % (n/N)</td>
<td>14.9 (107/739)</td>
<td>17.4 (398/232)</td>
<td>17.6 (469/507)</td>
<td>16.4 (84/520)</td>
<td>13.1 (920/7.008)</td>
</tr>
<tr>
<td>HCV RNA &gt;6x10^6 IU/ml, % (n/N)</td>
<td>10.6 (740/7.008)</td>
<td>12.9 (95/739)</td>
<td>11.6 (27/232)</td>
<td>13.4 (68/507)</td>
<td>11.6 (815/7.008)</td>
</tr>
<tr>
<td>SVR 12, % (n/N)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
</tr>
<tr>
<td>SVR 24, % (n/N)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
<td>94.8 (655/7008)</td>
</tr>
</tbody>
</table>

CONCLUSION
Data from this large real-world cohort showed high SVR12/24 rates in OST and NON-OST patients. Differences in SVR 12/24 in ITT analysis were mainly influenced by a higher LTFU rate after end of treatment in DI population and SI patients. SVR 12/24 rates according to HCV- genotype or underlying comorbidities did not differ significantly between OST and NON-OST patients. This analysis emphasis that HCV infection can be successfully treated with DAs in patients on OST. Due to a low relapse rate a high treatment efficacy can be assumed even in patients who do not show up for a control after end of therapy. Different medication used for opioid substitution therapy did not influence treatment success in our cohort.

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We thank all study nurses and all study investigators. Special thanks to Bianka Wiebner as well as Yvonne Serfert for the management of the German Hepatitis C-Registry.

DISCLOSURES
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Frequency and predictive value of detectable HCV RNA at the end of treatment with ledipasvir/sofosbuvir ± ribavirin in a large real world cohort: Results from the German Hepatitis C-Registry (DHC-R)

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INTRODUCTION

AASLD/IDSA guidelines for the management of hepatitis C virus (HCV) infection state that testing for quantitative HCV RNA can be considered at the end of antiviral treatment (EOT) with interferon-free regimens. However, it remains unclear how the respective results have to be interpreted.

The aim of this study was to analyze the frequency and predictive value of detectable HCV RNA results at the EOT with ledipasvir (LDV) and sofosbuvir (SOF) ± ribavirin (RBV) in a large real world cohort of HCV genotype 1 infected patients.

PATIENTS & METHODS

The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort that includes approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. Data base extract was done on Feb 15, 2016. The current data analysis is based on a subset of 471 patients fulfilling the following inclusion criteria:

- chronic HCV genotype 1 infection
- completion of a full course of antiviral treatment with LDV/SOF± RBV of either 8, 12 or 24 weeks
- available SVR12 data
- HCV RNA measurement with either the Roche COBAS Amplicon COBAS TaqMan (CAP/CTM) or the Abbott RealTime HCV assay.
- complete information on the qualitative HCV RNA result (positive/negative)

RESULTS

A significant number of patients had detectable HCV RNA at the end of LDV/SOF ± RBV therapy. Almost half of these patients even had quantifiable HCV RNA (Fig. 1). The only parameter that was associated with a positive HCV RNA result at EOT was using the ART assay (Fig. 2a).

Figure 1. Frequency of detectable HCV RNA at the end of LDV/SOF ± RBV therapy

CONCLUSION

- We observed a high number of detectable HCV RNA results at the end of LDV/SOF ± RBV therapy when using the Abbott RealTime HCV assay.
- SVR rates remain high in these patients. Therefore, treatment duration should not be extended.
- There seems to be no clinical benefit for testing HCV RNA at the end of LDV/SOF ± RBV therapy.

ACKNOWLEDGEMENTS

We thank all study nurses and all study investigators. Special thanks to Bianka Wiener as well as Yvonne Serfert for the management of the German Hepatitis C-Registry.

DISCLOSURES

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Dr. Benjamin Maasoumy (maasoumy.benjamin@mh-hannover.de)

[Insert Table and Diagrams as per the original document]
Estimation of liver fibrosis by the use of non-commercial serum scores in comparison to transient elastography in HCV patients receiving direct acting antiviral treatment

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INTRODUCTION

Treatment decision making with direct acting antivirals (DAA) in patients with chronic hepatitis C (CHC) is mainly based on baseline HCV RNA concentration, the HCV genotype and the presence or absence of liver cirrhosis. Since estimation of liver fibrosis by histology results has low acceptance, transient elastography (TE) and serum scores are often used in addition to clinical findings. Here, we assessed the diagnostic accuracy of a panel of non-commercial serum scores in comparison to TE.

PATIENTS & METHODS

The DHC-R (Deutsches Hepatitis C-Register, German Hepatitis C-Registry) is a national multicenter real-world cohort including approx. 9,500 patients. Patients are treated at the discretion of a physician. Data are collected by a web-based system. Data quality is analyzed by plausibility checks and on site monitoring. This data analysis is based on 6,034 patients who were observed for at least 40 weeks after initiation of antiviral treatment. Valid data on TE were available for 1,742 patients. For cut offs uses, see Table 1. In those patients, the non-commercial serum scores APRI score and FORNS index were calculated (for cut offs see below) and the diagnostic accuracy was compared to FS results.

RESULTS

Table 2. baseline characteristics in different patient groups

<table>
<thead>
<tr>
<th>TE &lt;=7 kPa</th>
<th>TE &gt;7 &lt; 12.5 kPa</th>
<th>TE &gt;=12.5 kPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0-1</td>
<td>F2-3</td>
<td>F4</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>50.9</td>
<td>54.6</td>
</tr>
<tr>
<td>Gender (male, %)</td>
<td>49.4</td>
<td>58.9</td>
</tr>
<tr>
<td>BMI (mean)</td>
<td>24.7</td>
<td>25.6</td>
</tr>
<tr>
<td>EDD (years)</td>
<td>19.1</td>
<td>19.8</td>
</tr>
<tr>
<td>Therapy experienced (%)</td>
<td>47.7</td>
<td>54.9</td>
</tr>
<tr>
<td>AST (U/l, mean)</td>
<td>68.5</td>
<td>67.4</td>
</tr>
<tr>
<td>Platelets (10^9)</td>
<td>230.2</td>
<td>205.4</td>
</tr>
<tr>
<td>Genotype 1 (%)</td>
<td>86.1</td>
<td>85.9</td>
</tr>
</tbody>
</table>

As estimated by TE, 625 (35.9%) patients had no significant fibrosis (SF) (<7,1kPa), 530 (30,4%) patients had SF (>7,1kPa) and 587 (33,7%) patients had liver cirrhosis (>12,5kPa) (Figure 1). Patients with liver cirrhosis were more frequently men, were older, had a higher BMI, had a longer estimated duration of disease (EDD) and were more likely treatment-experienced (Table 2).

Figure 1. Fibrosis estimation in patients by TE

Table 3. Sensitivity and specificity of serum scores in comparison to TE results

<table>
<thead>
<tr>
<th>Fibrosis score</th>
<th>APRI sensitivity</th>
<th>FORNS sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>98.2%</td>
<td>96.8%</td>
</tr>
<tr>
<td>No</td>
<td>92.4%</td>
<td>94.6%</td>
</tr>
</tbody>
</table>

CONCLUSION

• In our national multicenter real world cohort, significant fibrosis and cirrhosis were predicted with accuracy between 79-84% and 87% with non-commercial serum scores as compared to TE results.
• Our data support the use of serum scores when TE is not available for accurate cirrhosis estimation.
• Serum Scores may help for decision making, e.g. treatment duration
• SVR rates in patients with cirrhosis were numerically lower with current DAA regimens.

RESULTS (continued)

SVR rates following different DAA regimens with or without ribavirin for 8 – 24 weeks were 98.6%, 96.8%, and 92.4% for patients with no SF, SF, and cirrhosis, respectively. For discrimination of SF, AUROC were: 0.791 (APRI score), 0.840 (FORNS index). For discrimination of cirrhosis, AUROC was 0.879 (APIR index).

Table 3. Sensitivity and specificity of serum scores in comparison to TE results

<table>
<thead>
<tr>
<th>APRI</th>
<th>FORNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>98.2%</td>
</tr>
<tr>
<td>No</td>
<td>92.4%</td>
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</tbody>
</table>

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