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)

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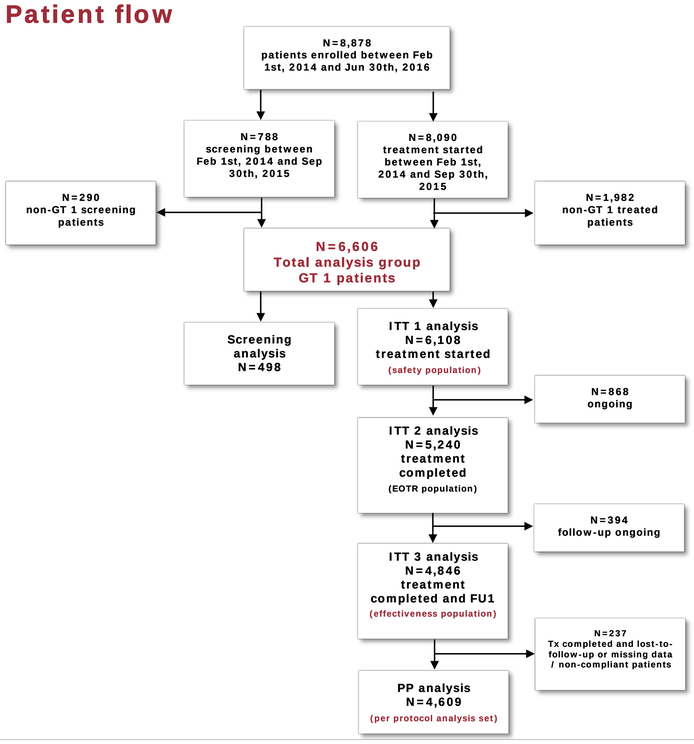
INTRODUCTION

In pivotal studies with modern direct acting antivirals (DAA) SVR rates in HCV genotype 1 (GT1) are >90%. However these data have to be replicated in less well controlled settings including patients more difficult to treat.

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 from 246 centers. 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. Data were analysed by descriptive statistics and logistic regression analysis.

Patient flow



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 regimen used (**figure 2**). HIV-coinfected patients (n=247) had an overall SVR12 of 92% which was the same as for HCV-monoinfected patients.

Figure 1: Efficacy according to regimen (ITT)

SVR12 PP (%)	88	91	98	98	98	98	96	97	96	97	98
Discontinuation (%)	3.3	1.2	0.6	0.0	1.0	0.4	0.8	0.5	0.0	1.3	0.3
Cirrhosis (%)	19	63	22	84	2	14	84	71	85	9	42

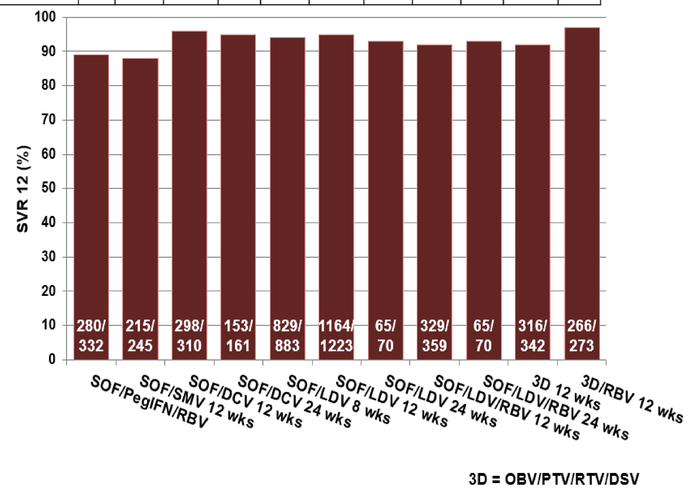
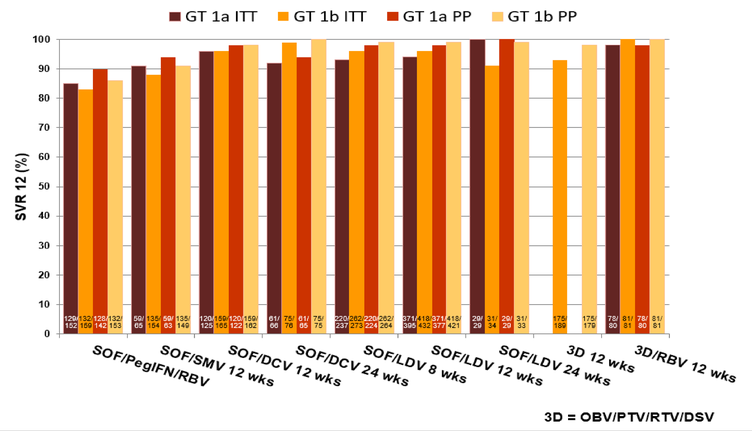


Figure 2: Comparison of efficacy GT1a vs. GT1b



In **multivariate analysis** adjusting for age, sex, platelets, cirrhosis, HCV RNA, GT1a/1b and treatment regime, SVR12 was associated with the choice of the antiviral regimen (OR 1.33 (1.24-1.43); p<0.001), cirrhosis (OR 0.71 (0.56-0.89); p<0.003) and sex (OR 1.52 (1.24-1.43); p<0.001).

Discontinuation rates were 2.3% total with only SOF/IFN/RBV 3.3% being higher than all other regimen.

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 withstanding a remaining lower SVR in cirrhotic patients.
- Discontinuation rates are low confirming good tolerance of the regimens and good adherence of patients.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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The German Hepatitis C-Registry is financially supported by AbbVie Deutschland GmbH & Co. KG, Bristol-Myers Squibb GmbH & Co. KGaA, Gilead Sciences GmbH, Janssen-Cilag GmbH, MSD Sharp & Dohme GmbH and Roche Pharma AG.

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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

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

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AASLD QR-Code

8 weeks treatment under real life conditions with Ledipasvir/Sofosbuvir in HIV co-infected treatment-naïve HCV genotype 1 infected patients with similar results to mono-infected HCV patients: data from the German Hepatitis C-Registry (DHC-R)

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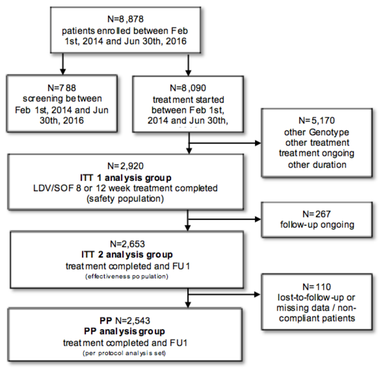
Introduction

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. .

Patient flow



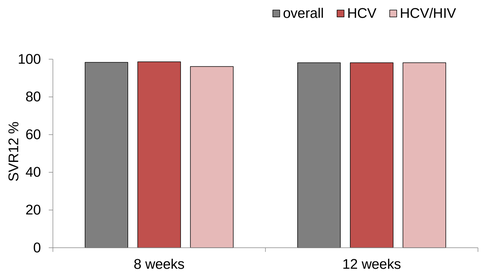
Results

- Characteristics of patients with HCV GT 1 receiving LDV/SOF for 8 or 12 weeks (n=2485) are given in table 1.
- Only patients not getting Ribavirin were included in this analysis. In general, we had a relative high number of patients with HIV coinfection (278) with in the 8 week LDV/SOF group 91 coinfected patients, 71 pat.with age > 70 and 78 treatment experienced patients.

Table 1: Patient characteristics

Patients	LDV/SOF 8 wk N=976	LDV/SOF 12 wk N=1,509
Male, n (%)	466 (48)	874 (58)
Mean age, years	50.0	54
Age >70 years, %	7.3	10,6
Treatment naïve, %	92	41,3
Fibroscan, mean (kPa)	6.5	9.3
Liver cirrhosis, %	2.4	13.9
Baseline viral load >6 million, %	3.0	14.2
HIV coinfection, n (%)	91 (9.3)	187 (12.4)

SVR12 – Rates (PP)



	8 week LDV/SOF	12 week LDV/SOF
Relapse, n (ITT)	12	19
D/C due to AEs, n (%)	3 (0.3)	2 (0.1)
Death, n (%)	5 (0.5)	6 (0.4)

All death are not related to treatment

	8 week SOF/LDV %(n)	12 week SOF/LDV %(n)
HIV - Coinfection	96.1 (73/76)	98.1 (158/161)
Pretreated patients	95.9 (70/73)	98.3 (773/786)
Age > 70 years	98.5 (65/66)	96.5 (138/143)
Patients on OST	98.7 (76/77)	96.8 (92/95)

- These data support the guidance to treat coinfected patients as monoinfected and this accounts for the possibility of 8 week treatment as well. Furthermore even patients with treatment experience were sufficiently treated with 8 weeks and older patients > 70 years do not have the need for longer treatment duration. Cirrhosis seems to be the only relevant factor, which qualifies for longer treatment. Cirrhosis was defined as Fibroscan > 12,5 kPa or ARFI ≥ 1,72 m/s or clear clinical signs of cirrhosis (e.g. varices). As shown in table 2 many patients eligible for 8 weeks get in real life 12 weeks of treatment. Even following the strict criteria outlined in the SmPC more patients qualify for 8 week treatment and taking into account the economic burden should get only 8 week.

Table 2: More patients are elegible

3 Criteria: init. VL < 6 Mio. IU/ml , treatment native , no cirrhosis

	2 criteria		All criteria		Total	
	N	%	N	%	N	%
LDV/SOF 8 W	127	10.7%	839	65.5%	976	33.4%
LDV/SOF 12 W	874	73.7%	410	32.0%	1508	51.7%
LDV/SOF/RBV 8 W	2	0.2%	2	0.2%	5	0.2%
LDV/SOF/RBV 12 W	183	15.4%	29	2.3%	430	14.7%
Total	1186	100.0%	1280	100.0%	2919	100.0%

Table 3 :Regression analysis

Subgroup (N)	yes %, (n/N)	no %, (n/N)	p-value	Odds Ratio (95%-CI)
HCV RNA, ≥ 6 million IU/ml (826)	100%, (21/21)	98.2% (791/805)	0.998	-
Cirrhosis (841)	90.5% (19/21)	98.5% (808/820)	0.014	0.141 (0.030-0.674)
Pretreated (841)	95.9 (70/73)	98.6 (757/768)	0.103	0.339 (0.092-1.244)
HIV infection (841)	96.1 (73/76)	98.6 (754/765)	0.118	0.355 (0.097-1.301)
OST (841)	98.7 (76/77)	98.3 (751/764)	0.793	1.316 (0.170-10.195)
Age > 70 years (841)	98.5 (65/66)	98.3 (762/775)	0.921	1.109 (0.143-8.611)

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 or 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 treatmemt duration .

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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Conflicts of Interests

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

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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)

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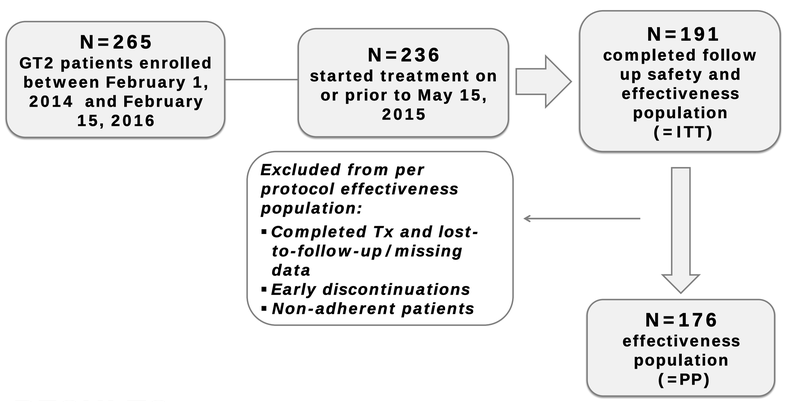
INTRODUCTION

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. This data analysis is based on 6,034 patients who were observed for at least 40 weeks after initiation of antiviral treatment. For the primary analysis descriptive statistics were used. A regression analysis was performed to identify risk factors for lower treatment response.

Patient flow



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+RBV >12 weeks in 10/11 (91%) patients and in 11/11 (100%) patients utilizing other regimen (PegIFN+SOF+RBV, SOF+DCV, LDV/SOF treatments.

Table 1. Patient characteristics and therapy

Characteristics	patients (n=236)
sex: male	141/236 (60%)
mean age [years] (IQR)	53.4 (46 – 61)
Caucasian	230/236 (98%)
Region of birth	
Germany	106/191 (55%)
Former Soviet Union	55/191 (29%)
HCV RNA [IU/mL] > 2 Mio IU/mL	66/236 (28%)
> 6 Mio IU/mL	33/236 (14%)
Liver cirrhosis	41/236 (17%)
Prior HCV treatment	65/236 (28%)
Diabetes mellitus	18/236 (9%)
Opioid substitution therapy (OST)	22/236 (9%)
Therapeutic regimen	
Sofosbuvir + ribavirin 12 weeks	n=178
Sofosbuvir + ribavirin >12 weeks	n=14
PegIFN + RBV + SOF	n=5
SOF + DCV	n=5
LDV/SOF	n=1

SVR rates for SOF+RBV 12 weeks (ITT) in different subgroups are shown in **Table 2**.

By logistic regression analysis, none of the variables reached statistical significance for predicting failure to the SOF+RBV 12 weeks regimen. In particular, low SVR12 rates were not related to Russian descent, arguing against a substantial number of patients infected with a chimeric GT 2k/1b virus.

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

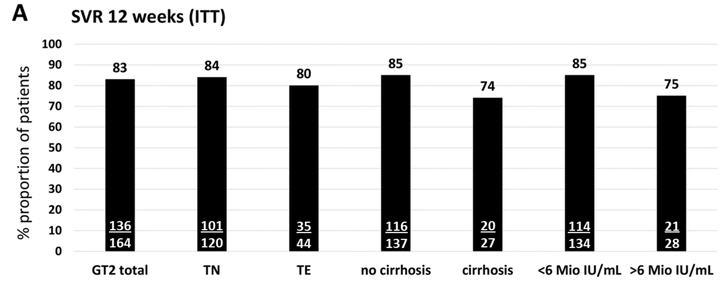
Variable subgroup 1	Variable subgroup 2	SVR ITT % (n/total) 1	SVR ITT % (n/total) 2
Non-cirrhotic	Cirrhotic	85% (116/137)	74% (20/27)
Naïve	Pretreated	84% (101/120)	80% (35/44)
Age <70 years	Age ≥70 years	84% (125/149)	73% (11/15)
HCV RNA* <6 Mio IU/mL	HCV RNA ≥6 Mio IU/mL	85% (114/134)	75% (21/28)
Non-diabetic	Diabetes mellitus	83% (126/152)	84% (10/12)
No opioid substitution	Opioid substitution	83% (123/149)	87% (13/15)
Origin outside former Soviet Union (SU)	Origin from former SU	84% (97/116)	81% (39/48)

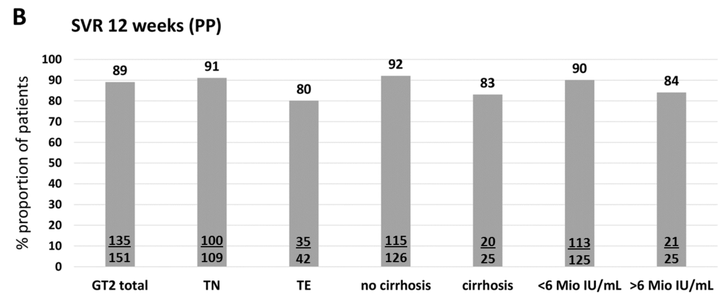
*data on initial viral load not available for 2 patients

The SVR rate for SOF+RBV 12 weeks 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, dyspnea, syncopal episode). No patient died.

SVR12 (SOF+RBV 12 weeks) in HCV-GT2





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.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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DISCLOSURES

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AASLD QR-Code

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 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

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

Figure 1A. Patient flow

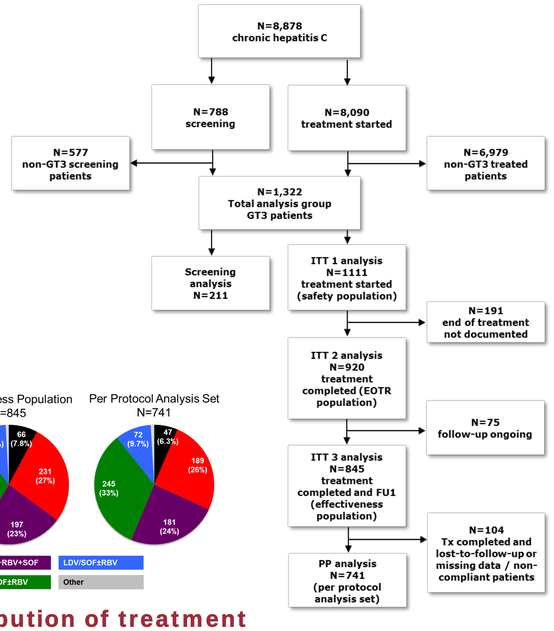


Figure 1B. Distribution of treatment regimens

Figure 2. Proportion of treatment regimens during the 20 months study period

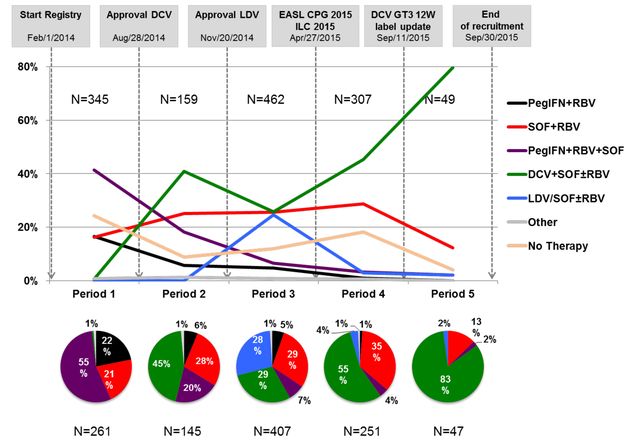


Table 1. Baseline characteristics of untreated (screened only) and treated GT3 patients

Characteristics, n (%)	patients only screened	patients treated (ITT 1)	p-value[¶]
Total, n	211	1,111	
Male	152 (72·0)	773 (69·6)	
Age, mean/median years	44·5 / 45·0	46·4 / 48·0	<0.05
treatment-naïve	164 (77·7)	742 (66·8)	<0.05
IFN pretreated	46 (21·8)	351 (31·6)	
DAA pretreated	1 (0·5)	17 (1·5)	
cirrhosis	19 (9·0)	355 (32·0)	<0.001
IFN pretreated, cirrhosis	8 (3·8)	153 (13·8)	
Platelets, mean/median	188·2 / 182·0	180·3 / 180·0	
Platelets <90/nl*	8 (6·7)	111 (10·8)	
Albumin, mean/median	n.a.	41·1 / 42·0	
Albumin <35 g/l**	n.a.	45 (9·3)	
HCV-RNA, mean/median IU/mL	3,073,390 / 780,000	3,150,249 / 900,500	
HCV-RNA <800,000 IU/ml	98 (46·4)	518 (46·6)	
HCV-RNA >2 M IU/ml	32 (15·2)	223 (20·1)	
HCV-RNA >6 M IU/ml	29 (13·7)	141 (12·7)	
MELD score, mean/median	n.a.	8·9/8·0	
CHILD A, B, C[#]	17 (89·5), 2 (10·5), 0 (0·0)	240 (84·2), 39 (13·7), 6 (2·1)	
Opioid Substitution Therapy (OST)	100 (47·4)	220 (19·8)	<0.001
IL28B-60 (CC, CT, TT)[##]	6 (2·8), 13 (6·2), (0·5)	70 (6·3), 107 (9·6), 20 (1·8)	
GFR <30	n.a.	8 (0·8)	
Diabetes mellitus	11 (5·2)	71 (6·4)	

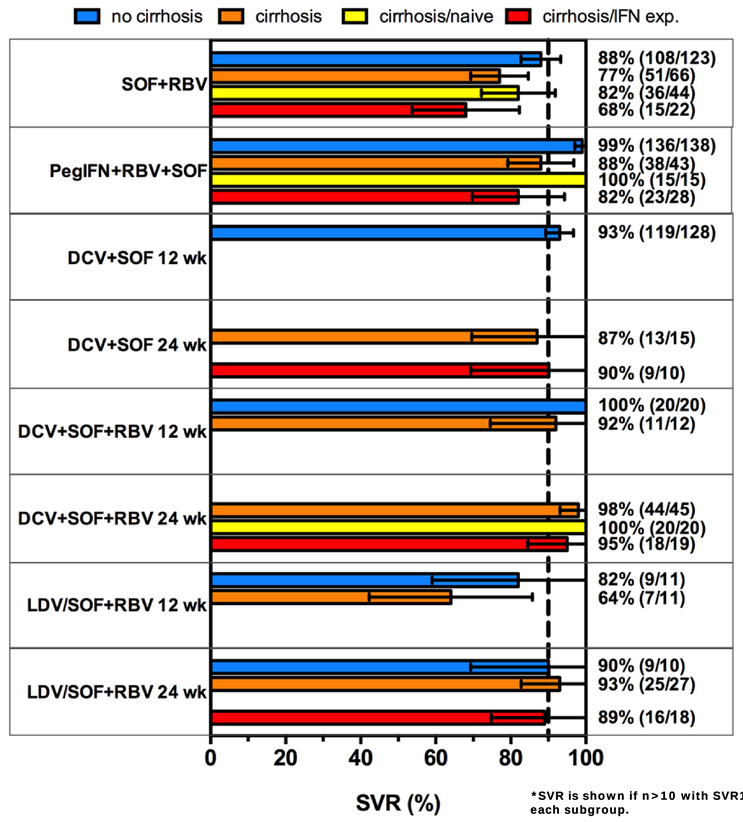
[¶]based on mean; *data on platelet count were available for 120 screened and 1,027 treated patients (ITT 1); **data on albumin were available for 483 treated patients (ITT 1)
[#]data on CHILD-PUGH were available for 19 screened and 285 treated patients (ITT1); [##]data on IL28 B-60 genotype were available for 20 screened and 197 treated patients (ITT 1)
[#¶]data on GFR were available for 981 treated patients (ITT 1);n.a., not available

Table 2. Overview of SVR in different treatment groups

Regimens	pts who started treatment n	% of all treatments	% cirrhosis of all treatments	% early termination of therapy[#]	SVR12 ITT3* n/total	SVR12 ITT3* %	SVR12 PP** n/total	SVR12 PP** %
PegIFN+RBV	91	8·2	3·3	18·3	39/66	59·1	38/47	80·9
PegIFN+RBV+SOF	213	19·2	22·1	4·0	178/197	90·4	174/181	96·1
SOF+RBV	308	27·7	33·4	10·0	165/231	71·4	159/189	84·1
SOF+DCV±RBV	364	32·8	33·5	5·6	230/262	87·8	228/245	93·1
SOF/LDV±RBV	124	11·2	63·7	6·6	61/82	74·4	61/72	84·7
Other[$]	*11*	*1·0*	*9·1*	-	*7/7*	*100·0*	*7/7*	*100·0*
Total	1111	100	32·0	7·5	680/845	80·5	667/741	90·0

*effectiveness population, **SVR12 (PP) was significantly associated with age, gender, cirrhosis, baseline albumin and baseline platelets (p<0·05; univariate regression analysis); #ITT2 (n=920). Early termination of therapy due to an SAE was reported in 7 patients among all treatment groups (PegIFN+RBV+SOF (n=1), SOF+RBV (n=2), DCV+SOF±RBV (n=4)). [$]*Other treatment regimens were rare, inconclusive and not included in the interpretation of data.*

Figure 3. SVR12 rates (PP) in different subgroups*



*SVR is shown if n>10 with SVR12 data in each subgroup.

SVR12 (PP) was significantly associated with age, gender, cirrhosis, baseline albumin and baseline platelets (p<0·05; univariate regression analysis).

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.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

Principal Investigator: Dietrich Hüppe, Herne

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AASLD QR-Code

Effectiveness and Safety of DAA Combination Therapies for Treatment of HCV in Elderly Patients (>70 yrs.): Results from the German Hepatitis C-Registry (DHC-R)

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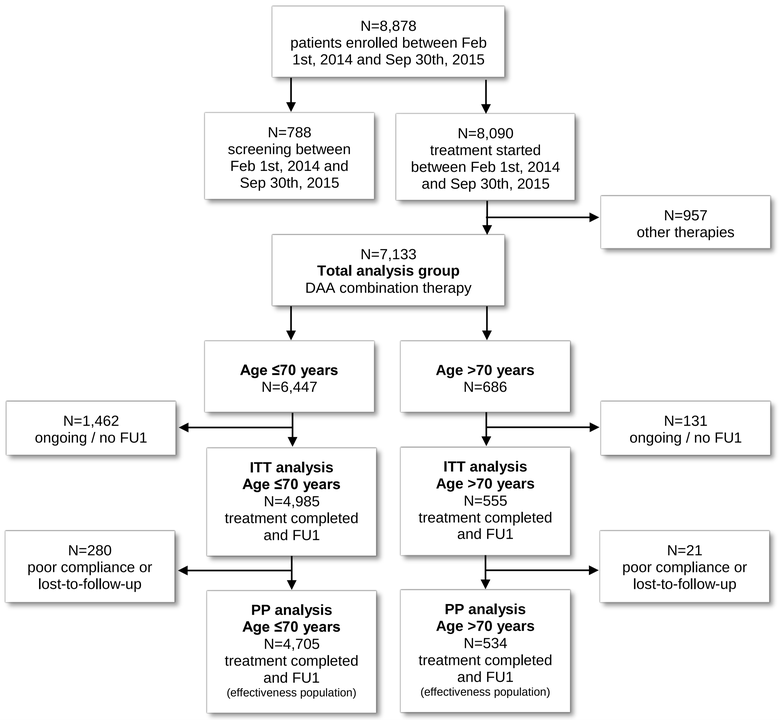
INTRODUCTION

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.

Figure 1. Patient disposition



RESULTS

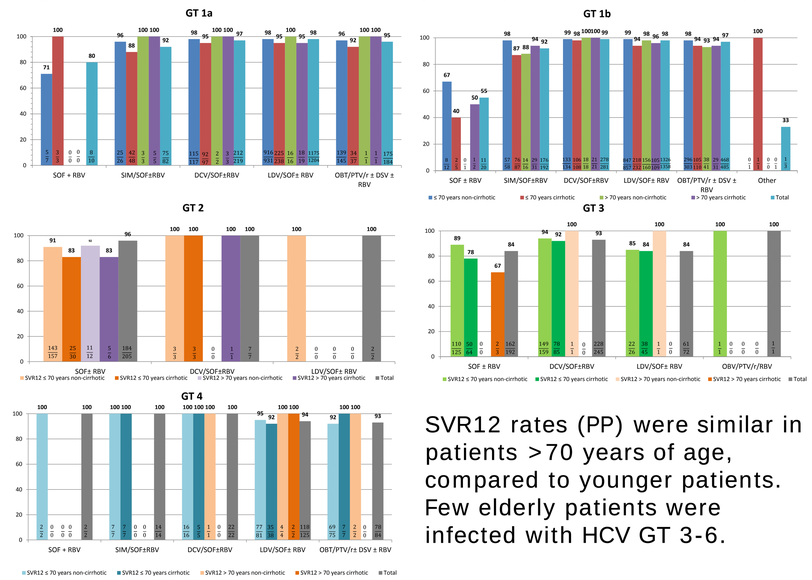
Of 7,133 patients who started all-oral DAA combination treatments, 686 (9.6%) were >70 years of age. Table 1 summarizes demographic and clinical characteristics of the patient population.

Table 1. Demographic and clinical characteristics by age group

	≤70 years (N = 6447)	>70 years (N=686)
Female % (n/N)	38.8% (2,502/6,447)	65.0% (446/686)
BMI (kg/m², mean ± SD)	25.9 (4.7)	25.7 (4.3)
White % (n/N)	96.3% (6,208/6,447)	98.8% (678/686)
HCV genotype, % (n/N)		
GT1	78.2% (5,041/6,447)	93.4% (641/686)
GT1a	36.5% (2,353/5,041)	10.6% (73/686)
GT1b	37.8% (,2437/5,041)	79.0% (542/686)
Other / unknown	3.9% (251/5,041)	3.8% (26/686)
GT2	4.0% (260/6,447)	3.6% (25/686)
GT3	12.3% (794/6,447)	0.9% (6/686)
GT4	5.4% (345/1,017)	1.7% (12/686)
GT5	0.1% (4/6,447)	0.3% (2/686)
GT6	0.0% (3/6,447)	0.0% (0/686)
HCV RNA (×10⁶ IU/ml, mean ± SD)	5.9 (0.9) (n=6,269)	5.9 (0.9) (n=650)
Treatment-experienced, % (n/N)	48.5% (3,127/6,447)	51.0% (350/686)
(peg)IFN ± RBV	96.1% (3,004/3,127)	96.9% (339/350)
Prior DAA failure	21.4% (670/3,127)	12.6% (44/288)
Other pretreatment	3.7% (116/3,127)	3.1% (11/350)
Cirrhosis, % (n/N)	27.3% (1,761/6,447)	44.0% (302/686)
Child-Pugh Score A, % (n/N)	85.3% (1,195/1,401)	87.4% (221/253)
Child-Pugh Score B, % (n/N)	12.6% (176/1,401)	11.9% (30/253)
Child-Pugh Score C, % (n/N)	2.1% (30/1,401)	0.8% (2/253)
Hepatic decompensation, % (n/N)	20.8% (367/1,761)	22.5% (68/302)
MELD score (median, Q1–Q3)	8 (7-10) (n=519)	8 (7-10) (n=93)
MELD score ≥15, % (n/N)	6.0% (31/519)	8.6% (8/93)
History of hepatocellular carcinoma (HCC)	1.2% (76/6,447)	2.5% (17/686)
Liver transplantation, %, (n/N)	1.9% (125/6,447)	2.5% (17/686)
Hemoglobin (g/dl, median, Q1–Q3)	14.5 (13.6–15.6) (n = 5,167)	13.7 (12.7-14.8) (n=561)
Platelets <90 × 10⁹/l, % (n/N)	10.1% (603/5,970)	14.4% (91/632)
Albumin <3.5 g/dl, % (n/N)	11.9% (330/2,767)	17.7% (57/322)
eGFR, % (n/N)		
eGFR >90 ml/min/1.73 m²	69.1% (3,903/5,651)	11.1% (68/613)
eGFR >60–90 ml/min/1.73 m	26.8% (1517/5,651)	66.4% (407/613)
eGFR >30–60 ml/min/1.73 m²	3.4% (190/5,651)	21.5% (132/613)
eGFR >15–30 ml/min/1.73 m²	0.4% (25/5,651)	0.7% (4/613)
eGFR 0–15 ml/min/1.73 m², incl. dialysis	0.3% (16/5,651)	0.3% (2/613)

RESULTS (continued)

Figure 2. Effectiveness of DAA therapies in patients ≤70 vs. >70 years



SVR12 rates (PP) were similar in patients >70 years of age, compared to younger patients. Few elderly patients were infected with HCV GT 3-6.

Table 2. Safety of all oral DAA regimen in patients ≤70 and >70 years

	≤ 70 years	> 70 years	Total
Any AE, n [%]	3,435/6,447 (53,3%)	374/686 (54,5%)	3,809/7,133 (53,4%)
Any serious AE, n [%]	235/6,447 (3,6%)	52/686 (7,6%)	287/7,133 (4,0%)
Death, n [%]	18/6,447 (0,3%)	2/686 (0,3%)	20/7,133 (0,3%)
Hemoglobin > 8mg/dL and < 10 mg/dL; n [%]	184/5,743 (3,2%)	46/616 (7,5%)	230/6,359 (3,6%)
Hemoglobin < 8 mg/dL; n [%]	25/5743 (0,4%)	8/616 (1,3%)	33/6,359 (0,5%)
RBV dose modification	234/2,034 (11,5%)	46/196 (23,5%)	280/2,230 (12,6%)
- In cirrhotics	127/954 (13,3%)	35/146 (24,0%)	162/1,100 (14,7%)
RBV discontinuation*	29/234 (12,4%)	3/46 (6,5%)	32/280 (11,4%)
- In cirrhotics	17/127 (13,4%)	3/35 (8,6%)	20/162 (12,3%)

*** in patients with RBV dose modifications**

Despite a higher proportion of SAEs and RBV dose modifications in patients >70 years, the rate of treatment discontinuations was low (1% in both age groups).

CONCLUSION

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

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

Principal Investigator: Dietrich Hüppe, Herne

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DISCLOSURES

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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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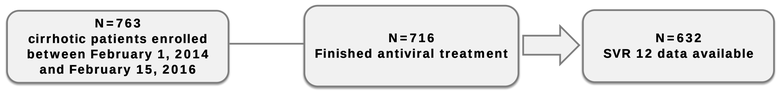
Introduction

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, thrombocytes <90,000/µl, albumin <35g/l or signs of liver decompensation, were analyzed.

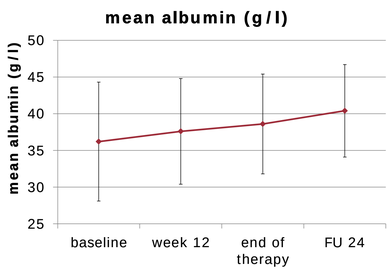
Patient flow

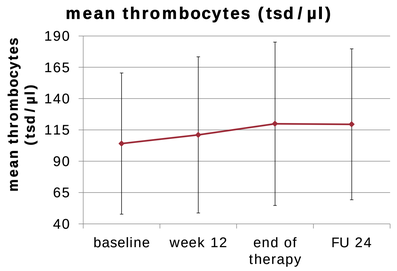


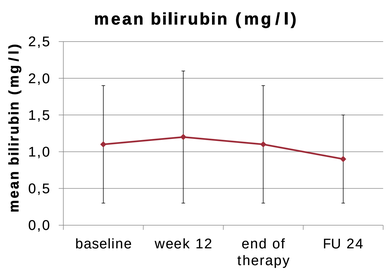
Patient characteristics

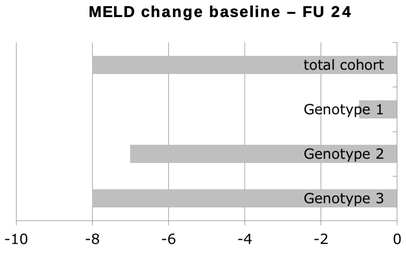
Characteristics	n (%)
Male/total	479/763 (63)
Age; mean (range)	58 (range 29-81)
HCV- genotype	
1	592 (78)
2	17 (2.2)
3	124 (16.3)
4	28 (3.7)
5	1 (0.1)
6	1 (0.1)
Child Pugh Score	
A	550 (72)
B	100 (13)
C	9 (1.2)
Oesophageal varices	265 (35)
Ascites at screening	79 (38)

Results









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	3	0.4
Total	**763**	**100.0**

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.

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**

- Overall, SVR was achieved in 88.0% of the patients (ITT). SVR rates according to the regimens ranged from 66 to 100%.
- DAA therapy lead to SVR rates (ITT) of 91%, 80%, 73% and 83% for HCV-genotype 1 (n =460), 2 (n =12), 3 (n=64) and 4 (n=19), respectively.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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Conflicts of Interests

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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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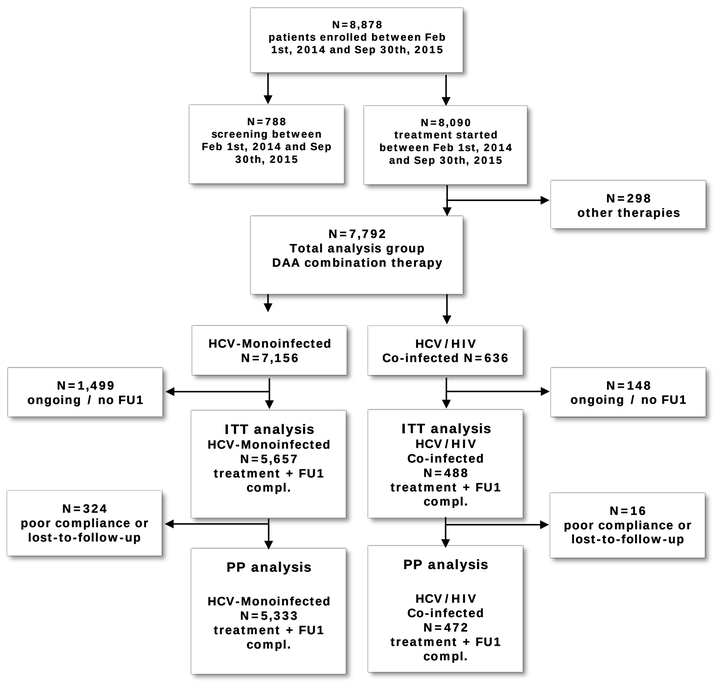
INTRODUCTION

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. 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.

FIGURE 1: Patient flow diagram



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. HIV coinfected patients mostly had good CD4-counts at baseline (63% >350 CD4-cells/µl; only 2.6% had a CD4-count below 200/µl).

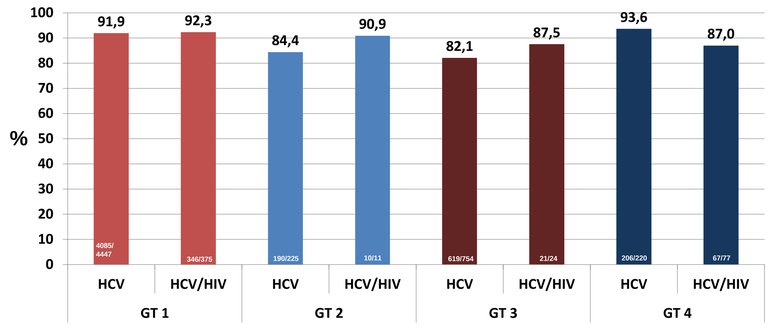
Table 1. Baseline characteristics

Baseline characteristics: ITT population	HCV mono infection (n=5657)	HIV/HCV coinfection (n=488)
Male (%)	57.2	84.7
Age (mean +/- SD)	53.8 +/- 12.5	46.5 +/- 9.0
Cirrhosis (%)	29.4	17.2
Genotype (GT) 1 (%)/ GT 2 (%)/ GT3 (%) /GT4 (%)	78.6/3.9/13/3.8	76.8/2.2/4.9/15.7
HCV Treatment-naive	51.4	53.5
LDV/SOF+/- RBV // or DAC + SOF +/-RBV// or OBV/PTV/r+DSV ± RBV for GT1 treatment (%)	58.4//11.9//15.1	67.7//8.8//9.4
SOF + RBV // SOF + PegIFN + RBV // SOF + DAC// SOF/LDV + RBV for GT3 (%)	29.2//25.7//22//8.5	45.8//12.5//16.7//12.5
SOF + PegIFN + RBV // or LDV/SOF+/- RBV // or OBV/PTV/r + RBV for GT4 treatment (%)	13.2//42.1//27.3	15.6//44.2//28.6

RESULTS

Overall, SVR12 rates across all genotypes in the ITT analysis were comparable between HCV mono- and HIV/HCV coinfected individuals with 90.3% and 91.2%, respectively. In addition no significant difference was noted between the various genotypes studied (see figure 2).

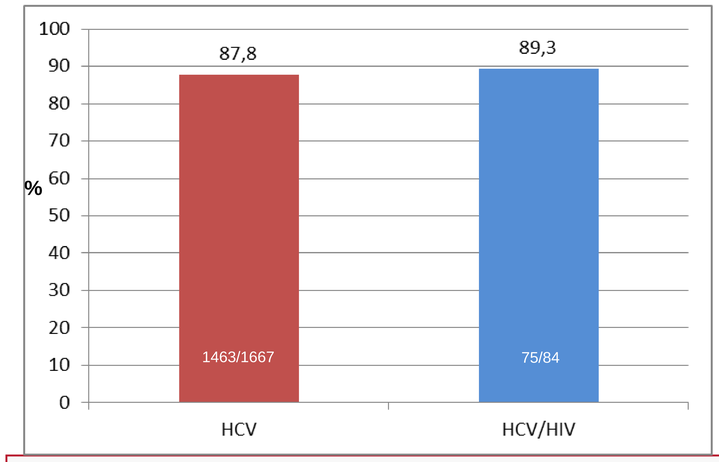
FIGURE 2: SVR12 results by genotype (ITT analysis)



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=74)). 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

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

Principal Investigator: Dietrich Hüppe, Herne

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The German Hepatitis C-Registry is financially supported by AbbVie Deutschland GmbH & Co. KG, Bristol-Myers Squibb GmbH & Co. KGaA, Gilead Sciences GmbH, Janssen-Cilag GmbH, MSD Sharp & Dohme GmbH and Roche Pharma AG.

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DISCLOSURES

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

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

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AASLD QR-Code

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)

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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= 739 were on OST. To get more insights if an integrated clinical setting influences treatment success positively we divided the OST group further more in patients with DAA therapy and OST in the same 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) have 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

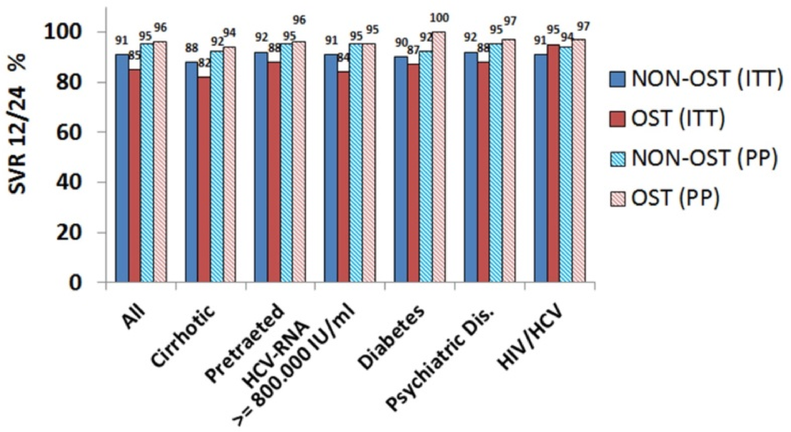
Baseline demographics of all patient groups are shown in **table 1** and distribution of therapy of chronic hepatitis C are shown in **table 2**. Compared to NON-OST more OST patients were younger (median age 46 vs. 54 years), male (79% vs. 57%), Genotype 3 infected (26% vs. 12%) and had a psychiatric 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=.0000), 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

	NON-OST	OST	SI	DI
Male, % (n/N)	57.2 (4.012/7.008)	79.4 (587/739)	79.3 (184/232)	79.5 (403/507)
Age (years, mean ± SD)	53.9 (12.4)	45.6 (8.9)	45.6 (8.9)	45.6 (8.9)
BMI (kg/m^2, mean ± SD)	25.9 (4.6)	25.7 (5.0)	25.2 (4.6)	26.0 (5.1)
Caucasian, % (n/N)	96.3 (6.746/7.008)	97.8 (723/739)	96.6 (224/232)	98.4 (499/507)
GT1	79.3 (5.554/7.008)	65.4 (483/739)	68.5 (159/232)	64.0 (324/507)
GT1a	31.7 (2.223/7.008)	50.6 (374/739)	55.6 (129/232)	48.3 (245/507)
GT1b	43.6 (3.056/7.008)	12.0 (89/739)	9.9 (23/232)	13.0 (66/507)
GT 2	3.6 (255/7.008)	4.5 (33/739)	6.5 (15/232)	3.5 (18/507)
GT 3	11.6 (815/7.008)	26.4 (195/739)	19.8 (46/232)	29.4 (149/507)
GT 4	5.3 (5.554/7.008)	3.8 (28/739)	5.2 (12/232)	3.2 (16/507)
HCV RNA >6x10^6 IU/ml, % (n/N)	10.6 (740/7.008)	12.9 (95/739)	11.6 (27/232)	13.4 (68/507)
HCV RNA ≤800.000 IU/ml, % (n/N)	39.6 (2.776/7.008)	40.5 (299/739)	39.2 (91/232)	41.0 (208/507)
Treatment-experienced, % (n/N)	49.4 (3.459/7.008)	31.1 (230/739)	79 (34.1/232)	29.8 (151/507)
Cirrhotic patients, % (n/N)	28.2 (1.973/7.008)	28.0 (207/739)	23.7 (55/232)	30.0 (152/507)
MELD score cirrhotic patients (median, Q1–Q3)	8.0 (7.0-10.0)	7.5 (6.5-8.5)	7.5 (6.5-9.0)	7.5 (6.5-8.5)
Platelets (x10^9/l, median, Q1–Q3)	192.0 (139.0-240.0)	183.0 (133.0-226.0)	186.5 (138.0-229.5)	181.0 (132.0-223.0)
ALT (IU/l, median, Q1–Q3)	67.0 (44.0-109.0)	59.4 (35.0-100.8)	49.7 (30.1-86.0)	63.0 (37.0-104.0)
Cardiovascular disease, % (n/N)	26.9 (1.888/7.008)	12.6 (93/739)	10.8 (25/232)	13.4 (68/507)
Diabetes mellitus, % (n/N)	10.3 (722/7.008)	3.8 (28/739)	3.0 (7/232)	4.1 (21/507)
Psychiatric diseases, % (n/N)	15.0 (1049/7.008)	24.8 (138/739)	32.3 (75/232)	21.3 (108/507)
Depression, % (n/N)	13.1 (920/7.008)	21.8 (161/739)	30.6 (71/232)	17.8 (90/507)
HCV/HIV co-infection, % (n/N)	7.9 (554/7.008)	11.1 (82/739)	16.8 (39/232)	8.5 (43/507)
OST Medication		100 (739/739)	100 (232/232)	100 (507/507)
Methadone, % (n/N)		35.0 (259/739)	36.6 (85/232)	34.3 (174/507)
L-Polamidone, % (n/N)		40.2 (297/739)	38.4 (89/232)	41.0 (208/507)
Buprenorphine, % (n/N)		19.9 (147/739)	22.4 (52/232)	18.7 (95/507)
Heroine, % (n/N)		1.4 (10/739)	0	2.0 (10/507)
Other, % (n/N)		3.4 (25/739)	2.6 (6/232)	3.7 (19/507)

Figure 1. Efficacy of HCV therapy for NON-OST and OST patients (ITT and PP analysis, SVR 12 and/or SVR 24)



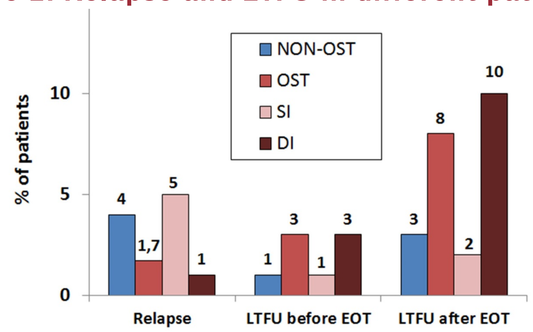
RESULTS (continued)

Table 2. Distribution of DAA regimes

	NON-OST	OST	SI	DI
SOF+PegIFN+RBV, % (n/N)	7,9 (556/7008)	9,3 (69/739)	10,3 (24/232)	8,9 (45/507)
SOF+RBV, % (n/N)	7,3 (514/7008)	14,6 (108/739)	12,1 (28/232)	15,8 (80/507)
SOF+SMV±RBV, % (n/N)	4,9 (343/7008)	2 (15/739)	1,7 (4/232)	2,2 (11/507)
SOF+DCV±RBV, % (n/N)	12,9 (906/7008)	13,3 (98/739)	10,8 (25/232)	14,4 (73/507)
SOF/LDV±RBV, % (n/N)	51,9 (3637/7008)	51 (377/739)	53,4 (124/232)	49,9 (253/507)
OBV/PTV/r ± RBV, % (n/N)	2,0 (143/7008)	1,5 (11/739)	2,6 (6/232)	1 (5/507)
OBV/PTV/r ± DSV ± RBV, % (n/N)	13 (909/7008)	8,3 (61/739)	9,1 (21/232)	7,9 (40/507)

Medication used for OST did not influence SVR12/24 rates with 84,4% (n=162/437) if Methadone, 84,3% (n=172/437) if L-Polamidon, 89% (n=97/437) if Buprenorphine and 75% (6/437) if Heroine was used for substitution (p=.546). A significant difference (p=.000) was seen in lost to follow (LTFU) with 2,2% in SI and 13% in DI patients, driven by a higher LTFU rate after end of treatment in DI (9,7%) vs. SI (1,5%) patients. The same effect is seen if LTFU is compared between NON-OST an OST patients (p=.000).

Figure 2. Relapse and LTFU in different patient groups



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 OST population and DI 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 DAAs 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.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

Principal Investigator: Dietrich Hüppe, Herne

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DISCLOSURES

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

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AASLD QR-Code

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) ± ribavrin (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:

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

The CAP/CTM HCV test has a limit of detection (LOD) and a lower limit of quantification (LOQ) of 15 IU/mL. The ART HCV assay has a LOD and LOQ of 12 IU/mL. In the present study, a positive (pos) viral load at the end of treatment was defined as detectable/above or below the LOQ of the respective assay.

RESULTS

Table 1. Baseline characteristics of the study cohort

	LDV/SOF		LDV/SOF+RBV		All	
HCV RNA at end of treatment	**pos**	**neg**	**pos**	**neg**	**pos**	**neg**
Male gender, n (%)	14 (8)	172 (92)	3 (7)	41 (93)	17 (7)	213 (93)
Female gender, n (%)	12 (6)	205 (94)	5 (21)	19 (79)	17 (7)	224 (93)
Treatment naive, n (%)	19 (9)	196 (91)	1 (4)	24 (96)	20 (8)	220 (92)
Treatment exp., n (%)	7 (4)	181 (96)	7 (16)	36 (84)	14 (6)	217 (94)
Treatment duration						
8-12 weeks, n (%)	24 (6)	359 (94)	7 (12)	50 (88)	31 (7)	409 (93)
24 weeks, n (%)	2 (10)	18 (90)	1 (9)	10 (91)	3 (10)	28 (90)
Mean Baseline VL (log_{10} IU/mL)	6.4	6.4	6.5	6.3	6.4	6.4
No Cirrhosis, n (%)	23 (7)	311 (93)	6 (35)	11 (65)	29 (8)	322 (82)
Cirrhosis, n (%)	3 (4)	66 (96)	2 (4)	49 (96)	5 (4)	115 (96)
Mean Albumin (g/l)	42.1	41.5	41.6	38.9	41.8	41.2
Mean ALT (U/l)	70.7	68.6	77.8	109.4	72.4	74.1
Mean GGT (U/l)	65.6	91.4	149.2	153.1	85.3	99.7
Mean Bilirubin (mg/dl)	0.5	0.6	0.7	0.9	0.6	0.6
Mean platelets (/µl)	220,000	219,051	172,000	135,534	208,364	207,680

RESULTS (continued)

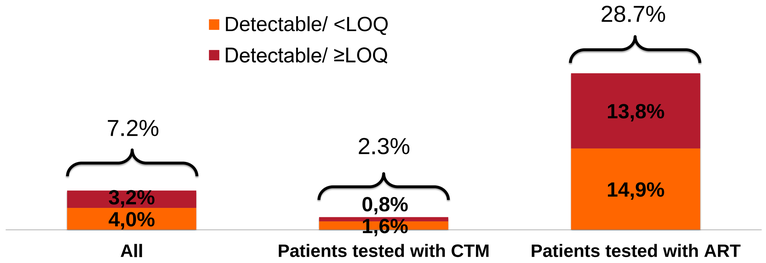


Figure 1. Frequency of detectable HCV RNA at the end of LDV/SOF ± RBV therapy

Percentages of patients with an HCV RNA result either detectable/below the limit of quantification (<LOQ) or detectable above the limit of quantification (>LOQ) are shown.

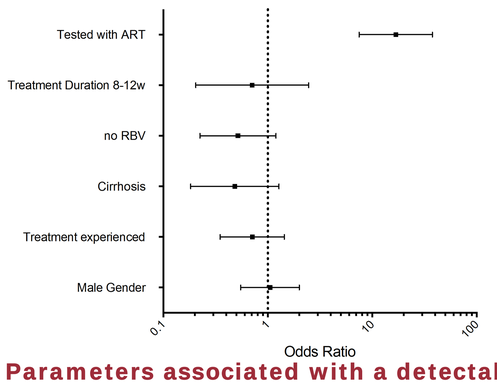


Figure 2a. Parameters associated with a detectable HCV RNA at the end of LDV/SOF ± RBV therapy

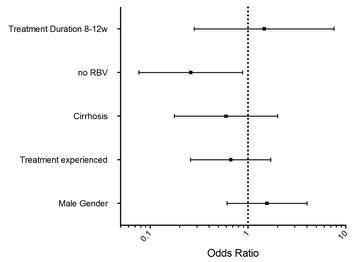
A significant number of patients had detectable HCV RNA at the end of LDV/SOV ± RBV therapy. Almost half of these patients even had quantifiable HCV RNA (Fig. 1). The only parameter that was associated with a positive HCV RNA result at EOT was using the ART assay (Fig. 2a).

Table 2a/b. Baseline characteristics of patients tested with CAP/CTM and ART

CAP/CTM	LDV/SOF		LDV/SOF+RBV		All	
HCV RNA at end of treatment	**pos**	**neg**	**pos**	**neg**	**pos**	**neg**
Male gender, n (%)	5 (3)	151 (97)	0	38 (100)	5 (3)	190 (97)
Female gender, n (%)	4 (2)	170 (98)	0	15 (100)	4 (2)	185 (98)
Treatment naive, n (%)	5 (3)	167 (97)	0	22 (100)	5 (3)	189 (97)
Treatment exp. , n (%)	4 (3)	154 (97)	0	32 (100)	4	186 (2)
Treatment duration						
8-12 weeks, n, (%)	8 (3)	308 (97)	0	46 (100)	8 (2)	354 (98)
24 weeks, n, (%)	1 (7)	13 (93)	0	8 (100)	1 (5)	21 (95)
Mean Baseline VL (log_{10} IU/mL)	6.5	6.4	-	6.3	6.5	6.4
No Cirrhosis, n (%)	8	265	0	10 (100)	8 (3)	275 (97)
Cirrhosis, n (%)	1	56	0	44 (100)	1 (0.9)	100 (99.1)
Mean Albumin (g/l)	43.0	41.6	-	38.6	43.0	40,1
Mean ALT (U/l)	79.5	69.1	-	116.4	79.5	92,8
Mean GGT (U/l)	59.6	89.8	-	157.3	59.6	123,6
Mean Bilirubin (mg/dl)	0.7	0.6	-	1.0	0.7	0.7
Mean platelets (/µl)	216875	218560	-	134962	216875	206618

ART	LDV/SOF		LDV/SOF+RBV		All	
HCV RNA at end of treatment	**pos**	**neg**	**pos**	**neg**	**pos**	**neg**
Male gender, n (%)	9 (30)	21 (70)	3 (60)	2 (40)	12 (34)	23 (66)
Female gender, n (%)	8 (19)	35 (81)	5 (56)	4 (44)	13 (25)	39 (75)
Treatment naive, n (%)	14 (33)	29 (67)	1 (34)	2 (66)	15 (33)	31 (67)
Treatment exp., n (%)	3 (10)	27 (90)	7 (64)	4 (36)	10 (24)	31 (76)
Treatment duration						
8-12 weeks, n (%)	16 (24)	51 (76)	7 (64)	4 (36)	23 (30)	55 (70)
24 weeks, n (%)	1 (17)	5 (83)	1 (34)	2 (66)	2 (22)	7 (78)
Mean Baseline VL (log_{10} IU/mL)	6.3	6.2	6.5	6.1	6.4	6.2
No Cirrhosis, n (%)	15 (25)	46 (75)	6 (86)	1 (14)	21 (31)	47 (69)
Cirrhosis, n (%)	2 (17)	10 (83)	2 (29)	5 (71)	4 (21)	15 (79)
Mean Albumin (g/l)	41.5	41.0	41.6	43.5	41,6	42,3
Mean ALT (U/l)	66.1	66.0	77.8	36.6	72.0	51,3
Mean GGT (U/l)	68.9	100.1	149.2	108.8	109,1	104,5
Mean Bilirubin (mg/dl)	0.5	0.6	0.7	0.6	0.6	0.6
Mean platelets (/µl)	221471	221784	172000	140500	205640	213918

RESULTS (continued)



There were no obvious differences in the baseline parameters between patients tested with the ART and those tested with the CAP/CTM assay (Table 2a/b)

Only the usage of RBV was linked to a higher risk for a positive EOT result among patients tested with the ART assay (Fig. 2b).

Figure 2b. Parameters associated with a detectable HCV RNA at the end of LDV/SOF ± RBV therapy in patients tested with the ART

Figure 3. Frequency of SVR depending on the HCV RNA result at the end of LDV/SOF ± RBV therapy

The overall SVR rate in our study was 99% (n=464/471). The SVR rate was numerically lower in patients with detectable HCV RNA at EOT (94%; n=32/34). However, this difference was not statistical significant. Only two patients with a detectable EOT result experienced a relapse (Fig. 3).

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.

Data were derived from the **German Hepatitis C-Registry** (Deutsches Hepatitis C-Register), a project of the German Liver Foundation (Deutsche Leberstiftung), managed by Leberstiftungs-GmbH Deutschland in cooperation with the Association of German gastroenterologists in private practice (bng).

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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

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

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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 sores APRI score and FORNS index were calculated (for cut offs see below) and the diagnostic accuracy was compared to FS results.

Table 1. Used TE cut offs to define different fibrosis stages

Transient Elastography (FibroScan, kPa)	N	%
TE <=7 kPa F0-1	625	35.9%
TE >7 - < 12.5 kPa F2-3	530	30.4%
TE >=12.5 kPa F4	587	33.7%
Total	1742	100.0%

APRI:

- Significant fibrosis: <0,5 for exclusion F2,3,4; >1,5 for diagnosis of F >= 2
- cirrhosis: <1 for exclusion, >2 for diagnosis of cirrhosis

FORNS index:

- Significant fibrosis: <4,2 for exclusion F2,3,4; >6.9 for diagnosis of F >= 2

(Lin et al., Hepatology 2011, Sebastiani et al., Aliment Pharm 2012, Forns et al., Hepatology 2002)

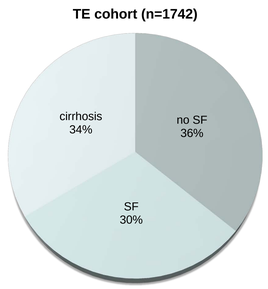
RESULTS

Table 2. baseline chraracteristics in different patient groups

Baseline demographic data	TE <=7 kPa F0-1	TE >7 - < 12.5 kPa F2-3	TE >=12.5 kPa F4	Total
Age (mean)	50.9	54.6	57.4	54.2
Gender (male, %)	49.4	58.9	64.4	57.3
BMI (mean)	24.7	25.5	26.5	25.5
EDD (years)	19.1	19.8	23.1	20.7
Therapy experienced (%)	47.7	54.9	62.4	54.8
AST iU/mL (mean)	48.5	67.4	97.5	70.9
Platelets /nl (mean)	230.2	205.4	139.9	192.0
Genotype 1 (%)	86.1	85.9	80.4	84.3

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



RESULTS (continued)

SVR rates following different DAA regimens with or without ribavirin for 8 – 24 weeks were 98,2%, 96,8%, and 92,4% for patients with no SF, SF, and cirrhosis, respectively. For discrimination of SF, AUROCS were: 0.791 (APRI score), 0.840 (FORNS index). For discrimination of cirrhosis, AUROC was 0.879 (APRI score).

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

Diagnostic accuracy of serum fibrosis scores in comparison to TE									
Fibrosis	**score**	**AUROC**	**sensitivity**	**specificity**	**NPV**	**PPV**	**+LR**	**-IR**	**Best cut**
Yes	APRI	.791	.602	.947	.606	.946	11.409	.420	.4958
Yes	FORNS	.840	.797	.203	.615	.916	4.315	.249	7.1647
cirrhosis	**score**	**AUROC**	**sensitivity**	**specificity**	**NPV**	**PPV**	**+LR**	**-IR**	**Best cut**
Yes	APRI	.879	.846	.853	.91	.75	5.77	.18	.4919

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 descision making, e.g. treatment duration
- SVR rates in patients with cirrhosis were numerically lower with current DAA regimens.

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