Barriers to Hepatitis C Virus Elimination in Germany in Patients Receiving Opioid Substitution Therapy

H Hinrichsen¹, P Buggisch², H Heiken³, S Mauss⁴, B Weber⁵, MC Jung⁶, H Görne⁷, R Heyne⁸, D Hidde⁹, B Koenig⁹, M Bondin¹⁰, C Niederau¹¹, H Wedemeyer¹², T Berg¹³

¹Centre for Gastroenterology and Hepatology, Kiel, Germany; ³Private practice, Hanover, Germany; ³Private practice, Hanover, Germany; ⁴Center for HIV and Hepatology, Düsseldorf, Germany; ³Private practice, Hanover, Germany; ⁴Center for HIV and Hepatology, Düsseldorf, Germany; ⁴Center for HIV and Hepatology, Düsseldorf, Germany; ⁴Center for HIV and Hepatology, Düsseldorf, Germany; ⁴Center for HIV and Hepatology, Ciel, Germany; ⁴Center for HIV and Hepatology, Düsseldorf, Germany; ⁴ Kassel, Germany; ⁶Liver Centre, Munich, Germany; ⁸Leberzentrum am Checkpoint, Berlin, Germany; ¹⁰AbbVie Inc., North Chicago, Illinois, United States; ¹¹Private practice, Oberhausen, Germany; ¹²Department of Gastroenterology, University Hospital Essen, University Medical Center, Leipzig, Germany; ¹³Division of Hepatology, University Medical Center, Leipzig, Germany; ¹⁴Division of Hepatology, University, Center, Leipzig, Germany; ¹⁴Division of Hepatology, Center, Leipzig, Germany; ¹⁴Division of Hepatology, Center, Leipzig, Cen

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BACKGROUND

- Globally, more than 70 million people are infected with hepatitis C virus (HCV);¹ people who inject drugs are the patient group with the highest number of chronic HCV (CHC) cases and new infections in the most high-income countries^{2,3}
- Despite the advent of effective and well-tolerated HCV treatment options such as direct-acting antivirals (DAAs),⁴ treatment uptake is still low, particularly among drug users⁵
- Barriers such as advanced age, alcohol and drug abuse, and comorbidities^{6–8} have been associated with low treatment uptake in patients with HCV
- In addition, stigma, ambivalence about opioid substitution therapy (OST), and health service funding priorities were some of the reasons reported by patients and healthcare providers (HCPs) for not initiating HCV treatment⁹
- The CURRENT-C 1.0 study, conducted in Germany in 2014, reported patient choice as the most cited reason for not initiating HCV treatment; however, this study was conducted in the interferon/early DAA era⁶
- In the current era of DAAs, it is therefore important to investigate the reasons for a lack of treatment initiation from both the patient and physician perspectives, as well as identify any significant patient demographic risk factors that may be associated with low treatment uptake

OBJECTIVE

• To describe reasons for physicians or patients not initiating HCV treatment, and identify significant demographic and clinical risk factors for not initiating DAAs in patients with CHC receiving OST

METHODS

STUDY DESIGN

- CURRENT-C 2.0 is an epidemiologic, multicenter, noninterventional, case-control study of patients attending 43 medical centers experienced in the treatment of HCV in Germany from 1 September 2017 to 30 June 2018
- The overall study duration was ≥20 months and included a 10-month retrospective observation period (from 1 September 2017 to 30 June 2018) followed by a documentation period

STUDY PARTICIPANTS

- Patients included were aged \geq 18 years, had CHC (HCV RNA–positive for \geq 6 months), and consulted their HCP at least once during the observation period
- Exclusion criteria consisted of acute HCV infection or treatment for CHC infection <3 months before the start of the planned observation period

STUDY OUTCOMES

- The primary objective of this study was to assess the reasons why either patients with CHC receiving OST or their HCPs decided not to initiate HCV therapy
- The secondary objective was to identify demographic and clinical risk factors for not initiating DAAs in patients with CHC receiving OST

DATA ANALYSIS

- Patient baseline characteristics and reasons for patient and HCP treatment decisions for HCV infection were collected
- Multivariate logistic regression analyses with backward elimination were performed to identify factors associated with not receiving therapy
- For patient baseline characteristics, subgroups analyzed were patients on OST initiating treatment for HCV and patients on OST who did not initiate treatment
- For reasons not to initiate HCV treatment, subgroups analyzed were patients on OST and patients not on OST

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RESULTS

STUDY POPULATION

- Of 793 total patients evaluated in the CURRENT-C 2.0 study, 259 (33%) were receiving OST (Table 1)
- Of those patients receiving OST, 166 (64%) initiated HCV treatment and the remaining 93 (36%) did not (*P* <.001)
- Descriptive comparison showed a higher percentage of untreated patients vs treated patients with nonfibrotic liver at baseline (70% vs 29%, respectively; P <.001)

Table 1. Patient Demographics and Clinical Characteristics

Characteristic	Patients on OST treated (n = 166)	Patients on OST untreated (n = 93)
Male	132 (80)	64 (69)
Age (years), median (Q1–Q3)	45 (37–51)	44 (38–50)
<40	57 (34)	32 (34)
40–60	104 (63)	59 (63)
>60	5 (3)	2 (2)
German language knowledge		
Mother language	118 (71)	67 (72)
Very good	117 (70)	62 (67)
Good	44 (27)	25 (27)
Poor	4 (2)	6 (6)
None	1 (<1)	0
Employment status, yes	39 (23)	24 (26)
HCV GT		
1	81 (49)	37 (40)
1a, n (% of GT1)	72 (89)	27 (73)
1b, n (% of GT1)	8 (10)	6 (16)
1 other/unknown, n (% of GT1)	1 (1)	4 (11)
2	8 (5)	5 (5)
3	70 (42)	39 (42)
4	4 (2)	4 (4)
Other/unknown	8 (5)	3 (3)
HCV treatment-naïve	139 (84)	78 (84)
Reinfection after pre-treatment, n (% of pre-treated)	6 (22)	3 (20)
Abnormal liver findings	66 (40)	36 (39)
Nonfibrotic [†]	48 (29)	65 (70)*
Cirrhosis status		
Cirrhotic	29 (17)	18 (19)
Noncirrhotic	135 (81)	72 (77)
Unknown	2 (1)	3 (3)
Duration of HCV infection		
Mean \pm SD	14.2 ± 8.7	14.6 ± 9.1
Median (Q1–Q3), [min–max]	14 (7–20), [0.5–35]	15 (7–20), [1–41]
Viral load		
>800 000 IU/mL [‡]	30 (55)	46 (50)
No value	110 (66)	0
Data are n (%) unless otherwise stated.	× /	

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*P < .001 (treated vs untreated patients, 2-sided Chi-square test); *Patients treated, n = 166; *Percentage of n = 55 treated patients, n = 92 untreated patients. GT, genotype; HCV, hepatitis C virus; OST, opioid substitution therapy; Q, quartile; SD, standard deviation.

• Comorbidities and risk behaviors in patients with CHC receiving OST by treatment status are shown in **Table 2**

- Significantly higher percentages of patients on OST who did not receive treatment showed human immunodeficiency virus coinfection, concomitant symptoms of current drug abuse or withdrawal (all P < .001), and concomitant psychiatric disease (P < .05) than those who did receive treatment

– Additionally, compared with patients on OST who received treatment, a higher number of patients on OST who did not receive treatment showed risk behaviors such as heavy alcohol intake, history of intravenous drug use (P < .001), and history of cannabis use (P < .05)

CREATED @ 100%

Table 2. Comorbidities and Risk Behaviors

Characteristic	Patients on OST treated (n = 166)	Patients on OST untreated (n = 93)	drug use (recent and ongoing) were significant predictors of not initiating HCV treatment (Table 3 Table 3. Multivariate Analysis of Predictive Factors For Receiving HCV Treatment				
HIV coinfection	9 (5)	18 (19)**	Parameter	<i>P</i> value	OR	95% CI	
Any concomitant disease	163 (98)	88 (95)	HIV coinfection	.020	0.250	0.078–0.805	
Concomitant CV disease	10 (6)	12 (13)	Nonfibrotic	.038	0.450	0.212-0.956	
Any concomitant psychiatric disease	46 (28)	41 (44)*	IV drug use (recent), yes vs no	.001	0.308	0.149-0.637	
Concomitant psychiatric disease "depression"	30 (18)	23 (25)	Current drug abuse	.024	0.327	0.124-0.864	
Concomitant psychiatric disease "psychosis"	9 (5)	7 (8)	Multivariate logistics regression analyses with back elimination for significant parameters with ≥75% valid cases (n = 175). CI, confidence interval; HIV, human immunodeficiency virus; IV, intravenous; OR, odds ratio. REASONS FOR NOT INITIATING TREATMENT • The top reasons reported by HCPs for not initiating HCV treatment by OST status are reported in Figure 1				
Current drug abuse	19 (11)	29 (31)**					
Current IV drug abuse	9 (5)	5 (5)					
State after drug abuse	32 (19)	16 (17)					
Other clinical symptoms [†]	59 (36)	55 (59)**	 In patients with CHC who were receiving OST, the most frequently reported reasons by the HCP for not initiating HCV therapy were patient preference against therapy, ongoing drug abuse, perceived or expected lack of compliance, psychiatric disease, and HCV reinfection 				
Alcohol intake	70 (42)	44 (47)					
Heavy alcohol intake, >40 g/day (male) or >30 g/day (female)	28 (17)	32 (34)**	 In patients with CHC who were not receiving OST, the most frequently reported reasons by the HCP for not initiating HCV therapy were advanced patient age and existing comorbidities, such heart disease, liver-, and non-liver-related malignancies 				
History of cannabis use	35 (21)	33 (35)*					
Recent history of IV drug use	34 (20)	45 (48)**	 Reported reasons that were significantly more frequent in patients on OST vs those who were not on OST: ongoing drug abuse (32% vs 2%), poor compliance (30% vs 3%), psychiatric disease (15% vs 2%), and HCV reinfection (9% vs 0%) (all P <.001) (Figure 1) 				
Duration of IV drug use (years), median (Q1–Q3)	21.5 (10–27)	21 (12–30)					
Data are n (%) unless otherwise stated.			- Regarding patient preference, significantly more patients who were not receiving OST decided				

*P <.05; **P <.001 (treated vs untreated, 2-sided Chi-square test); *Symptoms included fatigue, fever, skin changes, hair loss, joint pain, muscle pain, abdominal pain/complaints, diarrhea, constipation, flatulence, nausea, reflux, weight loss, anorexia, headache, sleeplessness, irritability, restlessness, depression, depressed mood, psychosis, poor concentration, icterus, pruritus, craving/withdrawal-like complaints, rash, taste disorder, dyspnea, or other. CV, cardiovascular; HIV, human immunodeficiency virus; IV, intravenous; OST, opioid substitution therapy; Q, quartile.



Figure 1. Top Reasons Reported For Not Initiating HCV Treatment

*P <.05; **P <.001 (receiving OST vs not receiving OST, 2-sided Chi-square test); †Include heroin, amphetamine, cocaine, and designer drugs. HCP, healthcare provider; HCV, hepatitis C virus; OST, opioid substitution therapy

TRANSPARENCY

AUTHOR DISCLOSURES

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• In multivariate logistic regression analyses, HIV coinfection, absence of fibrosis, and history of

- not to start HCV treatment because of fear of adverse effects than those who were on OST (23% vs 10%, respectively; P <.05); significantly more patients on OST decided not to start treatment because of imprisonment than those who were not on OST (3% vs 0%; P <.05)

CONCLUSIONS

- Significant risk factors contributing to patients on OST not commencing HCV treatment included HIV coinfection, concomitant psychiatric diseases, ongoing drug use, and absence of fibrosis
- Historical barriers to initiating HCV treatment, such as psychiatric disease, ongoing drug and alcohol use, and perceived or expected lack of compliance can lead to treatment postponement or noninitiation
- It is essential for HCPs to overcome historical barriers to initiating DAA therapy and educate patients on the importance of treatment to achieve HCV elimination in this patient population

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