Clinical Infectious Diseases

MAJOR ARTICLE

High Cure Rates With Grazoprevir-Elbasvir With or Without Ribavirin Guided by Genotypic Resistance Testing Among Human Immunodeficiency Virus/Hepatitis C Virus–coinfected Men Who Have Sex With Men

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Background. This study was performed to investigate the efficacy and safety of grazoprevir-elbasvir guided by baseline resistance-associated substitutions (RASs) in the Swiss HCVree Trial (clinicaltrials.gov NCT02785666).

Methods. We performed hepatitis C virus (HCV) RNA screening among all men who have sex with men (MSM) enrolled in the Swiss HIV Cohort Study. Individuals with replicating HCV genotype 1 or 4 infection were eligible for grazoprevir-elbasvir treatment. Genotype 1a–infected individuals with baseline RASs and genotype 4–infected individuals with prior failure of HCV treatment received 16 weeks of grazoprevir-elbasvir combined with ribavirin. All other individuals received 12 weeks of grazoprevir-elbasvir alone. Patients reporting unprotected sex with occasional partners were offered a HCV risk reduction–oriented behavioral intervention.

Results. We screened 3722 MSM and identified 177 (4.8%) with replicating infection. A total of 122 individuals (3.3%) were eligible for study treatment. Six of 76 patients infected with genotype 1a (7.3%) harbored baseline RASs. Sustained virological response after 12 weeks of follow-up was achieved in 121 patients (99%), including all with genotype 1a infection. Overall, 8 serious adverse events occurred, none of which was related to the study drug. Seventy-five percent of eligible MSM participated in the risk counseling program.

Conclusions. Grazoprevir-elbasvir for 12 or 16 weeks, with or without ribavirin, achieved high cure rates and had an excellent safety profile. Unique to other studies, the treatment duration was guided by the presence of baseline RASs among genotype 1a–infected individuals, and the treatment phase was accompanied by an HCV risk reduction–oriented behavioral intervention. This successful population-wide treatment approach lays the groundwork to achieve HCV elimination in coinfected MSM.

Keywords. Hepatitis C virus; HIV; resistance-associated substitutions; men who have sex with men; grazoprevir-elbasvir.

Hepatitis C virus (HCV) infection is one of the leading causes of death in human immunodeficiency virus (HIV)–infected persons [1–4]. In industrialized countries, the burden of HCV infection affected mainly persons who inject drugs until the first cases of sexually transmitted infection in HIV-infected men who have sex with men (MSM) were described a decade ago [5–9]. With the recently described epidemiological changes in HCV transmission, HIV-infected MSM are now the key population for targeted treatment interventions, with the goals of preventing transmission of HCV to other sex partners and liver-related complications [10]. Unfortunately, in many countries—including Switzerland until May 2017—treatment with highly effective HCV direct-acting agents (DAAs) was/is restricted to patients with advanced liver disease, owing to the exceptionally high costs of these DAAs.

The once-daily oral combination grazoprevir-elbasvir is a next-generation DAA and was approved by the US Food and Drug Administration in 2016 for the treatment of HCV genotype 1 or 4 infection [11]. Grazoprevir-elbasvir, with or without ribavirin, showed high efficacy, with cure rates of ≥95% and a favorable tolerability in both monoinfected and HIV/HCV-coinfected populations [12–18]. In some studies, the

Received 19 March 2018; editorial decision 10 June 2018; accepted 29 June 2018; published online XXXX XX, XXXX.

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Clinical Infectious Diseases® 2018;XX(XX):1–8

DOI: 10.1093/cid/ciy547

presence of baseline NS5A resistance-associated substitutions (RASs) significantly reduced rates of sustained virological response after 12 weeks of follow-up (SVR12) in genotype 1a–infected patients [19]. This observation resulted in the recommendation to perform HCV resistance testing of the NS5A region in genotype 1a–infected patients before grazoprevir-elbasvir therapy.

The Swiss HCVree Trial consists of population-based systematic HCV RNA polymerase chain reaction (PCR) testing among all MSM who participate in the Swiss HIV Cohort Study (SHCS) and thereafter provided free HCV treatment with grazoprevir-elbasvir to all MSM identified as having a replicating genotype 1 or 4 infection [20]. This was all in pursuit of a strategy with the primary goal of implementing an HCV elimination program at the population level. Individuals with contraindications to grazoprevir-elbasvir were treated with standard-of-care DAAs. Unique to other studies, the treatment duration of grazoprevir-elbasvir was a priori determined based on the presence of baseline RASs in genotype 1a–infected MSM. If baseline RASs were present, treatment extension to 16 weeks with the addition of weight-based ribavirin was recommended [21]. Here we report on the SVR12 data achieved with grazoprevir-elbasvir, with or without ribavirin, and the safety and tolerability of this regimen.

METHODS

Swiss HCVree Trial and SHCS

The Swiss HCVree Trial is a prospective, multicenter, nationwide, interventional trial (NCT02785666) within the SHCS, consisting of 3 phases. Detailed information on the SHCS is published elsewhere [22]. During period A, the screening period from 1 October 2015 to 30 June 2016, we performed a systematic HCV RNA PCR–based testing among all MSM participating in the SHCS. Participants were screened at least once using HCV PCR during the 9-month screening-period, at a regular 6-monthly SHCS visits.

During period B, from 1 June 2016 to 28 February 2017, HCV treatment with the once-daily combination grazoprevir-elbasvir was provided to all MSM with replicating genotype 1 or 4 infection, regardless of fibrosis stage. The study drug was provided by Merck Sharpe & Dohme in the context of this investigator-initiated trial. Individuals with genotype 2 or 3 infections were treated using standard-of-care DAAs in if reimbursement requirements were fulfilled. The treatment phase was accompanied by a risk behavioral intervention for MSM who reported unprotected sex with occasional partners.

During the rescreening period, period C, from 1 March to 30 November 2017, all MSM were retested with HCV PCR to assess preintervention and postintervention prevalence in the targeted population. Local ethics committees of all participating study sites approved the study, and written consent was obtained from all participants.

Study Population

HIV-infected MSM aged ≥18 years with treatment-naive or treatment-experienced HCV genotype 1 or 4 infections were eligible for grazoprevir-elbasvir treatment. Patients with compensated cirrhosis were allowed to be enrolled. Patients with decompensated liver disease, hepatitis B virus coinfection, or previous treatment with a DAA other than telaprevir or boceprevir were excluded. A complete description of the inclusion/exclusion criteria is provided in Supplementary Table 1.

Study Measurements

Between 1 October 2015 and 31 May 2016, all MSM participating in the SHCS and attending a clinical visit were screened at least once for a replicating HCV infection with HCV RNA PCR. Replicating HCV infection was defined as a HCV RNA result ≥100 IU/mL. HCV RNA testing was done centrally at the Institute of Medical Virology, Zurich, using the Abbott RealTime HCV test with a limit of quantification of 12 IU/mL.

In patients with a replicating genotype 1a infection, we performed a HCV resistance test, using a test developed by the Institute of Medical Virology, University of Zurich. The written report included the presence or absence of RASs M/L28T/A, Q/R30E/H/R/G/K/L/D, L31M/V/F, H58D, or Y93C/H/N in the NS5A gene, and a specific recommendation for 16 weeks of treatment if an RAS was present.

Specimens for HCV RNA measurements were collected at baseline (week 0) and at treatment weeks 4 and 12. Sustained virological response rates were assessed 12 weeks after cessation of study treatment. Liver fibrosis stage was determined with transient elastography (Fibroscan; Echosens) using the cutoffs proposed by Castera et al [23]. Prior failure of pegylated interferon alfa was defined as published elsewhere [24].

Study Treatment

MSM with a replicating HCV genotype 1 or 4 infection received a fixed-dose once-daily combination of grazoprevir (100 mg) and elbasvir (50 mg), with or without weight-adjusted ribavirin, twice daily, for 12 or 16 weeks. Treatment duration was determined based on the genotype, and for genotype 1a infection based on the HCV resistance result. Treatment-naive and treatment-experienced genotype 1a–infected patients without baseline NS5A RASs and treatment-naive genotype 4–infected patients were treated for 12 weeks with grazoprevir-elbasvir. Treatment-naive and treatment-experienced genotype 1a–infected patients with baseline NS5A RASs and treatment-experienced genotype 4–infected patients with a history of failed prior treatment with pegylated interferon alfa with ribavirin were treated for 16 weeks with grazoprevir-elbasvir in combination with weight-adjusted ribavirin. At the time of the study, if RAS testing was not available, the international guidelines recommended extending treatment to 16 weeks with the addition of weight-based ribavirin in genotype 1a–infected patients with baseline viral load >800 000 IU/mL [21].

Risk Reduction Intervention

All study participants received written and oral information on prevention of HCV reinfection at study visit 1 (week 0). In addition, all patients who reported any condomless sex with occasional partners at SHCS assessments in 2015, until study enrollment or baseline ,were offered a behavioral counseling intervention oriented toward HCV risk reduction. The 4 intervention sessions were provided by trained counselors and supported by an e-health tool. Participants were able to use the e-health tool at any time during the treatment phase. The counseling sessions took place at visit 2 (week 4), 3 (week 6), 4 (week 8), and 5 (week 12).

Statistical Analysis

We assessed the statistical significance of the difference between traits in screened and unscreened MSM in the SHCS, using χ^2 tests for categorical and t tests for 2 independent means for quantitative variables. The cutoff for statistical significance was set at $P \leq .05$. These statistical analyses were performed with R software (version 3.3.3).

RESULTS

Screening for Replicating HCV Infection

Overall, 3722 MSM were screened during a clinical visit in the screening period, of whom 177 MSM (4.8%) harbored a replicating HCV infection (Figure 1). Of these 177 patients, 3 had spontaneous clearance of the infection, and 1 died. Fifty-two MSM with a replicating HCV were not eligible for grazoprevir-elbasvir treatment. The reasons for exclusion were unwillingness to participate in the study (eg, to avoid a change in antiretroviral therapy because of drug-drug-interactions) (n = 25; 48%), harboring of HCV genotype 2 or 3 infections (n = 11; 21%); other exclusion criteria according to the study protocol (eg, medical comorbid conditions) (n = 6; 12%), loss to follow-up (n = 5: 10%), and logistic reasons (eg, living abroad) (n = 4; 8%). Finally, 122 patients were treated with grazoprevir-elbasvir. Thirty-eight of the 52 patients (75%) who were not eligible for grazoprevir-elbasvir received standard-of-care HCV treatment after the omission of the DAA reimbursement restrictions in Switzerland, and SVR12 was achieved in all. The remaining 13 patients will be considered for HCV treatment in the future (Figure 1).

Patient Characteristics

The first patient started treatment on 17 June 2016, and the last patient completed 12 weeks of follow-up on 23 May 2017. The baseline characteristics are shown in Table 1. The majority of patients were white (88%), the median patient age was 47 years, and the median CD4 cell count was 686/μL. Overall, 62 patients (51%) had HCV RNA levels >800 000 IU/mL, and 4 patients (3%) had cirrhosis. Five patients (4%) had a prior

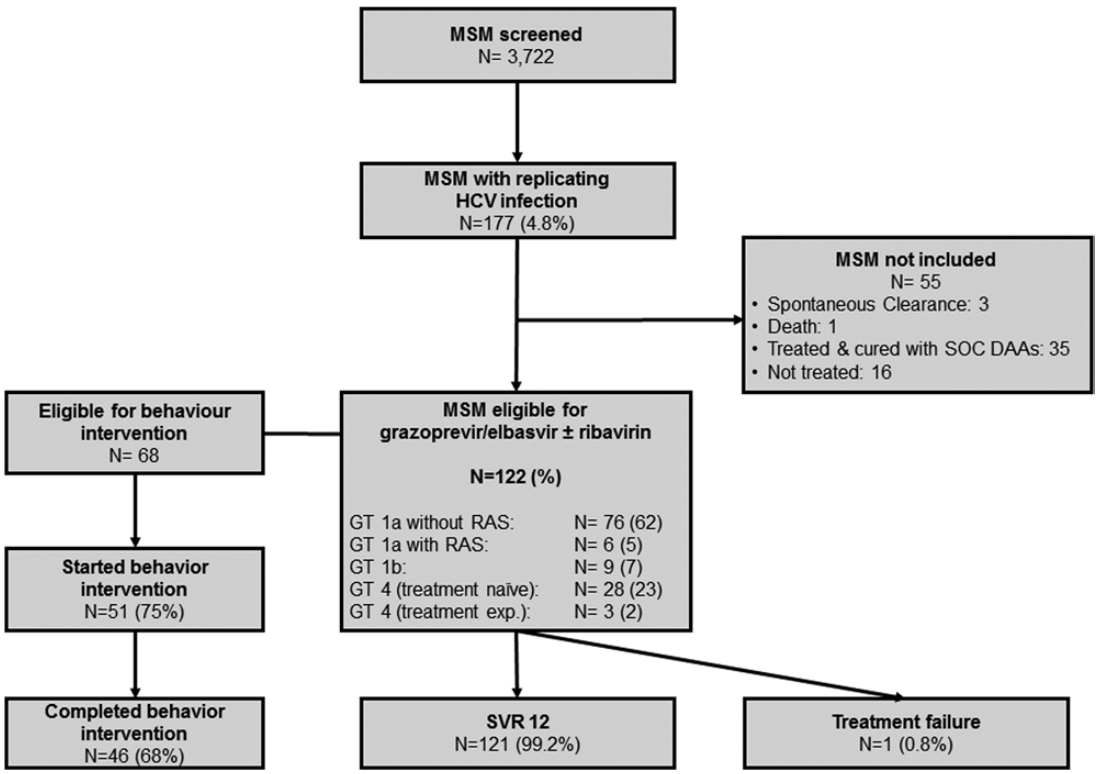

Figure 1. Flowchart of the Swiss HCVree trial. Abbreviations: DAAs, direct-acting agents; GT, genotype; HCV, hepatitis C virus; MSM, men who have sex with men; RASs, resistance-associated substitutions; SOC, standard-of-care; SVR12, sustained virological response after 12 weeks of follow-up.

Table 1. Baseline Characteristics of MSM Included in the Treatment Phase

Characteristic	MSM, No. (%)[a]
Age, median (IQR), y	46.7 (27–68)
Race	
White	107 (88)
Black	4 (3)
Asian	6 (5)
Latino/Hispanic	5 (4)
CD4 cell count, median (IQR), cells/μL	686 (199–1906)
HIV viral load, median (IQR), copies/mL	0 (0–9134)
HCV genotype	
1a	82 (67)
1b	9 (7)
4	31 (26)
Genotype 1a with baseline RASs	6 (7.3)
Previous HCV treatment	18 (15)
Patient population	
Genotype 1a without baseline RASs	76 (62)
Genotype 1a with baseline RASs	6 (5)
Genotype 1b	9 (7)
Genotype 4, treatment naive	28 (23)
Genotype 4, treatment experienced	3 (3)
Fibrosis stage at baseline (METAVIR score)	
F0–F1	95 (78)
F2	14 (12)
F3	4 (3)
F 4	4 (3)
Missing data	5 (4)
Time since HCV diagnosis, median (IQR), mo	36 (2–273)
HCV RNA at baseline, median (IQR), IU/L	865 279 (74–57 600 000)
Baseline HCV RNA concentration	
<800 000 IU/L	60 (49)
>800 000 IU/L	62 (51)
AST, median (IQR), U/L	44 (16–266)
ALT, median (IQR), U/L	63.5 (19–486)
Platelets, median (IQR), Giga/L	209 (113–368)
ART status	
HIV viral load <20 copies/mL	121 (99)
Currently not receiving ART	1 (1)
ART regimen	
Abacavir containing	47 (39)
Tenofovir containing	73 (60)
Other	1 (<1)
None	1 (<1)
ART 3rd agent	
Dolutegravir	64 (52)
Raltegravir	13 (11)
Rilpivirine	38 (31)
Other	6 (5)
None	1 (<1)

Abbreviations: ALT, alanine aminotransferase; ART, antiretroviral therapy; AST, aspartate aminotransferase; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; MSM, men who have sex with men; RASs, resistance-associated substitutions.

[a]Data represent No. (%) of MSM unless otherwise specified.

partial or null response to pegylated interferon and ribavirin. None of the patients had received prior therapy with telaprevir or boceprevir. Of 68 MSM eligible for the risk counseling program, 51 (75%) agreed to participate and 46 (68%) completed all 4 sessions.

Treatment Outcome

Overall, SVR12 was achieved in 121 of 122 patients (99%) (Figure 1). The SVR12 rate was 99% in the 12-week grazoprevir-elbasvir arm and 100% in the 16-week grazoprevir-elbasvir/ribavirin arm. One treatment-naive patient with genotype 4 infection experienced on-treatment failure. This patient had no advanced fibrosis and reported good adherence to the study drug throughout the study. His baseline HCV viral load of 6.5 log RNA (3 338 442 IU/mL) decreased to <1 log RNA (<12 IU/mL) at week 4, was detectable with 1.4 log RNA (27 IU/mL) at week 12 (end of treatment), and finally increased to 6.2 log RNA (1 737 800 IU/mL) at week 24 (12 weeks after treatment cessation).

RASs in Patients With Genotype 1a Infection

Six of 76 genotype 1a–infected MSM (7.9%) harbored baseline RASs in NS5A and therefore were treated for 16 weeks with grazoprevir-elbasvir in combination with ribavirin. The specific RASs detected in these 6 patients are shown in Table 2. In these patients, the presence of NS5A RASs at baseline did not reduce SVR12 rates. These rates were 100% in the patients with baseline NS5A RASs (Table 2). Of the 76 patients with genotype 1a infection and no baseline RASs, 41 (54%) had a HCV viral load >800 000 IU/mL. Two of the 6 patients with baseline RASs (33%) had a HCV viral load <800 000 IU/mL. The clinical characteristics of the genotype 1a–infected patients are shown in Table 3.

HCV Resistance Analysis of Patient With Treatment Failure

We retrospectively performed HCV resistance tests in genotype 4–infected patient with treatment failure for the NS3, NS5A and the NS5B regions from both the baseline sample at week 0 and the week 24 sample. The baseline sample showed no RASs in the NS3 and NS5B regions but a 58P mutation in NS5A, which is considered to result in reduced susceptibility according to the European Association for the Study of the Liver guidelines but is not scored as significant by the geno2pheno system [25]. The resistance test from the sample taken at week 24 newly revealed the 2 additional mutations 28S and 31I, with reduced susceptibility for genotype 4 only to ombitasvir, according to geno2pheno.

Safety and Tolerability

Overall, 8 serious clinical adverse events and 240 adverse events occurred. All serious adverse events were classified as treatment unrelated. The most common adverse events were upper respiratory tract infection (n = 41; 34%) and sexually transmitted infections (n = 31; 25%). Among possible drug-related clinical adverse events, the most common were fatigue (n = 7; 6%),

Table 2. Rates of Sustained Virological Response After 12 Weeks of Follow-up

Outcome	All Patients (N = 122)	Genotype 1a		Genotype 1b (n = 9)	Genotype 4	
		Without RASs (n = 76)	With RASs (n = 6)[a]		Treatment Naive (n = 28)	Treatment Experienced (n = 3)
SVR12, No. (%)	121 (99%)	76 (100)	6 (100)	9 (100)	27 (96)	3 (100)
Failure, No.	1%	0	0	0	4%	0

Abbreviations: RASs, resistance-associated substitutions; SVR12, sustained virological response after 12 weeks of follow-up.

[a]The following RASs were detected in the 6 patients: Q30H (n = 2), Y93N (n = 2), Y93C (n = 1), and L31LM (n = 1).

diarrhea (n = 6; 5%), nausea (n = 4; 3%), and pruritus (n = 4; 3%) (Table 4). The majority of clinical adverse events were of mild (n = 176; 73%) or moderate (n = 58; 24%) severity, and only 6 (2.5%) were classified as severe. Among the 29 laboratory adverse events, there were 5 (17%) grade 3 adverse events. The thresholds for the grading of laboratory adverse events are provided in Supplementary Table 2. We noted no late elevations of alanine aminotransferase or aspartate aminotransferase levels. There was no discontinuation of the study drug in the whole study population. Among the 9 patients who received ribavirin, 8 possible and 5 probable drug-related clinical adverse events occurred (Supplementary Table 3).

DISCUSSION

In this nationwide, prospective, multisite, interventional trial, once-daily grazoprevir-elbasvir for 12–16 weeks, with or without ribavirin, had a very high SVR12 rate of 99% and showed an excellent safety profile. Unique among other studies, we determined the treatment duration in HCV genotype 1a–infected patients based on the absence or presence of baseline RASs, and with this approach SVR12 was achieved in 100% of genotype 1a–infected patients with baseline RASs. In addition, the treatment phase was accompanied by an HCV risk reduction–oriented behavioral intervention, with the goal of preventing reinfection after successful HCV treatment.

To the best of our knowledge, this is the first HCV trial in which an a priori performed HCV resistance test guided the duration of HCV therapy, coadministered with or without ribavirin. Using this novel, personalized strategy, we achieved SVR12 rates similar to those reported in 4 HIV/HCV coinfection phase III trials with grazoprevir-elbasvir [12, 19, 26]. In our study, 6 of 76 genotype 1a–infected patients (7.9%) harbored RASs at baseline and therefore received 16 weeks of grazoprevir-elbasvir in combination with ribavirin. In all of them, SVR12 was achieved. Of note, 41 genotype 1a–infected patients without baseline RASs had a baseline HCV viral load >800 000 IU/mL. Thus, in the absence of RAS testing, all of these patients would have been treated for 16 weeks with grazoprevir-elbasvir with the addition of ribavirin, according to the guidelines at the time of the study [21]. In contrast, 2 patients with baseline RASs had a baseline viral load <800 000 IU/mL and therefore may have been treated unnecessarily for 16 weeks with the ribavirin combination. Hence, based on the 2 different strategies, the balance of potentially unnecessary treatments for 16 weeks was 2 versus 41 patients, resulting in a difference of 39 patients in whom prolonged treatment and the addition of ribavirin has been avoided.

The recommendations to prolong treatment duration to 16 weeks with the addition of ribavirin for genotype 1a–infected patients with baseline NS5A RASs is based mainly on the extrapolation of data from the C-EDGE TE study [19]. Among the genotype 1a–infected patients with baseline RASs, SVR12 was achieved in only 58%, compared with 99% in those without RASs. However, in genotype 1–infected patients with pretreatment NS5A RASs, who were treated with grazoprevir-elbasvir plus ribavirin for 16 or 18 weeks, SVR12 was achieved in all patients

Table 3. Clinical Characteristics of Genotype 1a–infected Patients With or Without Baseline RASs

Characteristic	Baseline RASs (n = 6)	No Baseline RASs (n = 76)	*P* Value
Age, mean, y	55	45	.01
Time since HCV diagnosis, median (IQR), mo	42 (23–103)	2.2 (1.0–5.7)	.53
HCV RNA at baseline, median (IQR), log IU/mL	6.2 (6.0–6.3)	6.0 (5.3–6.5)	.54
HCV RNA at baseline, No. (%)			
>800 000 IU/mL	4 (66.6)	41 (54)	.08
<800 000 IU/mL	2 (33.3)	35 (46)	
CD4 cell count, median (IQR), cell/μL	566 (556–644)	689 (526–835)	.20
HIV RNA, median (IQR), copies/mL	0 (0-0)	0 (0-0)l	.81
Fibroscan stiffness, median (IQR), kPa	5.3 (4.2–5.4)	5.7 (4.9–7.7)	.15

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; RASs, resistance-associated substitutions.

Table 4. Safety and Adverse Events in the Treatment Period and First 12 Weeks of Follow-up

Adverse Events	All Patients (N = 122)	Patients Treated With Ribavirin (n = 9)
All adverse events, No.	240	30
Patients with ≥1 adverse event, No. (%)	97 (80)	7 (78)
Serious adverse events, No.	9	1
Serious drug-related adverse events, No.	0	0
Discontinuation due to adverse event, No.	0	0
Deaths, No.	0	0
All clinical adverse events, No.	211	26
The numbers of clinical adverse events are number of events occuring in >5% of patients[a]		
Upper respiratory tract infection	41 (34)	5 (56)
Sexually transmitted infection	31 (25)	0
Fatigue	9 (7)	0
Skin rash	8 (7)	2 (22)
Headache	7 (6)	0
Diarrhea	7 (6)	2 (22)
Nausea or vomiting	7 (6)	4 (44)
The numbers of possible drug-related events are number of events occuring in >3% of patients[b]	35 (29)	8 (89)
Fatigue	7 (6)	0
Diarrhea	6 (5)	1 (11)
Nausea or vomiting	4 (3)	2 (22)
Pruritus	4 (3)	2 (22)
The numbers of probable drug-related clinical adverse events are number of events occurring in >3% of patients[c]	9 (7)	5 (56)
Laboratory adverse events, No. (%) of patients	29 (24)	4 (44)
ALT		
Grade 1	1 (<1)	0
Grade 2	0	0
Grade 3	1 (<1)	0
AST		
Grade 1	1 (<1)	0
Grade 2	1 (<1)	0
Grade 3	1 (<1)	0
Bilirubin		
Grade 1	0	0
Grade 2	2 (2)	1 (11)
Grade 3	3 (2)	0
Alkaline phosphatase		
Grade 1	1 (<1)	0
Grade 2–3	0	0
Creatinine		
Grade 1	11 (9)	2 (22)
Grade 2	2 (2)	0
Grade 3	0	0
Hemoglobin (grade 1–3)	0	0
Nonfasting glucose		
Grade 1	2 (2)	1 (11)
Grade 2–3	0	0
Decreased platelet count		
Grade 1	1 (<1)	0
Grade 2	2 (2)	0
Grade 3	0	0
Decreased WBC count (grade 1–3)	0	0

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell.

[a]List of specific clinical adverse events includes those occurring in >5% of all patients

[b]List of specific possible drug-related clinical adverse events includes those occurring in >3% of all patients.

[c]No specific probable drug-related clinical adverse events occurred in >3% of all patients.

achieved. Given the very high SVR12 rates observed in our study with a resistance-test guided treatment approach, this strategy can be considered a step toward precision medicine in the HCV field, ensuring the highest success rates. Although the newest pangenotypic DAAs show similarly high cure rates without previous RAS testing, our proof of principle using an RAS-guided approach will still be important for either further shortening treatment duration or for patients with DAA failure. Both aspects need to be considered while striving for HCV elimination.

The safety and tolerability of grazoprevir-elbasvir was excellent, and we noted no treatment discontinuation. In the 9 patients treated with the combination of grazoprevir-elbasvir and ribavirin, there were only a few probable drug-related clinical adverse events (n = 5) and laboratory adverse events (n = 4; all grade 1). In contrast to previous studies [14, 15, 26], no late elevations in alanine aminotransferase or aspartate aminotransferase were observed.

The majority of MSM in our study (94%) had a genotype 1 or 4 infection, and 78% of them revealed a liver fibrosis METAVIR score of <2. In Switzerland, until May 2017, treatment with the newest HCV DAAs was restricted to patients with a METAVIR score of ≥2, owing to the high costs of these drugs. Hence, for the majority of the coinfected MSM patients in Switzerland, DAA treatment was not covered by health insurance. The Swiss HCVree Trial offered HCV treatment with grazoprevir-elbasvir to all MSM with replicating genotype 1 or 4 infection, regardless of their fibrosis stage. By providing universal access to HCV treatment to all HIV-infected MSM, we were able to target a patient group at high risk for transmitting HCV to their sexual partners, and high risk for the development of liver-related complications, owing to the accelerated fibrosis process in HIV/HCV-coinfected individuals [27].

The strengths of our study include the use of a population-based, nationwide HIV/HCV cohort with prospectively collected laboratory and clinical data, including regular HCV screening. Seventy-five percent of all HIV-infected MSM in Switzerland participate in the SHCS [28, 29]; thus, our study population is highly representative in regard to the HIV-infected Swiss MSM population and includes the key population in regard of the new HCV epidemic in a real-life setting. Another strength is that we combined the treatment intervention with a risk counseling program. We believe that this is important in attempts to eliminate HCV, because reinfections after successful HCV treatment have been described frequently among HIV-infected MSM cohorts [30]. A limitation of our study is that the treatment intervention included only individuals with genotype 1 or 4 infections, owing to the limited activity of grazoprevir-elbasvir in genotype 2 or 3 infections. However, there were very few individuals with a genotype 2 or 3 infection, and most of them were treated and cured outside the study after the omission of the reimbursement restrictions.

In conclusion, our study confirmed the high efficacy and excellent safety and tolerability of treatment with once-daily

grazoprevir-elbasvir for 12 or 16 weeks, with or without ribavirin. A patient-individualized treatment approach based on the presence of baseline RASs in genotype 1a–infected patients was feasible and resulted in 100% SVR12 rates among those harboring RASs. To reduce the risk of a reinfection after successful HCV therapy, next to standard oral and written prevention information, a risk reduction–oriented behavioral intervention accompanied the treatment phase. Although the effectiveness of this approach for preventing reinfection is currently unclear and was not explicitly assessed in the current study, models suggest that sustained reductions in high-risk behavior in the MSM population could rapidly curb the epidemic [31]. Therefore, we strongly believe that such comprehensive approaches are needed to successfully end the ongoing HCV epidemic in HIV/HCV-coinfected MSM.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author contributions. D. L. B., A. R., H. F. G., and J. S. F. designed the study. D. L. B., B. H., M. F., M. S., A. C., C. B., P. K. H., D. N., P. S., J. D., M. R., E. B., H. F. G., J. B., and J. S. F. acquired the data. B. H., R. K., and H. N. performed statistical analysis. D. L. B. and J. S. F. supervised the study. D. L. B. and B. H. wrote the first draft of the manuscript. All investigators contributed to data collection and interpretation, reviewed drafts of the manuscript, and approved the final manuscript.

Acknowledgments. We are grateful to all patients who participated in the study. We thank all SHCS-affiliated private physicians and all study nurses, in particular Christina Grube, for their dedicated patient work, as well as all clinical and laboratory staff at the different SHCS sites who have contributed to this study. We acknowledge Erik Mossdorf, Silvana Renner, Daniele Viviani, and the team from Merck Sharp & Dohme for supporting the study. We thank the Institute for Medical Virology from the University of Zurich, particularly Alice Krause, Sarah Wicki, Ruth Hefti, Verena Anukege, and Nancy Kurmann, and all SHCS-affiliated laboratories for their excellent laboratory work; Maja Müller and Alexandra Matter from the Clinical Trials Center Zurich for great assistance and careful study monitoring; Danièle Perraudin and Mirjam Minichiello from the SHCS coordination center for their assistance; and Liliane Clausen for helpful data cleaning.

Disclaimer. The opinions expressed in this article are those of the authors and do not necessarily represent those of Merck Sharp & Dohme. Merck Sharp & Dohme had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Financial support. This work was supported by Merck Sharp & Dohme (research grant from its Investigator-Initiated Studies Program), the Swiss National Science Foundation (grants 33CS30-148522 and 324730-112594 to the SHCS and grants PZ00P3-142411 and BSSGI0-155851 to R. K.), SHCS project 772 (support for this work and the SHCS research foundation), and the University of Zurich's Clinical Research Priority Program' Zurich Primary HIV Infection Study (D. L. B., B. H., and H. F. G.).

Potential conflicts of interest. D. L. B reports support for travel from Merck Sharpe & Dohme (MSD) and consultancy fees from MSD, Gilead, and ViiV, outside the submitted work. R. K. reports payment for lectures from Gilead. M. S. reports board memberships with AbbVie, Gilead, and MSD. A. C. reports travel grants from MSD and Gilead. C. B. reports fees from AbbVie, MSD, and Gilead, outside the submitted work. P. K. H reports consultancy fees from Sigma-Tau, Norgine, and AbbVie and grants from ViiV, MSD, and Janssen. D. N. reports grants from MSD, Janssen, and ViiV. E. B. reports board memberships with Gilead, MSD, ViiV, AbbVie, Sandoz, and Pfizer and fees from Gilead, MSD, ViiV, and Pfizer, outside the submitted work. A. R. reports consultancy fees from MSD, Gilead, and AbbVie, grants from Gilead, and fees from Gilead, Pfizer, and AbbVie, outside the submitted work. H. F. G. reports board membership with Data Safety Monitoring Board; consultancies for Gilead, Sandoz, and Teva; grants from Swiss National Science Foundation, Gilead HIV Cure Grant, the National Institutes of Health, SHCS, Yvonne Jacob Foundation, and Systms.X (HIV.X). J. S. F. reports board membership with the Federal Commission for Sexual Health, grants from Janssen, MSD, and ViiV, and fees from MSD, outside the submitted work. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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