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Low SVR Rates in Clinical Practice for Treating Genotype 1 Chronic Hepatitis C with Protease Inhibitors Boceprevir and Telaprevir

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To the editor,

We read with great interest the research article, “Effectiveness of Telaprevir and Boceprevir Triple Therapy for Patients with Hepatitis C Virus in a Large Integrated Care Setting” by Price et al. [1]. To date, there have been few reports on treatment initiation and effectiveness of telaprevir- and boceprevir-based triple regimens in clinical practice. In this paper, only

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6.8 % patients were started on therapy and overall 54 % achieved SVR. A disappointing 37 % of cirrhotics achieved SVR.

Previously, our group showed that 18.7 % of patients from two large academic centers in Dallas and Miami were initiated on treatment with triple therapy during the first 12 months following approval of boceprevir and telaprevir [2]. Here, we would like to share our results of patients treated with triple therapy beginning 6/1/2011 through 11/30/2012 from this Dallas–Miami cohort.

A total of 154 patients were treated (Dallas—48, Miami—106). Data were collected through 6/30/13 to allow 6 months of follow-up. Protease inhibitor was chosen at the discretion of the provider.

Baseline variables (Tables 1, 2) included site, age, white blood cells, hemoglobin, platelets, alanine aminotransferase, albumin, body mass index (BMI, categorized by normal/overweight/obese), viral load (VL < or = 800,000 IU/L), specific protease inhibitor, presence of cirrhosis, and history of decompensation. The primary outcome was SVR at 12 or 24 weeks post-treatment. On-treatment measures included hospital admissions and need for blood transfusions.

Nearly 80 % of patients were treated with telaprevir and 20 % with boceprevir. In total, 53.2 % achieved SVR. SVR was particularly low in cirrhotic patients (38.9 %) versus non-cirrhotics (65.0 %). On multivariate analysis (Table 3), predictors of response included higher baseline albumin levels (OR 4.51, CI 1.76–11.5). Baseline VL ≥ 800,000 IU/mL (OR 0.30, CI 0.11–0.84), cirrhosis (OR 0.41, CI 0.17–0.95), and BMI ≥ 30.0 (OR 0.29, CI 0.10–0.81) were inversely associated with attaining SVR.

Despite considerable prior experience with first-generation directly acting antivirals, the overall SVR rate was lower than anticipated based on registration trials (a near 20 % drop in SVR [3]). Our data are consistent with the data presented in this paper [1] and also with the other published reports on SVR in clinical practice including the French Early Access Project (CUPIC)—which had cirrhotic SVR rates of 43 % (boceprevir) and 52 % (telaprevir) [4]; UCSF—which compared SVR rates in compensated (54 %) and mildly decompensated (35 %) cirrhotics [5]; and the national VA experience (SVR of 50 % for boceprevir and 52 % for telaprevir) [6].

It will be interesting to find out to what extent treatment initiation rates will rise with the use of second-generation directly acting antivirals available now and others nearing approval in the coming months. Our results are important to establish true SVR rates in clinical practice, specifically for patient profiles that were underrepresented in the registration trials. Also, these data will still be relevant in resource-poor regions of the world, which will continue to use boceprevir and telaprevir. Lastly, it is important to learn from our prior experiences, as often we face unexpected challenges in clinical practice.

References

1. Price JC, Murphy RC, Shvachko VA, Pauly MP, Manos MM. Effectiveness of telaprevir and boceprevir triple therapy for patients with hepatitis C virus infection in a large integrated care setting. *Dig Dis Sci.* (Epub ahead of print).
2. Chen EY, Sclair SN, Czul F, et al. A small percentage of patients with hepatitis C receive triple therapy with boceprevir or telaprevir. *Clin Gastroenterol Hepatol.* 2013; 11:1014.e2–1020.e2. [PubMed: 23602817]
3. Kanwal F, El-Serag HB. HCV treatment: The unyielding chasm between efficacy and effectiveness. *Clin Gastroenterol Hepatol.* 2014; 12(8):1381–1383. [PubMed: 24607698]
4. Hezode C, Fontaine H, Dorival C, et al. Effectiveness of telaprevir or boceprevir in treatment-experienced patients with HCV genotype 1 infection and cirrhosis. *Gastroenterology.* 2014; 147(1): 132.e4–142.e4. [PubMed: 24704719]
5. Saxena V, Manos M, Yee H, et al. Telaprevir or boceprevir triple therapy in patients with chronic hepatitis C and varying severity of cirrhosis. *Aliment Pharmacol Ther.* 2014; 39(10):1213–1224. [PubMed: 24654657]
6. Ioannou GN, Beste LA, Green PK. Similar effectiveness of boceprevir and telaprevir treatment regimens for hepatitis C virus infection, based on a nationwide study of veterans. *Clin Gastroenterol Hepatol.* 2013; 12(8):1371–1380. [PubMed: 24361415]

Table 1

Baseline and end-of-treatment variables meeting statistical significance or qualifying for multivariable analysis

Variable	Population (<i>n</i> = 154) median (IQR) or <i>n</i> (% of total)	SVR median (IQR) or <i>n</i> (% of variable)	No. SVR median (IQR) or <i>n</i> (% of variable)	Sig
Site				0.11
Dallas	48 (31.2 %)	21 (43.8 %)	27 (56.3 %)	
Miami	106 (68.8 %)	61 (57.5 %)	45 (42.5 %)	
Race				0.0004
White	114 (74.0 %)	68 (59.6 %)	46 (40.4 %)	
AA/Black	25 (16.2 %)	4 (16.0 %)	21 (84.0 %)	
Asian	5 (3.2 %)	4 (80.0 %)	1 (20.0 %)	
Other	4 (2.6 %)	1 (25.0 %)	3 (75.0 %)	
Unknown	6 (3.9 %)	5 (83.3 %)	1 (16.7 %)	
Ethnicity				0.0001
Non-hispanic/non-latino	105 (71.9 %)	45 (42.9 %)	60 (57.1 %)	
Hispanic/latino	41 (28.1 %)	32 (78.0 %)	9 (22.0 %)	
ALT	60 (7–402)	46 (7–350)	69 (14–402)	0.0094
Albumin	4.2 (1.4–5)	4.3 (1.4–5)	4.1 (2–4.7)	0.0001
Cirrhosis	72 (46.8 %)	28 (38.9 %)	44 (61.1 %)	0.0008
History of Decompensation	15 (9.7 %)	3 (20.0 %)	12 (80.0 %)	0.0066
VL (< 800,000 IU/L)	110 (73.8 %)	52 (47.3 %)	58 (52.3 %)	0.0083
Treatment history				0.0004
Naïve	49 (31.8 %)	32 (65.3 %)	17 (34.7 %)	
Non-responder	56 (36.4 %)	18 (32.1 %)	38 (67.9 %)	
Relapser	49 (31.8 %)	32 (65.3 %)	17 (34.7 %)	
BMI category				0.0313
Normal < 25	51 (33.1 %)	33 (64.7 %)	18 (35.3 %)	
Overweight 25–<30	54 (35.1 %)	30 (55.6 %)	24 (44.4 %)	
Obese ≥ 30	49 (31.8 %)	19 (38.8 %)	30 (61.2 %)	
On-treatment and end-of-treatment variables				
pRBC infusion	29 (18.8 %)	10 (34.5 %)	19 (65.5 %)	0.0249
Early discontinuation	69 (44.8 %)	11 (15.9 %)	58 (84.1 %)	<0.0001
Hospital admission during treatment	43 (27.9 %)	17 (39.5 %)	26 (60.5 %)	0.0338
Discontinuation reason				<0.0001
Completed therapy	84 (54.5 %)	72 (85.7 %)	12 (14.3 %)	
Non-responder/futility	18 (11.7 %)	0	18 (100.0 %)	
Side effects	33 (21.4 %)	7 (21.2 %)	26 (78.8 %)	
Heme side effects	15 (9.7 %)	3 (20.0 %)	12 (80.0 %)	
Financial/death/other	4 (2.6 %)	0	4 (100.0 %)	

Chi-squared and Fisher's exact test used when appropriate. Variables not meeting a significance criterion of $\alpha = 0.05$ are available in Table 2

IQR interquartile range, *SVR* sustained viral response, *Sig* significance, *AA* African American, *ALT* alanine aminotransferase, *VL* viral load, *IU/L* international units/liter, *BMI* body mass index, *pRBC* packed red blood cells

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Table 2

Non-statistically significant baseline variables

Variable	Population (<i>n</i> = 154) median (IQR) or <i>n</i> (%)	SVR (<i>n</i> = 82) median (IQR) or <i>n</i> (%)	No SVR (<i>n</i> = 72) median (IQR) or <i>n</i> (%)	Sig
DAA				0.54
Boceprevir	31 (20.1 %)	15 (48.4 %)	16 (51.6 %)	
Telaprevir	123 (79.9 %)	67 (54.5 %)	56 (45.5 %)	
Male	94 (61.0 %)	51 (54.3 %)	43 (45.7 %)	0.75
Age (years)	57 (20–73)	57 (20–73)	57 (28–71)	0.35
White blood cells	5.5 (0.3–36.7)	5.4 (0.3–36.7)	5.5 (1.7–9.8)	0.95
Hemoglobin	14.6 (7.7–17.7)	14.6 (9.8–17.7)	14.4 (7.7–17.4)	0.46
Platelets	155 (39.5–449)	154 (39.5–343)	158 (42.1–449)	0.66
HCV genotype				0.51
1a	83 (53.9 %)	41 (49.4 %)	42 (50.6 %)	
1b	52 (33.7 %)	31 (59.6 %)	21 (40.4 %)	
1 Undetermined	19 (12.3 %)	10 (52.6 %)	9 (47.4 %)	

None of the variables were included in the multivariable analysis

IQR interquartile range, *SVR* sustained viral response; *Sig* significance

Table 3

Multivariable logistic regression

Variable	Odds ratio	95 % CI	Sig
Cirrhosis ^a	0.41	0.17–0.95	0.0388
Age	1.01	0.97–1.05	0.76
Ethnicity ^a	5.12	1.82–14.4	0.0019
Alanine aminotransferase	0.99	0.99–1.00	0.53
Albumin ^a	4.51	1.76–11.5	0.0017
Viral load 800,000 IU/L ^a	0.30	0.11–0.84	0.0210
BMI 30 ^a	0.29	0.10–0.80	0.0172
25 BMI < 30	0.70	0.26–1.89	0.48
Site	1.34	0.53–3.34	0.54

Overall logistic regression analysis was significant at $p < 0.0001$

Sig significance, *ALT* alanine aminotransferase, *IU/L* international units/liter, *BMI* body mass index

^aIndicates continual significance after multivariable analysis