**Integrated Efficacy and Safety Analysis of GT1-6 Treatment-Naïve, Non-Cirrhotic
and Compensated Cirrhotic Patients Who Received 8 Weeks of
Glecaprevir/Pibrentasvir**

EASL 2020 Aug 27-29 virtual
Reported by Jules Levin

Eli Zuckerman¹, Julio Gutierrez², Douglas E Dylla³, Victor de Ledinghen⁴, Andrew Muir⁵, Michael Gschwantler⁶, Massimo Puoti⁷, Jihad Slim⁸, Frederik Nevens⁹, Linda M Fredrick³, Ana Gabriela Pires dos Santos³, Lino Rodrigues Jr³, John Dillon¹⁰ Liver Unit, Carmel Medical Center, Faculty of Medicine, Technion Institute, Haifa, Israel; ²St. Vincent Medical Center, Los Angeles, California, United States; ³AbbVie Inc., North Chicago, Illinois, United States; ⁴Centre d'Investigation de la Fibrose Hepatique, Bordeaux University Hospital, Pessac, France; INSERM U1053, Bordeaux University, Bordeaux, France; ⁵Duke Clinical Research Institute, Durham, North Carolina, United States; ⁶Department of Internal Medicine IV, Wilhelminenspital, Vienna, Austria; Sigmund Freud University, Vienna, Austria; ⁷Niguarda ca Grande Hospital, Milan, Italy; ⁸Infectious Disease Division, Department of Internal Medicine, St. Michael's Medical Center, Newark, New Jersey, United States; ⁹Department of Gastroenterology and Hepatology, University Hospitals Leuven, KU Leuven, Belgium; ¹⁰Division of Molecular and Clinical Medicine, School of Medicine, University of Dundee, Dundee, United Kingdom

CONCLUSIONS

- High SVR rates with 8-week G/P were observed regardless of baseline patient and viral characteristics, including patients with compensated cirrhosis
- G/P was well tolerated, and no new safety signals were observed
- These data support recent American Association for the Study of Liver Diseases/Infectious Diseases Society of America simplified treatment recommendations for 8-week G/P to be used in treatment-naïve, non-cirrhotic and compensated cirrhotic patients with minimal pre-treatment assessments, without the need for GT or resistance testing, and with minimal to no on-treatment monitoring¹⁵

BACKGROUND

- With increased treatment in the direct-acting antiviral (DAA) era, the remaining patient population is generally younger, treatment-naïve, and without cirrhosis^{1,2}
- In the United States and the European Union (EU), the DAA combination glecaprevir (developed by AbbVie and Enanta) and pibrentasvir (G/P) is approved for an 8-week duration in hepatitis C virus (HCV) genotype (GT)1–6, treatment-naïve patients without cirrhosis and with compensated cirrhosis^{3,4}
- Simplification of HCV treatment choice may facilitate expanded willingness to treat by non-specialists

G/P is Approved for Patients With HCV GT1–6 Infection

Glecaprevir
pangenotypic NS3/4A
protease inhibitor

Pibrentasvir
pangenotypic NS5A
inhibitor

Coformulated: G/P

- 8-week duration in treatment-naïve patients (without cirrhosis or with compensated cirrhosis)³
- Pangenotypic SVR12 rate of 98% in more than 4500 patients in clinical trials
- Favorable safety profile in indicated populations (eg, Child-Pugh A, CKD, patients ≥12 years)
- Real world clinical outcomes consistent with those observed in clinical trials, also including historically underserved patients^{5–7}
- No recommendation for baseline resistance testing [EASL & AASLD guidelines]

G/P dosed as 3 pills taken at the same time once daily with food (total daily dose of 300 mg GLE/120 mg PIB).
Glecaprevir was identified by AbbVie and Enanta.

OBJECTIVE

- This integrated analysis of label-consistent data evaluates the pooled efficacy and safety of 8-week G/P treatment in HCV treatment-naïve patients with chronic HCV GT1–6 infection without cirrhosis or with compensated cirrhosis

METHODS

- Data were pooled from eight Phase 2 and 3 clinical trials of G/P: SURVEYOR-1⁸ (Part 2; NCT02243280), SURVEYOR-2^{8,9} (Part 2 and Part 4; NCT02243293), ENDURANCE-1¹⁰ (NCT02604017), ENDURANCE-3¹⁰ (NCT02640157), EXPEDITION-2¹¹ (NCT02738138), ENDURANCE-5,6¹² (NCT02966795), EXPEDITION-5¹³ (NCT03069365), and EXPEDITION-8¹⁴ (NCT03089944)
- Patients received 8 weeks of oral, once-daily G/P 300/120 mg
- The inclusion and exclusion criteria for each study have been previously reported^{8–14}

ENDPOINTS AND ASSESSMENTS

- The efficacy endpoint was the percentage of patients with a sustained virologic response after 12 weeks of treatment (SVR12), defined as an HCV RNA concentration below the lower limit of quantification at post-treatment Week 12
- SVR12 rates for subgroups of interest were also assessed
- Treatment-emergent adverse events (AEs) and clinical laboratory abnormalities during treatment were described

ANALYSIS POPULATIONS

- The intention-to-treat (ITT) population included all treatment-naïve patients who received ≥1 dose of G/P
- The modified ITT (mITT) population excluded patients with SVR non-response due to reasons other than virologic failure
- The GT1–6 data set included all patients with no cirrhosis or with compensated cirrhosis; the GTΔ3CC data set (representative of EU label at the time of analysis) excluded patients with GT3 infection with compensated cirrhosis

RESULTS

- Demographics and clinical characteristics for the GT1–6 data set at baseline are summarized in **Table 1**
 - Of 1248 patients, 343 (27%) had compensated cirrhosis
 - Most patients were white (80%) and had HCV GT1 (47%) or GT3 (22%); median age was 54 years
- The GTΔ3CC data set included 1185 patients and demographic characteristics were similar to those in the GT1–6 data set

Table 1. Demographics and Clinical Characteristics at Baseline (ITT Population; GT1–6 Data Set)

	GT1-6 Treatment-Naïve		
	Non-cirrhotic N = 905	Cirrhotic N = 343	Overall N = 1248
Male	492 (54.4)	217 (63.3)	709 (56.8)
Age, median, years	52.0	58.0	54.0
<65 years	800 (88.4)	257 (74.9)	1057 (84.7)
Race			
White	708 (78.2)	285 (83.1)	993 (79.6)
Black/African American	67 (7.4)	28 (8.2)	95 (7.6)
Asian	112 (12.4)	28 (8.2)	140 (11.2)
Other*	18 (2.0)	2 (0.6)	20 (1.6)
Ethnicity			
Hispanic or Latino	92 (10.2)	43 (12.5)	135 (10.8)
Not Hispanic or Latino	813 (89.8)	300 (87.5)	1113 (89.2)
BMI, mean, kg/m ²	26.3	28.3	26.8
≥30 kg/m ²	160 (17.7)	101 (29.4)	261 (20.9)
HCV GT			
1	352 (38.9)	231 (67.3)	583 (46.7)
2	202 (22.3)	26 (7.6)	228 (18.3)
3	217 (24.0)	63 (18.4)	280 (22.4)
4	53 (5.9)	13 (3.8)	66 (5.3)
5	19 (2.1)	1 (0.3)	20 (1.6)
6	62 (6.9)	9 (2.6)	71 (5.7)
Fibrosis stage			
F0-F1	741/902 (82.2)	0	741/1245 (59.5)
F2	53/902 (5.9)	0	53/1245 (4.3)
F3	107/902 (11.9)	0	107/1245 (8.6)
F4	1/902 (0.1)	343 (100)	344/1245 (27.6)
HCV RNA			
≥1 000 000 IU/mL	547 (60.4)	231 (67.3)	778 (62.3)
Platelet count			
<100 × 10 ⁹ /L	6 (0.7)	63 (18.4)	69 (5.5)
History of injection drug use†			
Recent (≤12 months prior to G/P)	22/624 (3.5)	4 (1.2)	26/967 (2.7)
>12 months prior to G/P	226/624 (36.2)	88 (25.7)	314/967 (32.5)
No history	376/624 (60.3)	251 (73.2)	627/967 (64.8)
Stable OST	69 (7.6)	27 (7.9)	96 (7.7)
HIV coinfection	121 (13.4)	0	121 (9.7)
History of diabetes	60 (6.6)	68 (19.8)	128 (10.3)
History of depression or bipolar disorder	206 (22.8)	11 (3.2)	217 (17.4)
Severe renal impairment	67 (7.4)	0	67 (5.4)
Concomitant PPI use	101 (11.2)	39 (11.4)	140 (11.2)
Alcohol use			
Drinker	349 (38.6)	70 (20.4)	419 (33.6)
Ex-drinker	284 (31.4)	126 (36.7)	410 (32.9)
Non-drinker	267 (29.5)	144 (42.0)	411 (32.9)
Unknown	5 (0.6)	3 (0.9)	8 (0.6)

Data are n (%) or n/N (%) unless otherwise stated; percentages are calculated from non-missing values.

*Other races include American Indian or Alaska native, multiple, and native Hawaiian or other Pacific Islander categories; †Patient-reported; SURVEYOR-1 and 2 trial did not capture this information and are excluded from this assessment.

BMI, body mass index; G/P, glecaprevir/pibrentasvir; GT, genotype; HCV, hepatitis C virus; HIV, human immunodeficiency virus; ITT, intention-to-treat; OST, opioid substitution therapy; PPI, proton pump inhibitor; RNA, ribonucleic acid.

- Overall SVR12 rates were 97.6% (1218/1248) in the ITT and 99.3% (1218/1226) in the mITT populations (**Figure 1**)
 - Similar results were observed in the GTΔ3CC data set, with overall SVR12 rates >99% for the ITT and mITT populations, respectively (data not shown)
- SVR12 rates were high regardless of cirrhosis status (**Figure 1**) and across subpopulations of interest (**Figure 2**)

Figure 1. SVR12 Rates After G/P Treatment for 8 Weeks by Cirrhosis Status (GT1–6 Data Set)

Numbers represent the number of patients with SVR12 and the total number of patients in each group. Error bars represent 95% confidence intervals by Wilson score method.

d/c, G/P discontinuation; G/P, glecaprevir/pibrentasvir; GT, genotype; ITT, intention-to-treat; LTFU, lost to follow-up; mITT, modified ITT excluding patients with non-virologic failure; OTVF, on-treatment virologic failure; SVR12, sustained virologic response at post-treatment Week 12.

Figure 2. SVR12 Rates After G/P Treatment for 8 Weeks by Subgroups of Interest (mITT Population; GT1–6 Data Set)

Numbers represent the number of patients with SVR12/the total number of patients in each subgroup. Error bars represent 95% confidence interval Wilson score method. *History of injection drug use was patient-reported; recent was defined to be within 12 months prior to G/P initiation. APRI, aspartate aminotransferase-to-platelet ratio index; BMI, body mass index; FIB-4, Fibrosis-4 score; G/P, glecaprevir/pibrentasvir; GT, genotype virus; HIV, human immunodeficiency virus; mITT, modified intention-to-treat excludes patients with non-virologic failure; OST, opioid substitution therapy; RNA, ribonucleic acid; SVR12, sustained virologic response at post-treatment Week 12.

- Treatment with G/P for 8 weeks was safe and well-tolerated, regardless of cirrhosis status (Table 2)

Table 2. Treatment-Emergent AEs and Post-Baseline Clinical Laboratory Abnormalities (ITT Population; GT1–6 Data Set)

AEs, n (%)	GT1–6 Treatment-naïve		
	Non-cirrhotic N = 905	Cirrhotic N = 343	Overall N = 1248
Any AE	563 (62.2)	158 (46.1)	721 (57.8)
Any serious AE	24 (2.7)	6 (1.7)	30 (2.4)*
Any serious AE possibly related to G/P	0	0	0
Any AE leading to G/P discontinuation	2 (0.2)	0	2 (0.2)*
Any serious AE leading to G/P discontinuation	2 (0.2)	0	2 (0.2)*
Deaths†	2 (0.2)	0	2 (0.2)
AEs in ≥10% of any group			
Headache	120 (13.3)	28 (8.2)	148 (11.9)
Fatigue	115 (12.7)	30 (8.7)	145 (11.6)
Laboratory abnormalities (Grade ≥3), n/N (%)			
Alanine aminotransferase (>5 × ULN)	0/903	1/342 (0.3)	1/1245 (<0.1)
Aspartate aminotransferase (>5 × ULN)	1/903 (0.1)	0/342	1/1245 (<0.1)
Total bilirubin (>3 × ULN)	4/903 (0.4)	0/342	4/1245 (0.3)

*8 patients with serious AEs and 1 patient with an AE leading to G/P discontinuation were from EXPEDITION-5, which included patients with stage 4/5 chronic kidney disease; †Includes non-treatment emergent deaths.

AE, adverse event; G/P, glecaprevir/pibrentasvir; GT, genotype; ITT, intention-to-treat; ULN, upper limit of normal.

TRANSPARENCY

AUTHOR DISCLOSURES

Eli Zuckerman: Speaker, consultant, and advisory board participant for AbbVie, Gilead, and Merck. Julio Gutierrez: Speaker and scientific advisor for AbbVie, Gilead, and MSD. Victor de Ledinghen: Advisory board participant and/or speaker for Gilead, AbbVie, Intercept, Medac, Supersonic Imagine, Promethera, Echoscans, MYR-Pharma, Alfasigma, Bristol-Myers Squibb, Pfizer, Indivior, Spimaco. Andrew Muir: Advisory board participant for AbbVie and Gilead; Research support: AbbVie, Gilead, and Merck. Michael Gschwanner: Speaker/advisor: Janssen, MSD, Bristol-Myers Squibb, Gilead, and AbbVie; Research support: Gilead, AbbVie, and MSD. Massimo Puoti: Speaker/advisor: MSD, Gilead, AbbVie. Jihad Slim: Speaker and advisory board participant for AbbVie, Gilead, MSD, and Janssen. Frederik Nevens: Consultant for Gilead. John Dillon: Research support and lecturer for AbbVie, Abbott, Bristol-Myers Squibb, Gilead, Janssen, Merck Sharpe & Dohme, Roche, Douglas E Dylla, Linda M Fredrick, Ana Gabriela Pires dos Santos, and Lino Rodrigues Jr: Employee of AbbVie Inc., and may hold stock or options.

ROLE OF AUTHORS AND SPONSOR

AbbVie sponsored the study; contributed to its design; and participated in the collection, analysis, and interpretation of the data and in the writing, reviewing, and approval of the abstract. All authors had access to relevant data, and participated in the writing, review, and approval of the final poster.

ACKNOWLEDGMENT OF CONTRIBUTORS

Medical writing support was provided by Hayley Ellis, PhD, and Jennifer Mayes, PhD, of Fishawack Communications Ltd, funded by AbbVie.