A Sub-Analysis of Puerto Rican Hepatitis C Infected Patients Enrolled in Phase 2 & 3 Glecaprevir-Pibrentasvir Clinical Program

Sepúlveda-Arzola G[1], Rosado-Carrión B[2], Lovell S[3], Bugarin G[4], Aponte F[5], Crown E[6], Rodríguez-Pérez F[7]

[1]Instituto de Investigación Científica del Sur, Ponce, Puerto Rico; [2]GHGCPR Research Institute, Ponce, Puerto Rico; [3]Abbvie, S.A, Chicago, Estados Unidos; [4]AbbVie. S.A., Buenos Aires, Argentina; [5]Abbvie, S.A, San Juan, Puerto Rico; [6]Abbvie, S.A, Chicago, Estados Unidos; [7]Klinical Investigations Group, San Juan, Puerto Rico

Presented at HIV & Hepatitis in the Americas 2019 • Bogotá, Colombia • 4–6 April 2019

BACKGROUND

- Chronic hepatitis C virus (HCV) infection is a leading cause of cirrhosis and advanced liver disease, and achieving a sustained virologic response (SVR) is associated with reduced risk of developing cirrhosis, hepatic decompensation, and death[1]
- Glecaprevir (NS3/4A protease inhibitor) and pibrentasvir (NS5A inhibitor) are direct-acting antivirals (DAAs) co-formulated as a once-daily, fixed-dose combination regimen (G/P) to treat genotype (GT) 1–6 HCV infection
- HCV therapies with simpler treatment algorithms and shorter treatment durations are critical to achieving the World Health Organization goal of eliminating HCV by the year 2030[2,3]

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

Glecaprevir
pangenotypic NS3/4A protease inhibitor

Coformulated: G/P

Pibrentasvir
pangenotypic NS5A inhibitor

- 8-week duration approved for treatment-naïve patients with HCV GT1–6 infection without cirrhosis[4]
- Overall SVR12 rate of 98% across GT1–6 in more than 2200 HCV-infected patients
- Potent against common polymorphisms (eg, Y93H in NS5A and Q80K in NS3)
- Favorable safety profile irrespective of baseline factors such as compensated cirrhosis or advanced renal disease
- Recent real-world results demonstrate that G/P achieved high SVR12 rates consistent with those observed in clinical trials[5,6]

G/P is orally dosed as 3 pills taken once daily with food for a total dose of 300 mg/120 mgGlecaprevir was identified by AbbVie and Enanta.

OBJECTIVE

- To describe the clinical characteristics and virologic response rate of patients in Puerto Rico treated with G/P in phase 2, 3, and 3b clinical studies

METHODS

- Data were pooled from 14 Phase 2, 3, and 3b clinical trials conducted in 32 countries and representing 3,233 treatment-naive and treatment-experienced patients with chronic HCV GT1–6 infection who received G/P once-daily for 8, 12, or 16 weeks
  - Included studies were SURVEYOR-I and -II, ENDURANCE-1, -2, -3, and -4, EXPEDITION-1, -2, -4, -5, and -8, MAGELLAN-1 and -2, and M16-133 (APRI study)
- Patients included in this sub-analysis were those who participated in these trials in sites in Puerto Rico

KEY ELIGIBILITY CRITERIA

- Adults with chronic HCV GT 1, 2, 3, 4, 5, or 6 infection
- Age ≥18 years
- Compensated liver disease with or without cirrhosis
- Absence of co-infection with hepatitis B virus with or without HIV coinfection
- Treatment-naive or treatment-experienced
- Normal renal function or any degree of renal impairment, including severe renal impairment or end-stage renal disease/dialysis

ENDPOINTS AND ANALYSIS

- Percentage of patients with SVR12 (HCV RNA <lower limit of quantification 12 weeks after the last dose of study drug)
  - SVR12 was determined in the intent-to-treat (ITT) population which included all patients who received one dose of study drug and in a modified ITT (mITT) population which excluded patients with nonvirologic failure
- Percentage of patients with treatment-emergent adverse events (AEs), including AEs leading to treatment discontinuation, AEs occurring in ≥5% of patients, and serious AEs

ADHERENCE

- Adherence for study drug within the treatment period was calculated as the percentage of tablets taken relative to the total tablets expected to be taken
- Patients were considered adherent if the percentage was between 80% and 120% (if a patient took more tablets than expected over a period of time, adherence would be >100%)
- Adherence was summarized for patients who received glecaprevir and pibrentasvir as coformulated tablets

RESULTS

PATIENTS

- From the 3,233 patients included in the G/P phase 2, 3, and 3b program, this sub-analysis included 79 (2.4%) patients from sites in Puerto Rico
- The Puerto Rico population was predominantly infected with HCV genotype 1 and was predominantly treatment-naïve (**Table 1**)
- The population included 25 (32%) patients with compensated cirrhosis (**Table 1**)
- Over a quarter of patients had HIV co-infection and nearly half reported injection drug use (**Table 1**)
- Additional baseline patient and viral characteristics are shown in **Table 1**

Table 1. Baseline Patient and Viral Characteristics

Characteristic		N=79
Male, n (%)		52 (66)
Race, n (%)	White	64 (81)
	Black or African-American	15 (19)
Median age (range), years		56 (29–78)
Median BMI (range), kg/m^2		26.6 (18.1–42.6)
BMI ≥30, n (%)		17 (22)
Median baseline HCV RNA level (range), $\log_{10}$ IU/mL		6.2 (3.4–7.4)
HCV genotype*	GT1, n (%)	69 (87)
	GT1a, n/N (%)	49/69 (71)
	GT1b, n/N (%)	20/69 (29)
	GT2, n (%)	5 (6)
	GT3, n (%)	4 (5)
	GT4, n (%)	1 (1)
HCV treatment history	Treatment-naïve, n (%)	63 (80)
	Treatment-experienced†, n (%)	16 (20)
	DAA-experienced‡, n/N (%)	3/16 (19)
Baseline fibrosis stage, n (%)	F0–F1	39 (53)
	F2	3 (4)
	F3	6 (8)
	F4	25 (34)
	Missing	6
Median eGFR¶ (range), mL/min/1.73 m^2		87.5 (6.8–188.1)
G/P treatment duration, n (%)	8 weeks	49 (62)
	12 weeks	28 (35)
	16 weeks	2 (3)
	History of diabetes, n (%)	13 (16)
	Injection drug use, n (%)	35 (44)
	Opiate substitution therapy, n (%)	7 (9)
	HIV co-infection, n (%)	22 (28)

BMI, body mass index; DAA, direct-acting antiviral agent; eGFR, estimated glomerular filtration rate; GT, genotype; IFN, interferon; pegIFN, pegylated interferon; RBV, ribavirin.
* No HCV GT5- or GT6-infected patients were enrolled in Puerto Rico;
† Treatment-experienced to IFN/pegIFN ± RBV or sofosbuvir + IFN ± RBV;
‡ All three DAA-experienced patients were previously treated with boceprevir + IFN + RBV;
¶ Data available for 76 patients.

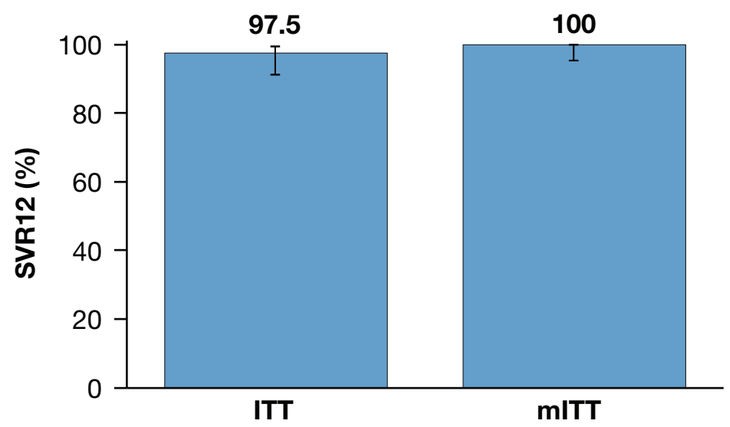
ADHERENCE

- There was a high rate of adherence to the co-formulated G/P regimen, with 100% (71/71) of patients defined as being adherent during the treatment period
  - Mean adherence was 99.6% (standard deviation = 1.4%)
  - Adherence rates ranged from 92.9% to 101.8%

EFFICACY

- The overall SVR12 rate was 97.5% (77/79; 95% confidence interval: 91.2–99.3) in the ITT population (**Figure 1**)
  - Two patients did not achieve SVR12 due to nonvirologic reasons, both of whom were missing SVR12 data
- The SVR12 rate in the mITT population was 100% (77/77; 95% confidence interval: 95.2–100) (**Figure 1**)

Figure 1. Efficacy of G/P in Patients in Puerto Rico from the G/P Clinical Trial Program



ITT, intent-to-treat; mITT, modified intent-to-treat (excluding those with nonvirologic failure).

SAFETY

- Overall, 38 patients (48%) experienced an AE, most of which were Grade 1 or 2 (mild-to-moderate) in severity (**Table 2**)
- The most common AEs (occurring in ≥5% of patients) were pruritus, diarrhea, fatigue, and headache (**Table 2**)
- Serious AEs were reported in four patients (5%) (**Table 2**)
  - Serious AEs were bronchitis, pneumonia, venous stenosis, and upper gastrointestinal hemorrhage
  - No serious AEs were assessed by investigators to be related to study drug
- There were no AEs or serious AEs leading to discontinuation of study drug
- There were no deaths during the treatment period or during follow-up
- There were 4 (5%) Grade ≥3 laboratory abnormalities, none of which were deemed to be clinically meaningful (**Table 2**)

Table 2. Treatment-emergent Adverse Events

Safety, n (%)		N=79
Any AE		38 (48)
Any DAA-related AE*		13 (16)
Serious AE		4 (5)
DAA-related serious AE*		0
AE leading to discontinuation of study drug		0
Any fatal AE		0
Deaths		0
AEs occurring in ≥5% of total population	Pruritus	5 (6)
	Diarrhea	4 (5)
	Fatigue	4 (5)
	Headache	4 (5)
	Any Grade ≥3 laboratory abnormality	4 (5)

AE, adverse event; DAA, direct-acting antiviral agent.
* As assessed by investigator.

CONCLUSIONS

- G/P achieved 97.5% SVR12 with no virologic failures in patients enrolled in Puerto Rico from phase 2, 3, and 3b clinical studies
- G/P was effective in this population that included numerous patients with cirrhosis, HIV coinfection, and injection drug use
- G/P was well-tolerated, with no DAA-related serious AEs or AEs leading to discontinuation of study drug
- The efficacy and safety profile of G/P in patients in Puerto Rico was comparable to that of the overall patient population in the global registrational trial program
- SVR12 rates in G/P clinical trial patients in Puerto Rico were comparable to SVR rates observed in real-world studies of G/P

REFERENCES

1. Manns MP, et al. *Nat Rev Dis Primers* 2017; 3:17006.
2. Pawlotsky JM, et al. *J Hepatol* 2015; 62(suppl):S87–S99.
3. World Health Organization. Combating hepatitis B and C to reach elimination by 2030. May 2016, available at https://www.who.int/hepatitis/publications/hep-elimination-by-2030-brief/en/ (accessed March 2018).
4. MAVYRET [package insert]/MAVIRET [SmPC], AbbVie 2018.
5. D'Ambroio R, et al. *J Hepatol* 2019;70:379–387.
6. Weigand J, et al. *Hepatology* 2018; 68(suppl):364A (poster presentation).

DISCLOSURES & ACKNOWLEDGEMENTS

Medical writing support was provided by Scott Battle, PhD, of Medical Expressions, funded by AbbVie.

The design, study conduct, analysis, and financial support of the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the content. All authors had access to all relevant data and participated in writing, review, and approval of this presentation.

Sepúlveda-Arzola G: Investigator in AbbVie-sponsored clinical trial. **Rosado-Carrión B:** Investigator in AbbVie-sponsored clinical trial. **Lovell S, Bugarin G, Aponte F, Crown E:** Employees of AbbVie and may hold stock or options. **Rodríguez-Pérez F:** Investigator in AbbVie-sponsored clinical trial.

abbvie