**BACKGROUND**

- In Egypt, chronic hepatitis C virus (HCV) infection is a leading cause of liver cirrhosis and liver cancer.
- Although HCV genotype (GT) 4 accounts for approximately 8% of HCV infections globally, it constitutes 7% of HCV infections in Egypt.
- Achievement of sustained virologic response (SVR) at 12 weeks post-treatment (SVR12) is associated with improved liver function and reduced risk of liver decompensation and need for transplant.

**METHODS**

- **Trial Design**:  The phase 3 AGATE-II study, OBV/PTV/r + RBV for 12 or 16 weeks achieved high SVR12 rates in GT4-infected patients with compensated cirrhosis from Europe and North America.
- In the phase 3 AGATE-I study, OBV/PTV/r + RBV for 12 or 16 weeks achieved high SVR12 rates (97% and 93% for 12- and 16-week regimens, respectively) and improved markers of liver fibrosis and synthetic function in GT4-infected patients with compensated cirrhosis from Europe and North America.

**OBJECTIVES**

- The primary objectives of the AGATE-II study were to assess the efficacy and safety of OBV/PTV/r + RBV in Egyptian GT4-infected patients with compensated cirrhosis.

**DISCLOSURES**

- Authors:  Summary of affiliation details: None.

**RESULTS**

**Patients**

- Patient demographics and baseline disease characteristics for patients with compensated cirrhosis are presented in Table 1.

**Immunization in Biomarkers of Liver Injury in Patients With Compensated Cirrhosis**

- Biomarkers of liver injury at baseline and PTW24 are presented in Figure 3.

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**Safety**

- **Summary**
  - The majority of TEAEs were mild to moderate in severity
  - No TEAE led to discontinuation of treatment
  - Two patients in Arm C experienced severe TEAEs, neither were considered to be related to study drug
  - All patients who received RBV in combination with OBV

**Conclusions**

- **High SVR rates were achieved with both the 12- and 16-week OBV/PTV/r + RBV regimens in Egyptian HCV GT4-infected patients with compensated cirrhosis.**
- **OBV/PTV/r + RBV treatment resulted in improvements in most biomarkers of liver synthetic function, liver injury, and liver fibrosis.**
- **Liver biomarker improvements were independent of duration of treatment.**
- **Treatment was well tolerated with no discontinuations due to AEs.**

**REFERENCES**


INTRODUCTION

• Hepatitis C virus (HCV) genotypes (GT2) and 2 and 3 account for approximately 40% of HCV infections and are highly prevalent in Europe, South Asia, and Australia.

• In the direct-acting antiviral (DAA) era, GT3 has emerged as the most refractory HCV genotype, especially in patients with cirrhosis and prior treatment experience.

2D Regimen + Sofosbuvir

OBJECTIVE

• The design, study conduct, analysis, and financial support of the QUARTZ (NCT0229719) 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.

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REFERENCES

• High SVR rates were seen among GT3-infected patients without cirrhosis treated with 2D + SOF or without RBV for 12 weeks.

• A 2B role of GT2 + SOF or RBV achieved an SVR rate of 91% of GT3-infected non-cirrhotic patients.

• Shortening treatment duration to 6 weeks resulted in a high rate of relapse.

• 2D + SOF ± RBV had a favorable safety profile consistent with previous observed regimens of 2D or SOF ± RBV.

• These results suggest that 2C or SOF ± RBV may be a useful treatment option for patients with GT3 infection with or without cirrhosis.

CONCLUSIONS

ENDPOINTS AND ANALYSES

• There were no virological failures in GT3-infected patients who completed treatment.

• One GT3-infected patient without cirrhosis treated with 12-week 2D + SOF + RBV discontinued treatment on Day 8 due to an adverse event of influenza-like illness deemed unrelated to DAAs; this patient did not achieve SVR12.

• Addition of RBV did not improve treatment response among patients without cirrhosis.

Table 1. Baseline Demographics and Disease Characteristics

RESULTS

• No serious AEs were related to DAAs.

• There were no Grade 4 or higher laboratory abnormalities.

RESULTS (CONTINUED)

• With 8 weeks of treatment, 1/10 patients with GT2 infection relapsed, but with the shorter 6-week treatment duration, 6/9 patients relapsed.

• None of the 6 patients had resistance-associated polymorphisms at baseline in NS3, NS5A, or NS5B, nor did any have treatment-emergent substitutions at the time of failure.

• Exposures of the DAAs and ritonavir were comparable between non-cirrhotic patients who achieved SVR12 and those who failed treatment with 2D + SOF.

• There were no virological failures in GT3-infected patients who completed treatment.

Figure 1. Efficacy

A. Rates of Virological Response in Patients With GT3 Infection

Table 3. Safety and Laboratory Abnormalities

OBJECTIVE

• quartz (NCT0229719) is an open-label, multicenter, phase 2 study designed to evaluate the safety and efficacy of 6- and 8-week treatment durations of 2D + SOF ± RBV in patients with GT2 infection, and 12-week treatment with 2D + SOF ± RBV in patients with GT3 infection, including those with cirrhosis.

• 2D + PTV/r + SOF ± RBV had a favorable safety profile and effectiveness.

• These results suggest that 2D + SOF ± RBV may be a useful treatment option for patients with GT3 infection with or without cirrhosis.
The full-length NS5A gene was sequenced by population or next-generation sequencing (NGS) from 12 GT4-infected patients in PEARL-I (53.2% of the samples) or 118/120 patients (AGATE-I) GT4-infected patients.

The full-length NS4A gene was sequenced by population- or next-generation sequencing from baseline samples of GT4-infected patients in PEARL-I.

NS4A sequences were included in a phylogenetic analysis to assess genetic relationships among and within GT4 subtypes by country.

Prevalence of baseline polymorphisms in NS4A were frequently detected in NS4A regions of the hepatocellular carcinoma (HCC) patients

Baseline SVR12 rates among previously untreated patients who received treatment with OBV/PTV/r ± RBV at week 12 were 100%

Patients who experienced virologic failure were infected with HCV GT4a in EGY and the Middle East Africa, Europe and North America.

The majority of patients enrolled in North America were subtype 4a, patients enrolled in France, Spain, and the United States were infected with a strain of HCV subtype 4a that was predominantly NS5B- and/or NS3/4A-ps11

Prevalence of baseline polymorphisms in NS3/4A and/or NS5A among GT4-infected patients in PEARL-I and AGATE-I

Baseline polymorphisms at resistance-associated amino acid positions in NS4A were prevalent in 13.2% (18/120) of the GT4 samples. The most prevalent polymorphisms were L28S/M31I/T58P (23/120) in GT4a, K54T/168V in GT4d, and N50T/T58P in GT4f.

Baseline polymorphisms at resistance-associated amino acid positions in NS5A were prevalent in 23/120 (19%) GT4-infected patients in PEARL-I and AGATE-I. For GT4a patients who achieved SVR in study AGATE-I.

The majority of GT4a-infected patients from France, Spain, and the United States were infected with a strain of HCV subtype 4a that was predominantly NS5B- and/or NS3/4A.

The majority of GT4a-infected patients from Egypt and the Middle East Africa, Europe and North America were infected with a strain of HCV subtype 4a that was predominantly NS5B- and/or NS3/4A.

Baseline polymorphisms at resistance-associated amino acid positions in NS5A were prevalent in 13.2% (18/120) of the GT4 samples. The most prevalent polymorphisms were L28S/M31I/T58P (23/120) in GT4a, K54T/168V in GT4d, and N50T/T58P in GT4f. There was no apparent impact of GT4 baseline polymorphisms on treatment outcome (Figure 5).

The treatment-emergent substitutions revealed 2 sequence clusters within subtype 4a which were found to segregate by country of origin and suggest a genetically distinct strain of 4a circulating in Egypt and Europe-North America.

Baseline polymorphisms at resistance-associated amino acid positions in NS5A were prevalent in 23/120 (19%) GT4-infected patients in PEARL-I and AGATE-I. For GT4a patients who achieved SVR in study AGATE-I.