**Clinically Meaningful Differences in Health-Related Quality of Life and Fatigue in Patients With Hepatitis C Virus (HCV) Infection Treated With Elbasvir/Grazoprevir (EBR/GZR) Compared to Sofosbuvir (SOF) With Pegylated Interferon and Ribavirin (PR)**

### Introduction

- Hepatitis C Virus (HCV) leads to decreased health-related quality of life (HRQoL) and fatigue in patients with chronic liver disease.
- HCV treatment can improve chronic HCV patients who respond to treatment, but on-treatment HCV may vary based on the tolerability profile of the treatment regimens used.
- This potential variation in on-treatment HCV between regimens can be assessed using data from randomized trials, although some clinical meaningfulness of often-reported change scores in HVRQoL between regimens sometimes may not be intuitively apparent.
- C-EDGE H72 was a randomized, open-label multinational trial that compared the efficacy and safety of elbasvir/grazoprevir (EBR/GZR) versus sofosbuvir with pegylated interferon and ribavirin (SOF/PR) in patients with genotype 1, 2, or 6 chronic HCV infection.
- The study sample consisted of 255 patients, with the majority of patients having HCV GT infection (82.0%) and taking treatment-naive (72.4%) and treatment-experienced (31.3%) patients.
- Patients were randomized to one of two treatment regimens: SOF/PR 100 mg once daily (PEGylarin®) 0.5 mg/day once weekly + weight-based ribavirin 1000-1200 mg daily for 12 weeks.
- Elbasvir 50 mg + grazoprevir 100 mg once daily for 12 weeks.
- The primary efficacy objective was sustained virologic response (SVR) 12 weeks after the end of therapy (SVR12).
- SVR12 was observed to have superior efficacy, safety, and tolerability in patients with HCV GT 1 or 4 infection compared with SOF/PR, with SVR12 rates of 99.2% (126/128) and 99.5% (114/114) in the EBR/GZR and SOF/PR groups, respectively.
- As a part of the study on HVRQoL and fatigue, the same patients were also collected using the SF-36v2 and FACIT-Fatigue scale to measure the Functional Assessment of Chronic Hepatitis-B Therapy-Fatigue (FACIT-Fatigue) Scale.

### Aim

- Therefore, the aims of the current study were to:
  - Describe and compare the impact of EBR/GZR versus SOF/PR on changes in HVRQoL and fatigue during and after treatment.
  - Assess whether any observed differences in HVRQoL and fatigue between the two treatment groups are clinically meaningful.

### Methods

- Data sources:
  - 247 study patients from the C-EDGE H72 study had a baseline and follow-up assessment on the SF-36v2 and FACIT-Fatigue and so were included in the analysis.
  - SF-36v2 Health Survey Acute (1-week recall):
    - Consists of 36 items, used to create health domains that transform 0 to 100 scale.
    - Higher scores indicate better health status.
    - Physical functioning
    - Role limitations due to physical health
    - Role limitations due to emotional problems
    - Vitality
    - Social functioning
    - General health
    - Bodily pain
  - FACIT-Fatigue Scale:
    - Consists of 13 items, used to create a total Fatigue score of 0 – 120, where a lower score indicates better functioning.

### Results

#### Overall

- There was a decrease in HRQoLs from baseline to week 4 in both groups during treatment, with patients in the SOF/PR treatment arm showing a higher decrement in HRQoL (Figure 1 and 2).
- This trend of a reduction in HRQoL was also observed at week 12 of treatment for the SOF/PR treatment arm, while for patients in the EBR/GZR treatment arm, a trend of improvement in HRQoL was observed (Figure 1 and 2).
- At follow-up week 12, the observed improvement in HRQoL in week 12 was maintained in patients in the EBR/GZR treatment arm.
- HRQoL for patients in the SOF/PR treatment arm was similar to baseline except for general health and role limitations – physical, where improvements were observed (Figure 1 and 2).

- After the completion of treatment, ES ranged from 0.07 (body pain) to 0.15 (MCS), reflecting a small effect.
- The results reflected overall improvement in comparison with baseline HRQoLs for both groups at follow-up, with no clinically meaningful difference between the arms.
- MCID for Vitality Domain:
  - Difference in mean change from baseline for each group for Vitality exceeded the MCID of -0.12 during treatment only. After treatment the difference was -0.42.

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#### SF-36v2 Health Survey

- Baseline mean scores were similar between treatment arms.
- During treatment, the ES for the difference between treatment arms was 0.56 at week 4, 0.15 at week 12 (Figure 4).
- These differences between the arms represent a clinically meaningful impact on HRQoL favoring EBR/GZR, reflecting a moderate ES (Figure 4).
- After the completion of treatment, the ES reduced to 0.04, reflecting a small effect that was not considered to be clinically meaningful.

#### FACIT-Fatigue Scale

- Baseline mean scores were similar between treatment arms.
- During treatment, the ES for the difference between treatment arms was 0.56 at week 4, 0.15 at week 12 (Figure 4).
- These differences between the arms represent a clinically meaningful impact on Fatigue for this patient population favoring EBR/GZR, reflecting a moderate ES (Figure 4).

### Conclusions

- Overall, a trend of an improvement in HRQoL and fatigue was observed in patients in the EBR/GZR treatment arm at week 12, whereas a trend of a decrease in HRQoL and fatigue was observed at week 12 in the SOF/PR treatment arm.
- HVRQoL was statistically significantly better for patients treated with EBR/GZR as compared to SOF/PR, as measured by all 8 SF-36v2 domains and Physical and Mental Component Summary scores as well as FACIT-Fatigue scale differences also significantly different at weeks 4 and 12, with no significant differences between the arms at week 12.
- Effect sizes were moderate at weeks 4 and 12.
- One reason for this observed difference during treatment may be attributable to the difference in the tolerability profile of the two regimens, with EBR/GZR demonstrating better safety and tolerability relative to SOF/PR in the study.

- Clinically meaningful differences between groups were not present by the 12-week follow-up visit on all measures.
- However, for EBR/GZR patients, there still were some improvement in SF-36v2 physical functioning, role limitations-physical, vitality, social functioning, role limitations-emotional, and mental health domains as well as Physical and Mental Component Summary scores FACIT-Fatigue scale differences also significantly different at weeks 4 and 12, with no significant differences between the arms at week 12.
- Effect sizes were moderate at weeks 4 and 12.
- One reason for this observed difference during treatment may be attributable to the difference in the tolerability profile of the two regimens, with EBR/GZR demonstrating better safety and tolerability relative to SOF/PR in the study.

- This was an open-label trial, and it is unknown how much of an impact the treatment assignment had on the results.

### References

- McDonald SA, Hutchinson SJ, Palmateer NE, et al. Decrease in health-related quality of life measured by all 8 SF-36v2 physical, vitality, social functioning.
- Vary JH, Levy M, Gralnick HR, et al. Tolerance and safety of elbasvir/grazoprevir 100% and 50% confidence intervals was estimated.
- Effect sizes were calculated as the mean difference divided by the standard deviation of the difference.
- The literature was reviewed for established minimal clinically important differences (MCID) for the SF-36v2 and FACIT-Fatigue Scale.
- The study sample consisted of 255 patients, with the majority of patients having HCV GT infection (82.0%) and taking treatment-naive (72.4%) and treatment-experienced (31.3%) patients.
- Patients were randomized to one of two treatment regimens: SOF/PR 100 mg once daily (PEGylarin®) 0.5 mg/day once weekly + weight-based ribavirin 1000-1200 mg daily for 12 weeks.
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### Figure 1

**EBR/GZR treatment arm: change from baseline for SF-36v2 (PRO FAS)**

#### Figure 2

**SOF/PR treatment arm: change from baseline for SF-36v2 (PRO FAS)**

#### Figure 3

**Summary of differences between treatment arms and effect sizes for changes from baseline for SF-36v2 by domain (PRO FAS)**

#### Figure 4

**Summary of differences between treatment arms and effect sizes for changes from baseline in FACIT-Fatigue scale (PRO FAS)**

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