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# Impact of Elbasvir/Grazoprevir (EBR/GZR) on Health-Related Quality of Life (HRQOL) and Fatigue in Patients With Chronic Hepatitis C Virus (HCV) Infection and Inherited Blood Disorders (IBLD): Data From the C-EDGE IBLD Study

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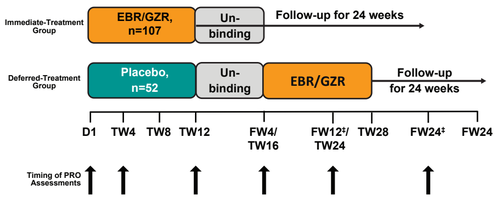
## Background

- Chronic HCV infection and IBLD negatively impact patients' HRQOL and cause fatigue It is important to describe the impact of HCV treatment on patients' HRQOL, including functional health and well-being
- EBR/GZR, a fixed-dose combination tablet administered once daily, without regard to food intake, is approved for the treatment of genotype (GT) 1 and GT4 HCV infections in Europe, the United States, Canada, and other countries worldwide
- Efficacy and safety demonstrated in treatment-naive and treatment-experienced patients, cirrhotic and non-cirrhotic patients, HIV/HCV co-infected patients, and those with chronic kidney disease[1-5]
- C-EDGE IBLD, a double-blind, placebo-controlled, multinational Phase III trial, randomized patients with HCV genotype 1, 4, or 6 infection and IBLD (hemophilia A/B, von Willebrand disease, β-thalassemia, or sickle cell anemia) in a 2:1 ratio to either an immediate-treatment group (ITG; 12 weeks of EBR/GZR) or deferred-treatment group (DTG; 12 weeks of placebo, followed by open-label EBR/GZR)[6]
  - SVR12: ITG: 93.5% (100/107) (full analysis set)
  - Incidence of adverse events was generally comparable between EBR/GZR and placebo
- An exploratory objective was to evaluate whether treatment with EBR/GZR impacts HRQOL and fatigue during treatment and follow-up

## Methods

### Study design




‡PRO assessments only completed by subjects in ITG
D: Day, TW: Treatment Week, FW: Follow-up Week

### Patient-reported outcomes (PRO)

- Patients completed 3 questionnaires using an electronic data-capture tool:
  - SF-36v2® Acute Health Survey (1-week recall), 8 Health Domains (Score: 0-100), Component Summary (Score: normalized to US population with mean 50, SD 10)
  - EuroQol Visual Analog Scale [EQ-VAS] (Score: 0-100)
  - Fatigue: FACIT-Fatigue Scale (Score: 0 to 52)
  - Higher scores indicate better health status

## Methods (continued)

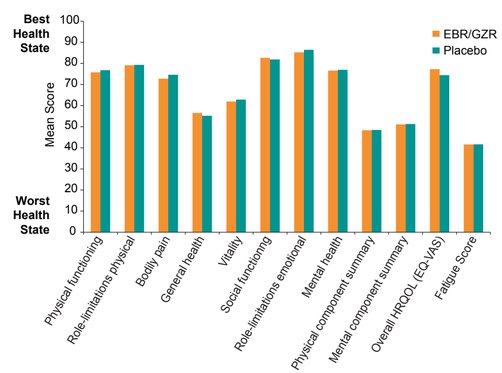
- Descriptive analyses:
  - Mean change (95% CI) from baseline in HRQOL and fatigue scores within treatment groups
  - Difference between treatment groups in mean change in HRQOL and fatigue scores (95% CI)

## Results

| Baseline Characteristics | EBR/GZR | Placebo |
|---|---|---|
| Male | 75% | 75% |
| Age (yr), median (range) | 42 (19-69) | 42 (24-64) |
| Race | | |
| Black/African American | 18% | 17% |
| White | 76% | 77% |
| HCV genotypes (GT) | | |
| GT1 | 89% | 87% |
| GT4 | 11% | 12% |
| GT6 | 0% | 2% |
| Cirrhosis | 24% | 23% |
| HIV co-infection | 6% | 8% |
| Treatment-naïve | 50% | 52% |
| Blood disorders | | |
| Sickle cell anemia | 18% | 19% |
| ß thalassemia | 38% | 38% |
| Von Willebrand or hemophilia A or B | 44% | 42% |

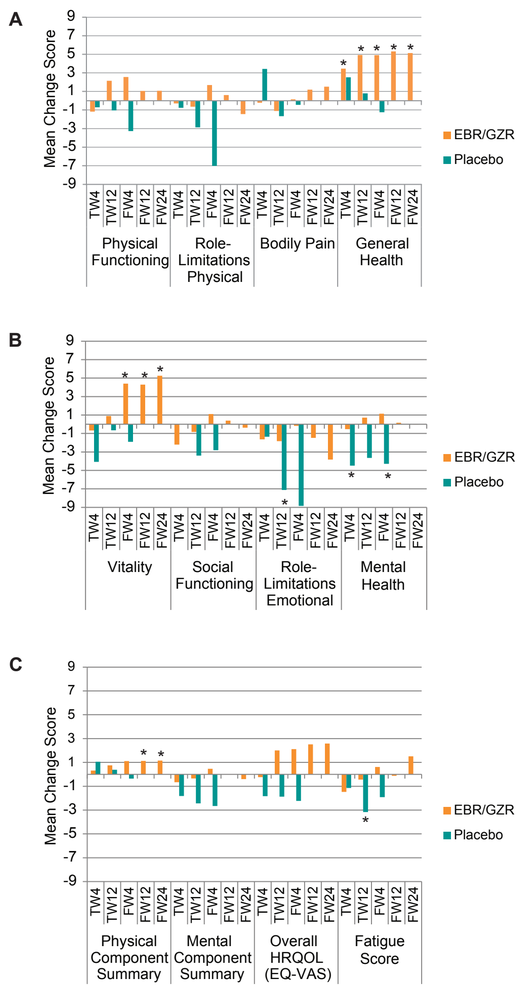
- Compliance rates for the PRO assessments were high across the time points (>92%) and comparable between treatment groups

### Figure 1. Comparable baseline mean scores between treatment groups



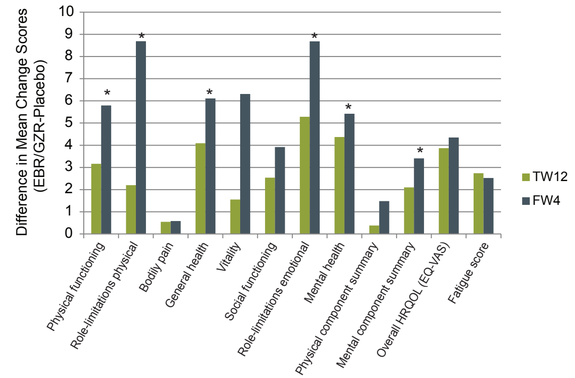

## Results (continued)

### Figure 2. Mean change from baseline in HRQOL and fatigue scores*




*Within treatment group: significant mean change from baseline score, with 95% CI excluding 0.

### Figure 3. Treatment difference in mean change from baseline HRQOL and fatigue scores [EBR/GZR – placebo]*




*Between treatment groups: significant treatment difference in mean change from baseline score, with 95% CI excluding 0.

## Conclusions

- Patient-reported outcomes provide meaningful information that comes directly from the patients, giving their own perception on their overall health, including functional and well-being, during the course of the study
- Treatment with EBR/GZR had a more favorable impact on the HRQOL profile than treatment with placebo
- At FW4, the EBR/GZR group had more favorable mean change from baseline scores than the placebo group in:
  - Physical Functioning, Role-Limitations Physical, General Health, Role-Limitations Emotional, Mental Health, and Mental Component Summary
- Overall, the changes in HRQOL in this study were substantially more favorable than the large declines in HRQOL historically associated with interferon- and ribavirin-containing regimens

**References**

1. Zeuzem S, Ghalib R, Reddy KR, et al. *Ann Intern Med.* 2015;163(1):1-13.
2. Rockstroh JK, Nelson M, Katlama C, et al. *Lancet HIV.* 2015;2(8):e319-e327.
3. Dore GJ, Altice F, Litwin AH, et al. *Ann Intern Med.* 2016;165(9):625-634.
4. Roth D, Nelson DR, Bruchfeld A, et al. *Lancet.* 2015;386(10003):1537-1545.
5. Bruchfeld A et al. ERA EDTA 2016.
6. Hezode C et al. EASL 2016. Hézode C et al. *Hepatology 2017 - Early Online* - Mar 3, 2017.

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- BE, LM, ML, RT, and JMA are current employees of and/or own stock in Merck & Co., Inc., Kenilworth, NJ, USA