# Elbasvir/Grazoprevir Does Not Worsen Renal Function in Patients With Hepatitis C Virus Infection and Pre-existing Renal Disease

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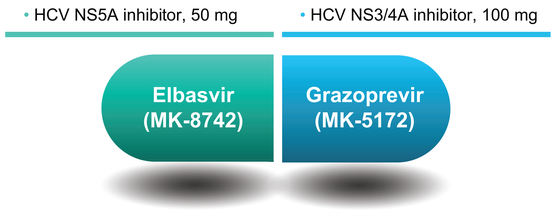
## Background

- Hepatitis C virus (HCV) infection in patients with chronic kidney disease (CKD) is associated with an increased risk for loss of kidney function, kidney transplant failure, and death[1-3]
- Decreased estimated glomerular filtration rate (eGFR) has been reported in patients with HCV infection receiving direct-acting antiviral agents
  - Among patients receiving sofosbuvir/ledipasvir, those with baseline eGFR <60 mL/min/1.73 m$^2$ were more likely to have on-treatment worsening of kidney function than those with normal eGFR[4]
- Elbasvir (EBR) is a once-daily NS5A inhibitor and grazoprevir (GZR) is a once-daily HCV NS3/4A protease inhibitor (**Figure 1**)[5]
  - Approved in Europe, the US, Canada, and other countries worldwide
  - Broad activity vs most HCV genotypes in vitro[6-8]
  - Efficacious in treatment-naive and treatment-experienced patients, cirrhotic and noncirrhotic patients, HIV/HCV co-infected patients, and those with CKD[9-12]

### Figure 1. EBR/GZR




- <1% of EBR/GZR is renally excreted[13]
  - Phase 1 trial demonstrated no need for dose adjustments in CKD
- EBR/GZR was safe and efficacious in patients with CKD stage 4/5, including those receiving hemodialysis in the C-SURFER study[10]
  - Sustained viral response at 12 weeks achieved in 99% of patients
  - On-treatment changes in eGFR and creatinine were similar in patients receiving EBR/GZR and placebo

## Aim

- To evaluate the impact of EBR/GZR on eGFR in patients with CKD stage 3 (CKD 3; eGFR <60 to ≥30 mL/min/1.73 m$^2$)

## Patients and Methods

### Study Design

- This was an integrated analysis of data from the EBR/GZR phase 2/3 clinical development program
  - Pooled dataset of 1689 patients who received EBR/GZR (50 mg/100 mg) with or without ribavirin (RBV) for 8, 12, 16, or 18 weeks
  - 32 patients with CKD 3 were identified
- Patients were treatment-naive or treatment-experienced, and included cirrhotics and those with HIV co-infection
- Creatinine values were assessed at baseline and ≥1 postbaseline time point
- eGFR was calculated using the Modification of Diet in Renal Disease equation at baseline, end of treatment, and 12 weeks post-therapy

## Results

### Demographics and Characteristics

- Patient characteristics and treatment were similar in patients with normal renal function (baseline eGFR ≥60 mL/min/1.73 m$^2$) and those with CKD 3 (baseline eGFR <60 to ≥30 mL/min/1.73 m$^2$) (**Table 1**)

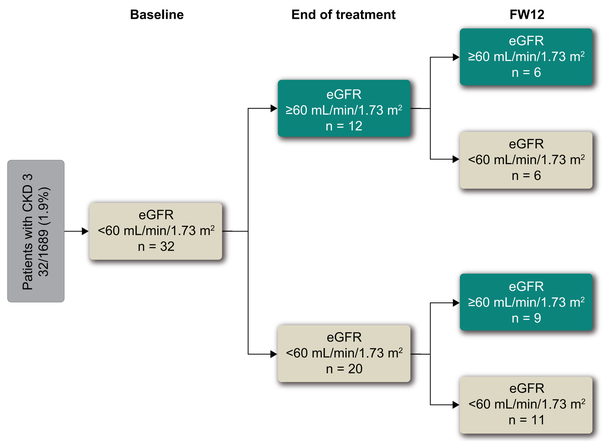
### Table 1. Patient demographics

| | Baseline eGFR <60 to ≥30 mL/min/1.73 m$^2$ n = 32 | Baseline eGFR ≥60 mL/min/1.73 m$^2$ n = 1657 |
|---|---|---|
| Mean age, years (range) | 58.5 (32-82) | 52.5 (18-79) |
| Male, n (%) | 15 (47) | 1023 (62) |
| Black/AA, n (%) | 7 (22) | 211 (13) |
| Treatment-naive, n (%) | 25 (78) | 1018 (61) |
| Cirrhotic, n (%) | 8 (25) | 449 (27) |
| HIV co-infected, n (%) | 13 (41) | 285 (17) |
| Mean baseline viral load (× 10$^6$ IU/mL) | 3.3 | 4.0 |
| Treatment duration, n (%) | | |
| 12 weeks | 27† (84) | 1302‡ (78) |
| 16 weeks | 2 (6) | 209 (13) |
| 18 weeks | 3 (9) | 146 (9) |
| RBV-containing regimen, n (%) | 10 (31) | 646 (39) |
| eGFR, median (IQR) | 56 (51.5, 58.0) | 100 (86.0, 117.0) |

AA, African American.
†One patient received 8 weeks of therapy.
‡Ninety patients received 8 weeks of therapy.

- Change in renal function during treatment and follow-up is shown in **Figure 2**

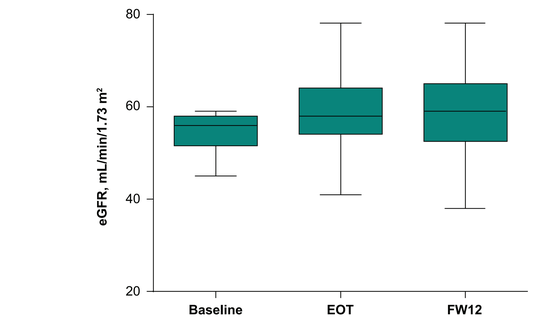
### Figure 2. Patient disposition and change in renal function




FW, follow-up week.

- There was no decline in median eGFR in patients with HCV infection and CKD 3 receiving EBR/GZR for 8-18 weeks (n = 32) (**Figure 3**)

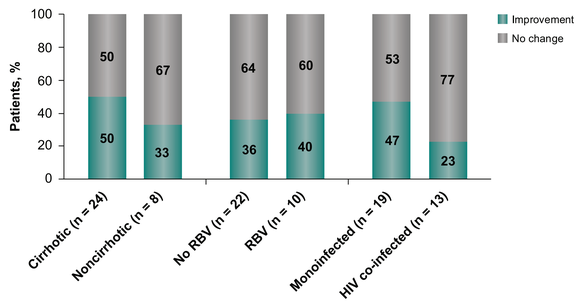
### Figure 3. Median eGFR† during treatment and follow-up in patients with CKD 3 at baseline




CKD 3 defined as baseline eGFR <60 to ≥30 mL/min/1.73 m$^2$.
EOT, end of treatment.
†eGFR assessed using the Modification of Diet in Renal Disease equation.

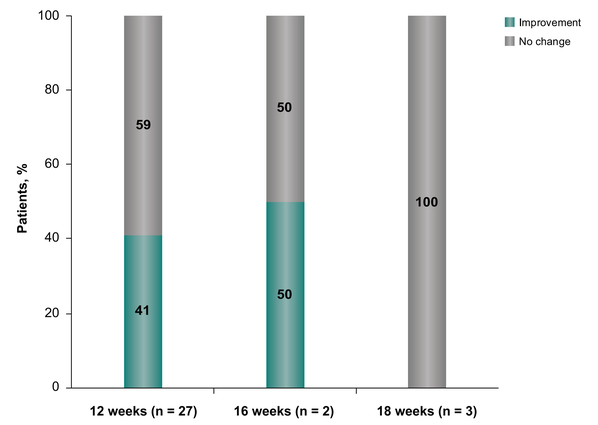
- No patient with CKD 3 at baseline exhibited a decline in CKD stage during treatment with EBR/GZR (**Figure 4**)

### Figure 4. Change in CKD stage between baseline and EOT in selected subgroups among patients with CKD 3 at baseline (n = 32)




- 12 of 32 patients with CKD 3 showed an improvement in CKD stage during treatment with EBR/GZR (**Figure 5**)

### Figure 5. Change in CKD status between baseline and EOT according to treatment duration among patients with CKD 3 at baseline (n = 32)




## Conclusions

- eGFR remained stable or improved in patients with HCV infection and CKD 3 who received EBR/GZR for 8-18 weeks
- No patient with CKD 3 at baseline exhibited a decline in CKD stage during treatment with EBR/GZR
  - 12/32 patients with CKD 3 at baseline showed an improvement in CKD stage during treatment with EBR/GZR
  - Future studies should focus on identifying factors associated with improvements in renal function after successful HCV therapy
- Presence of cirrhosis or HIV co-infection, or treatment with RBV, had no impact on CKD status during treatment with EBR/GZR

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