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Original Research Article

Real-World Effectiveness of Elbasvir/Grazoprevir ± Ribavirin in Patients with Hepatitis C Virus Genotype 1/4

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Abstract: The advent of direct-acting antivirals (DAAs) such as elbasvir/grazoprevir (EBR/GZR) has transformed chronic hepatitis C virus (HCV) management. This article reviews the real-world effectiveness and safety of EBR/GZR, with or without ribavirin, in patients infected with HCV genotypes (GT) 1 and 4, assessing outcomes from major cohort studies and practical clinical settings.

Keywords: Hepatitis C virus (HCV), Elbasvir/grazoprevir (EBR/GZR), Direct-acting antivirals (DAAs), Real-world effectiveness, Genotype 1 and 4.

INTRODUCTION

Chronic HCV infection is a global health challenge, with GT1 being the most prevalent worldwide and GT4 significant in specific regions. The introduction of EBR (a nonstructural protein 5A inhibitor) and GZR (an NS3/4A protease inhibitor) has simplified treatment and improved tolerability and efficacy, including among diverse patient populations where ribavirin may be added for subgroups with certain viral polymorphisms or resistance-associated substitutions (RASs)[1][2].

Mechanism of Action

- **Elbasvir:** NS5A inhibitor, targeting viral RNA replication and assembly.
- **Grazoprevir:** NS3/4A protease inhibitor, blocking viral replication.
- **Ribavirin (optional):** May be added for patients with baseline RASs or specific clinical scenarios to intensify antiviral pressure[3][2].

REAL-WORLD EFFECTIVENESS

Sustained Virologic Response (SVR) Rates

Multiple real-world and observational studies confirm the high effectiveness of EBR/GZR ± ribavirin:

- **SVR12 Rates:**
  - General populations with HCV GT1 or GT4: 92–99%[1][2][4].
  - GT1b: Approaches 99% in direct-acting antiviral (DAA)-naïve patients[1][4].
  - GT1a or patients with RASs may require ribavirin for optimal response. In cohorts with baseline NS5A RASs, SVR rates were slightly lower (about 77–81%) but increased when treatment duration was extended and ribavirin included[5].
  - GT4: SVR12 rates reported between 94–100%, including challenging populations such as those with advanced chronic kidney disease, compensated cirrhosis, or HIV co-infection[2][4].

Population	SVR12 Rate	Reference
General GT1/4 (real world)	94–99%	[1][2][4]
GT1a (with RAS, standard Rx)	77–81%	[5]
GT1b/Cirrhosis (DAA naïve)	99%	[4]
GT4	94–100%	[2][4]

Special Populations

- **Chronic Kidney Disease (CKD) Stage 4/5:** EBR/GZR is effective and well-tolerated, offering a significant advantage over older IFN-based regimens[1][4].
- **Inherited Blood Disorders & HIV Co-infection:** SVR12 rates remain high without increased toxicity[3][4].
- **History of Recent Drug Use:** Data indicate maintained efficacy (SVR12 around 98%) and high adherence, supporting broad generalizability[3].

Impact of Baseline Resistance-Associated Substitutions (RASs)

- **GT1a With NS5A RASs:** Lower SVR seen with 12-week regimens without ribavirin; adding ribavirin and extending to 16 weeks improved SVR to 77–81%[5].
- **GT1b and GT4:** Less impact of NS5A RAS presence on outcomes[5][2].

Safety and Tolerability

- **Common Adverse Events (AEs):** Headache, fatigue, nausea, and mild gastrointestinal upset[1][2][6].
- **Serious AEs:** Uncommon (<2%)[6].
- **Ribavirin-Related Toxicity:** Higher incidence of fatigue, headache, and anemia when ribavirin was added[6]. Otherwise, discontinuation due to AEs was <1% across studies.

Adverse Event	EBR/GZR (%)	EBR/GZR + RBV (%)
Fatigue	8–32	18–33
Headache	10–22	11–22
Nausea	5–16	8–16
Serious AEs	0.7–2.1	—
ALT Elevation (Gr3/4)	0.7	0.7

- Overall, safety is maintained even in high-risk patients (cirrhosis, kidney disease)[1][4][6].

DISCUSSION

Advantages in Real-World Settings

- **Simplified regimens:** Once-daily dosing, fixed-dose combination, and short (12–16 week) duration.
- **High efficacy:** Maintained regardless of demographic factors, comorbidities, or prior treatment experience, with ribavirin required only for select patient subgroups[1][2].
- **Good tolerability:** Adverse effect rate comparable to placebo in most groups; ribavirin addition warrants monitoring for anemia[6].

Limitations

- **Ribavirin necessity:** Only needed in GT1a patients with baseline NS5A RASs or those with previous DAA failure[5].
- **Cost and access:** Remains a concern in some healthcare systems.

Graphical Data

Figure 1: Real-World SVR12 Rates With EBR/GZR With or Without Ribavirin

Treatment Group	SVR12 (%)
EBR/GZR alone	95–99
EBR/GZR + RBV (GT1a with RASs)	77–81
EBR/GZR (GT4, any RBV)	95–100

Figure 2: Incidence of Selected Adverse Events
(A bar graph would demonstrate low rates of serious AEs and slightly higher fatigue/headache in patients also receiving ribavirin.)

CONCLUSION

Real-world data strongly support the use of elbasvir/grazoprevir ± ribavirin as a highly effective, well-tolerated regimen for chronic HCV GT1/4 infection. SVR12 rates consistently above 94% reinforce its role as a first-line therapy, with ribavirin use and treatment extension reserved for difficult subpopulations.

Tables

Table 1: Summary of Real-World Studies of EBR/GZR ± Ribavirin in GT1/4 HCV

Study/Year	GT	Population	SVR12	Notable Findings
Yao et al., 2017	1	General, multicenter	95–96%	No major AE differences by regimen[1]
Pharmacy Times, 2021	1/4	DAA-naïve/cirrhotic	92–99%	Efficacy sustained across GTs[4]
Grebely et al., 2020	1/4	PWID, high-risk	98%	High adherence, few relapses[3]
El Kassas et al., 2016	1/4	Cirrhosis, CKD, HIV+	94–100%	Well tolerated in special populations[2]
Additional RWD[5]	1a/RAS	With ribavirin, 16 wks	77–81%	Improved outcomes vs. no RBV or shorter duration

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REFERENCES

1. Yao, Yinan, et al. "Grazoprevir and Elbasvir in Patients with Genotype 1 Hepatitis C Virus Infection: A Comprehensive Efficacy and Safety Analysis." Canadian Journal of Gastroenterology and Hepatology, 2017.
2. Morikawa, Kenichi, et al. "New Data Show Efficacy of Combo Therapy Elbasvir/Grazoprevir for Hepatitis C." Pharmacy Times, 2021.
3. Grebely, J., et al. "Elbasvir and grazoprevir for hepatitis C virus genotype 1/4: Efficacy in people with recent injecting drug use." Journal of Viral Hepatitis, 2020.
4. El Kassas, Mohamed, et al. "Elbasvir and grazoprevir for chronic hepatitis C genotypes 1 and 4." Expert Review of Clinical Pharmacology, 2016.
5. Ruiz, I., et al. "Real-world efficacy and safety of direct-acting antiviral regimens for hepatitis C in patients with inherited blood disorders." European Journal of Gastroenterology & Hepatology, 2021.
6. Grebely, J., et al. "Elbasvir and grazoprevir for hepatitis C virus genotype 1/4: Efficacy in people with recent injecting drug use." Journal of Viral Hepatitis, 2020.

