

## Treatment-Naive Genotype 2 Without Cirrhosis

Recommended and alternative regimens listed by pangenotypic, evidence level and alphabetically for:

### Treatment-Naive Genotype 2 Patients Without Cirrhosis

RECOMMENDED	DURATION	RATING 
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) <sup>a</sup>	8 weeks	I, A
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)	12 weeks	I, A

<sup>a</sup> Dosing is 3 coformulated tablets (glecaprevir [100 mg]/pibrentasvir [40 mg]) taken once daily. Please refer to the prescribing information.

## Recommended Regimens

### Glecaprevir/Pibrentasvir

ENDURANCE-2 was a randomized, double-blind, placebo-controlled trial of the daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) administered as three 100 mg/40 mg fixed-dose combination pills for 12 weeks among 302 genotype 2-infected treatment-naive or -experienced participants. Treatment-experienced patients included those previously treated with interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon. Patients randomized to placebo later received open-label treatment with glecaprevir/pibrentasvir for 12 weeks. Among 202 patients randomized to active treatment, 70% (141/202) were treatment naive and none had cirrhosis. The SVR12 rates were 99% and 100% by intention-to-treat and modified intention-to-treat analysis, respectively. There were no virologic failures. One participant who achieved SVR4 was lost to follow-up before the SVR12 evaluation. There was no effect of baseline RASs on SVR12 rate. Overall, therapy was well tolerated and the adverse event profile was not different compared to placebo ([Asselah, 2018b](#)).

A shorter duration of glecaprevir/pibrentasvir for 8 weeks was evaluated in the SURVEYOR-II, part 4 study. This was a single-arm, phase 2 study that evaluated glecaprevir/pibrentasvir for 8 weeks among 203 treatment-naive or -experienced patients (previously treated with interferon or peginterferon ± ribavirin, or sofosbuvir plus ribavirin ± peginterferon) with genotype 2, 4, 5, or 6 infection without cirrhosis. Of the 142 genotype 2-infected patients, 137 (96%) were treatment naive. Among the treatment-naive, genotype 2-infected participants, 135/137 (99%) achieved SVR12. The presence of baseline RASs had minimal effect on SVR12 rates. Fifty-three of 126 (42%) treatment-naive and -experienced participants with genotype 2 had the L31M RAS within the NS5A gene at baseline. Fifty-one of 53 (96%) of these participants achieved SVR12 ([Asselah, 2018b](#)).

While not a head-to-head comparison, the results of ENDURANCE-2 and SURVEYOR-II, part 4 indicate that glecaprevir/pibrentasvir administered for 8 or 12 weeks is highly efficacious among genotype 2-infected, treatment-naive patients without cirrhosis. In an integrated analysis of 297 DAA-naive, noncirrhotic patients with genotype 2 infection treated with 8 weeks of glecaprevir/pibrentasvir in 6 phase 2 or 3 clinical trials, SVR12 was 98% (252/257) ([Naganuma, 2019](#)). Additionally, a real-world cohort of treatment-naive, noncirrhotic genotype 2 patients from Italy treated with

glecaprevir/pibrentasvir for 8 weeks achieved an SVR rate of 98% (173/175) ([D'Ambrosio, 2019](#)). A meta-analysis of real-world cohorts that examined glecaprevir/pibrentasvir treatment response among adults demonstrated SVR12 rates of 99.0% (n=274) and 98.0% (n=29) among participants with genotype 2 infection without or with compensated cirrhosis, respectively, with 8 weeks of treatment ([Lampertico, 2020](#)).

## Sofosbuvir/Velpatasvir

The daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg) for 12 weeks was approved by the FDA for the treatment of genotype 2 infection in patients without cirrhosis or with compensated cirrhosis. ASTRAL-2 compared 12 weeks of sofosbuvir/velpatasvir to 12 weeks of sofosbuvir plus ribavirin in 266 treatment-naïve and -experienced patients without cirrhosis or with compensated cirrhosis. The study showed superior efficacy of sofosbuvir/velpatasvir (SVR12 99% vs 94%); ([Foster, 2015a](#)). ASTRAL-1 also included 104 genotype 2 treatment-naïve and -experienced participants without cirrhosis or with compensated cirrhosis, all of whom achieved SVR12 ([Feld, 2015](#)). Pooled analysis of all genotype 2 patients in ASTRAL-1 and ASTRAL-2 demonstrated 100% SVR12 in participants with compensated cirrhosis (29/29) and 99% SVR12 in treatment-naïve participants (194/195). Among patients with genotype 2 receiving sofosbuvir/velpatasvir, the presence of baseline NS5A or NS5B RASs was not associated with virologic failure ([Asselah, 2018](#)).

The POLARIS-2 phase 3 study randomized DAA-naïve patients to 8 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg) versus 12 weeks of sofosbuvir/velpatasvir. Fifty-three patients with genotype 2 were included in the sofosbuvir/velpatasvir arm and all achieved SVR12 (100%). This study confirms the high efficacy and safety of this 12-week regimen in patients with genotype 2 infection ([Jacobson, 2017](#)).

In a single-arm, phase 3 study from Asia that included 375 treatment-naïve and -experienced patients with genotype 1, 2, 3, 4, 5, or 6 infection (18% with cirrhosis) treated with 12 weeks of sofosbuvir/velpatasvir, SVR was achieved in 95% (362/375) ([Wei, 2019](#)). Of the 62 patients with genotype 2 infection, 100% achieved SVR. A real-world, pooled analysis of 12 cohort studies demonstrated an SVR of 99.3% (1535/1546) among adults with genotype 2 infection (with or without compensated cirrhosis) who were treated with 12 weeks of sofosbuvir/velpatasvir ([Mangia, 2020](#)).

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## Related References

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