Sofosbuvir-Based Treatment Failures

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

Sofosbuvir-Based Treatment Failures, With or Without Compensated Cirrhosis[a]

RECOMMENDED	DURATION	RATING
Daily fixed-dose combination of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg)[b]	12 weeks	I, A
ALTERNATIVE	**DURATION**	**RATING**
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) except for NS3/4 protease inhibitor inclusive combination direct-acting antiviral regimen failures[c] • **Not** recommended for genotype 3 infection with sofosbuvir/NS5A inhibitor experience.	16 weeks	I, A

[a] For decompensated cirrhosis, please refer to the appropriate section.
[b] Genotype 3: Add weight-based ribavirin if cirrhosis is present and there are no contraindications.
[c] This regimen is not recommended for persons with prior exposure to an NS5A inhibitor plus NS3/4 PI regimens (eg, elbasvir/grazoprevir).

Recommended Regimen

Sofosbuvir/Velpatasvir/Voxilaprevir

In general, people who have experienced treatment failure with a sofosbuvir-based regimen should be retreated with 12 weeks of sofosbuvir (400 mg)/velpatasvir (100 mg)/voxilaprevir (100 mg). The main exception is persons with genotype 3 infection and cirrhosis for whom the addition of weight-based ribavirin to sofosbuvir/velpatasvir/voxilaprevir for 12 weeks is recommended. These recommendations are supported by data from clinical trials (El-Kassas, 2023); (Bourlière, 2018); (Bourlière, 2017), real-world cohorts (Graf, 2024); (Katiyar, 2024); (Ruiz-Cobo, 2024); (Wang, 2024); (Heo, 2023); (Liu, 2023); (Carson, 2022); (Gupta, 2022); (Dietz, 2021); (Dietz, 2021b); (Onofrio, 2021); (Smith, 2021); (Da, 2020); (Belperio, 2019); (Degasperi, 2019); (Llaneras, 2019); (Sarrazin, 2018); (Vo-Quang, 2018) and 2 meta-analyses (Devan, 2023); (Xie, 2022). The combination of sofosbuvir/velpatasvir/voxilaprevir was studied in a prospective open-label multicenter trial among people with HIV/HCV coinfection who experienced prior treatment failure with sofosbuvir-based regimens; SVR rate was 90.9% (Wilson, 2019).

Alternative Regimen

Glecaprevir/Pibrentasvir

Sixteen weeks of glecaprevir (300 mg)/pibrentasvir (120 mg) can be used as an alternative retreatment regimen based on efficacy data from the phase 3 MAGELLAN-1 clinical trial part 2 (Poordad, 2018); (Poordad, 2017), which revealed a superior SVR rate in the 16-week arm (91%, 43/47) compared with the 12-week arm (89%, 39/44). An HCV-TARGET cohort study of treatment response to glecaprevir/pibrentasvir demonstrated a superior SVR rate in the 16-week versus 12-week arms among DAA-experienced (sofosbuvir plus an NS5A inhibitor) persons with genotype 1 infection without cirrhosis (94% versus 90%) and with cirrhosis (97% versus 86%) (Lok, 2019). A meta-analysis of 14 studies involving people with prior DAA treatment failure (n= 1294) further supports the potential role of glecaprevir/pibrentasvir as an alternative retreatment regimen with a pooled SVR12 rate of 97% (Shen, 2020). However, limited data are available for persons with genotype 3 infection and prior sofosbuvir/NS5A inhibitor treatment failure. Therefore, glecaprevir/pibrentasvir is not recommended for these individuals.

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