Retreatment approach and potential regimens (including other NS5A regimen containing failures)

For patients with cirrhosis or other patients who require retreatment urgently, testing for RAVs that confer decreased susceptibility to NS3 protease inhibitors (eg, Q80K) and to NS5A inhibitors should be performed using commercially available assays prior to selecting the next HCV treatment regimen. For patients with no NS5A inhibitor RAVs detected, retreatment with ledipasvir/sofosbuvir or sofosbuvir/velpatasvir, both with ribavirin, for 24 weeks is recommended. For patients who have NS5A inhibitor RAVs detected and who do not have NS3 inhibitor RAVs detected, treatment with simeprevir, sofosbuvir, and ribavirin for 24 weeks is recommended. For patients who have both NS3 and NS5A inhibitor RAVs detected there are several small studies that provide some insight on salvage regimens. Limited data suggest a retreatment approach based on sofosbuvir combined with either elbasvir/grazoprevir or PrOD may be efficacious. (Lawitz, 2015e); (Poordad, 2015a) In a retreatment arm of the C-SWIFT study, 23 patients who had failed shorter courses of elbasvir/grazoprevir plus sofosbuvir were retreated with 12 weeks of this combination plus weight-based ribavirin. In a per protocol analysis a 100% SVR12 rate was achieved (23/23), including SVR in 9/9 patients with dual NS3 and NS5A RAVs. (Lawitz, 2015e) A second phase II study of 22 patients, including 14 PrOD failures, evaluated retreatment with 12-24 weeks of PrOD plus sofosbuvir. Treatment duration and ribavirin usage were determined by cirrhosis status, HCV RNA response on therapy, and genotype subtype. SVR12 data was available on 15 patients with 14/15 (93%) attaining SVR12. Based on these limited data, patients with dual NS3 and NS5A class RAVs may be retreated with elbasvir/grazoprevir plus sofosbuvir with weight-based ribavirin for 12 weeks or PrOD plus sofosbuvir for 12 weeks in genotype 1b and 24 weeks with weight-based ribavirin in those with genotype 1a. If these regimens are unavailable, retreatment should be conducted in a clinical trial setting, as an appropriate treatment regimen cannot be recommended at this time. Another approach in patients with prior non-response to NS5A-containing therapy has been studied in genoptype 1, 2, and 3 patients who did not respond to velpatasvir-containing regimens including sofobuvir/velpatasvir and sofosbuvir/velpatasvir/GS-9857. (Gane, 2016) Retreatment with sofosbuvir/velpatasvir with ribavirin for 24 weeks yielded high overall response rates (91% or 59/65). Among genotype 1 patients, 97% (33/34) achieved SVR. Baseline NS5A RAVs did not appear to effect SVR rates. In 34 genotype 1 patients, 6 patients had NS5A RAVs prior to retreatment, all of whom achieved SVR. Although data is extremely limited, retreatment with sofosbuvir/velpatasvir + ribavirin for 24 weeks should be considered in genotype 1 patients who have not responded to prior NS5A-based therapy, especially if there is urgency for treatment.