Treatment-Naive Genotype 1

Four highly potent DAA combination regimens are recommended for patients with genotype 1 infection, although there are differences in the recommended regimens based on the HCV subtype, the presence or absence of baseline NS5A resistance-associated substitutions (RASs), and the presence or absence of compensated cirrhosis.

With certain regimens, patients with genotype 1a may have higher virologic failure rates than those with genotype 1b. Genotype 1 infection that cannot be subtyped should be treated as genotype 1a infection.

Approximately 10% to 15% of genotype 1-infected patients without prior exposure to NS5A inhibitors have detectable NS5A RASs prior to treatment. The clinical impact of NS5A RASs varies across regimens and baseline patient characteristics. In patients with genotype 1a infection, the presence of baseline NS5A RASs that cause a large reduction in the activity of NS5A inhibitors (>5 fold) adversely impacts response to some NS5A inhibitor-containing regimens (Zeuzem, 2017); (Jacobson, 2015b). These RASs are found by population sequencing in roughly 5% to 10% of patients and relevant RASs vary by DAA regimen. Given that baseline NS5A RASs are one of the strongest pretreatment predictors of therapeutic response with certain regimens in those with genotype 1a infection, testing for these RASs prior to deciding on a therapeutic course is recommended in select situations (Zeuzem, 2015c). In clinical settings where RAS testing is unavailable, regimens for which the presence of specific RAS(s) factor into treatment selection should be avoided. For further guidance, please see the HCV Resistance Primer section.

Compared to interferon-based therapy, DAAs are associated with a higher rate of drug-drug interactions with concomitant medications. Thus, attention to drug interactions is an important treatment consideration (see Drug Interactions table). The product prescribing information and other resources (eg, http://www.hep-druginteractions.org) should be referenced regularly to ensure safety when prescribing DAA regimens. Important interactions with commonly used medications (eg, antacids, lipid-lowering drugs, anti-epileptics, antiretrovirals, etc) exist for all the regimens discussed.

The following pages include guidance for management of treatment-naive patients with genotype 1 infection.

- Treatment-Naive Genotype 1a Without Cirrhosis
- Treatment-Naive Genotype 1b Without Cirrhosis
- Treatment-Naive Genotype 1a With Compensated Cirrhosis
- Treatment-Naive Genotype 1b With Compensated Cirrhosis
- Simplified HCV Treatment for Treatment-Naive Patients Without Cirrhosis

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Related References

Jacobson IM, Asante-Appiah E, Wong P, et al. Prevalence and impact of baseline NSA resistance associated variants (RAVs) on the efficacy of elbasvir/grazoprevir (EBR/GZR) against GT1a infection [abstract LB-22]. *The Liver Meeting*. 2015.

Zeuzem S, Rockstroh JK, Kwo PY, et al. Predictors of response to grazoprevir/elbasvir among HCV genotype 1 (GT1)–infected patients: integrated analysis of phase 2-3 trials [abstract 700]. In: *Liver Meeting 2015*. Liver Meeting 2015. San Francisco, CA; 2015.

Zeuzem S, Mizokami M, Pianko S, et al. NS5A resistance-associated substitutions in patients with genotype 1 hepatitis C virus: prevalence and effect on treatment outcome. *J Hepatol*. 2017;66(5):910-918.