


HCV Resistance Primer

Resistance Testing in Clinical Practice

Regimen-Specific Recommendations for Use of RAS Testing in Clinical Practice	
RECOMMENDED	RATING 
<p>Elbasvir/grazoprevir NS5A RAS testing is recommended for genotype 1a-infected, treatment-naïve or -experienced patients being considered for elbasvir/grazoprevir. If present, a different regimen should be considered.</p>	I, A
<p>Ledipasvir/sofosbuvir NS5A RAS testing can be considered for genotype 1a-infected, treatment-experienced patients with and without cirrhosis being considered for ledipasvir/sofosbuvir. If clinically important^a resistance is present, a different recommended therapy should be used.</p>	I, A
<p>Sofosbuvir/velpatasvir NS5A RAS testing is recommended for genotype 3-infected, treatment-naïve patients with cirrhosis and treatment-experienced patients (without cirrhosis) being considered for 12 weeks of sofosbuvir/velpatasvir. If Y93H is present, weight-based ribavirin should be added or another recommended regimen should be used.</p>	I, A

^a Clinically important = ≥100-fold shift in the in vitro EC₅₀ to ledipasvir

Table 1. Most Common, Clinically Important RASs by DAA, Genotype, and Fold Change

DAA	Genotype 1a				Genotype 1b		Genotype 3a	
	M28T	Q30R	L31M/V	Y93H/N	L31V/I	Y93H/N	A30K	Y93H
Ledipasvir	20x	>100x	>100x / >100x	>1000x / >10,000x	>100x >50x	>100x / --	NA	NA
Elbasvir	20x	>100x	>10x >100x	>1000x / >1000x	<10x	>100x / --	50x	>100x
Velpatasvir	<10x	<3x	20x / 50x	>100x / >1000x	<3x	<3x / --	50x	>100x

Pibrentasvir	<3x	<3x	<3x	<10x	<3x	<3x	<3x	<3x
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Color Key: light green = <3-fold change; dark green = <10-fold change; orange = >10- to 100-fold change; pink = >100-fold change

Table 2. Clinically Important RASs by DAA Regimen and Genotype

DAA Regimen	Genotype		
	1a	1b	3
Ledipasvir/sofosbuvir	Q30H/R L31M/V Y93C/H/N	L31V ?Y93H	NA
Elbasvir/grazoprevir	M28A/T Q30H/R L31M/V Y93C/H/N	Y93H	NA
Sofosbuvir/velpatasvir	NA	NA	Y93H
Glecaprevir/pibrentasvir	NA	NA	A30K

Table 3. NS5A RAS Testing Recommendations Prior to Initiation of DAA Treatment Among Genotype 1 Patients by DAA Regimen, Virus Subtype, Prior Treatment Status, and Cirrhosis Status

DAA Regimen	1b TN ^a or TE ^b	1a TN	1a TE No Cirrhosis	1a TE Cirrhosis	3 TN Cirrhosis	3 TE No Cirrhosis
Ledipasvir/sofosbuvir	No	No	Yes	Yes	N/A	N/A
Elbasvir/grazoprevir	No	Yes	Yes	Yes	N/A	N/A
Sofosbuvir/velpatasvir	No	No	No	No	Yes	Yes
Glecaprevir/pibrentasvir	No	No	No	No	No	No

^a TN = treatment naive
^b TE = treatment experienced

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