586 ★ Presidential Poster of Distinction

Real-World Impact of Resistance-Associated Substitutions on Re-Treatment after Ledipasvir/Sofosbuvir Virologic Failure in Hepatitis C Patients

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Abstract Text

Background: Understanding the real-world impact of resistance-associated substitutions (RAS) on re-treatment after ledipasvir/sofosbuvir (LDV/SOF) virologic failure in hepatitis C virus (HCV)-infected patients is necessary for informed treatment decisions.

Methods: Observational, intent-to-treat cohort analysis from the Veterans Affairs' Clinical Case Registry of genotype (GT) 1a patients with RAS testing after LDV/SOF virologic failure who were then retreated with an end of treatment (EOT) by 31 Jan 2018. Data were available through 15 May 2018. SVR was defined as HCVRNA below the limit of quantification >10 weeks after EOT.

Results: 439 GT1a veterans were included. The mean age was 63 years, 98% were male, 44% were black, 35% had cirrhosis defined as FIB4>3.25, 19% had history of decompensation. 234 patients had NS3 testing with 114 (48.7%) having 130 RASs. 419 patients had NS5A testing with 326 (77.8%) having 419 RASs. 159 patients had NS5B testing with 9 (5.7%) having 10 RASs. The most common RASs were: NS3 Q80K (101); NS5A Q30R (103), L31M (70), Y93H (55), Q30H (41); NS5B S282T (3), S556G (3). The three most commonly used re-treatment regimens were elbasvir/grazoprevir (ELB/GRZ)+SOF+ribavirin (RBV) (100, 23%), velpatasvir(VEL)/SOF+RBV (81, 18%) and SOF/VEL/voxilaprevir (VOX) (58, 13%). The number of people who had a documented RAS to the re-treatment regimen prior to initiation was NS3 5, NS5A 202, NS5B 2. Re-treatment duration was <12 weeks 7.5%, 12 weeks 48.7%, 16 weeks 14.1%, 24 weeks 26.7%. SVR data was available for 404 patients; data on the full cohort will be presented. Overall SVR rates based on the presence of RASs to any of the three genes or just RASs for NS5A respectively were 84.5% (180/213) and 83.7% (164/196) with no RASs to the re-treatment regimen and 84.3% (161/191) and 84.7% (160/189) with RASs to the re-treatment regimen (Table). SVR rates without and with individual codon changes were: NS3 Q80K 86.4% (108/125) and 81.4% (79/97) p=0.41, NS5A M28A/G 84.8% (318/375) and 60.0% (6/10) p=0.09, Q30E/G/H/K/R 82.8% (192/232) and 86.3% (132/153) p=0.43, H58D 85.0% (318/374) and 54.5% (6/11) p=0.02, Y93C/H/N/S 84.5% (229/271) and 83.3% (95/114) p=0.89.

Conclusion: In this real-world cohort of LDV/SOF virologic failures, the presence of NS5A RASs did not appear to substantially affect SVR for most re-treatment regimens, which were low overall. Individual mutations were associated with varying effect on SVR with the NS5A M28A/G and H58D most important. Other host or viral factors may be contributing to the less than expected SVR rates.

	No NS5A RAS SVR % (n/N)	With NS5A RAS SVR % (n/N)	P
Overall	83.7 (164/196)	84.7 (160/189)	0.90
ELB/GRZ+SOF+RBV	100 (14/14)	89.7 (70/78)	0.46
VEL/SOF+RBV	66.7 (24/36)	80.0 (28/35)	0.32
VEL/SOF/VOX	78.9 (15/19)	92.6 (25/27)	0.36
LDV+RBV	93.8 (15/16)	86.7 (13/15)	0.95
ELB/GRZ+RBV	100 (13/13)	45.5 (5/11)	0.009

Disclosures

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