Poster # 57442

Mutations May Be Important in Second Generation DAA Treatment Failures

Glen Abergel, MD, Robert H K Eng, MD, Sandra Kaminski, MS PA-C , Alexandra Sonyey, MD
Infectious Diseases, New Jersey Healthcare System, East Orange, NJ

RUTGERS New Jersey Medical School

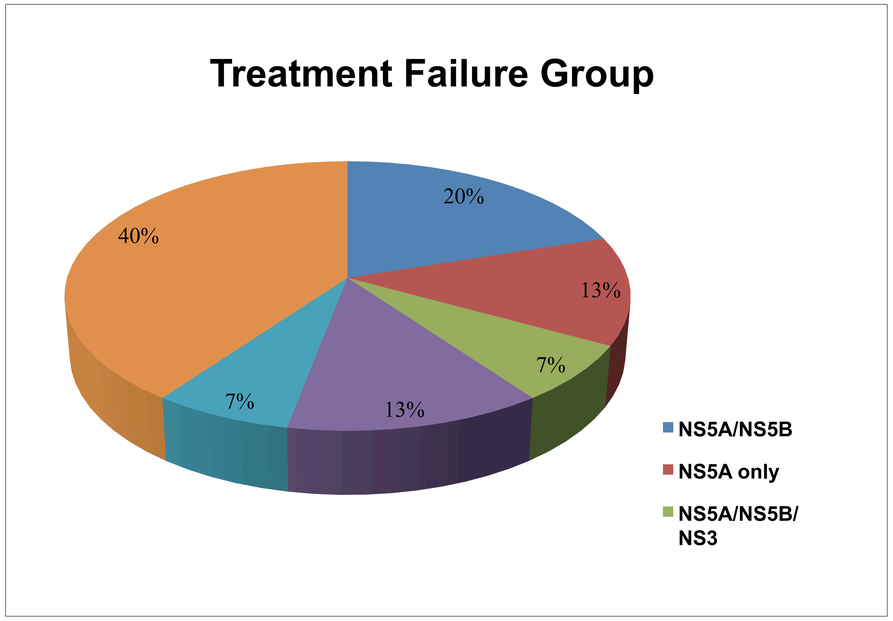
Contact Info:
G Abergel: glenabergel@gmail.com
RHK Eng: Robert.eng@va.gov
A. Sonyey: Alexandra.Sonyey@va.gov

Background

- The use of direct acting antivirals (DAA) has significantly improved treatment outcomes in patients with chronic HCV.
- The data on DAA treatment failure is limited. Resistance associated variants (RAVs) seem to play an important role .
- We analyzed treatment outcomes and causes of DAA failure in NJ VA patients over a period of 1.5 years.

Methods

- We performed a retrospective health record review of all HCV patients treated between 9/24/14 and 3/4/16.
- HCV genotypes (GT), the presence of cirrhosis and HIV, DAA type, length of therapy, and RAVs post treatment were evaluated in the treatment failure (TF) group.
- TF was defined as an inability to achieve the sustained virological response at week 12 post therapy (SVR12).



Results

- 238 HCV patients were treated in the study period. Treatment success rate was 89.9% and 93.4% (14/229) when adjusted for number of patients who fully completed therapy
- Failure rate in the latter group was 6.6%
- TF group had 1 patient with HIV co-infection; 10 with cirrhosis, 7 with GT 1a, 2-GT 1b, 4-GT 2b, and 2-GT 3a
- 8/9 patients with GT 1 received ledipasvir/ sofosbuvir (LDV/SOF) +/- ribavirin (RBV) for 12 weeks
- 1of 9 received paritaprevir/ritonavir/ombitasvir plus dasabuvir (PrOD) + RBV for 12 weeks
- GT 2b patients were treated with SOF/RBV for 12 or 16 weeks
- GT 3a were on LDV/SOF +RBV or SOF/RBV for 12 or 24 weeks
- Resistance panels were available for 9 patients
- GT 1 patients had Q30H/Q80K, Q30H/Y93H, Q30R/Q80K, Q30E/Q80K, and Q30E/S556G RAVs.
- The patient on PrOD had M28T, M141 M/T, E446 E/K, Q80K, D168 E/Y, and Y93H RAVs
- 1 of the 4 GT2b patients had available resistance panel with L159F RAV
- Both patients with GT3a had no RAVs to sofosbuvir or dasabuvir

Conclusion

- HCV treatment failure rate in patients who fully completed therapy at NJ VA over 1.5 years was 6.6% and 3% for those with detected RAVs.
- All GT1 patients with available resistance analyses had NS5a RAVs. One patient with GT2b had NS5b RAV.
- Data on GT3a was incomplete since the full resistance panel was not performed.
- As information on pre-treatment RAVs was not available, we could not determine whether mutations were natural or emerged during treatment.
- Analysis of available data indicates that the presence of RAVs might be the major cause of treatment failure among HCV patients treated with DAA at NJ VA.

References

1. Pawlowtsky et al.”Hepatitis C Virus Resistance to Direct-Acting Antiviral Drugs in Interferon-Free Regimens” Gastroenterology Volume 1, Issue 1. July 2016, Pages 70–86
2. Linh Thuy Nguyen, et al. “Naturally occurring HCV NS5A/B inhibitor resistance-associated mutations to direct-acting antivirals”, Antiviral Therapy, January 2016
3. Julia Dietz, et al. Consideration of Viral Resistance for Optimization of Direct Antiviral Therapy of Hepatitis C Virus Genotype 1-Infected Patients, August 28, 2015
4. Paolucci, Stefania, et al. "Naturally occurring resistance mutations to inhibitors of HCV NS5A region and NS5B polymerase in DAA treatment-naïve patients." *Virology journal* 10.1 (2013):
5. Svarovskaia ES, et al. Infrequent development of resistance in genotype 1-6 hepatitis C virus-infected subjects treated with sofosbuvir in phase 2 and 3 clinical trials. Clin Infect Dis 2014; 59:1666–1674.
6. Soriano V, et al. Treatment failure with new hepatitis C drugs. Expert Opin Pharmacother 2012; 13:313–323.
7. Nakamoto S, et al. Hepatitis C virus NS5A inhibitors and drug resistance mutations. World J Gastroenterol 2014; 20:2902–2912.