Background & Aim

Chronic hepatitis C virus (HCV) infection is a major health burden, affecting approximately 71 million people worldwide who are at risk of developing chronic liver disease, cirrhosis and hepatocellular carcinoma. Among the introduction of direct acting antiviral agents (DAAs), the majority of patients with chronic HCV infection can now be cured with only 8-12 weeks of antiviral therapy. However, some patients do not achieve a sustained virologic response (SVR), regardless of the HCV genotype and/or DAA treatment involved. For these patients, retreatment failure is also limited.

Retreatment may be particularly difficult due to the higher prevalence of negative predictors such as cirrhosis, prior treatment with interferon (IFN), and presence of resistance-associated substitutions (RASs). The aim of the present study was to assess the clinical and virologic characteristics and retreatment options of patients who failed all courses of DAA therapies in a real-world setting.

Methods

In a large resistance database, clinical and virologic data were collected from patients who failed at least two DAA regimens. HCV NS3, NS5A and NS5B amplification and population-based sequencing was performed. Retreatment was primarily based on guideline recommendations, i.e. patients who failed on a regimen containing an NS5A inhibitor were retreated with a protease inhibitor and sofosbuvir, and patients who failed on a protease inhibitor-based regimen were retreated with an NS5A inhibitor and sofosbuvir. However, detailed recommendations for retreatment were also given based on the resistance analysis, where available. All patients were retreated at the discretion of the treating physician. Thus, some patients did not receive guideline-recommended and/or resistance-based regimens.

Conclusion

- The majority of patients who did not respond to multiple DAA therapies were male (76%) and had cirrhosis (79%)
- Resistance testing was performed in 71% of patients after the first failed course of DAA therapy. Despite this, retreatment was not consistently tailored to the RASs detected

- Importantly, treatment failure was even observed in patients in whom the best- available retreatment option was chosen
- Some patients who do not respond to multi-targeted rescue therapies may never be cured

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