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Letters to the Editor

JOURNAL OF HEPATOLOGY

Retreatment with direct-acting antivirals of genotypes 1-3-4 hepatitis C patients who failed an anti-NS5A regimen in real world

To the Editor:

Treatment with direct-acting antivirals (DAA) has shown high efficacy, but a substantial proportion of patients (5–15%) remain resistant to DAAs.[1] As previously reported, treatment failure is generally associated with the emergence of HCV resistance-associated substitutions (RASs), which reduce susceptibility to DAA agents.[1–7] Recent studies have identified emerging RAS patterns following DAA-based treatment failures and have evaluated how new treatment regimens could potentially be selected based on documented or presumed resistance.[1,8,9] Little is known about the efficiency or guidelines of retreatment, and only a few studies are available.[2,10,11]

The aim of this "real-world" study was to analyze retreatment according to baseline nonstructural protein 5A (NS5A) RASs after the failure of first-line DAA treatment.

Patients and methods

From January 2014 to March 2016, 2,995 patients infected with HCV were exposed to NS5A inhibitors in six French liver referral centers; 80 (2.7%) patients relapsed. This "real-world" study included 24 of those 80 patients who had failed to achieve SVR on previous NS5A-based therapies. According to Article

NS3-4A mutation at baseline. The presence of NS5A RASs/polymorphisms was found in 20 (80%) patients at baseline of retreatment (Table 1). Among these 20 patients, 16 were re-treated with at least one anti-NS5A DAA; the remaining four patients were re-treated with a combination of anti-NS5B and anti-NS3/4A DAAs. Among the four patients with no RAS at baseline of retreatment, all were retreated with NS5A inhibitors; three patients were retreated with a combination of NS5A + NS5B inhibitors, and one patient was retreated with a combination of NS5A + NS5B+NS3/4A inhibitors. Overall, 24 weeks of DAA therapy was administered more as a second-line treatment than it was as a first-line treatment: 15/24 (63%) *vs.* 5/24 (21%), respectively (Fisher $p = 0.0043$).

Among the 17 GT1 patients, 14 (82%) had a least one NS5A RAS at the time of failure. The SVR rate was 100% for all regimens except for ombitasvir + paritaprevir + ritonavir + dasabuvir + ribavirin; one patient out of four failed to achieve SVR (failure occurred in a patient with a 93N RAS).

Discussion

Given the emergence and persistence of RASs, retreatment of patients after first-line DAA therapy failure remains a challenge. The present study showed that retreatment of patients after a

FEEDBACK