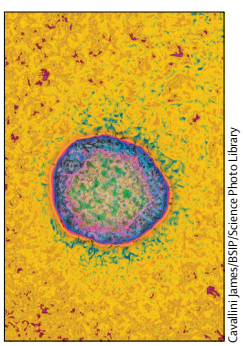
Sustained virological response with sofosbuvir and ledipasvir for hepatitis C virus genotype 5

The main goal of treatment for hepatitis C virus (HCV) is to achieve sustained viral supression (defined as a sustained virological response [SVR]), which substantially delays disease progression and hence improves the survival of the patient.[1] The development of interferon-free therapies that use directly acting antivirals has improved the efficacy and safety profile of HCV treatment, which enhances the possibility of a successful treatment response being achieved.[2,3] Although six major genotypes of HCV, 1 to 6, have been described, studies of the efficacy and safety of directly acting antivirals in the treatment of HCV have focused on the genotypes that are most prevalent in high-income countries (ie, genotypes 1 to 4).[2,3] There is, by contrast, little information about other genotypes, such as genotype 5.

Most cases of chronic HCV genotype 5 infection occur in sub-Saharan Africa, where they represent 40% of cases in some areas.[4] Although the genotype is largely confined to that region, cases of chronic HCV caused by this viral genotype have been reported in Europe. Because of the small number of patients with HCV genotype 5 infection in high-income countries, where clinical studies are generally done, information about the efficacy of combinations of directly acting antivirals for HCV genotype 5 infection is scarce.[2,3] The absence of data and the cost of new treatments are substantial obstacles to the control of HCV in these areas.

In *The Lancet Infectious Diseases*, Armand Abergel and colleagues present the first study done with patients with HCV genotype 5 infection to assess the efficacy and safety of an interferon-free regimen.[5] In this small open-label, non-randomised clinical trial, patients who were both treatment naive and treatment experienced received a single tablet combination of sofosbuvir (400 mg) and ledipasvir (90 mg) once per day for 12 weeks. Overall SVR with this combination was achieved by 39 (95%, 95% CI 83–99) of 41 patients, which is significantly better than in a meta-analysis[6] that included 423 patients who received pegylated interferon plus ribavirin. Despite the small number of patients included in Abergel and colleagues' study (mainly because of the low frequency of HCV genotype 5 in Europe), their study represents the first strong evidence that sofosbuvir plus ledipasvir is effective for the treatment of HCV genotype 5 infection and should therefore be considered as a first-line option for treating HCV in this setting.

Abergel and colleagues detected no differences in SVR with respect to the presence of liver cirrhosis or previous treatment experience. Nonetheless, reduced SVR was reported for patients with the *IL28B* TT genotype (a genetic marker that was associated with a low probability of treatment response during the era of interferon treatment for HCV).[7] The two patients who did not achieve SVR both had the *IL28B* TT genotype. SVR for patients with *IL28B* TT genotype was 50% (achieved by two of four patients). This result agrees with the findings of a clinical trial by Feld and colleagues, who assessed a new combination consisting of sofosbuvir plus velpatasvir once per day for 12 weeks.[8] Among the 35 patients with HCV genotype 5 infection recruited to the study, just one patient (who had the *IL28B* TT genotype) did not achieve SVR, and SVR in patients with the *IL28B* TT genotype (two [67%] of three patients) was similar to that reported by Abergel and colleagues. Because of the small numbers of patients included in both studies, no association can be established between the *IL28B* TT genotype and reduced SVR in patients with HCV genotype 5 infection who are receiving interferon-free regimens. Nevertheless, these results show that studies to assess this possible association will be important for the optimisation of treatment for patients with HCV genotype 5 infection and the *IL28B* TT genotype. These findings could also reopen the debate about the need to establish *IL28B* as a predictive factor in the interferon-free era. The fact that HCV genotype 5 does not represent a major health problem in high-income countries should not preclude larger clinical trials being done to assess the efficacy of interferon-free combinations in this subset of patients. Meanwhile, the combination of sofosbuvir and ledipasvir represents a substantial advance for the treatment of patients with HCV genotype 5 infection.



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We declare no competing interests.

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