

High efficacy of resistance-guided retreatment of HCV patients failing NS5A inhibitors in the real world

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## Abstract

### Background & Aims

Most hepatitis C virus (HCV)-infected patients failing NS5A inhibitors develop resistance-associated substitutions (RASs). Here we report the use of resistance-guided retreatment of patients who failed prior NS5A inhibitor-containing regimens in the GEHEP-004 cohort. This is the largest direct-acting antiviral (DAA)-resistance cohort study conducted in Spain. We aim to provide indications on how to use resistance information in settings where sofosbuvir/velpatasvir/voxilaprevir may not be available.

### Methods

GEHEP-004 is a prospective multicenter cohort enrolling HCV-infected patients treated with interferon (IFN)-free DAA regimens. Prior to retreatment, population-based sequencing of HCV NS3, NS5A and NS5B genes was performed. After receiving a comprehensive resistance interpretation report, the retreatment regimen was chosen and the sustained virological response (SVR) at 12 weeks after treatment completion (SVR12) was recorded.

### Results

A total of 342 patients experiencing virological failure after treatment with sofosbuvir/ledipasvir±ribavirin (54%), sofosbuvir/daclatasvir±ribavirin (23%), or paritaprevir-ritonavir/ombitasvir±dasabuvir±ribavirin (20%) were studied. After a resistance report, 186 patients were retreated. An SVR12 was achieved for 88.1% of the patients who failed after sofosbuvir/ledipasvir±ribavirin, 83.3% of the patients who

failed after sofosbuvir/daclatasvir±ribavirin, 93.7% of the patients who failed after paritaprevir-ritonavir+ombitasvir±dasabuvir±ribavirin.

## Conclusions

In our study, we show how resistance-guided retreatment in conjunction with an interpreted report allows patients to achieve SVR rates close to 90%. We hypothesize that SVR rates may even be improved if resistance data are discussed between experienced virologists and treating clinicians. We believe that our data may be relevant for countries where the access to new DAA combination regimens is limited.

## Keywords

1. [HCV](#)
2. [RASs](#)
3. [Treatment failure](#)
4. [Resistance testing](#)
5. [Resistance-associated substitution](#)
6. [Direct-acting antivirals](#)
7. [Ribavirin](#)