tion of L31 plus Y93 double-substituted variants in HCV genotype 1b. Long-term follow-up of these NS5A variants is required to fully understand their fitness versus that of the wild-type sequence.

There are several limitations in this study based on the use of ultradeep sequencing and 36-nucleotide-read-length fragments without being able to examine linkages with other viral domains. Further analysis using ultradeep sequence technologies with longer read lengths is needed to clarify the relationship between multiple substitutions and treatment response.

In conclusion, 8 patients with HCV genotype 1b infection were treated with DCV, PEG-IFN alpha-2b, and RBV triple therapy. This treatment is expected to improve the SVR rate greatly, but viral breakthrough might develop in some patients with the emergence of DCV-resistant variants. In this study, preexisting DCV-resistant variants had no effect on the results of DCV plus PEG-IFN and RBV treatment. Ultradeep sequence analysis of preexisting DCV variants is not useful to predict the response to combination treatment; however, it might be useful to detect the early emergence of resistant variants. A larger-scale study would be required to establish the methods for the early detection of DCV-resistant variants during treatment with DCV-containing regimens. It is expected that in the near future, DAAs will be preferentially used for the treatment of chronic HCV infection. Therefore, it is important to devise strategies for preventing the emergence and selection of DAA-resistant variants and suppress the replication of preexisting DAA-resistant viral populations.

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