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***Retrospective Study***

**Efficacy of direct-acting antiviral treatment for chronic hepatitis C: A single hospital experience**

Rena Kaneko*et al.*Efficacy of Direct-Acting Antivirals

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**Abstract**

***AIM***

To evaluate the efficacy of direct-acting antivirals (DAAs) in Kanto Rosai Hospital.

***METHODS***

All patients with hepatitis C virus (HCV) who underwent DAA prescription were enrolled in this study. The present study was a single center retrospective analysis using patients infected with HCV genotype 1 or 2. Resistance analysis was performed by using direct sequencing and cycleave PCR in genotype 1 patients treated with interferon (IFN)-free DAA. The primary endpoint was sustained virologic response at 12 wk after therapy (SVR12).

***RESULTS***

Total 117 patients. 135 with genotype 1 and 42 with genotype 2. Of 135 patients with genotype 1, 16 received protease inhibitor+interferon+ribavirin and all achieved SVR. Of the 119 patients who received IFN-free DAA (in different combinations), 102 achieved SVR while 9 failed; 7/9 were on DCV/ASV and 2/9 on LDV/SOF. Efficacy analysis was done only for 42 patients who received DCV/ASV. From this analysis, Y93 resistance-associated substitutions(RASs) were significantly correlated with SVR.

***CONCLUSION***

The SVR rate was 98% for genotype 1 and 100% for genotype 2. However, caution is needed for HCV NS5A RASs that are selected by HCV NS5A inhibitors because cerebrovascular adverse events are induced by some DAA drugs.

**Key words:** Direct-acting antivirals; Resistance-associated substitutions; Hepatitis C; Sustained viral response

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**Core tip:** Direct-acting antivirals (DAAs) have been approved for the treatment of hepatitis C virus (HCV) genotype 1 and 2 infection in Japan since 2011. In the new era of DAA therapy, predictors who fail to respond to DAA might be compromised by resistance-associated substitutions.There have been few reports of DCV/ASV(DAA) failure because DCV/ASV is limited in Japan. Therefore, it might be important to report these cases for future research and treatment of HCV.

Kaneko R, Nakazaki N, Omori R, Yano Y, Ogawa M, Sato Y. Efficacy of direct-acting antiviral treatment for chronic hepatitis C: A single hospital experience. *World J Hepatol* 2017; In press

**INTRODUCTION**

Hepatitis C is a worldwide health problem with 170 million carriers globally and 4 million new cases appearing per year[1]. Approximately 70% of hepatocellular carcinoma cases in Japan are attributable to hepatitis C virus (HCV) infection[2,3]. Since the late 1990s in Japan, the management of HCV infection has improved and there has been a decrease in the widespread use of non-sterile needles and blood transfusions[4-7]. Protease inhibitors such as simeprevir or telaprevir resulting in highly sustained virologic responses (SVR) in HCV patients were introduced in 2011[8-10]. More recently, interferon (IFN)-free DAA inhibiting key viral functions have become the mainstay of anti-HCV treatment[11-13]. Prior to the introduction of these therapeutic agents, IFN-based treatments were the standard therapy against HCV infection[14], despite the suboptimal SVR induced by this treatment (40%-50%). However, patients responding to IFN therapy and sustaining a loss of HCV RNA are generally regarded as being at low risk of developing liver cirrhosis or HCC[4]. However, these continuous efforts and advances in anti-HCV therapy may influence improvements in the long-term outcome of patients with HCV.

In the new era of DAA therapy, the reason for patients’ failure in responding to DAA might be related to the presence or development of resistance-associated substitutions (RASs)[15,16]. The aim of this study was to characterize the treatment response of new DAAs in patients infected with HCV.

**MATERIALS AND METHODS**

***Patients***

Japanese patients aged 30-87 years with chronic HCV genotype 1 and genotype 2 infection without decompensated cirrhosis were commenced with DAA treatment. Overall, 177 participants treated with telaprevir or simeprevir with PEG-IFN and RBV or IFN-free DAA and in whom SVR12 was judged between November 2012 and March 2017 at Kanto Rosai Hospital were included. Treatment-naïve and treatment experienced patients were included.

***Assessments***

Parameters were defined by standard laboratory techniques in Kanto Rosai Hospital. HCV NS5A resistance- associated substitutions (RASs) at Y93 and L31 were detected by commercial direct sequencing and cycleave PCR (SRL Laboratory, Tokyo, Japan) as well as PCR-invader methods (BML Laboratory, Tokyo, Japan). HCV-RNA was measured by COBAS TaqMan PCR assay version 2.0 (Roche, Tokyo, Japan) with a lower limit of quantification (LLOQ) of 25 IU/mL. For 10 patients who received either telaprevir or simeprevir with PEG-IFN treatment, the IL28B genotype was defined by PCR amplification and sequencing of the rs8099917, rs1188122, rs88103142 nucleotide polymorphisms (SRL Laboratory). HCV core amino acids 70 and 99 were defined by PCR direct sequencing (LSI Laboratory Tokyo, Japan). Liver cirrhosis was diagnosed by ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI) or a liver biopsy.

 The primary efficacy end point was the proportion of patients with undetectable HCV-RNA at 12 wk post-treatment (SVR12).

***Statistical analysis***

Analyses were performed using STATA/MP14.0 software (Stata-Corp LP, College Station, TX, United States).

***Ethical statement***

Before any study procedures were undertaken, informed consent was obtained from all patients. This study conformed to the ethical guidelines of the Declaration of Helsinki, and was approved by the ethics committee of Japan Organization of Occupational Health and Safety Kanto Rosai Hospital (2015-17).

**RESULTS**

***Baseline demographics and characteristics***

Among 177 cases, 16 patients with genotype 1 were assigned to telaprevir or simeprevir with PEG-IFN and RBV, and 119 were assigned to IFN-free DAA (DCV/ASV, LD/SOF, OBV/PTV/r). Forty-two patients were treated with SOF and RBV for genotype 2. The average age ± standard deviation of the patients was 67.8 ± 11.0 years. Of these, the group with the highest average age of 72.7 ± 8.3 years was prescribed DCV/ASV. The number and proportion of males and females were 79 (44.6%) and 98 (55.4%), respectively. There were 74 cases (46.2%) with cirrhosis including 21 cases diagnosed pathologically and 58 (29.7%) patients experienced IFN based treatment previously. Twenty-six (14.7%) patients had a history of curative hepatocellular carcinoma (Table 1).

Among 16 patients with IFN based protease inhibitor treatment, 10 patients carried out the polymorphism NS5A region of IL28B, and HCV core amino acids 70 and 91. In both treatment groups, patients with the mutation who were predicted to have a low treatment response were included (Table 2).

***Treatment response and efficacy of all DAA therapy***

A sustained virological response at 12 wk post-treatment (SVR12) was achieved in 167 of 177 (94.4%) patients.

All 16 who received protease inhibitor with PEG-IFN and RBV (5 with teraprevir, 11 with simeprevir) achieved SVR12. All 42 patients with genotype 2 who received the treatment with SOF with RBV achieved SVR 12. There was no relapse until today. The response rate of the IFN-free DAA regimen (DCV/ASV, LDV/SOF, OBV/PTV/r) is shown in Table 3. Of the 43 patients who were treated with DCV/ASV, one patient broke through and 6 relapsed. Of the 66 patients on LDV/SOF, 2 relapsed and 2 patients had SAE; subarachnoid hemorrhage and cerebral hemorrhage. Although medication was stopped at 8 wk and 6 wk after prescription, SVR was achieved. Two patients also relapsed with LDV/SOF treatment. Of the 10 patients who have been on OBV/PTV/r one was lost for follow up.

***Analysis of RASs***

NS5A RASs were analyzed in 82 patients with IFN-free DAA treatment (Figure 1). Of these, 2 relapsed patients with wild type Y93 and 1 with Y93 hetero were treated with DCV/ASV. Three relapsed patients with wild type L31 were also treated with DCA/ASV. Another 6 patients that failed to achieve SVR with DAA treatment had not obtained NS5A RASs prior to treatment. Of the 9 failure patients, 7 were diagnosed as cirrhosis before DAA treatment, and 4 patients had a history of curative HCC (Table 4).

Patients who failed to respond to the initial IFN-free DAA regimen were given second-line therapies. Four patients were enrolled to LDV/SOF with RBV therapy in another hepatitis core hospital in Kanagawa prefecture and SVR was achieved in 3 of these patients and 1 relapsed. One patient treated with LDV/SOF achieved SVR. One patient is now undergoing DCV-TRIO (daclatasvir/asunaprevir/beclabuvir) treatment (Table 4).

Of the 25 having HCC history patients treated with IFN-free DAA, 4 had recurrence until today. Of these, 2 came back with extremely rapid growth of HCC.

Multivariable logistic regression for SVR factors using patients with DCV/ASV treatment was performed using 2 models. Regression using all baseline variables as covariates (Model 1) showed HCV-RNA levels were independently associated with SVR. Model 2 built with suspected variables from DAA failure patients in Table 5 showed that only Y93 RAS was associated with SVR (Table 5).

**DISCUSSION**

This study of patients with HCV infection demonstrated that high SVR rates can be achieved with DAA regimens including IFN based protease inhibitor and IFN-free DAAs. DAA agents confirmed good effectiveness and safety for both treatment naïve patients and previously treated cases.

Until recently, PEG-IFN combined with ribavirin therapy was the only antiviral drug capable of terminating HCV infection[8]. However, SVR was only achieved in about 50% of treated patients[17-19]. Many DAAs have been designed to improve this situation[20]. To activate the IFN pathway, telaprevir, boceprevir and simeprevir were introduced as 1st and 2nd generation HCV protease inhibitors[8-10,20]. However, these agents increase the risk of adverse events such as anemia, renal failure, and severe drug rash. In the initial IFN-free regimen, DCV/ASV eliminated IFN-related toxicity and achieved a SVR24 rate of 84% in chronic hepatitis C patients and 90.9% in liver cirrhosis cases in Japan[21]. The SVR12 rate of LDV/SOF was 100%[12] and for OBV/PTV/r it was 98%[22] in genotype 1 HCV. SOF/RBV and OBV/PTV/r have been approved for genotype 2 HCV, which accounts for up to 30% of chronic HCV infection, which is increasing in prevalence in Japan[23]. Although OBV/PTV/r was limited to use for genotype2b, the SVR rate was 95-98% when ribavirin is used[23-25]. The use of IFN-free DAA enables the treatment of IFN ineligible/intolerant individuals with HCV infection.

A low rate of virological failure in genotype 1 was observed in patients with baseline Y93 or L31 variants in NS5A receiving DCV/ASV or OBV/PTV/r treatment[13,22]. It has been reported that pretreatment with NS5A RASs did not impact LDV/SOF therapy[26].

Moreover, there have been few reports of DCV/ASV failure because DCV/ASV is limited in Japan. Therefore, it might be important to report these cases for future research and treatment of HCV.

In the present report, the SVR rate of each therapy in Kanto Rosai Hospital was similar to previous reports[12, 13, 21, 23, 27]. In genotype 1 patients, 7 failures with DCV/ASV and 2 with LDV/SOF were reported. Among these, 7 patients were diagnosed cirrhosis and 4 patients with a history of HCC were also reported. Y93 RAS was correlated to SVR failure in DCV/ASV cases. In two relapsers with LDV/SOF, DAA RAS could not detected. Subsequently, it was revealed that the core genotype of HCV was 1a and 2a in these patients.

We experienced two patients with subarachnoid hemorrhage and cerebral hemorrhage, and these discontinued LDV/SOF therapy. They were 51 and 68 year-old female without cirrhosis and other medical history. In 2016, post-marketing surveillance were reported in Japan, and 31 cases of severe cerebrovascular disease were reported[28]. As far as we know, there is no detailed report about cerebrovascular adverse reaction. Therefore the physiological mechanism underlying the cerebrovascular adverse events is unclear. Caution is needed when prescribing LDV/SOF therapy.

Two patients had aggressive and rapid HCC recurrence after treatment with DAA. The assumption that the use of DAA may induce HCC relapse had been reported [29]. The surveillance of HCC must be taken strictly after DAA treatment in patients with prior HCC.

Recent reports demonstrated that the SVR rate was only 69% for salvage therapy for patients who failed to respond to NS5A inhibitors[30]. Prior DCV/ASV treatment is associated with a failure of LDV/SOF for multiple HCV NAS5A RASs[30, 31].

We could not treat patients with LDV/SOF and RBV simultaneously because this treatment regimen has not been approved for general insurance. However, the ratio of SVR increased to 75% in initial DAA failure patients, even though multiple NS5A RASs were observed.

The achievement of an SVR of 100% for overall patients with HCV infection may be accomplished in the future.

This study had some limitations. First, data for RASs were not available for all cases. Due to the small sample size, the power of the multiple regression analysis remains low rebel. Second, because this was a study from one hospital, the total number of treatment cases was small. Third, because DCV/ASV has only been approved in Japan, there are some limitations regarding the generalizability of the results. However, this study provides some important knowledge about HCV treatment.

In conclusion, direct-acting antiviral treatment for HCV infection is highly effective in Kanto Rosai Hospital. However, caution is needed for HCV NS5A RASs that are selected by HCV NS5A inhibitors because cerebrovascular adverse events are induced by some DAA drugs.

**ARTICLE HIGHLIGHTS**

***Research background***

In a previous study, it was shown that resistance-associated substitutions (RASs) were predictors of DAA failure. No significant adverse effect was reported in the DAA treatment in clinical trails. In this study, the pre-study hypothesis was that another predictors might exist concerning about DAA failure. An anther hypothesis was that the severer adverse effect must occur in the real world because patients conditions were severer than those of clinical trials.

***Research motivation***

Direct-acting antivirals (DAAs) have been approved for the treatment of hepatitis C virus (HCV) genotype 1and 2 infection in Japan since 2011. In the new era of DAA therapy, predictors who fail to respond to DAA might be compromised by resistance-associated substitutions (RASs).There have been few reports of DCV/ASV failure because DCV/ASV is limited in Japan. Therefore, it might be important to report these cases for future research and treatment of HCV.

***Research objectives***

All patients with hepatitis C virus (HCV) who underwent DAA prescription were enrolled in this study. Overall, 177 participants treated with DAA and in whom SVR12 was judged between November 2012 and March 2017 at Kanto Rosai Hospital were included.

***Research methods***

HCV patients who underwent DAA prescription were enrolled in this study. Resistance analysis was performed by using direct sequencing and sycleave PCR. Multiple regression analysis was performed to evaluate factors related to loss of HCV-RNA.

***Research results***

Total 117 patients. 135 with genotype 1 and 42 with genotype 2. Of 135 patients with genotype 1, 16 received protease inhibitor + interferon + ribavirin and all achieved SVR. Of the 119 patients who received IFN-free DAA (in different combinations), 102 achieved SVR while 9 failed; 7/9 were on DCV/ASV and 2/9 on LDV/SOF. Efficacy analysis was done only for 42 patients who received DCV/ASV. From this analysis, Y93 resistance-associated substitutions(RASs) were significantly correlated with SVR.

***Research conclusions***

The SVR rate was 98% for genotype 1 and 100% for genotype 2. NS5A RASs are most likely to affect the outcomes of DAA therapy in our facility.

***Research perspectives***

The SVR rate was 98% for genotype 1 and 100% for genotype 2. However, caution is needed for HCV NS5A RASs that are selected by HCV NS5A inhibitors because cerebrovascular adverse events are induced by some DAA drugs.

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**Figure 1 Sustained virologic response rates for NS5A resistance-associated substitution and each interferon-free agent.** The number above each column is the number of cases with SVR (numerator) and total cases (denominator). Two relapsed patients with wild type Y93, 1 with Y93 hetero and 3 relapsed patients with wild type L31 were treated with DCV/ASV. Another 6 patients that failed to achieve SVR with DAA treatment had not obtained NS5A RASs prior to treatment. Another patients had no relapse regardless of the presence or absence of RASs. RAS: Resistance-associated substitution; SVR: Sustained virologic response; DCV/ASV: Daclatasvir/asunaprevir; DAA: Direct-acting antivirals.

**Table 1 Baseline demographics and patient characteristics**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Overall*****n =* 177** | **Genotype 1** | **Genotype 2** |
| **IFN/TVR/RBV** | **IFN/SMV/RBV** | **DCV/ASV** | **LDV/SOF** | **OBV/PTV/r** | **SOF/RBV** |
| ***n =* 5** | ***n =* 11** | ***n =* 43** | ***n =* 66** | ***n =* 10** | ***n =* 42** |
| Age, median1 | 67.8 (11.0) | 62.9 (8.7) | 60.2 (8.9) | 72.7 (8.3) | 66.0 (11.2) | 70.9 (6.5) | 67.5 (12.6) |
| > 65, *n* (%) | 118 (66.7) | 3 (60) | 4 (36.4) | 37 (88.1) | 39 (59.0) | 7 (70) | 29 (67.4) |
| Gender |  |  |  |  |  |  |  |
| Male, *n* (%) | 79 (44.6) | 3 (60) | 7 (63.6) | 14 (32.6) | 31 (47.0) | 4 (40) | 20 (47.6) |
| Female, *n* (%) | 98 (55.4) | 2 (40) | 4 (36.4) | 29 (67.4) | 35 (53.0) | 6 (60) | 22 (52.4) |
| HCV RNA,median Log10 LGE1 | 6.1 (0.8) | 6.5 (0.56) | 6.2 (1.1) | 6.30 (0.5) | 6.16 (0.6) | 5.4 (0.9) | 5.8 (0.9) |
| > 100000 IU/mL, *n* (%) | 109 (61.6) | 4 (80) | 9 (81.8) | 32 (76.2) | 43 (0.7) | 2 (20) | 19 (45.2) |
| Cirrhosis present |  |  |  |  |  |  |  |
| Yes, *n* (%) | 74 (41.8) | 0 (0) | 0 (0) | 34 (79.0) | 29 (44.0) | 3 (30) | 8 (18.6) |
| No, *n* (%) | 103 (58.2) | 5 (100) | 11 (100) | 9 (20.1) | 37 (56.0) | 7 (70) | 34 (81.4) |
| HCV treatment history |  |  |  |  |  |  |  |
| Naïve, *n* (%) | 132 (70.3) | 1 (20) | 2 (18.2) | 25 (58.1) | 63 (95.5) | 9 (90) | 32 (76.2) |
| Prior IFN-based treatment, *n* (%) | 45 (29.7) | 4 (80) | 9 (81.8) | 18 (41.8) | 3 (4.5) | 1 (1) | 10 (23.8) |
| History of HCC |  |  |  |  |  |  |  |
| Yes, *n* (%) | 26 (14.7) | 1 (20) | 0 (0) | 19 (44.1) | 3 (4.5) | 0 (0) | 3 (9) |
| No, *n* (%) | 151 (85.3) | 4 (80) | 11 (100) | 24 (55.8) | 63 (95.5) | 10 (100) | 39 (90.7) |
| Laboratory values |  |  |  |  |  |  |  |
| Baseline platelet count, mean (×104/μL)1 | 15.1 (6.5) | 15.4 (3.4) | 15.1 (6.2) | 11.5 (5.8) | 15.5 (6.5) | 18.0 (5.96) | 17.6 (6.0) |
| Baseline ALT level, mean (IU/L)1 | 51.2 (37.3) | 41.8 (9.7) | 50.1 (50.5) | 53.1 (27.8) | 60.3 (45.2) | 39.9 (26.8) | 38.9 (28.6) |
| Baseline AFP level, mean (ng/mL)1 | 12.1 (17.6) | 5.6 (1.6) | 7.18 (9.1) | 23.4 (27.2) | 8.99 (11.6) | 9.9 (11.6) | 6.8 (6.9) |

1The standard deviation is given in parentheses. HCV: Hepatitis C virus; ALT: Alanine aminotransferase; AFP: Alpha fetoprotein; TVR: Telaprevir; SMV: Simeprevir; IFN: Interferon; LDV/SOF: Ledipasvir/sofosbuvir; OBV/PTV/r: Ombitasvir/paritaprevir/ritonavir; DCV/ASV: Daclatasvir/asunaprevir; RBV: Ribavirin.

**Table 2 Baseline characteristics of IL-28B and NS5A polymorphisms**

|  |  |  |
| --- | --- | --- |
|  | **IFN/TVR/RBV** | **IFN/SMV/RBV** |
|  | ***n =* 5** | ***n =* 5** |
| IL28B SNP (*n*) |  |  |
|  *rs8099917* |  |  |
|  T/T | 4 | 1  |
|  T/G | 1 | 2  |
|  G/G | 0 | 1 |
|  *rs11881222* |  |  |
|  A/A | 4 | 1 |
|  A/G | 0 | 2 |
|  G/G | 1 | 1 |
|  *rs88103142* |  |  |
|  T/T | 4 | 1 |
|  T/C | 1 | 2 |
|  C/C | 0 | 1 |
| NS5A aa701 |  |  |
|  Wild | 3 | 0 |
|  Mutant | 2 | 4 |
|  Competitive | 0 | 1 |
| NS5A aa911 |  |  |
|  Wild | 3 | 0 |
|  Mutant | 2 | 2 |
|  Competitive | 0 | 3 |

1aa HCV core amino acid. IFN: Interferon; TVR: Telaprevir; SMV: Simeprevil; RBV: Ribavirin.

**Table 3 Response during and after treatment with direct-acting antivirals**

|  |  |  |  |
| --- | --- | --- | --- |
| **Response** | **Overall*****n =* 119** | **Genotype 1** | **Genotype 2** |
| **DCV/ASV** | **LDV/SOF** | **OBV/PTV/r** | **SOF+RBV** |
| ***n =* 43** | ***n =* 66** | ***n =* 10** | ***n =* 42** |
| HCV RNA<LLOQ during treatment1, *n* (%) | 119 (100) | 41 (100) | 66 (100) | 9 (90)3 | 42 (100) |
| HCV RNA<LLOQ after end of treatment1, *n* (%) | 118 (98.3) | 42 (97.6) | 66 (100) | 9 (90)3 | 42 (100) |
| SVR122, *n* (%) | 109 (91.6) | 35 (83.3) | 64 (97) | 9 (90)3 | 42 (100) |
| On-treatment failure, *n* (%) | 1 (0.8) | 1 (2.3) | 0 (0) | 0 (0) | 0 (0) |
| Relapse, *n* (%) | 8 (6.7) | 6 (16.7) | 2 (3) | 0 (0) | 0 (0) |

1LLOQ (lower limit of quantification) = 25 IU/Ml; 2SVR: Sustained virologic response; 3One case lost to follow-up.

**Table 4 NS5A RASs and clinical course in patients with failure of direct-acting antivirals**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient No.** | **Gender** | **Age (yr)** | **LC1** | **HCC2** | **Initial DAA** | **NS5A RASs** | **Second DAA** | **Second result** |
| **Before DAA** | **After DAA (invader)** | **After DAA (cycleave)** |
| 1 | Female | 73 | No | No | DCV/ASV | NA | Y93H L31F Q54H A92V | Y93mutant L31mutant | LDV/SOF/RBV | SVR |
| 2 | Female | 77 | Yes | Yes | DCV/ASV | NA | Y93H L31M Q24Q/R | Y93mutant L31mutant | LDV/SOF/RBV | Relapse |
| 3 | Female | 71 | Yes | No | DCV/ASV | NA | NA | Y93wild L31mutant | LDV/SOF/RBV | SVR |
| 4 | Female | 78 | Yes | No | DCV/ASV | NA | NA | Y93mutant L31mutant | LDV/SOF/RBV | SVR |
| 5 | Male | 74 | Yes | Yes | DCV/ASV | NA | Y93H L31V Q54y Q62D | Y93mutant L31mutant | LDV/SOF | SVR |
| 6 | Female | 83 | Yes | Yes | DCV/ASV | Y93Y/H L31L | Y93H L31M L31V | Y93mutant L31wild | No | NA |
| 7 | Male | 71 | Yes | No | DCV/ASV | Y93Y L31L | NA | Y93wild L31mutant | DCV-TRIO | Undergoing |
| 8 | Female | 66 | No | No | LDV/SOF | Y93Y L31L | NA | Failure | Waiting | NA |
| 9 | Male | 78 | Yes | Yes | LDV/SOF | NA | NA | Failure | Waiting | NA |

1Diagnosed as cirrhosis; 2A history of curative treatment for hepatocelluler carcinoma. RAS: Resistance-associated substitution; DAA: Direct-acting antivilals; SVR: Sustained virologic response; DCV/ASV: Daclatasvir/asunaprevir; LDV/SOF:　Ledipasvir/sofosbuvir; RBV: Ribavirin; DCV-TRIO: Daclatasvir/asnaprevir/beclabuvir; NA: Data not available; Failure: Could not be detected.

**Table 5 Multivariable logistic regression models for SVR in patients with DCV/ASV**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Odds ratio** | **95%CI** | ***P* value** |
| Model 1: All variables  |  |  |  |
|  | Platelet count | 0.00 | -0.01-0.27 | 0.71 |
|  | AFP level | 0.00 | -0.00-0.01 | 0.44 |
|  | ALT level | 0.00 | -0.00-0.01 | 0.31 |
|  | HCV RNA level | 0.26 | 0.02-0.45 | 0.04a |
|  | Age  | 0.02 | -0.01-0.04 | 0.14 |
|  | Gender | -0.13 | -0.39-0.12 | 0.28 |
|  | Y93 | 0.23 | -0.31-0.77 | 0.38 |
|  | L31 | -0.17 | -1.05-0.70 | 0.68 |
|  | History of HCC | -0.29 | -0.68-0.92 | 0.13 |
|  | Cirrhosis | -0.30 | -0.38-0.26 | 0.67 |
|  | Prior IFN  | -0.15 | -0.41-0.99 | 0.21 |
| Model 2: Limited suspicious covariates |  |  |  |
|  | Age | 0.00 | -0.13-0.14 | 0.93 |
|  | Y93 | 0.48 | 0.08-0.87 | 0.02a |
|  | L31 | -0.42 | -1.09-0.24 | 0.2 |
|   | Cirrhosis | -0.15 | -0.37-0.08 | 0.19 |

Model 1: The baseline model considered with all covariates obtained. Model 2: Limited to covariates suspected from Table 4. a*P* < 0.05were considered statistically significant.