# Dual oral therapy with daclatasvir plus asunaprevir for patients with HCV genotype 1b infection: A Chang Gung Medical Branches multicenter experience

Chih-Lang Lin [1], Tsung-Hui Hu[2], Chien-Hung Chen[2], Chao-Hung Hung[3], Sen-Yung Hsieh[4], Chau-Ting Yeh[4], Chun-Yen Lin[4], Sheng-Nan Lu[3], Rong-Nan Chien[4]

Liver research center, Chang Gung Memorial Hospital and University, College of Medicine, Keelung[1] and Kaohsiung[2] and Chiayi[3] and Linkou[4], Taiwan

***Objectives:***

Daclatasvir (DCV) and Asunaprevir (ASV) are NS5A and NS3 protease-targeted antivirals currently under development for treatment of chronic hepatitis C (CHC) virus genotype 1b (HCV-1b) infection with potent antiviral activity. However, the real-world efficacy and safety of DCV plus ASV for CHC patients with HCV genotype 1b infection remain limited in Taiwan. In this study, we aim to investigate the anti-viral response and safety of dual therapy with DCV and ASV for CHC patients with HCV-1b infection in four institutions of Chang Gung Medical Branches.

***Methods:***

A total of 344 HCV-1b patients intended in receiving DCV 60 mg once daily plus ASV 100 mg twice daily for 24 weeks and 196 (57%) completed with sustained virological response at 12 weeks (SVR12) has been enrolled. (Figure 1)

***Results:***

Of the 196 patients, 176 (89.8 %) and 191 (97.4 %) achieved serum HCV RNA levels below lower limit of quantification (LLOQ) at 4 and 24 weeks of treatment, respectively. The SVR12 was achieved in 187 of 196 patients (95.4 %). (Figure 2) The stratified SVR12 rates were comparable in terms of sex, age, baseline viral load, liver function, platelet count, and FIB-4. Of note was that multivariate logistic regression analysis showed that higher viral load more than 3 million IU/ml (OR=0.219; 95% CI=0.056-0.854; P=0.029) independently associated with SVR12. (Table 1) All except 9 (97.4%) patients tolerated treatment well without interruption of treatment. (Figure 1) Additionally, another two patients experienced isolated hyperbilirubinemia without ALT elevation or therapy withdrawal.

**Figure 1**

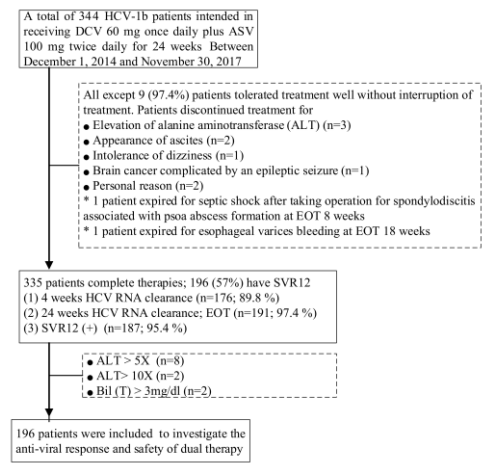


**Figure 2**

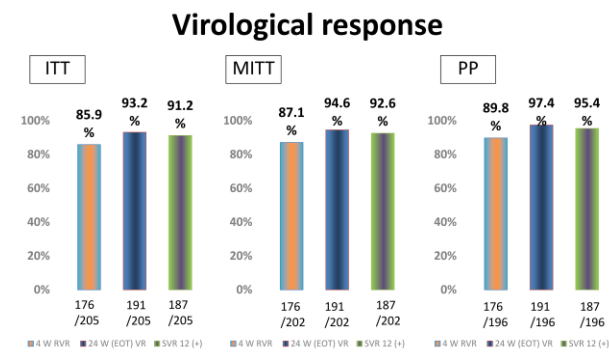


**Table 1. Prediction factors for SVR 12**

| | All patients | SVR12 (-) | SVR12 (+) | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|---|---|---|
| | (n=196) | (N=9) | (N=187) | OR (95% CI) | p value | OR (95% CI) | p value |
| Age (mean ± SD) | 64.5 ± 9.7 | 60.7 ± 10.9 | 64.7 ± 9.6 | 1.040 (0.976 -1.109) | 0.225 | | |
| Male (%) | 77 (39.3%) | 5 (55.6 %) | 72 (38.5 %) | 1.997 (0.519 -7.681) | 0.315 | | |
| HCC (%) | 29 (14.8%) | 0 (0 %) | 29 (15.5 %) | 0 (0- 0) | 0.998 | | |
| Liver cirrhosis (%) | 106 (54.1 %) | 3 (33.3 %) | 103 (55.1 %) | 0.408 (0.099 - 1.679) | 0.214 | | |
| IFN experience (%) | 117 (59.7 %) | 5 (55.6 %) | 112 (59.9 %) | 0.837 (0.218 -3.219) | 0.796 | | |
| Hemodialysis (%) | 3 (1.5%) | 0 (0%) | 3 (1.6%) | 0 (0- 0) | 0.999 | | |
| HCV RNA (logIU/mL) | 5.94 ± 0.83 | 6.24 ± 0.56 | 5.93 ± 0.84 | 0.548 (0.192 -1.566) | 0.261 | | |
| High viral load (>1*$10^6$ IU/mL) | 117 (60%) | 6 (66.7 %) | 111 (59.7 %) | 0.740 (0.179 -3.051) | 0.677 | | |
| High viral load (>3*$10^6$ IU/mL) | 45 (23.1%) | 5 (55.6 %) | 40 (21.5 %) | 0.219 (0.056 -0.854) | 0.029 | 0.219 (0.056-0.854) | 0.029 |
| High viral load (>6*$10^6$ IU/mL) | 20 (10.3 %) | 1 (11.7 %) | 19 (10.2 %) | 0.910 (0.108 -7.677) | 0.931 | | |
| Albumin | 4.1 ± 0.4 | 4.1 ± 0.5 | 4.1 ± 0.4 | 0.881 (0.188 -4.101) | 0.872 | | |
| AST | 82.3 ± 68.9 | 54.2 ± 18.9 | 83.7 ± 70.1 | 1.018 (0.995 -1.041) | 0.129 | | |
| ALT | 83.3 ± 75.9 | 61.3 ± 31.4 | 84.4 ± 77.3 | 1.010 (0.992 -1.029) | 0.28 | | |
| Bilirubin (T) | 1.0 ± 0.5 | 1.0 ± 0.5 | 1.0 ± 0.5 | 0.920 (0.225 -3.763) | 0.908 | | |
| platelet | 129.1 ± 62.6 | 128.2 ± 53.7 | 129.2 ± 63.2 | 1.000 (0.990 -1.011) | 0.964 | | |
| Cr | 0.97 ± 1.23 | 0.82 ± 0.26 | 0.98 ± 1.26 | 1.348 (0.248 -7.341) | 0.73 | | |
| FIB-4 | 7.71 ± 8.79 | 7.80 ± 9.91 | 7.71 ± 8.76 | 0.999 (0.927 -1.076) | 0.975 | | |

***Conclusions:***

Dual therapy with DCV plus ASV provides a highly effective and well-tolerated treatment option for Taiwanese patients with HCV-1b infection. Univariate followed by multivariate analysis revealed that SVR12 independently associated with higher HCV RNA levels (p=0.029).