free direct-acting antiviral agents (DAAs) in chronic hepatitis C patients. **Methods:** Total 1291 patients who achieved SVR by IFN-free DAA therapies from September 2014 through December 2017 were enrolled in multicenter in Japan. Patients with a history of hepatocellular carcinoma (HCC) before DAA treatment and had carcinogenesis within 1 year after end of treatment (EOT) were excluded in this analysis. Serum Mac 2 binding protein glycosylated isomer (M2BPGi), albumin, α-fetoprotein (AFP), Fiborsis-4(Fib-4) index were measured at pre-treatment (pre-Tx) and post-treatment (post-tx, SVR24). In addition, *TLL1* (rs17047200) SNP associated with HCC development after SVR24 achievement with IFN-based therapy was examined. The median observation periods after DAA treatment were 97 weeks. This study protocol was approved by the appropriate institutional ethics review committees and written informed consents were obtained from all patients.**Results:** Of the 1291 patients, the median age of the patients was 70 years (range 21-87), male gender was 41%, and 328 (25.4%) were liver cirrhosis (LC). The median platelet (PLT) counts were $16.3*10^4$ and AFP was 3.3 ng/ml at the SVR 24. Seventeen (1.3%) patients developed an initial HCC during the follow-up periods. Several clinical data at SVR24 (age, gender, albumin, AFP, Fib-4 index and M2BPGi) and host genetic factor [*IL28B* (rs8099917) genotype, and *TLL1* (rs17047200) genotype] were evaluated for univariate and multivariate analysis. Post-Tx median M2BPGi, AFP and Fib4 index were improved, but significantly higher in those with HCC development. Multivariate analysis showed that high age (HR 1.10; 95%CI 1.01-1.20; p=0.020) and *TLL1*(rs17047200) AT/TT (HR 3.24; 95%CI 1.06-9.90; P=0.039) were independent risk factors for developing HCC after HCV eradication with DAA. Whereas, in the LC group, AFP>5.0 ng/ml at SVR24 was associated with incidence of HCC occurrence (HR 4.16, 95%CI 1.12-15.38; p=0.030). Cumulative carcinogenesis rate of patients with *TLL1* (rs17047200) AT/TT was significantly higher than that of patients with AA (4.0% and 4.3% vs. 1.3% and 1.7% at the 1st and 2nd year, respectively, p = 0.006). Comparing the *TLL1* (rs17047200) genotypes, pre-Tx M2BPGi, pre-Tx and post-Tx Fib4 index were significantly higher in patients with AT/TT genotype than those with AA genotype [pre-Tx M2BPGi was 2.5 vs. 2.0 (C.O.I.) (p<0.001), pre-Tx Fib4 index was 3.8 vs. 3.1(p=0.040) and post-Tx Fib4 index was 3.1 vs. 2.6 (p=0.014)]. **Conclusion:** ***TLL1*** genotype and high age were independent risk factors for HCC development in patients after HCV eradication by IFN-free regimen. Further study is needed to elucidate the association between *TLL1* SNP and carcinogenesis and fibrosis during the long-term follow up.

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Changing Cascade of Care for Hepatitis C in the Era of Direct-Acting Antivirals

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Background: The landscape of hepatitis C virus (HCV) has changed dramatically in the recent years with the advent of direct-acting antivirals (DAAs), updates in HCV screening policies, and expansion of insurance coverage. Our objective was to project changes in the cascade of care for HCV considering these factors. **Methods:** We used a previously-validated mathematical model, Hepatitis C Disease Burden Simulation model (*HEP-SIM*), that projects the changing prevalence of HCV in National Health and Nutrition Examination Survey (NHANES) and non-NHANES population groups. HEP-SIM simulated the clinical management of HCV from 2010 onwards, which included risk-based screening until 2013 and inclusion of birth-cohort screening afterwards; the rising HCV incidence resulting from new patterns of injection drug use; insurance expansion included in the Affordable Care Act; and antiviral treatment options in different waves starting with peginterferon followed by the launch of first- and second-generation DAAs, including pan-genotypic drugs. Treatment efficacy was extracted from clinical studies and treatment rates were based on insurance status and drug sales. We projected different steps of the HCV cascade of care for years 2010, 2015, and 2020. **Results:** Our model estimated that in 2010, 4.0 million people had chronic viremia, and among those 1.5 million people (37.5%) were aware of their HCV infection status (**Figure 1**). In 2015, 3.35 million people were viremic and 1.35 million were aware of their status. Under current clinical practice, by 2020, 2.16 million are projected to remain viremic and 0.65 million (30%) aware of their infection. The number of people who achieved cure is projected to increase from 0.47 million in 2010 to 1.89 million in 2020. **Conclusion:** Our model predicts that the HCV cascade of care has changed substantially with the advent of DAAs, with a predicted increase in the number of HCV infected people expected to be cured by 2020. Despite that, under current screening and treatment practice, 1.89 million people will remain infected in 2020 and 70% of those people unaware of their infection. Policies aimed at aggressive screening for HCV alongside controlling the rising HCV incidence could help further reduce the burden of HCV in the United States.