Disclosures:

The following people have nothing to disclose: Fadi-Luc Jaber, Yogeshwar Sharma, Erica Chung, Sanjeev Gupta

★ 1500

PANGENOTYPIC THERAPIES GLECAPREVIR-PIBRENTASVIR (G-P) AND SOFOSBUVIR-VELPATASVIR-VOXILAPREVIR (S-V-V) AFTER FAILURE WITH INTERFERON (IFN)-FREE DIRECT-ACTING ANTIVIRAL (DAA) TREATMENT FOR HEPATITIS C

Steven L Flamm[1], Naoky C. S. Tsai[2], Bruce R Bacon[3], Michael P. Curry[4], Scott Milligan[5], Nicole Wick[5], Zobair M. Younossi[6] and Nezam H Afdhal[4], (1)Division of Hepatology, Northwestern University, Feinberg School of Medicine, (2) University of Hawaii, Honolulu, Hawaii, USA, (3)Saint Louis University School of Medicine, St. Louis, Missouri, USA, (4)Beth Israel Deaconess Medical Center, (5)Trio Health Analytics, La Jolla, CA, (6)Center for Liver Diseases and Department of Medicine, Inova Fairfax Hospital, Falls Church, VA, United States

Background: Despite the remarkable effectiveness of IFN-free DAA treatment in real-world HCV care, treatment failures remain a challenge in disease eradication. Here, we examine outcomes with G-P or S-V-V after DAA failure/relapse. **Methods:** Inclusion: patients who failed or relapsed following IFN-free DAA therapy and were subsequently treated with G-P (n=55) or S-V-V (n=176) between July 2017 and Dec 2018. Data were collected electronically from providers and specialty pharmacies through Trio Health's disease management program. Variable comparisons were via chi-square or Exact tests with subsequent z-tests of column proportions. Significantly different variables were used in a logistic regression to generate propensity scores for 1-1 matching without replacement with G-P as the test group. Therapy duration was not included in matching due to sample limitations. **Results:** In comparison to S-V-V, the G-P group had a higher percentage of baseline eGFR <30 ml/min (8% v. 1%, p=0.015), genotype (GT) 2 HCV (9% v 2%, p=0.040), hypertension (60% v. 42%, p=0.016), and care at academic centers (42% v. 26%, p=0.021). G-P and S-V-V treatment groups were not significantly different for age, gender, insurance, ribavirin (RBV), anxiety, depression, diabetes, HCC, HIV, or HBV and had characteristics of GT1 (82% G-P v. 78% S-V-V, p=0 .589) and baseline FIB4 >3.25 (37% G-P v. 38% S-V-V, p=0.651). Therapy duration for G-P was 16 weeks (69%), 12 weeks (16%), and 8 weeks (15%); for S-V-V, 99% patients received 12 weeks (p<0.001). Prior therapy was mostly ledipasvir-sofosbuvir (L-S) for both G-P (64%) and S-V-V (58%). SVR rates were significantly lower for G-P compared to S-V-V for both intent to treat (ITT, 84% v. 94%, p=0.017) and per protocol (PP, 85% v. 98%, p<0.001) populations [TABLE]. After propensity score matching, treatment groups (n=39 pairs) significantly differed only by therapy duration (G-P 69% 16 weeks, 15% 12 weeks, 15% 8 weeks v. S-V-V 100% 12 weeks, p<0.001) and had the following characteristics: 95% GT1, 5% GT 3, 100% eGFR>30 ml/min, 33% (G-P) to 36% (S-V-V) FIB4 >3.25,and prior therapy predominantly L-S (80%). In the matched sample, SVR rates were significantly lower for G-P compared to S-V-V for ITT (85% v. 97%, p=0.048) and PP (85% v. 100%, p=0.012). **Conclusion:** In patients with prior DAA failure/relapse, significantly higher ITT and PP SVR rates were observed with S-V-V compared to G-P both before and after adjustment for clinical differences.

Before adjustment	ITT SVR n/N (%)			PP SVR n/N (%)		
Prior Therapy	G-P	S-V-V	p	G-P	S-V-V	p
DCV + SOF	1/1 (100%)	11/11 (100%)		1/1 (100%)	11/11 (100%)	
EBR-GZR	1/1 (100%)	18/20 (90%)	0.905	1/1 (100%)	18/18 (100%)	
G-P		3/4 (75%)			3/4 (75%)	
L-S	29/35 (83%)	97/102 (95%)	0.021	29/35 (83%)	97/98 (99%)	<0.001
PrOD	2/2 (100%)	11/12 (92%)	0.857	2/2 (100%)	11/11 (100%)	
SMV + SOF	1/1 (100%)	1/1 (100%)		1/1 (100%)	1/1 (100%)	
SOF + RBV	7/8 (88%)	5/5 (100%)	0.411	7/7 (100%)	5/5 (100%)	
S-V	5/7 (71%)	20/21 (95%)	0.078	5/7 (71%)	20/21 (95%)	0.145
Total	46/55 (84%)	166/176 (94%)	0.017	46/54 (85%)	166/169 (98%)	<0.001

After adjustment	ITT SVR n/N (%)			PP SVR n/N (%)		
Prior Therapy	G-P	S-V-V	p	G-P	S-V-V	p
L-S	26/31 (84%)	30/31 (97%)	0.086	26/31 (84%)	30/30 (100%)	0.022
PrOD	2/2 (100%)	2/2 (100%)		2/2 (100%)	2/2 (100%)	
SOF + RBV	1/1 (100%)	1/1 (100%)		1/1 (100%)	1/1 (100%)	
S-V	4/5 (80%)	5/5 (100%)	0.292	4/5 (80%)	5/5 (100%)	0.292
Total	33/39 (85%)	38/39 (97%)	0.048	33/39 (85%)	38/38 (100%)	0.012

DCV+SOF = daclatasvir+sofosbuvir, EBR-GZR = elbasvir-grazoprevir, G-P = glecaprevir-pibrentasvir, L-S = ledipasvir-sofosbuvir, PrOD = paritaprevir-ritonavir-ombitasvir + dasabuvir, SMV+SOF = simeprevir+sofosbuvir, SOF+RBV = sofosbuvir+ribavirin, S-V = sofosbuvir-velpatasvir, S-V-V = sofosbuvir-velpatasvir-voxilaprevir.

Disclosures:

Steven L Flamm – Gilead Sciences, Inc.: Advisory Committee or Review Panel; Gilead Sciences, Inc.: Speaking and Teaching; Gilead Sciences, Inc.: Grant/Research Support; AbbVie: Advisory Committee or Review Panel; AbbVie: Speaking and Teaching; AbbVie: Grant/Research Support; Merck: Advisory Committee or Review Panel; Merck: Speaking and Teaching

Naoky C. S. Tsai – Gilead Sciences, Inc.: Speaking and Teaching; Gilead Sciences, Inc.: Consulting; Intercept: Advisory Committee or Review Panel; Intercept: Speaking and Teaching

Bruce R Bacon – Merck: Consulting; Merck: Speaking and Teaching; Merck: Grant/Research Support; AbbVie: Advisory Committee or Review Panel; AbbVie: Speaking and Teaching; AbbVie: Grant/Research Support; Gilead Sciences, Inc.: Advisory Committee or Review Panel; Gilead Sciences, Inc.: Speaking and Teaching; Gilead Sciences, Inc.: Grant/Research Support; Janssen: Advisory Committee or Review Panel; Janssen: Speaking and Teaching; Bristol-Myers Squibb: Advisory Committee or Review Panel; Bristol-Myers Squibb: Grant/Research Support; Valeant: Speaking and Teaching

Michael P. Curry – Gilead Sciences: Consulting; Trio Health: Consulting; Gilead Sciences: Grant/Research Support; Mallinckrodt: Grant/Research Support; Conatus: Grant/Research Support; Salix: Grant/Research Support; Affimune: Grant/Research Support

Scott Milligan – Trio Health: Employment; Gilead Sciences, Inc.: Grant/Research Support; AbbVie: Grant/Research Support; Merck: Grant/Research Support

Nicole Wick – Trio Health: Employment; Gilead Sciences, Inc.: Grant/Research Support; Merck: Grant/Research Support; AbbVie: Grant/Research Support

Zobair M. Younossi – Gilead: Consulting; Terns: Consulting; Viking: Consulting; Intercept: Consulting; Novo Nordisk: Consulting; Merck: Consulting; Abbvie: Consulting; Novartis: Consulting; BMS: Consulting; Shionogi: Consulting; Siemens: Consulting

Nezam H Afdhal – Merck: Consulting; Gilead: Consulting; Echosens: Consulting; Ligand: Consulting; Shionogi: Consulting

★ 1501

THE EFFICACY AND SAFETY OF RAVIDASVIR COMBINED WITH DANOPREVIR IN THE 12-WEEK ORAL REGIMEN FOR TREATMENT-NAÏVE HCV GENOTYPE 1 ADULT PATIENTS WITHOUT CIRRHOSIS IN CHINA: PHASE II/III CLINICAL TRIAL

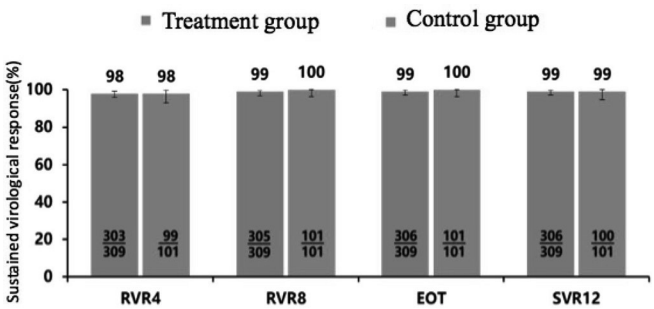
Lai Wei, Tsinghua Changgung Hospital, School of Clinical Medicine, Institute for Precision Medicine, Tsinghua University, Xiaoyuan Xu, Infectious Diseases, Peking University First Hospital, Sujun Zheng, Beijing Municipal Key Laboratory of Liver Failure and Artificial Liver Treatment Research, Beijing Youan Hospital Affiliated to Beijing Capital Medical University, Yujuan Guan, Guangzhou Eighth People's Hospital, Jifang Sheng, The First Affiliated Hospital of Medical School of Zhejiang University, Xingxiang Yang, Sichuan Provincial People's Hospital,, Yuanji Ma, West China Hospital, Sichuan University,, Yan Huang, Hunan Key Laboratory of Viral Hepatitis, Yi Kang, Henan People's Hospital,, Xiaofeng Wen, Department of Hepatology, Liuzhou People's Hospital, Jun Li, Department of Infectious Disease, The First Affiliated Hospital with Nanjing Medical University, Youwen Tan, Zhenjiang No.3 People's Hospital, Qing He, The Third People's Hospital of Shenzhen, Qing Xie, Department of Infectious Diseases, Ruijin Hospital, Shanghai Jiaotong University School of Medicine,

Maorong Wang, 81th Hospital of People's Liberation Army, Nanjing, China, Ping An, Shenyang Sixth People's Hospital, Guozhong Gong, The 2nd Xiangya Hospital of Central South University, Changsha, China, Huimin Liu, Xixi Hospital of Hangzhou,, Qing Ning, Tongji Medical College of Hust, Wuhan, China, Rui Hua, Department of Hepatology, The First Hospital of Jilin University, Bo Ning, Baoji Center Hospital, Wen Xie, Center of Liver Diseases, Beijing Ditan Hospital, Capital Medical University, Beijing, China, Jiming Zhang, Huashan Hospital, Shanghai, China, Wenxiang Huang, Chongqing Medical University No.1 Affiliated Hospital, Yongfeng Yang, Department of Hepatology, The Second Hospital of Nanjing, Minghua Lin, Fujian Fuzhou Municipal Infectious Disease Hospital, Yingren Zhao, Department of Liver Diseases, The 1st Teaching Hospital, SOM, Xi'an Jiaotong University, Yanhong Yu, The First Affiliated Hospital of Guangxi Medical University, Jidong Jia, National Clinical Research Center for Digestive Diseases, Beijing, China, Dongliang Yang Sr., Wuhan Union Hospita, Wuhan, China, Liang Chen, Shanghai Public Health Clinical Center, Shanghai, China, Yinong Ye Sr., Department of Infectious Diseases, Foshan First People's Hospital, Yuemin Nan, Department of Traditional and Western Medical Hepatology, Third Hospital of Hebei Medical University, Zuojiong Gong, Wuhan University Renmin Hospital, Wuhan, China, Quan Zhang, The Affiliated Hospital of Guizhou Medical University, Peng Hu, Department of Infectious Diseases, The Second Affiliated Hospital of Chongqing Medical University, FuSheng Wang, PLA 302 Hospital, Yongguo Li, The First Affiliated Hospital of Harbin Medical University, Dongliang Li, Fuzhou General Hospital of Nanjing Military Command, Zhansheng Jia, Center of Diagnosis and Treatment for Infectious Diseases of Chinese PLA, Tangdu Hospital, the Fourth Military Medical University,, Jinlin Hou, Department of Infectious Diseases , Nanfang Hospital, Southern Medical University, Chengwei Chen, 85th Hospital of People's Liberation Army, Shanghai, China and Jinzi Wu, Ascletis Bioscience Co., Ltd.

Background: Ravidasvir (RDV) is a new generation and pan-genotypic NS5A inhibitor with a high resistance barrier developed by Ascletis BioScience in China. This study was conducted to analyze the efficacy and safety of RDV and DNVr (Ritonavir-boosted Danoprevir) combined with Ribavirin in the 12-week oral regimen for treatment-naïve HCV GT1 adult patients without cirrhosis in China. **Methods:** This multi-centered, randomized, double-blind, placebo-controlled phase II/III trial enrolled 424 treatment-naïve, non-cirrhotic HCV GT1 adult patients from 42 centers in China. These patients were randomized to receive RDV 200mg+DNVr 100mg/100mg+RBV 1000/1200mg/day (administered by weight) (n=318) or placebo (n=106) at a ratio of 3:1 for 12 weeks. After unblinding, the placebo-controlled group continued to receive the same regimen as the treatment group. The primary efficacy endpoint was SVR12 rate (with a lower limit detection of 15 IU/mL). **Results:**

- Of the 424 patients, the mean age was 45 years (range 21-73 years), 47% were male, 82% were of IL-28B CC genotypes, 72% with a baseline of HCV RNA ≥ 800,000 IU/mL. The proportions of patients with NS5A resistance-associated substitution (RAS) in baseline in the treatment and control groups were 25% and 29%(per protocol set ,PPS), respectively. The most common NS5A RAS in the treatment group was R30Q (12.3%), Y93H (6.8%) and R30Q/Y93H (2.6%); the most common NS5A RAS in the control group was R30Q (20.8%), Y93H (5.9%), R30Q/Y93H (0.99%).
- The overall SVR12 rates of these two groups were both 99% (PPS). The SVR12 rates of the patients with HCV RNA <400,000 IU/ml, 400,000-800,000 IU/ml, and >800,000 IU/ml in the treatment and control groups were 100%, 100%, 99% and 100%, 100%, 99%, respectively. The SVR12 rates of the patients aged <65 years were both 99% in these two groups, and were both 100% for patients ≥65 years old. The SVR12 rates of the male patients in the treatment and the control groups were 99% and 100%, respectively, and 99% and 98% for the female patients.
- SVR12 rates of the patients with baseline NS5A RAS were both 100% (PPS)in these two groups.
- The incidence rates of virological breakthrough were 0.97% and relapse were 0.99% (PPS)in the treatment and the control groups, respectively. No RAS was detected at baseline for those patients.
- There were no serious adverse events related to treatment during the study period, most of the abnormal laboratory tests of liver function were mild or moderate severity.

Conclusion: RDV combined with DNVr in the 12-week oral regimen for Chinese treatment-naïve non-cirrhotic GT1 HCV adult patients can achieve high cure rates, and the efficacy is not affected by age, gender, IL28B genotype, HCV RNA levels and NS5A RAS in the baseline. The regimen has high safety.



Disclosures:

Jinlin Hou – AbbVie: Consulting; Arbutus: Consulting; Johnson &Johnson: Consulting; Bristol Myers Squibb: Consulting; Gilead Sciences: Consulting; Roche: Consulting; Bristol Myers Squibb: Grant/Research Support; Johnson &Johnson: Grant/Research Support

The following people have nothing to disclose: Lai Wei, Xiaoyuan Xu, Sujun Zheng, Jifang Sheng, Yan Huang, Xiaofeng Wen, Qing Xie, Rui Hua, Wen Xie, Yongfeng Yang, Jidong Jia, Peng Hu, Yongguo Li

Disclosure information not available at the time of publication: Yujuan Guan, Xingxiang Yang, Yuanji Ma, Yi Kang, Jun Li, Youwen Tan, Qing He, Maorong Wang, Ping An, Guozhong Gong, Huimin Liu, Qing Ning, Bo Ning, Jiming Zhang, Wenxiang Huang, Minghua Lin, Yingren Zhao, Yanhong Yu, Dongliang Yang, Liang Chen, Yinong Ye, Yuemin Nan, Zuojiong Gong, Quan Zhang, FuSheng Wang, Dongliang Li, Zhansheng Jia, Chengwei Chen, Jinzi Wu