

influenced the achievement of SVR, administration of EPA might produce higher SVR on the combination therapy.

Disclosures:

The following people have nothing to disclose: Shintaro Takaki, Yoshiiku Kawakami, Kiminori Uka, Keitaro Yamashina, Nami Mori, Syutetsu Tei, Akira Hiramatsu, Hideaki Kodama, Michio Imamura, Hiroshi Aikata, Syoichi Takahashi, Kazuaki Chayama

1145

LONG-TERM LOW DOSE TREATMENT WITH PEGYLATED INTERFERON ALPHA 2B LEADS TO A SIGNIFICANT REDUCTION IN FIBROSIS AND INFLAMMATORY SCORE IN CHRONIC HEPATITIS C NONRESPONDER PATIENTS WITH FIBROSIS OR CIRRHOSIS Peer Stephan Kaiser, Holger Hass, Bettina Lutze, Birgit Sauter, Michael Gregor; *Medicine I, University of Tuebingen, Tuebingen, Germany*

Objective: Treatment with current standard antiviral therapy leaves about 50% of patients without viral clearance with the risk of progression of their liver disease. Recent studies have suggested an antifibrotic effect of low dose interferon treatment. **Methods:** The efficacy of low dose pegylated interferon alfa 2b with 0.5 ug/kg weekly given for 36 months as monotherapy was evaluated based on histological examination and liver function in 142 patients with chronic HCV, nonresponse to antiviral combination therapy and significant fibrosis / cirrhosis (Ishak staging 3-6) and compared to an observational control group (n=64). Histology was evaluated at baseline, at 18 months of treatment and 6 months after end of treatment. **Results:** At 18 months therapy an increase in fibrosis score from 3.86 to 4.09 and at 6 months post observation to 4.86 was detectable in the control group (n=57). In the treatment group a decrease from 3.91 at baseline to 2.42 at 18 months and 2.13 at 6 months post therapy was noted (n=119). The necroinflammatory score showed constant levels with 7.32 at baseline, 7.84 at month 18 and 7.48 at 6 months post observation in the control group. In the treatment group the score decreased from 8.24 at baseline to 5.77 at month 18 and then relapsed again to 7.38 post therapy. 59% of patients in the treatment group showed an HCV viral load decline of > 1 log, and 8% had a negative PCR, which however was not maintained for any patient upon cessation of therapy. The drop out rate was 4% and the dose reduction rate was 12%. 17 SAEs were observed, of which 15 were complications of cirrhosis (6 hydropic decompensations, 3 variceal bleeds and 3 HCC development). There was no significant difference of these complications between treatment and observational groups. **Conclusions:** Low dose therapy with pegylated interferon alfa 2b in patients with HCV and advanced fibrosis or cirrhosis shows a significant and persistent decrease in fibrosis in comparison to a control group. In contrast the also observed significant decrease in the necroinflammatory score is only temporary as long as treatment lasts. As treatment was well tolerated even for patients with cirrhosis, this treatment could evolve as a salvage therapy for patients with advanced liver disease with HCV where standard antiviral therapy has failed.

Disclosures:

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1146

RAPID VIROLOGIC RESPONSE (RVR) IS ENHANCED BY HIGHER DRUG EXPOSURE AMONG PATIENTS RECEIVING TARIBAVIRIN IN COMBINATION WITH PEGYLATED INTERFERON ALFA-2B FOR THE TREATMENT OF HCV INFECTION Mitchell L. Shiffman¹, Maribel Rodriguez-Torres², Stuart Gordon³, Melissa Palmer⁴, Paul Pockros⁵, Christian Treppe⁶, Yong Kim⁷, Brian Murphy⁷; ¹Division of Gastroenterology, Hunter Holmes McGuire VAMC, Richmond, VA; ²Fundacion de Investigacion de Diego, Piso Oficina, Puerto Rico; ³Gastroenterology, Henry Ford Health System, Detroit, MI; ⁴Digestive Disease Center, Plainview, NY; ⁵Scripps Clinic, La Jolla, CA; ⁶Hopital Hotel-Dieu, Lyon, France; ⁷Valeant Pharmaceuticals International, Costa Mesa, CA

Background: Previous studies have demonstrated that the later during treatment with peginterferon (PEGIFN) and ribavirin

(RBV) a patient with chronic HCV becomes HCV RNA undetectable, the higher is the likelihood of relapse and the lower the SVR rate. In a recent Phase 3 study, the combination of taribavirin (TBV) plus PEGIFN alpha-2b or was found to have a lower SVR compared to weight base dosed RBV and PEGIFN alfa 2b (38% and 52%, respectively). To try and understand why TBV was associated with a lower SVR a post-hoc analysis of the ITT population was performed to examine the impact of treatment on viral kinetics and other demographic features such as patient age, body weight and total drug exposure. **Methods:** This Phase 3 study randomized 970 patients in a 2:1 ratio into a fixed dose taribavirin arm versus a weight base dosed RBV arm, stratifying patients on the basis of genotype, baseline viral load, and weight. Viral load was assessed throughout the study using the NGI SuperQuant Assay with a lower limit sensitivity of 39 IU/ml. Variables assessed included percent of patients younger than 45yo as well as average drug exposure expressed in mg/kg based on response activity at treatment weeks 4, 12, 24, and week 24 follow-up. **Results:** See table. **Conclusions:** Patients achieving rapid virologic response (RVR) had similar an SVR approaching 90%, when treated with either TBV or RBV. In contrast, patients who had a slower virologic response, particularly those who failed to drop HCV RNA by 2 logs within the first 4 weeks of treatment, had a marked increase in SVR when treated with TBV when compared to RBV (63% vs 36% if HCV RNA undetectable at week 12 and 23% vs 12% if HCV RNA undetectable at week 24, respectively). The improvement in SVR in patients who fail to clear HCV RNA early during treatment is likely secondary to the improved tolerability of TBV over RBV.

	TBV				RBV			
	N	% <45 yo	mean mg/kg	SVR %	N	% <45 yo	mean mg/kg	SVR %
wk 4/ wk 12/ wk 24 response								
neg/neg/neg	144	71%	16.4	87%	103	58%	14.8	88%
≥2 log ↓ / neg / neg	146	49%	16.1	57%	73	32%	14.7	78%
<2 log ↓ / neg / neg	24	50%	15.6	63%	14	36%	13.7	36%
≥2 log ↓ / ≥2 log ↓ / neg	27	30%	15.6	26%	10	40%	12.6	20%
<2 log ↓ / ≥2 log ↓ / neg	35	37%	15.8	23%	25	56%	14.7	12%

Disclosures:

Yong Kim - Employee: Valeant Pharmaceuticals International
Brian Murphy - Employee: Valeant Pharmaceuticals International
The following people have nothing to disclose: Mitchell L. Shiffman, Maribel Rodriguez-Torres, Stuart Gordon, Melissa Palmer, Paul Pockros, Christian Treppe

1147

AN OPEN LABEL, COMPARATIVE, MULTICENTER STUDY OF PEGINTERFERON ALFA-2A PLUS RIBAVIRIN IN THE TREATMENT OF PATIENTS WITH CHRONIC HEPATITIS C/HEPATITIS B CO-INFECTION VERSUS THOSE WITH MONOINFECTED CHRONIC HEPATITIS C: AN INTERIM REPORT Chun-Jen Liu¹, Pei-Jer Chen¹, Jia-Hong Kao Kao¹, Ming-Yang Lai¹, Chi-Ling Chen¹, Chen-Hua Liu¹, Ming-Lung Yu², Chia-Yen Dai², Zu-Yau Lin², Wan-Long Chuang², Sheng-Nan Lu³, Jing-Houng Wang³, Tsung-Hui Hu³, Chao-Hung Hung³, Chau-Mo Lee³, Wei-Wen Su⁴, Shun-Shen Wu⁴, Chih-Lin Lin⁵, Li-Ying Liao⁵, Hsing-Tao Kuo⁶, Hung-Da Tung⁶, You-Chen Chao⁷, Shui-Yi Tung⁸, Sien-Sing Yang⁹, Ding-Shinn Chen¹; ¹National Taiwan University College of Medicine and National Taiwan University Hospital, Taipei, Taiwan; ²Kaohsiung Medical University Hospital, Kaohsiung, Taiwan; ³Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung, Taiwan; ⁴Changhua Christian Hospital, Changhua, Taiwan; ⁵Tai Pei City Hospital, Taipei, Taiwan; ⁶Chi-Mei Medical Center, Tainan, Taiwan; ⁷Tri-Service General Hospital, Taipei, Taiwan; ⁸Chang Gung Memorial Hospital, Chia-Yi, Taiwan; ⁹Cathay General Hospital, Taipei, Taiwan

Introduction: Pilot studies using standard interferon in combination with ribavirin for 6 months to treat patients with dual chronic hepatitis C and B infection have shown that a sustained hepatitis C virus (HCV) clearance rate could be achieved to an extent comparable to that observed in HCV monoinfected patients. We have therefore conducted a multicenter clinical trial using pegin-