

CMV were relatively preserved during antiviral therapy. **Conclusions:** Combination antiviral therapy results in contraction of immune responses specifically directed against HCV. These decreases in the memory population are independent of race and virologic outcome. *This study is funded by the NIDDK through a cooperative agreement with partial support from Roche Laboratories Inc. through a CRADA with the NIH.*

Disclosures:

The following people have nothing to disclose: James R. Burton, Jared Klarquist, Kyung Im, Sue Smyk-Pearson, Lucy Golden-Mason, Hugo R. Rosen

368

BETTER PREDICTION OF SVR IN PATIENTS WITH HCV GENOTYPE 1 (G1) WITH PEGINTERFERON ALFA-2A (PEGASYS) PLUS RIBAVIRIN: IMPROVING DIFFERENTIATION BETWEEN LOW (LVL) AND HIGH BASELINE VIRAL LOAD (HVL) Elmar Zehnter¹, Stefan Mauss², Christine John³, Renate Heyne⁴, Bernd Moller⁴, Thomas Lutz⁵, Bernd Bokemeyer⁶, Robert Kihn⁷, Gero Moog⁸, Ulrich Alshuth⁹, Dietrich Hueppe¹⁰, ¹Center of Gastroenterology, Dortmund, Germany; ²Center of Gastroenterology and Hepatology, Dusseldorf, Germany; ³Center of Gastroenterology, Berlin, Germany; ⁴Livercenter, Berlin, Germany; ⁵Center of Infectiology, Frankfurt, Germany; ⁶Center of Gastroenterology, Minden, Germany; ⁷Center of Gastroenterology, Frankfurt, Germany; ⁸Center of Gastroenterology, Kassel, Germany; ⁹Hepatitis/HIV/Infectiology, Roche Pharma AG, Grenzach-Wyhlen, Germany; ¹⁰Center of Gastroenterology, Herne, Germany

Recently, baseline VL has become an important predictive factor in the development of a treatment algorithm in pts with G1; however, it is unclear whether the cut-off should be 600,000 or 800,000 IU/mL HCV RNA. Both were derived historically from 2×10^6 cps/mL using different conversion factors for the PCR assay used. In an analysis of predictive factors using data from a German observational study (DDW 2006, abs #219003), developed by the Association of German Independent Gastroenterologists (bng) and Roche Pharma AG, categorized baseline VL (800,000 IU/mL cut-off) was not significant in uni- or multivariate analyses. Therefore, this analysis investigated the optimal VL cut-off for SVR prediction. **Methods:** Analyses included 916 naive patients with G1 who received treatment with peginterferon alfa-2a + ribavirin for 48 weeks according to current guidelines and for whom complete relevant data was recorded. The influence of logarithmic VL on SVR was estimated as a continuous variable in univariate logistic regression (ULR) and by analyzing the receiver operating characteristic curve (ROC). The optimized cut-off was then compared to both existing cut-offs using multivariate logistic regression (MLR) analysis. **Results:** In ULR, continuous VL was a strong predictor of SVR ($p < .0001$; OR=0.79; CI: 0.69-0.89), but the effect of VL was non-linear. The ROC-plot revealed a cut-off level of VL of $5.6 \log_{10}$ IU/mL ($\sim 400,000$ IU/mL). According to this result, the predictability of baseline VL using a cut-off level of 400,000 IU/mL, 600,000 or 800,000 IU/mL was compared by MLR. Of the three, 400,000 IU/mL best predicted SVR ($p < .0001$; OR=0.48; CI:0.37-0.63). Using this cut-off, 62.0% of patients with LVL and 43.7% with HVL had an SVR. SVR rates according to VL cut-off are shown in the table. While in pts with LVL, SVR rate increased with decreasing cut-off, in pts with HVL, the SVR rate was 43% regardless of cut-off, i.e. pts with VL >400,000 IU/mL had low SVR rates similar to pts with VL >800,000/mL and belong in the same VL category. **Conclusion:** The well-accepted former cut-off of 2×10^6 copies/mL was statistically optimized for treatment with standard interferon. In the era of pegylated interferon, this cut-off is not the best way to differentiate between LVL and HVL with regard to likelihood of SVR. These data suggest that to use VL as a reliable predictor of successful treatment outcome, the optimized cut-off of 400,000 IU/mL should be used.

SVR rate by VL cut-off, n (%)

400,000 IU/mL		600,000 IU/mL		800,000 IU/mL	
LVL	HVL	LVL	HVL	LVL	HVL
267/431	212/485	323/552	156/364	355/628	124/288
62.0	43.7	58.5	42.9	56.5	43.1

Disclosures:

Elmar Zehnter - Grant/Research Support: Hoffman-La Roche AG, Germany
Stefan Mauss - Grant/Research Support: Hoffman-La Roche AG, Germany
Christine John - Grant/Research Support: Hoffman-La Roche AG, Germany
Renate Heyne - Grant/Research Support: Hoffman-La Roche AG, Germany
Bernd Moller - Grant/Research Support: Hoffman-La Roche AG, Germany
Thomas Lutz - Grant/Research Support: Hoffman-La Roche AG, Germany
Bernd Bokemeyer - Grant/Research Support: Hoffman-La Roche AG, Germany
Robert Kihn - Grant/Research Support: Hoffman-La Roche AG, Germany
Gero Moog - Grant/Research Support: Hoffman-La Roche AG, Germany
Ulrich Alshuth - Employee: Hoffman-La Roche AG, Germany
Dietrich Hueppe - Grant/Research Support: Hoffman-La Roche AG, Germany

369

RESPONSE TO PEGINTERFERON ALFA-2B AND RIBAVIRIN FOR CHRONIC HEPATITIS C IN PATIENTS WITH BODY WEIGHT >125 KG: RESULTS FROM THE WIN-R TRIAL Ira m. Jacobson¹, Robert Brown², Bradley Freilich³, Nezam Afjal⁴, Paul Kwo⁵, John Santoro⁶, Scott Becker⁷, Adil Wakil⁸, Louis Griffel⁹, Clifford Brass⁹, WIN-R Study Group The¹; ¹Weill Medical College of Cornell University, Center for the Study of Hepatitis C, New York, NY; ²Columbia Presbyterian Medical Center, New York, NY; ³Baptist Medical Center, Kansas City, MO; ⁴Beth Israel Deaconess Medical Center, Boston, MA; ⁵Indiana University School of Medicine, Indianapolis, IN; ⁶Atlantic Gastroenterology Associates, PA, Egg Harbor Township, NJ; ⁷Austin Gastroenterology, Austin, TX; ⁸East Bay Liver Clinic, San Francisco, CA; ⁹Schering-Plough Research Institute, Kenilworth, NJ

PURPOSE In WIN-R, a US study of >4900 HCV patients from community and academic sites that prospectively compared PEG-IFN alfa-2b 1.5ug/kg/wk + fixed dosing (FD; 800 mg/d) or weight-based dosing (WBD; 800-1400 mg/d) of ribavirin (RBV), sustained virological response (SVR) rates were significantly greater with WBD than FD of RBV (AASLD'05). WBD patients weighing >105-125 kg received RBV 1400 mg/d and had SVR rates similar to other WBD patients. The current study evaluated SVR rates among patients weighing >125 kg, for whom data are limited, who entered the study as protocol exceptions. **METHODS** In WIN-R, patients were randomized to PEG-IFN alfa-2b 1.5ug/kg/wk (max: 150 ug/wk) + FD RBV 800 mg/d or WBD RBV: <65 kg, 800 mg/d; 65-<85kg, 1000 mg/d; 85-<105 kg, 1200 mg/d; 105-125 kg, 1400 mg/d. Genotype 1 (G1) patients received 48 wks of therapy, and G2/3 patients were randomized to 24 or 48 wks of therapy. All patients were monitored for 24 wks post-treatment. HCV RNA levels were determined by PCR (Taqman/SPRI, LLQ 29 IU/ml) at wks 0, 24, 48 and 72. RBV dose reductions and discontinuation were required for hemoglobin <10 gm/dl and <8.5 gm/dl. **RESULTS** In total, 42 patients >125 kg were enrolled in the trial (Table); 20 received FD RBV (800 mg/d) and 22 received WBD RBV (1400 mg/d). SVR occurred in 45% of patients—33% of G1 and 61% of G2/3 patients, rates nearly identical to those for the overall study cohort. SVR rates for the 20 FD RBV patients and the 22 WBD RBV patients were 25% and 64% overall ($P=.015$); 17% and 50% in G1 ($P=.096$), and 38% and 50% in G2/3 ($P=.078$). Only 2/42 (5%) had nadir Hgb <10 gm/dl and 3/42 (7%) had neutrophils <750/mm³; for the overall study cohort (n = 4913) these percentages were 16% and 20%. Dose reductions of PEG-IFN occurred in 8/42 (19%) patients and 9/42 (21%) had dose reductions of RBV. **CONCLUSIONS** In WIN-R, patients with very high body weight and BMI had SVR rates similar to those of other study patients, and like the other patients, WBD RBV conferred superior efficacy to FD RBV in these patients. The low rates of nadir hemoglobin and neutropenia and low dose reduction rates probably reflect lower levels of drug exposure. These results suggest that severe obesity should not preclude consideration of antiviral therapy for chronic hepatitis C; however, further studies of such patients are needed. Supported by Schering Plough.

Mean body weight	132.5 kg (125.4-149.5)		
Mean body mass index	41.5 (35.3-55.70)		
		SVR, %	
All patients	n = 42	45 (19/42)	
Genotype 1 Genotype 2/3	n = 24 (57%) n = 18 (43%)	33 (8/24) 61 (11/18)	
FD RBV (800 mg/d) WBD RBV (1400 mg/d)	n = 20 n = 22	All 25 64 P=.015	G1 17 50 P=.096 G2/3 38 80 P=.078

Disclosures:

Ira m. Jacobson - Consultant, Speaker, Research support: Schering Plough
 Robert Brown - Speakers Bureau: Schering-Plough
 Bradley Freilich - Speakers Bureau: Schering-Plough
 Nezam Afdhal - Speakers Bureau: Schering-Plough
 Paul Kwo - Speakers Bureau: Schering-Plough
 Louis Griffel - Employee: Schering-Plough
 Clifford Brass - Employee: Schering-Plough
 The following people have nothing to disclose: John Santoro, Scott Becker, Adil Wakil, WIN-R Study Group The

370

HEPATITIS C SCREENING AND TREATMENT AMONG DRUG USERS IN AMSTERDAM: INTERIM RESULTS OF THE INCLUSION PROCEDURE IN THE DUTCH C PROJECT

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Objective: Although injecting drug users (IDU) are at high risk for Hepatitis C Virus (HCV) infection, they are less likely to be treated than other populations. We started to offer HCV testing and treatment combined with methadone programs in a setting where active drug use is tolerated. Here, we evaluate the inclusion procedure 1.5 year after the start of our pilot project. **Methods:** The study population comprises DU participating in the Amsterdam Cohort Studies (ACS) in 2005. Hepatologists, methadone specialists, cohort staff and a special project-nurse collaborate closely to provide optimal HCV care. DU chronically infected with HCV are offered additional medical and psychiatric screening. HCV treatment is directly observed and combined with methadone provision. **Results:** 466 DU were offered HCV screening: 70% male, 8% homeless and median age 43 years. HCV screening was refused by 110/466 (24%). An additional 10% (49/466) was willing but lacked medical insurance, leaving 307/466 (66%) to be tested. HCV antibodies were found in 179/307 (58%), 125/179 (70%) were chronically infected. Of these, 110/125 (88%) returned to obtain their test result. Of 76 HIV-negative HCV-infected DU, 56/76 (74%) were willing to undergo additional medical screening which was completed by 43/56 (77%). For 26/43 (60%) a final treatment decision was made: 13/26 (50%) started treatment, 5/26 (19%) refused, for 5/26 (19%) treatment was not indicated based on a liver biopsy, and for 3/26 (12%) there were medical contraindications. For 19/43 (44%) the decision on HCV treatment initiation is pending: 2/19 (11%) due to alcohol problems, 7/19 (37%) due to social, medical or psychiatric problems, and 8/19 (42%) due to multiple problems. Among the 13 persons who started HCV treatment 9/13 (70%) were active DU while 12/13 (92%) were on methadone. Six individuals finished treatment and were HCV RNA negative at the end of treatment. Compliance in this group was 98%. 4/13 (31%) are still on treatment while 3/13 (23%) stopped: 1 due to a serious adverse event, 1 due to social and medical problems, and 1 subject with HCV genotype 1 failed treatment at week 12. **Conclusion:** 66% of the participants of the ACS among DU is willing to undergo HCV screening. We observed a high return rate among screened DU and great willingness to undergo additional medical screening. Screening appears to be time-consuming, but once DU start HCV therapy they are fully compliant. These findings suggest that active DU can successfully undergo treatment for HCV in a multidisciplinary approach. However, social, medical, psychiatric and abuse related problems postpone or interfere with HCV treatment initiation.

Disclosures:

The following people have nothing to disclose: Karen Lindenburg, Christine Weegink, Janke Schinkel, Peter Jansen, Marcel Beld, Anneke Krol, Gertie Casteelen, Gerrit van Santen, Roel Coutinho, Maria Prins

371

PEGYLATED INTERFERON AND RIBAVIRIN IN HAEMODIALYZED PATIENTS WITH CHRONIC HEPATITIS C: A PROSPECTIVE STUDY

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In haemodialyzed patients, ribavirin is contraindicated due to a high risk of hemolytic anemia related to the end-stage renal failure. HCV eradication before kidney transplantation may be an attractive option when considering the deleterious impact of HCV after kidney transplantation. The aims were: 1) to determine the tolerance of combinative therapy with pegylated interferon (Pegasys) and a weekly individual schedule of ribavirin; 2) to provide preliminary data on virological response. **Patients and methods:** Fourteen haemodialyzed HCV patients waiting for renal transplant were treated with combinative therapy with Pegasys and weekly dose of ribavirin for 6 or 12 months according to genotype. Doses of ribavirin and erythropoietin (EPO) were adjusted according to hemoglobin level (Hb) to maintain levels up to 10 g/dl. There were 9 patients with genotype 1, 5 with non-1 genotype. Median viral load was 962000 IU/mL (95 % CI: 146000-3610000). Liver fibrosis was mild or moderate ($\leq F2$) in all but 1 patient. Mean time on dialysis was 16 years. **Results:** Median doses of Pegasys was 180 μ g/week (95 % CI: 135-180 μ g) and of ribavirin 800 mg/week (95 % CI: 600-1000 mg). Before initiation of antiviral therapy, 11 out of 14 patients were already treated by EPO. After 2 months of treatment, 13 out of 14 patients received EPO. As compared to baseline, the median increase of EPO dose was 200 % (95 % CI: 100-305%, range: 92-525%). Median Hb levels decreased during the first 2 months of treatment from 11.9 (95 % CI: 10.2-12.8) to 10.2 g/dl (95 % CI: 8.9-11.1, p=0.03) and remained stable throughout the period of treatment. Five patients required transfusion but only 2 of them had Hb level lower than 7 g/dl. Eleven patients completed treatment. Treatment was withdrawn in the 3 remaining patients for severe asthenia (n=2) and retinal hemorrhage (n=1). After 1 and 3 months of treatment, more than 2 log decrease in viral load was reached in 86% (12 out of 14 patients) and in 92% (11 out of 12 patients), respectively. End-of-treatment virological response (ETR) was reached in 11 out of 14 patients and sustained virological response (SVR) in 5 out of the 8 patients reaching 6 months post-treatment follow-up. **Conclusions:** Despite a theoretical contraindication, ribavirin may be used in haemodialyzed HCV patients, a particular high-difficult-to-treat group of patients. This use required a weekly adaptation of ribavirin dose and 200 % increase of EPO. This combinative therapy with an individualized schedule of ribavirin permits to reach ETR and SVR in 79 % and 63 % of cases, respectively. These results are similar to those observed in non-haemodialyzed HCV patients.

Disclosures:

The following people have nothing to disclose: Pierre Deltenre, Valérie Canva, François Provôt, François Glowacki, Sébastien Dharancy, Housseem Ben Ali, Alexandre Louvet, Jeanne Boitard, Jean Henrion, Christian Noël, Philippe Mathurin

372

ECONOMIC EVALUATION OF INDIVIDUALIZED VERSUS STANDARD TREATMENT APPROACH FOR PATIENTS WITH CHRONIC HEPATITIS C VIRUS GENOTYPE-1 (G1)

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Purpose: A 24-week course of therapy for G1 LVL patients who become viral negative after 4 weeks of treatment with peginterferon alpha-2b + ribavirin was recently approved by the EMEA. Clinical evidence suggests sustained virologic response (SVR) in this population is comparable to a 48-week course of therapy. The long-term clinical and economic impacts of shorter treatment duration are unknown. This study evaluated the cost-effectiveness of 24-week