P.255 Long term follow-up of previous hepatitis C virus positive non-responders to interferon monotherapy successfully re-treated with combination therapy: are they really cured?

A. Ciancio[1]*, A. Smedile[1], C. Giordanino[1], C. Colletta[2], G. Croce[3], M. Pozzi[4], G. Cariti[5], A. Macor[6], A. Biglino[7], A. Di Napoli[8], G. Tappero[9], M. Andreoni[10], A. Manca[11], G. Prandi[12], G. Calleri[13], P. Orsi[14], G. Ciccone[15], M. Rizzetto[1], G. Saracco[1]. [1]*Dipartimento di Gastroenterologia, Ospedale Molinette, Torino;* [2]*Divisione di Medicina, Ospedale Madonna del Popolo, Omegna;* [3]*Dipartimento di Gastroenterologia, Ospedale S. Carlo Borromeo, Milano;* [4]*Divisione di Medicina, Ospedale S. Gerardo, Monza;* [5]*Clinica Malattie Infettive,* [6]*Divisione B, Ospedale Amedeo di Savoia, Torino;* [7]*Divisione di Malattie Infettive, Ospedale Civile, Asti;* [8]*Dipartimento di Gastroenterologia, Ospedale Giovanni Bosco,* [9]*Dipartimento di Gastroenterologia, Ospedale Gradenigo, Torino;* [10]*Divisione di Malattie Infettive, Ospedale degli Infermi, Biella;* [11]*Dipartimento di Gastroenterologia, Ospedale S. Croce e Carle, Cuneo;* [12]*Divisione di Medicina, Ospedale S. Lazzaro, Alba;* [13]*Divisione A, Ospedale Amedeo di Savoia, Torino;* [14]*Divisione di Malattie Infettive, Ospedale S.S. Antonio e Biagio, Alessandria;* [15]*Unità di Epidemiologia dei Tumori – CPO Piemonte, Ospedale Molinette, Torino, Italy*

Objective: to evaluate whether in chronic hepatitis C-positive patients who failed to respond to Interferon monotherapy a sustained response obtained with retreatment using the combination therapy of Interferon + ribavirin can be safely considered to reflect eradication of the infection.

Methods: prospective follow-up of a cohort of 97 patients who responded to retreatment with different regimens of Interferon + ribavirin after failing to respond to a first Interferon monotherapy course. The patients were followed throughout 7 years of follow-up with determinations of HCV viremia every 6 months.

Results: at the end of the follow-up, 11 patients (11.3%) showed a viremic reappearance. HCV late relapse rates were 0%, 13%, 20% and 12% in patients retreated respectively with 3 MU Interferon + ribavirin for 12 months (Group 1), 5 MU Interferon + ribavirin for 12 months (Group 2), 3 MU Interferon + ribavirin for 6 months (Group 3) and 5 MU Interferon + ribavirin for 6 months (Group 4) (Group 2 vs Group 3, $p = 0.005$).

The virologic relapses occurred within 2 years from therapy withdrawal. Among patients with genotype 1 and 4, the long term response was significantly higher in Group 2 than in Group 3 (15% vs 3%, $p = 0.03$). In patients with genotype 2 and 3, the long term virological response was not affected by the different regimens.

Conclusion: non-responders to Interferon monotherapy who achieve a sustained virologic response after retreatment with Interferon + ribavirin stand a discrete risk of HCV reactivation within two years post therapy.

P.256 HCV relapse in sustained responders to interferon therapy for chronic hepatitis C genotype 4

M. El-Raziky[1], W. El-Akel[1], M. Soliman[1], S. El-Kafrawy[2], M. Abdel-Hamid[2], G. Esmat[1]*. [1]*Tropical Medicine, Cairo University,* [2]*Viral Hepatitis Reference Laboratory, National Hepatology and Tropical Medicine Research Institute, Cairo, Egypt*

Background: Prevalence of chronic hepatitis C virus (HCV) infection in Egypt is 8–24%. Ninety percent are genotype 4. Administration of pegylated interferon and combination therapy with ribavirin improved considerably the virological response rates. However, assessment of chronic hepatitis C outcome in sustained responders to interferon requires prolonged observation and close monitoring. Data on long term follow up of patients treated with genotype 4 are limited.

Objectives: (1) To assess the occurrence of relapse on long term follow up among Sustained Virological Responders (SVR) to Pegylated Interferon or Interferon therapy and to study the characteristics of relapsers. (2) To assess the possibility of persistence of HCV RNA in peripheral blood mononuclear cells (PBMNCs) of SVR as a risk for relapse.

Methods: Two hundred patients with chronic HCV (90% genotype 4) were included in a randomized controlled clinical trial for treatment of chronic HCV with either Pegylated Interferon or Interferon-alpha both with ribavirin for 48 weeks. Eighty-three subjects are SVR. We followed the responders by clinical and ALT levels evaluation as well as HCV RNA testing in serum and PBMCs.

Results: We followed the responders for a median follow up period of 37 months (min 26, max 44) after end of therapy. Most of the patients (84.3%) reported the disappearance of side effects developed while on treatment with significant increase in their Body Mass Index. Blood picture showed neutropenia or thrombocytopenia in 20% of cases. Elevated ALT was found in 7.5% (max 1.9-fold) and viraemia relapsed in 9% on follow up. Testing for HCV RNA in PBMCs has been done; 8% tested positive with no concordance to viraemia.

Conclusion: HCV relapse might occur in genotype 4 patients with SVR to interferon based combined therapies which proved to be safe on the long term. Persistence of HCV RNA in PBMNCs of SVR occurs in few subjects.

P.257 Hepatitis C genotype 4 in Belgium: a multicentric registry

G.J.M. Hemmink[1], C. de Galocsy[2]*, J. Delwaide[3], P. Langlet[4], S. Francque[1], L. Lasser[4], E. Bottieau[5], P.P. Michielsen[1]. [1]*Gastroenterology and Hepatology, University Hospital Antwerp, Edegem;* [2]*Gastroenterology and Hepatology, HIS Bracops, Brussels;* [3]*Gastroenterology and Hepatology, CHU, Liège;* [4]*Gastroenterology and Hepatology, CHU Brugmann, Brussels;* [5]*Internal Medicine, Institute of Tropical Medicine, Antwerp, Belgium*

Background and Objectives: Genotype 4 is predominant in Central African and Middle Eastern Hep C patients, but is rare in the West. Reports on treatment results are scarce. We aim to describe the patients' characteristics and treatment results in 4 Belgian centres and to identify predictive factors for response.

Methods: A retrospective review of all genotype 4 patients in 4 participating centres from 1990 to 2006 was performed. Results were analysed with Chi square or Student's t-test and logistic regression where appropriate.

Results: 192 patient files were analysed: 46% of the patients were male, 134 (70%) Black (B), 53 (28%) Caucasian (C), 4 (2%) North African. B were significantly more of female gender [41% vs. 54%, $p = 0.039$] and older (mean age 49.1 ± 1.6 y vs. 39.7 ± 3.0 y, $p = 0.012$) compared to C. Twenty-one had a HIV co-infection.

Body mass index was elevated in 60% (36 overweight and 16 obese in 93 patients). Fasting glycaemia was >100 mg/dl in 21 of 116 patients (25%), 8/119 (7%) had renal insufficiency, and 30/98 (31%) had dyslipidaemia. In 156 patients 160 biopsies were scored. Ninety (56%) had METAVIR F0 or F1, 48 (30%) F2 or F3 and 22 (14%) F4. The ratio minimal (F0–F1)//advanced fibrosis (F2-F4) was not significantly different between B and C. 64 patients (39%) were not treated: for minimal disease in 34, contraindications in 23, patients' refusal or non-compliance in 7. 139 treatments were given to 120 patients: interferon (IFN) only ($n = 12$), IFN+ribavirin (R) ± amantadine (A) ($n = 34$), peginterferon (PegIFN) ($n = 1$), PegINF+R±A ($n = 92$). Early viral response (HCV RNA neg. or $\geqslant$2 log drop at week 12) was assessed in 62 patients treated with PegIFN and R. It was absent in 32 (52%). SVR was achieved in 11/45 (24%) evaluable treatments so far. Four of 46 patients treated with INF+R±A responded (HCV RNA negative at week 24), none of them had SVR. The SVR was not significantly different between B and C or between male and female. Overweight or obesity, hyperglycemia, dyslipidaemia and renal insufficiency did not significantly influence the SVR in univariate and multivariate analysis. Only dose reduction of R was an independent negative predictive factor ($p = 0.024$).

Conclusion: Overall SVR is poor, both in B and C. Although known negative predictive factors of response are frequent (advanced fibrosis, overweight, hyperglycaemia, dyslipidaemia) and might influence the poor results, only dose reduction for R was an independent negative predictive factor for response.