controls were studied. The intracytoplasmic expression of IL-4, IFNγ and TNFα, and surface CD4 and CD8 markers from PBMCs, resting and stimulated, were measured using flow-cytometry. SVR was analysed after 6 months of follow-up.

Results: All 44 patients finished the study. Healthy controls presented a higher percentage of CD8 than CHC patients (22.1±7 vs 16.9±10;$p < 0.004$), higher expression of IFNγ by resting CD4 (0.03±0.02 vs 0.8±1.3;$p < 0.02$), higher expression of TNFα by CD8 (29.8±17.3 vs 19.5±17.3;$p < 0.05$) and CD4 stimulated T cells (36.3±9.9 vs 26.7±22.3; $p < 0.02$) and lower of IL-4 by CD4 T cells (1.3±0.7 vs 2.7±2.9;$p < 0.01$). After follow-up, 26 patients had SVR (59.1%), 13 relapsed (29.5%) and 5 were non-responders (11.4%). At the first month, expression of TNFα by CD4 was higher in patients with a SVR than in NR (36.46±24.9 vs 17.2±20.7;$p < 0.01$). At the third month, the percentage of CD4 was lower in patients with a SVR (34±16 vs 44±15.3; $p < 0.04$), stimulated-IL-4 expression by CD4 cells was lower in patients with SVR than in non-responders (1.9±4.2 vs 3.9±4.2;$p < 0.05$) and TNFα expression by CD4 was higher in SVR patients (48.8 ±20.9 vs 31.2 ±23;$p < 0.01$). At the end of treatment, expression of IFNγ by CD8 and CD4 stimulated cells was higher in SVR respectively (17.3±14 vs 10±8.5; $p < 0.04$ and 10.7±8.2 vs 5.9 ±5.5; $p < 0.03$). Predictive factors of SVR: CD4 T cells and expression of TNFα by CD4 stimulated T cells at first month, expression of IFNγ by CD4 T cells at third month, and expression of TNFα and IFNγ by CD8 stimulated T cells at the end of treatment.

Conclusions: IFNγ and TNFα expression by CD4 and CD8 T cells (cytokine response type 1) during combination treatment is associated with SVR suggesting the replication control and later clearance of HCV.

614 KINETIC ANALYSIS OF INSULIN RESISTANCE AND SERUM ADIPOCYTOKINES LEVELS DURING PEGINTERFERON ALPHA-2A PLUS RIBAVIRIN THERAPY IN NON-DIABETIC HCV PATIENTS

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Background and Aims: Insulin resistance (IR), steatosis and adipocytokines levels have been associated with severity and progression of liver fibrosis. Aims of this study were to evaluate, in non-diabetic HCV patients, the role of host metabolic factors in determining the progression of liver fibrosis and response to antiviral therapy (AVT), and to investigate the changes of IR and adipocytokines levels related to AVT.

Methods: Forty-eight naïve patients with biopsy-proven CHC (28M/20F; age: 50±12.7 years, genotype 1–4: 66.7%), were treated according to genotype for 24–48 weeks with standard schedule of Peginterferon α-2a (Pegasys, Roche) plus Ribavirin. Biochemical and virological assessment, HOMA-IR and serum leptin, adiponectin and resistin were determined, after an overnight fasting, at baseline, after 3 months, and at the end of therapy (ET) and follow-up (FU).

Results: Mean BMI of patients was 26.4±4.0 kg/m^2 and visceral obesity (according to ATP III definition) was present in half of them. At multivariate analysis, grade 2–3 liver steatosis was associated with older age (RR 1.1; 95%CI: 1.01–1.2), visceral obesity (7.8; 1.3–46.1) and serum insulin (1.4; 1.08–1.9). Independent variables associated with hepatic fibrosis (F2–F4) were higher necroinflammatory activity (27.5; 2.7–277.8) and grade 2–3 of steatosis (6.4; 1.1–38.2). A SVR was achieved in 62.5% (30/48) of patients and was associated with younger age ($p < 0.01$), genotype non-1 ($p < 0.04$) and absence of visceral obesity ($p < 0.01$). When we compared basal vs. end of follow-up levels we observed a significant decrease of insulin (12.09±5.0 vs 5.6±5.6; $p < 0.000$), HOMA-IR (2.8±1.4 vs 1.3±1.28; $p < 0.000$) and an increase of adiponectin levels (19.65±7.8 vs 26.11±17.6; $p < 0.02$). Leptin levels significantly decreased only during AVT (basal: 19.9±11.5 vs ET: 9.4±9.4; $p < 0.000$) but returned to basal levels after stopping therapy. Mean levels of these variables did not differ among patients with SVR and non responders. Resistin levels did not significantly changed during and after therapy when compared to basal.

Conclusions: Visceral obesity and clinical expression of IR have a major role to determine the severity of liver steatosis and fibrosis. Independently from the outcome, AVT produces significant changes of IR and adipocytokines levels. Visceral obesity is an independent predictor of SVR and maybe another target in the management of CHC patients.

615 TREATMENT COMPARISON OF PATIENTS WITH CHRONIC HEPATITIS C AND ELEVATED ALT VS PATIENTS WITH PERSISTENTLY NORMAL ALT – PRELIMINARY RESULTS OF A PROSPECTIVE OPEN TRIAL

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There is evidence that patients with persistently normal ALT (PNALT) respond similarly to those with elevated ALT to treatment with interferon and ribavirin, however, further studies are needed. In this prospective, multicenter, open-labeled clinical trial 240 de novo patients with biopsy-proven CHC with normal or elevated ALT levels received PegIntron 1.5 μg/kg/wk & Rebetol 0.8–1.2 g/d for 48 weeks (genotype 1/4) or 24 weeks (genotype 2/3).

Study design: Patients were stratified according to elevated or normal (>3 measurements over >3 months) ALT, high or low viral titer (cut-off 800,000 IU/ml, bDNA HCV RNA 3.0 assay; Bayer Diagnostics) and genotypes (GT) 1/4 or 2/3. Baseline data are available from 225 patients: 107 patients with PNALT (83 patients with GT 1/4, median ALT was 29 U/l, 24 patients with GT 2/3, median ALT was 25 U/l) and 118 patients with elevated ALT (88 patients with GT 1/4, median ALT was 79 U/l, 30 patients with GT 2/3, median ALT was 135).

Results: There was no statistical significant difference in pretreatment characteristics between the two groups. 65.1% of patients with PNALT had a viral load lower or equal 800,000 IU/ml vs 66.4% of patients with elevated ALT.

For 114/225 patients viral load was determined after week 4: 51.8% had undetectable RNA (49.2% PNALT and 54.9% high ALT; 37% of GT 1/4 pts. and 93% of GT 2/3 pts). After week 12 167/225 pts. were evaluated: 71.3% had undetectable RNA (76.3% PNALT and 67% high ALT; 66% of GT 1/4 and 90% of GT 2/3). 195 patients have so far completed the study. 14.4% of these patients withdrew because of AEs; 4.1% had a breakthrough on therapy, and 14.9% did not show a 2 log drop at week 12. Of these 195 patients 71.3% had undetectable RNA at end of treatment (74.1% normal ALT and 69.1% high ALT; 64% GT 1/4 and 89% GT 2/3). The differences in responses between the normal and high ALT group are not significant.

Conclusions: Patients with elevated or normal ALT stratified for genotypes and viral load show at least the same ETR receiving PegIntron 1.5 μg/kg/wk & Rebetol 0.8–1.2 g/d.