P124
Efficacy and toxicity of tacrolimus in steroid resistant ulcerative colitis cannot be predicted by genetic polymorphisms of the CYP3A4, CYP3A5, ABCB1 and NR112 genes
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Objectives: Tacrolimus (FK506) is an effective immunosuppressive treatment in steroid refractory ulcerative colitis (UC) but a substantial percentage of patients fail to respond to the drug and its use is limited by unpredictable toxicity. Tacrolimus is substrate to the metabolizing enzymes cytochrome P450 (CYP) 3A4, CYP3A5 and the multidrug efflux pump P-glycoprotein, encoded by ABCB1 (MDR1). An individual’s response to tacrolimus may in part be genetically determined by their functional genetic variation. Here, we report the first pharmacogenetic evaluation of tacrolimus in UC.

Methods: We studied 95 IBD patients (84 ulcerative colitis – UC, 11 indeterminate colitis – IC) treated with tacrolimus for steroid resistant disease. All subjects were genotyped for the following polymorphisms: CYP3A4*1B, CYP3A5*3, ABCB1 C1236T, C3435T, G2677T,A and NR112 (PXR) A7635G. Genotype-phenotype associations were evaluated by univariate and multivariate analysis with respect to efficacy and toxicity of tacrolimus therapy.

Results: Forty-eight (50%) patients achieved remission and 21 (22%) achieved response. Twenty-seven (28%) patients failed to respond to therapy. Overall forty-six (48%) patients experienced side effects. The most frequent adverse events were tremor (n = 9), hyperglycemia (7), reversible renal impairment (6) and nausea (5). None of the selected candidate SNPs were associated with efficacy or toxicity of tacrolimus therapy.

Conclusions: In this study response to tacrolimus in patients with steroid resistant UC or IC could not be attributed to SNPs in the genes encoding for CYP450, ABCB1 or NR112. These data support previous findings in liver and kidney transplant patients receiving tacrolimus. Application of genome wide approaches may be used as an alternative strategy for identification of predictive markers for drug failure.

P125
Influence of disease duration on adalimumab efficacy in Crohn’s disease: subanalysis of the CARE trial
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Introduction: Adalimumab, a fully human anti-tumor necrosis factor (anti-TNF) monoclonal antibody, is approved for the treatment of Crohn’s disease (CD) and has been shown to induce and maintain remission in patients with CD. Subanalyses of the CHARM trial demonstrated substantial rates of disease remission in patients with early CD [1].

Methods: In the Crohn’s Patients Treated With Adalimumab: Results of a Safety and Efficacy Study (CARE), we evaluated efficacy and safety of adalimumab in a large patient population whose treatment approximated usual clinical practice. Patients with Harvey-Brashaw Index (HBI) scores ≥7 enrolled in this multicenter, open-label, European, Phase IIIb trial. Patients received induction therapy of 160-mg/80-mg adalimumab at Weeks 0/2, followed by adalimumab 40-mg every-other-week maintenance therapy through at least Week 20 (patients with flares/nonresponse could receive 40mg weekly at or after Week 12). Modifications to CD-related concomitant treatments were allowed as clinically indicated and at the investigator’s discretion at or after Week 12. In this analysis, we evaluated adalimumab’s ability to induce remission (defined as HBI ≤4) in subgroups stratified by duration of disease (<2 years, 2 to ≤5 years, and >5 years).

Results: Of 945 patients in CARE, 107 had CD for <2 years, 217 had CD for 2 to ≤5 years, and 621 had CD for >5 years. Patients with disease <2 years were more likely to be immunomodulator- and anti-TNF-naïve than the other disease duration subgroups (data not shown). By Week 8, remission was achieved in more than half of patients whose duration of CD was <2 years and in approximately half of patients whose disease duration was 2 years or longer. For all subgroups, remission rates were maintained from Week 4 to Week 20 (table).

P126
Implementation of a day care unit for inflammatory bowel disease: patients’ satisfaction
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Introduction: Patients with IBD require continued attention, with multiple admissions due to activity periods of their illness and to receive treatments, with the following bother and loss of productivity. In order to reduce these admissions a Day Care Unit (DCU) was set in our hospital during year 2007, to administer biological treatments and other techniques related to the disease on an outpatient basis, sitting and through the application of a clinical protocol followed by a specialized nurse. Previously these treatments took place during ordinary hospital admission in a medical ward.

Material and Methods: All 50 patients with inflammatory bowel disease receiving biological treatment filled in a satisfaction survey form before the first and after several treatment sessions in the Day Care Unit (DCU). Seven patients refused to answer or did not fulfill it. The form included also the presence of problems in DCU, medical visit or recommendations at home. Three patients reported minor complaints, related with the need for more information. Quantitative variables were compared using Chi square test and qualitative variables with t student. The tables show the analysed variables and the results obtained.

| Age (years) |            | 36.9 (18–71) |
| Gender (male) |           | 20 (46.5%) |
| Study level (Elementary (21%); Secondary (42%); College (37%)) |       | Previous admissions 86% |
| Knowledge of physician’s name | 97.7 |
| Knowledge of nurse’s name | 93% |

Data are presented as mean (range) or percentage.