Parameter	Corr. coeff*
Discharge	-0.528
Pain/restriction of activities	-0.263
Restriction of sexual activity	-0.410
Type of perianal disease	0.185
Induration	-0.232
Total PCDAI	-0.474
VAS score	-0.591

* Change in score vs PGI-I (all subjects)

W1211

P-Glycoprotein 170 (P-GP) Functional Activity in Peripheral Blood Lymphocytes (Pbl) According Therapeutic Response in Ulcerative Colitis (UC)

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BACKGROUND: P-gp, encoded by MDR-1 gene, is a transmembrane efflux pump described overexpressed in cancer refractoriness by pumping treatment drugs out of cells. It is expressed in PBL, other haematopoietic cells, apical superficial epithelium of colon, ileum and other tissues with barrier function. It is an interesting and controversial candidate for UC therapeutic response and pathogenesis. Increased expression has been reported associated with steroid UC refractoriness. Conversely, deficient P-gp function has been postulated as UC susceptibility/severity factor **AIM:** to investigate the role of MDR1 gene in the therapeutic response of UC by studying the P-gp functionality in PBL **METHODS:** P-gp functional activity was evaluated in PBL of 27 patients (15 M, 12 F) median age 30 (16-71) yrs with active UC (Mayo score: severe n 9, moderate n 9, mild n 9) categorized in: S-REFR (steroid-refractory, n 16) and S-RESP (steroid-responders, n 11); healthy controls (HC, n 68): similar age/gender. Rhodamine123 (a fluorescent P-gp substrate) efflux was studied by flow cytometry, (FACS Calibur, Becton-Dickinson) in absence and presence of P-gp modulators: Verapamil 100 µM, Valspodar 1µM reassessment. Data were expressed evaluating the behaviour of two markers (M1, M2) defined based on % of cells with different fluorescence levels. M1 (high fluorescence, low P-gp pump activity) and M2 (low fluorescence, high activity) were compared in the three groups. After inhibition, it should be expected that Rhodamine123 remain in the intracellular leading to an increase of % of cells in M1 vs. M2 **RESULTS:** (X±SD) Significant differences were observed in absence and presence of verapamil inhibition, showing increased P-gp functional activity in S-REFR vs. S-RESP ($p<0.01$) and HC ($p<0.001$), but not between S-RESP and HC (ANOVA and Student-Newman-Keuls post-test)**(Tabla)** Results were not influenced by cumulative steroids. Three out of 4 severe patients showing M2>M1 in the assay with verapamil required surgery. Clinical disease activity correlated with M2 (with inhibitor= r:0.57, p=0.000056, Spearman). Interestingly, S-REFR showed a shift (M2 to M1) in an early new assay when some newly added drug reached effectiveness (6-MP n:4, infliximab n:1) **CONCLUSION:** our results suggest: 1)a relevant role of P-gp in UC treatment response 2)a possible usefulness of P-gp functional assay in the early detection of individual therapeutic response.

	WITHOUT INHIBITOR		WITH INHIBITOR	
	M1	M2	M1	M2
CONTROLS	47±12	50±12	82±8	14±9
S-RESP	48±10	49±10	88±6	10±5
S-REFR	34±13	63±14	62±22	35±22

W1212

Anti-Infliximab Antibodies in Routine Clinical Practice - Is It Worth to Assess Them?

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Aim: To assess the role of anti-infliximab antibodies (ATI) formation in therapeutic response and occurence of allergic reactions in patients with inflammatory bowel disease. Material and methods: We included Crohns disease (CD) and ulcerative colitis (UC) patients, treated consequently with infliximab at our tertiary IBD center, in whom the presence of ATI was prospectively measured. Response to infliximab was classified retrospectively as: 1. Prolonged response (initial good response maintained during the long-term treatment); 2. Loss of therapeutic response (initial good response with secondary loss of response) and 3. No response (initial no response). Blood samples were taken prior to each administration of infliximab infusion and analyzed for ATI using commercial ELISA test (Matriks Biotek). Fisher exact test with significance level of 5% was used for the statistical evaluation. Results: A total of 133 IBD patients (56 males), 95 CD and 38 UC, were included with median follow-up time of 6 months (2 -12 month) Eighteen (14%) patients were found to be positive for ATI. Significantly higher occurence of ATI was observed in patients with loss of response (secondary non-reponders) to infliximab compared to those with prolonged response (55% vs. 9%, p=0.001). None of the patients with primary no response was positive for ATI. Seven (5%) patients experienced allergic reaction. However, no significant difference in the presence of ATI between those with and without allergic reaction was found (29% vs. 13%, p=0.19). Conclusion: The presence of ATI seems to be responsible for secondary loss of response to infliximab in significant proportion of patients. However, no association with primary non-response or allergic reactions was observed. Assessment of ATI may be useful when deciding for further treatment strategy.

W1213

Determination of 5-ASA and Its Derivatives in the Colonic Mucosa of Ulcerative Colitis Patients: A Surrogate Marker of Oxidative Damage?

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Background and Objectives Mesalamine (5-aminosalicylic acid or 5-ASA)-containing formulations represent the first-line therapy in the treatment of mild to moderately active ulcerative colitis (UC) and in relapse prevention. *In Vivo* metabolism of 5-ASA produces two hydroxylated derivatives (2,3- and 2,5-DHBA). 2,3-DHBA can be formed by direct hydroxyl radical attack. thus appearing a useful marker of *In Vivo* OH. production. The aim was to evaluate the mucosal concentration of both 5-ASA and 2,3-DHBA in UC patients with active and non-active disease. Patients and Methods The study included 130 consecutive ulcerative colitis patients (mean age 48.5, range 23-84; 62 males and 38 females) on continuous oral 5-ASA treatment (2.4g/day). After informed consent, patients undergoing colonoscopy had two biopsies taken from the sigmoid region (25 cm from the anal verge) for conventional histology and 5-ASA concentration. Endoscopic and histological disease activity were recorded as remission or active disease. 5-ASA (ng/mg) and 2,3-DHBA (pg/mg) concentrations were measured in tissue homogenates by high-pressure liquid chromatography equipped with electrochemical detector. The t-test was used for statistical analysis. Results Patients with endoscopic remission showed higher concentrations of mucosal 5-ASA than those with a mild to moderately active endoscopic disease (58.4 ± 5.9 vs. 42.6 ± 5.2, p=0.04). Similarly, mucosal 5-ASA concentrations in patients with normal histology were higher than in those with active histological inflammation (67.04 ± 7.11 vs. 39.6 ± 4.4, p=0.001). Conversely, 2,3-DHBA mucosal levels were significantly lower in patients in remission with respect to patients with active disease both endoscopically and histologically (0.6 ± 0.1 vs. 4.9 ± 1.9, p=0.03 and 0.6 ± 0.1 vs. 3.6 ± 1.3 p=0.03, respectively). Conclusions Patients with active ulcerative colitis show lower 5-ASA concentration in the colonic mucosa while its hydroxylation product increases. The determination of 2,3-DHBA in the colonic mucosa may be suggested as a novel marker of inflammation-derived oxidative damage.

W1214

A Prospective, Single-Center Study Assessing the Adherence to Long-Term Anti-TNF Treatment in IBD

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Introduction: Patients with Inflammatory Bowel Disease in long-standing remission self-report low adherence to oral therapies (5-ASA, azathioprine, 6-MP). In contrast, the issue of adherence to anti-TNF [infliximab (IFX) and adalimumab (ADA)] maintenance treatment has only recently been addressed. Methods: This was a prospective, single-centre study assessing the adherence to IFX and ADA scheduled maintenance treatment of patients with steroid-dependent luminal and/or fistulizing CD who achieved remission on induction therapy with IFX (5mg/kg at wks 0,2,6) or ADA (160/80mg, at wks 0,2). Patients were followed prospectively from January 2002 until December 2008 with monthly visits to the outpatient clinic or the infusion area. At each visit a review of the medical history between infusions, physical examination, adverse events check, and concomitant medication were assessed, and routine hematological and biochemical tests were performed. Adherence to treatment was determined as the ratio of active to expected visits for IFX infusions or ADA prescriptions (and return of the used syringes). Turning on for an infusion session which was not performed or a prescription that was not given for other reasons was not considered as non adherence. The study was prematurely stopped for loss of response or severe adverse events to treatment, moving area, or for personal choice or other medical reasons. Results: 72 patients (43 males), mean age 27.2 (17-58) years with luminal (54) or luminal/perianal CD (18) received scheduled IFX either as monotherapy (n=33), or combined with AZA (n=30), or initially combined AZA+IFX that was switched later to IFX monotherapy (9) for a mean (range) of 35.1 (12-81) months. Fifteen patients were active and 17 ex-smokers; 23 had extraintestinal manifestations (EIM); 120 were of rural origin. 22 patients received top-down therapy for perianal CD or EIM. At the end of the trial patients received a mean (range) of 21.5 (5-42) infusions. Treatment was switched to adalimumab in 16 patients for loss of response (7), infusion reactions (5), and adverse events (4) to IFX and was maintained on 40 mg ew or eow for 2 (0.2-4) years (mean, range). Two patients stopped treatment temporarily (two pregnancies and personal choice, respectively) and 11 (18%) are receiving 10 mg/kg IFX. Adherence to IFX was 98%, and to ADA 100%. Adherence to AZA of patients receiving combined AZA+IFX therapy was 65%. Conclusion: Even in quiescent CD, adherence to IFX or ADA approximates 100%. This may be due to selection bias, satisfaction with effectiveness of treatment, and/or acceptable dose regimen.

W1215

Assessing Changes in Reported Medication Adherence Over a Three Year Period: the Manitoba IBD Chort Study

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This study reports on medication adherence over time from the Manitoba IBD Cohort Study, a longitudinal, population-based study of multiple determinants of health outcomes in IBD. Methods: Adherence was assessed at 2 time points 3 yrs apart, using data available from 290 participants. Adherence was measured using a validated multi-item patient report tool, the Medication Adherence Response Scale (MARS-5). The MARS-5 rates the frequency of adherence behaviours with 25 representing complete adherence. Poor adherence was defined as a score <20 based on our previously published work on this scale. Differences in response patterns were analyzed, as well as potential correlates of adherence such as beliefs about medication, memory strategies, obstacles to compliance (e.g. cost, dose frequency), and disease activity. Results: Adherence scores were comparable to those reported 3 yrs previously by this sample (Time 1= 20.56, SD = 4.01; Time 2= 20.86, SD = 3.94; r =0.594, p <0.001). Most participants (58.4%) reported scores within 2 points of their previous responses even