PO27
FUNCTIONAL MODULATION OF CRONIN’S DISEASE MYOFIBROBLASTS BY ANTI-TNF ANTIBODIES
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Background & Aims: Infliximab induces immune cell apoptosis by outside-to-inside signalling through transmembrane tumor necrosis factor (TNF)-alpha (mTNF). However, in inflamed gut, myofibroblasts also produce TNF-alpha, and the effects of anti-TNF-alpha on these structural cells has not been studied. We therefore investigated the action of infliximab on apoptosis, matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (TIMP)-1 production, and migration of Cronin’s disease (CD) myofibroblasts.

Methods: Colonic myofibroblasts were isolated from patients with active CD and controls. mTNF was evaluated by Western blotting and flow cytometry. Infliximab-treated myofibroblasts were analysed for apoptosis by Annexin V staining and caspase-3. TIMP-1 and MMPs were measured by Western blotting, and fibroblast migration was assessed using in vitro wound-healing assay.

Results: CD myofibroblasts showed higher mTNF expression than control myofibroblasts. Infliximab had no effect on CD myofibroblast apoptosis, caspase-3 activation and production of MMP-3 and MMP-12. However, infliximab induced a significant dose-dependent increase in TIMP-1 production, which was inhibited by the p38 mitogen-activated protein kinase inhibitor SB 203580. The anti-TNF antibodies adalimumab, certolizumab pegol, onercept and etanercept increased TIMP-1 production. Migration of CD myofibroblasts was significantly enhanced by infliximab and recombinant human transforming growth factor for clinical response.

Conclusion: Our findings show a novel therapeutic pathway for anti-TNF therapies in enhancing TIMP-1 production and fibroblast migration which may reduce MMP activity, and facilitating the wound healing.

PO28
OPEN-LABEL INFlixIMAb THERAPY IN ULCErATIVE COLITIS: A MULTICENTER SURVEY OF RESULTS AND PREDICTORS OF RESPONSE
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Aim: Results of randomized controlled trials showing efﬁcacy of infliximab in ulcerative colitis (UC) must be conﬁrmed in clinical practice. Our aim was to evaluate the efﬁcacy and safety of infliximab in UC patients of the Madrid area, looking for clinical predictors of response.

Methods: Retrospective survey of all UC patients treated with infliximab in Madrid (Spain) followed up for at least 2 weeks.

Results: 47 UC patients were included (45 males, mean age 44.1±15 years), with a mean follow up of 4.7 months (range 0.5-21), and a total number of 211 infliximab infusions. Infliximab was prescribed for steroid-resistance in 34% of the patients, and for steroid-dependence in 66%. Response and remission rates were, respectively, 97% and 42% at the 2nd week, 93% and 69% at the 6th week, and 80% and 65% at the long-term follow up (mean 8.2 months, range 3.5-21). Overall, 85% of the patients were considered to achieve a favourable outcome, and 15% did not respond or lose the response. Age, gender, disease duration, indication for infliximab (steroid-resistance/dependence), disease severity, C-reactive protein, concomitant thiopurinuric therapy, or smoking habit, did not influence on efﬁcacy. Extent of the disease was the only predictive factor: patients with pancolitis had better response than those with left sided colitis (p=0.02). Adverse events were reported in only 4 cases (8.5%), all of them mild.

Conclusion: Infliximab is safe and effective for UC. Short and long term response rates of this large multicenter study are better than those reported in randomized controlled trials. Extent of the disease was the only predictive factor for clinical response.

PO29
A NEW ‘CALPROTECTIN POC DEVICE’ CORRELATES WITH ELISA AND SEPARATES BETWEEN ENDOSCOPIC ASSESSED MUCOSAL HEALING AND ACTIVE ULCERATIVE COLITIS
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Calprotectin (Cpt) is a neutrophil marker protein that is stable in stools for 7 days at ambient temperature and can be sent by mail to the local laboratory. It correlates with the 3 days excretion of 111-In labeled leukocytes as well as with histology in IBD; normalization of Cpt is a strong indicator of mucosal healing in such pts. Furthermore, determination of Cpt in stools by ELISA is accepted by the FDA for the diagnosis of IBD and to separate between IBD and IBS. We have designed a rapid POC device, making it possible for the physician to obtain a reliable result in less than 15 minutes. Aim of the study: Evaluation of this Cpt-POC device in a relevant clinical material.

Method: 66 consecutive patients referred for colonoscopy were included. 41 had previous known UC, 25 were referred due to chronic diarrhea, 30 was diagnosed with endoscopic active UC, 11 had mucosal healing. All endoscopic procedures were done by one physician (AR) and biopsies were collected in all pts. All pts were asked to send in a stool sample 3-4 days after colonoscopy and before starting treatment. Cpt was assessed both by ELISA and the POC device at two different times, in two separate stool extracts.

Results: The correlation between the two methods was excellent (r=0.92, p<0.001). In pts with diarrhea and normal histology, all except three had Cpt<50mg/kg (71,85,220). Among UC pts with mucosal healing, all had normal Cpt levels except 3 (67,75,97) All but two pts with active disease had Cpt>100 (median 600, range 48-2150)

Conclusion: This POC device is a quantitative rapid format test for the determination of fecal calprotectin; it correlates strongly with the ELISA. It will soon be available for clinical use.

PO30
LONG-TERM EFFECTIVENESS OF AZATHIOPRINE (AZA) FOR CRONIN’S DISEASE (CD) AND ULCERATIVE COLITIS (UC)
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Objective: The long-term effectiveness of AZA and the beneficial effect of this drug on UC, are less clear than in CD. Our aim was to evaluate and compare the long-term effectiveness of AZA therapy in patients with CD and UC.

Methods: Prospective study including 394 consecutive patients with IBD treated with AZA (25 mg/kg). Control visits were performed weekly for the first month, and then every 6 months. Truefalse-index/CDAI were used to assess clinical response. Hospitalizations and surgical procedures before and after starting AZA were recorded.

Results: Of the 394 patients included, 238(60%) had CD and 156(40%) UC. Patients receivd AZA treatment for a median of 34 months (range:1-187 months). Effectiveness: Response/remission was achieved in 20%/60% of the patients, without significant differences between CD/UC. In the multivariate analysis, the type of disease did not influence the efficacy. Differences were neither observed when Kaplan-Meier-curves were compared depending on CD/UC. At the end of the study, clinical relapse was documented in 8% of patients (9% CD and 5% UC). Steroid treatment: At the beginning of the study, 49% of CD patients were receiving steroids, while this therapy was necessary by only 8% at the end of the study (p<0.01). Corresponding figures for steroid-dependency in UC were 39%/9%, before/after AZA (p<0.01). Hospitalizations: Prior to AZA, 82% of CD patients had been hospitalized, while after AZA treatment this figure decreased to 21%(p<0.01). Hospitalization rates in UC, before/after AZA, were 64%/9%(p<0.01). Surgical procedures: performed in CD patients before/after AZA was 38%/5%(p<0.01). Corresponding figures for UC patients were 22%/11%(p<0.01).

Conclusion: Long-term treatment with AZA is similarly effective for the clinical management of both CD and UC. AZA therapy reduced both the number of hospitalizations and of surgical procedures performed during treatment. At the same time, a clinically meaningful steroid sparing effect was achieved by the thiopurin treatment.