Results and Conclusion: CAI in patients with UC in 2 months after infusion of MSCs decreased from 8.2±1.2 to 0.6±0.2 ($p < 0.05$), EAI decreased from 6.5±1.5 to 2.0±0.3 ($p < 0.05$). CDAI in patients with CD in 2 months after infusion decreased from 213.3±53.4 to 102.0±24.3 ($p < 0.05$). Healing of the mucosa within the period of observation was noted in most of the patients with UC and CD, including those, who had continuous course of the diseases. None of the patients showed aggravation of the disease. There were not any adverse effects of infusion. Thus MCSs are effective for mucosal healing in ulcerative colitis and Crohn's disease.

P086

Which activity index for ulcerative colitis (UC)? Evaluation of inter-observer variation in clinical, endoscopic and composite indices

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Background: Clinical trials of ulcerative colitis use many different activity indices, making it difficult to compare data between trials. It is unclear which index is most reproducible and how inter-observer variation (IOV) impacts on trial inclusion and outcomes.

Methods: Our aims were to assess IOV in all commonly used indices and to determine the impact that IOV has on inclusion criteria and outcomes in key published trials. 100 patients with UC were seen independently, each patient on the same day, in random order, by 4 gastroenterologists. Each clinician completed a proforma to calculate the following indices: Mayo Index (MAYO), UC Disease Activity Index (UCDAI), Simple Colitis Clinical Activity Index (SCCAI), Seo Index (SEO), Modified Truelove and Witts Severity Index (MTW) and Colitis Activity Index (CAI). A separate clinician performed video sigmoidoscopy on the same day. The video record was later scored by the 4 assessing clinician, blinded to other results. An experienced blinded clinician assigned each patient to an appropriate clinical category (ACC) [remission, mild, moderate, severe] by assessing symptoms, examination findings, blood results, FS and histology. To assess the impact of IOV in recruiting patients to, or meeting outcome criteria of clinical trials, pivotal papers were selected for each index. Quadratic weighted kappa (κ) statistics assessed agreement within and between indices, in which disagreements are weighted in relation to their magnitude (number of categories).

Results: Of 100 patients, 50% were male, median age 49 y (range 19–82) and median duration of disease 107 mo (range 0–575). Maximum disease extent: proctitis 27%, left-sided colitis 39% and pancolitis 34%. 23% were in remission, 40% had mild, 32% moderate and 5% severe colitis. For reproducibility between the 4 clinicians the SEO (κ 0.95) scored highest and CAI lowest (κ 0.78). The scores with highest correlation with ACC were MAYO and UCDAI (κ 0.81 and 0.82 respectively). The score with lowest correlation with ACC was the SEO (κ 0.66). For endoscopic indices, κ for agreement between Baron and Mayo, and Baron and modified Baron indices were 0.83 and 0.89 respectively. For trial inclusion, the median mismatch was 23% (complete concordance in 65–97%), with most agreement for severe UC by MTWSI and least for mild-moderate UC by UCDAI. Median mismatch for remission was 21% (complete concordance in 77–91%) with most agreement for SCCAI and least for UCDAI.

Conclusions: With 4 independent specialists assessing the same patients, about 1 in 5 patients would have been affected by disagreement on whether they met entry criteria or achieved remission for published clinical trials. IOV in the assessment of UC is substantial and should be taken into account when calculating the power of clinical trials.

P087

SONIC: a randomized, double-blind, controlled trial comparing infliximab and infliximab plus azathioprine to azathioprine in patients with Crohn's disease naive to immunomodulators and biologic therapy

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Purpose: To assess the induction of steroid-free remission and the safety of infliximab (IFX) monotherapy and IFX+azathioprine (AZA) combination therapy, with AZA monotherapy in moderate-to-severe CD pts.

Methods: 508 pts who were naive to immunomodulators were randomized to: 1) AZA 2.5 mg/kg capsules + placebo (PBO) infusions, 2) IFX 5 mg/kg infusions + PBO capsules, or 3) IFX 5 mg/kg infusions + AZA 2.5 mg/kg capsules through wk30. The infusions were administered at wks 0, 2, and 6 followed by q8wk infusions. Final efficacy assessments were collected at wk26, including endoscopy for pts with mucosal ulcerations at baseline.

Results: 52% of pts were male and 93% were Caucasian. The median age was 34 yrs (range, 18–80 yrs). The median CD duration was 2.3 yrs (range, 0 to 43 yrs). The median CDAI score was 275 (25^{th}–75^{th} percentile, 244–323) and the median baseline CRP was 1.1 mg/dL (range, 0.3–19.0). 41% of pts were on steroids at baseline. The proportion of pts in steroid-free remission (CDAI < 150) at wk26 (primary endpoint) was 56.8% with IFX+AZA, 44.4% with IFX, 30.6% with AZA ($p < 0.001$ IFX+AZA vs. AZA; $p = 0.009$ IFX monotherapy vs AZA monotherapy; $p = 0.022$ IFX+AZA vs. IFX monotherapy). Results of a subanalysis by baseline CRP and endoscopy status are shown in Table 1. The proportion of pts with mucosal healing at wk26 was 43.9% with IFX+AZA, 30.1% with IFX, and 16.5% with AZA ($p < 0.001$ IFX+AZA vs. AZA; $p = 0.023$ IFX vs AZA; $p = 0.055$ IFX+AZA vs. IFX). The proportion of pts with serious infections was similar in all treatment groups. One pt, treated with IFX+AZA, developed tuberculosis. Colon cancer developed in 2 pts, both treated with AZA monotherapy. One death occurred following colectomy in a pt treated with AZA alone.

Table 1. Patients achieving corticosteroid-free clinical remission at week 26 by baseline CRP and endoscopy status.

Baseline status	AZA	IFX	AZA+IFX	p-value		
	n (%)	n (%)	n (%)	IFX vs. AZA	IFX+AZA vs. AZA	IFX+AZA vs. IFX
CRP < 0.8 mg/dL	25/71 (35.2)	27/67 (40.3)	35/69 (50.7)	0.503	0.121	0.314
CRP ⩾ 0.8 mg/dL	27/98 (27.6)	48/101 (47.5)	61/96 (63.5)	0.004	<0.001	0.027
Lesions	35/115 (30.4)	50/99 (50.5)	68/111 (61.3)	0.003	<0.001	0.117
No lesions	11/27 (40.7)	12/36 (33.3)	12/30 (40.0)	0.372	0.927	0.688
Lesions UTD/NP	6/28 (21.4)	13/34 (38.2)	16/28 (57.1)	0.139	0.003	0.074
CRP ⩾0.8 mg/dL and lesions	21/75 (28.0)	37/65 (56.9)	44/64 (68.8)	<0.001	<0.001	0.169

UTD/NP = unable to determine or no endoscopy performed.

Conclusions: Moderate-severe CD pts treated with IFX monotherapy or IFX+AZA (when initiated together) are more

likely to achieve steroid-free clinical remission and complete mucosal healing than those receiving AZA alone. IFX+AZA was more effective than IFX monotherapy for steroid-free remission. Patients with evidence of active inflammation, by CRP and/or baseline endoscopic lesions, showed a particularly strong benefit from the IFX-based regimens compared to AZA monotherapy. Safety among the treatment groups was similar.

P088

Prevention of postsurgical recurrence of Crohn's disease by infliximab: a three years follow-up study

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Aim: Prevention of recurrence of Crohn's disease after surgery remains a fundamental goal of gastroenterology. None of the aminosalicylates, immunosuppressives, steroids and antibiotics used for the purpose have shown a great benefit. By contrast, we already reported that infliximab given two weeks after surgery completely protects against endoscopic and clinical recurrence at two years when compared to mesalamine (Arch Intern Med. 2007;167:1804). However, in the absence of large RCT's, additional evidence as proof of efficacy may be desirable. In addition, it is not clear for how long infliximab should be continued after surgery. This study focused on these two issues.
Methods: Ten patients (four females and six males) were treated two weeks after curative surgery with infliximab (5 mg/kg body weight: 0, 2, 6 weeks and then q8wk) and compared to sixteen controls (five females and eleven males) treated with mesalamine (800 mg tid). The groups were comparable with regard to age, duration of disease, involved intestinal tracts, reasons for surgery, type of surgery and risk factors for recurrence (smoking, previous surgery). In both groups, all medications were stopped at least a month before surgery. The groups were compared at two years: recurrence was defined according to endoscopic (Gut 1984;25:665 Rutgeerts score $\geqslant$2) or clinical criteria (Gastroenterology 2004;127:723). The patients treated with infliximab were followed-up for an additional year, at which time we performed a colonoscopy, stopped the medication for four months and performed another colonoscopy. The study was conducted after approval of the institution ethics committee and full informed consent by the patients.
Results: In the group treated with infliximab none of the patients had endoscopic or clinical recurrence at two years. No abnormality of blood tests was detected during the period of study and at two years. We did not record any potential infliximab-related side effect. By contrast, only four out of the sixteen mesalamine treated patients (25%) were disease free two years after surgery. In particular, of the twelve patients with recurrent disease, seven had endoscopic relapse while five fullfilled both the endoscopic and the clinical criteria of recurrence. At three years after surgery all ten infliximab treated patients continued to be disease free both on endoscopic and clinical grounds. Endoscopic reevaluation four months after stopping infliximab showed clear endoscopic signs of recurrence in eight out of ten patients (80%, with Rutgeerts score $\geqslant$3 in six patients). Such result was comparable to what observed in the mesalamine group and consistent with well known recurrence rates – in the absence of medications – reported in the literature.
Conclusions: This study provides additional strong evidence of the remarkable efficacy of infliximab in preventing postsurgical recurrence of Crohn's disease. It also shows that the medication should be continued beyond three years to mantain its benefit.

P089

Results from a prospective study combining infliximab, surgery, and methotrexate in severe fistulising ano-perineal Crohn's disease

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Introduction: Infliximab (IFX) is effective in treating fistulising Crohn's disease (CD). However, clinical recurrence may happen because of persistence of fistula tracks as observed with MR-imaging. Initial IFX induction associated with an optimal surgical procedure, then followed by a maintenance therapy should be evaluated regarding anatomic healing and prolonged clinical response.
The aim of this open prospective study was to evaluate the short- and long-term efficacy of a combined schedule comprising short course of IFX, associated with local optimal surgery, followed by long-term methotrexate (MTX) in patients with severe fistulising ano-perineal CD.
Patients and Methods: From January 2006 to November 2007, all consecutive patients with severe fistulising ano-perineal CD were prospectively included after primary abscess drainage. At inclusion, patients received MTX (25 mg/week IM during all the study) and 3 IFX infusions (5 mg/kg at weeks 0, 2, and 6). During second surgical step performed at week 4, all setons were removed and an optimal surgical procedure (including fistula laying out, fibrin glue injection, flap . . .) was done. IFX was then stopped and MTX continued as maintenance therapy. Clinical response was defined by a reduction in 50% or more of draining fistulas at two or more consecutive study visits. The primary end-point was clinical response at week 14. Secondary end-points were: (i) time to loss of response for responders at week 14; (ii) Perineal Disease Activity Index – PDAI – and van Assche MR-imaging score at weeks 0, 14 and 50; (iii) safety.
Results: Thirty-four CD patients (26W; mean age 38.5 years) were included. All had complex fistula, including 9 recto-vaginal, and 10 ano-rectal stenosis. At week 14, 85% had clinical response, and it was complete in 73.5%. Median time to loss of response was 69 weeks. Median PDAI decreased from 11 to 3, and 0 ($p < 0.001$), and median van Assche score decreased from 15 to 9, and 6 ($p \leqslant 0.001$) at weeks 0, 14, and 50 respectively. Adverse events occurred in 62% of cases, with 15% severe infections.
Conclusion: Treatment combining initial IFX induction, and two steps sphincter-sparing surgical procedure was very effective in achieving short-term response in severe fistulising ano-perineal CD. MTX as a maintenance therapy may provide long-term remission. MTX should be compared to IFX in maintenance therapy after an optimised induction treatment.

P090

Autologous mesenchymal stem cell therapy in patients with refractory Crohn's disease

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Background and Aims: Crohn's disease (CD) is a chronic inflammatory disorder with significant morbidity and major impact on quality of life. Despite the availability of a range of medications there still remains a need for therapeutic alternatives since patients not always respond to existing therapeutic choices, become refractory to their medication, or develop treatment limiting toxicities.