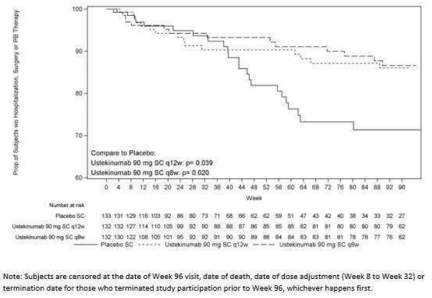
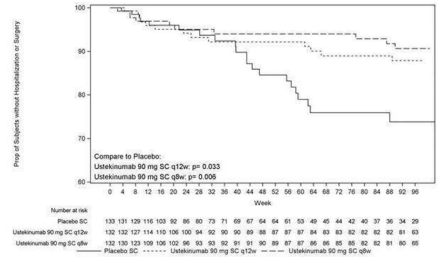
Figure 1. Kaplan-Meier curve for the time to the first Crohn's disease-related hospitalization, surgery or first prohibited biologic therapy due to worsen of Crohn's disease through Week 96 (with dose adjustment time as a censoring time); Randomized subjects in IM-UNITI



Note: Subjects are censored at the date of Week 96 visit, date of death, date of dose adjustment (Week 8 to Week 32) or termination date for those who terminated study participation prior to Week 96, whichever happens first.

Figure 2. Kaplan-Meier curve for the time to the first Crohn's disease-related hospitalization or surgery through Week 96 (with dose adjustment time as a censoring time); Randomized subjects in IM-UNITI



Note: Subjects are censored at the date of Week 96 visit, date of death, date of dose adjustment (Week 8 to Week 32) or termination date for those who terminated study participation prior to Week 96, whichever happens first.

Sa1744

CANNABIS INDUCES CLINICAL AND ENDOSCOPIC IMPROVEMENT IN MODERATELY ACTIVE ULCERATIVE COLITIS

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Background: Cannabis is frequently used by patients with ulcerative colitis UC, although it was never investigated in a controlled trial. **Aim**: We aimed to assess the effects of Cannabis in moderately active UC in a randomized placebo controlled trial. **Patients and Methods**: Patients with UC who did not respond to conventional medical treatment were randomized to receive 2 cigarettes of cannabis or placebo daily. Each cigarette contained 0.5 g of cannabis, corresponding to 11.5mgTHC. The placebo contained cannabis leaves from which THC was extracted. Disease activity (DAI), endoscopic findings and laboratory tests were assessed before and after 8 weeks of treatment. All other medication remained unchanged. **Results**: Twenty-eight patients completed the study, mean age 33 (20-61), 17 males. The colitis was extended in 11 and left sided in 17 patients. During treatment the DAI decreased from 10±3 to 4±3.2 and from 10±2.7 to 8±2 (p<0.01), while the Mayo endoscopic score decreased from a median of 2 (IQR2-2.5) to 1 (IQR 0-2) (p=0.01) and from 2 (IQR2-2) to 2 (IQR 1.25-2) (p=0.059) in the THC and placebo groups, respectively. The mean CRP changed from 0.8±0.9 to 0.7±1.2 and from 1.8±1.9 to 1±1.6(mg/dl) (p=0.5), whereas fecal Calprotectin changed from 135±113 to115±103and from 226±100 to 229±230 (mg/dl)in the THC and placebo groups, respectively (p=0.7). No serious side effects were observed. **Conclusion:-** Tetrahydrocannabinol-rich cannabis is safe and can induce clinical as well as endoscopic improvement in moderately active UC.

Sa1745

BIOLOGICAL INTERVENTIONS FOR INDUCTION AND MAINTENANCE OF MUCOSAL HEALING IN CROHN'S DISEASE: A COCHRANE SYSTEMATIC REVIEW

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Background Clinical trials of biologics in Crohn's disease (CD) have focused on clinical outcomes. Their ability to achieve mucosal healing (MH) is less clear. In this Cochrane review, we synthesized the randomized controlled trial (RCT) evidence on the efficacy of biologics to induce and maintain MH in CD. **Methods** MEDLINE, EMBASE, Cochrane Library (CENTRAL) and the Cochrane IBD Group Specialized Trials Register were searched to October 10 2017 for RCTs investigating biologics for inducing and/or maintaining MH in CD at 4 to 26, and >26 weeks, respectively. Endoscopic response (ER), safety and quality of life (QOL) were examined as secondary outcomes. Pooled risk ratio (RR) estimates were calculated using a random-effects model. The quality of the evidence was rated using GRADE. **Results** The search yielded 7 induction trials (5 low, 2 unclear risk of bias). Infliximab (IFX) was superior to placebo (PBO) for inducing MH at week 10 (RR 8.4, 95% CI 1.2-61, n=74, low quality), and IFX mono- and combination therapy with azathioprine (AZA) were superior to AZA for inducing MH at week 26 (RR 1.9, 95% CI 1.1-3.1, n=218, low quality, and RR 2.7, 95% CI 1.7-4.3, n=232, respectively, moderate quality). MH rates did not differ significantly between adalimumab (ADA) and PBO treated patients, but ADA users were more likely to achieve CDEIS ≤4 at week 12 (RR 1.9, 95% CI 1.2-3.0, n=123, low quality). Neither natalizumab (RR 2.8, 95% CI 0.4-20, n=50, low quality), nor ustekinumab (UST) (RR 2.1, 95% CI 0.81-5.4, n=302, low quality) were superior to PBO for inducing MH, but UST users displayed significantly greater SES-CD reductions in one study (low quality). The search identified 3 maintenance trials, each examining a different biologic (2 low, one high risk of bias). Neither IFX nor ADA was superior to PBO for maintaining MH achieved during induction, but patient numbers were extremely small. Comparable data were not available for UST. Amongst all randomized patients (regardless of MH status at induction completion), only ADA was associated with higher 1-year MH rates than PBO (RR 30.5, 95% CI 1.9-499, moderate quality for ADA; RR 2.4, 95% CI 0.94-6.4, low quality for IFX; RR 2.2, 95% CI 0.86-5.6, very low quality for UST). All 3 biologics displayed a significant benefit for ER at 1 year. Adverse event rates were similar between groups, but one case of progressive multifocal leukoencephalopathy was observed with natalizumab. IFX and UST were associated with improved QOL. **Conclusions** The evidence supports the efficacy of IFX for inducing MH (low-to-moderate quality), and of ADA and UST for inducing ER (low quality), in CD. ADA was associated with higher maintenance MH rates than PBO at 1 year, with ADA, IFX and UST displaying significantly higher rates of ER. There is no RCT evidence for certolizumab or vedolizumab.

Sa1746

LONG-TERM SAFETY AND EFFICACY OF THE ANTI-MADCAM MONOCLONAL ANTIBODY SHP647 FOR THE TREATMENT OF CROHN'S DISEASE: THE OPERA II STUDY

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Background: Despite available treatments, patients with Crohn's disease (CD) often experience symptoms and complications of uncontrolled intestinal inflammation. SHP647 is a fully human IgG2κ anti-MAdCAM monoclonal antibody, in development for induction and maintenance of remission in patients with CD and ulcerative colitis. OPERA II was a 72-week, multicentre, open-label, phase 2 extension study (NCT01298492), designed to assess the long-term safety and efficacy of SHP647 in patients with moderate to severe CD. **Methods:** Included patients had completed 12 weeks' treatment (placebo or 22.5 mg, 75 mg or 225 mg s.c. SHP647) in OPERA I (NCT01276509), or had a clinical response (≥3-point decrease in Harvey Bradshaw Index [HBI] score) to 225 mg SHP647 in the open-label study, TOSCA (NCT01387594). Patients received SHP647 (75 mg, s.c.) every 4 weeks from baseline to week 72, and were followed up monthly for a further 6 months. Dose de-escalation to 22.5 mg owing to intolerance/AEs, or escalation to 225 mg owing to clinical deterioration/poor response, was allowed as judged by the investigator. Primary endpoints were frequency of AEs, AEs leading to withdrawal and SAEs. HBI scores were used to define remission (score <5) and assessed as exploratory efficacy measures. **Results:** In total, 268 patients (mean age 36.5 years; 56.3% women) were enrolled and entered the treatment period; 149 completed the study. Mean±SD HBI score at OPERA II baseline was 4.9±3.01. A total of 1150 and 461 AEs were reported during the treatment and follow-up periods, respectively. The most common treatment-related AEs during treatment were nasopharyngitis (5.6%), arthralgia (6.0%) and headache (5.2%). No patient experienced progressive multifocal leukoencephalopathy. Eighty patients experienced SAEs; these were considered treatment-related in 10 patients. Among patients who had AEs leading to discontinuation (n=54) the most common AE was CD flares. Two patients died: one (75 mg) of multiple organ failure after postoperative aspiration following a resection of the terminal ileum. The second (225 mg) died of metastatic neoplasm of unknown primary, with adenocarcinoma identified on cytology. Neither death was considered drug-related. HBI remission and response rates showed no unexpected decay over time (Figure 1). **Conclusion:** SHP647 was well-tolerated. The sustained HBI response rate suggests efficacy of SHP647 over 72 weeks of treatment. These results add to evidence for the long-term safety and efficacy of SHP647.