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Background: We performed a systematic review and network meta-analysis to assess efficacy and impact on patient-reported outcomes (PRO) of pharmacological therapies for moderate to severe ulcerative colitis (UC).
Methods: Medline, Embase, CENTRAL, and grey literature sources were systematically searched up to October 2016. We included randomized controlled trials in adults with moderate to severe UC that compared infliximab, adalimumab, golimumab, vedolizumab and tofacitinib to each other or placebo. Efficacy outcomes were induction and maintenance of remission, response and mucosal healing. PRO endpoints included change in IBDQ score and IBDQ response (a ≥16-point increase from baseline). We combined direct and indirect evidence through multivariate random-effects network meta-analyses and relative ranking of treatments was assessed using surface under the cumulative ranking (SUCRA) probabilities. We conducted subgroup analyses based on prior anti-TNF therapy.
Results: We included thirteen randomized, double-blind, placebo-controlled trials (4 with infliximab, 3 with adalimumab, 2 with golimumab, 1 with vedolizumab and 3 with tofacitinib). All interventions were effective against placebo. When used for induction, infliximab had higher rates of clinical response and mucosal healing compared to adalimumab (OR 2.27; 95% CI 1.47 to 3.50 and OR 2.03; 95% CI 1.32 to 3.12 respectively) and golimumab (OR 1.88; 95% CI 1.18 to 3.02 and 1.68; 95% CI 1.05 to 2.69 respectively), and was ranked first (SUCRA 97.5 and 89.7, respectively). However, it was comparable (SUCRA 75.1) with vedolizumab (SUCRA 72.6) and tofacitinib (SUCRA 72.4) in achievement of clinical remission.
In patients who prior anti-TNF exposure, tofacitinib was ranked as the most effective agent and it was superior to adalimumab for all efficacy outcomes. Infliximab (OR 2.35; 95% CI 1.62 to 3.41), adalimumab (OR 1.38; 95% CI 1.07 to 1.79) and tofacitinib (OR 2.07; 95% CI 1.59 to 2.70) resulted in higher IBDQ response rates compared to placebo. Greater improvement in IBDQ score was observed following treatment with vedolizumab (OR 18.00; 95% CI 11.08 to 24.92) and infliximab (OR 18.58; 95% CI 13.19 to 23.97).
Finally, we could not synthesize indirect effect estimates for maintenance of remission for all agents due to differences in study designs. Remission (OR 0.95; 95% CI 0.49 to1.83) and response (OR 0.79; 95% CI 0.45 to 1.39) rates were comparable between infliximab and adalimumab at the end of maintenance phase.
Conclusions: All pharmacological therapies equally improved quality of life. Infliximab was ranked first across efficacy outcomes. Short-term treatment with tofacitinib seems effective with high ranking, especially in patients with previous anti-TNF exposure.

P422
Patient-near Infliximab trough-level testing by a novel quantitative rapid test; the Quantum Blue Infliximab assay

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Background: Therapeutic drug monitoring (TDM) has become standard clinical practice and overwhelming clinical evidence indicates that dose-optimization improve clinical outcome by decreasing the risk for anti-drug-antibodies (ADA) and improves the efficacy of the drug itself. There is also another aspect for advocating TDM, that is improving the health economic aspect of these very expensive drugs. However, this has been hampered by the high cost of and the absence of a near patient testing.
Aims of the study: The study had two aspects; first is to correlate a CE -marked rapid test for IFX trough level, the Quantum Blue Infliximab test (QB-IFX) (BÜHLMANN Laboratories, AG, Basel, Switzerland) to an assay very similar to the Loeven assay. Secondly, to correlate the performance of such a test done by; A) a nurse and B) a trained laboratory person
Methods: The study comprised 64 pts with IBD receiving IFX treatment; 14 Remicade and 50 Remsina. At the day of infusion, blood for IFX-trough level was collected in addition to 3 ml serum for QB-IFX rapid test.
Part A: A nurse (IL) received one hour of "laboratory" training before running the QB-IFX under supervision of AR. The serum was diluted 10uL in 190 uL assay buffer and vortexed for 5 sec. 70uL was applied to the rapid test cassette and read after 15 min using the Q B reader.
Part B: The same procedure was followed by an experienced lab technician (GHM). In addition, 5 aliquots from three sera-levels was collected (3, 7 and 10ug/ml) and tested to establish CV for the upper and lower trough level values as well as for one high level value.
Results: The was a very good correlation between the QB-IFX rapid test and the laboratory ELISA test, r=0.90, p<0.001, the slope was 1.1. Furthermore, the correlation between the results obtained by the nurse and a skilled lab person was acceptable with r=0.92, p<0.001. The CV for the upper and lower trough level was 4.7 and 7.8% respectively. CV for the high level was 14.7%
Conclusions: This is the first study that documents a close correlation between a 15 min. rapid test for IFX trough level with that of an standard lab-test. We have shown that such a test can accurately be performed by a nurse. The CV for the three different serumlevels was way lower than expected for a lateral flow rapid test. This means that TDM now can be moved from a distant laboratory to the near patient facility like the infusion centre to ensure correct dosing in IBD and other patients on IFX treatment.
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P423
Early improvement in quality of life in patients with luminal Crohn's disease treated with adalimumab. Data from RAPIDA trial

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Background: Clinical response and patient's quality of life improve as a result of the direct benefit of Crohn's disease (CD) effective treatment. Rapidity of response to treatment in CD is a field of major interest, due to the importance of achieving the highest benefit in the shortest possible time. There are no studies specifically designed for early evaluation of the quality of life in patients with active CD receiving adalimumab therapy.

The aim of this study was to evaluate the rapidity of improvement of quality of life in response to adalimumab therapy in adult antiTNF naïve patients with active luminal (Harvey-Bradshaw Index ≥8) moderate-to-severe CD, and with no response to a full and adequate course of therapy with corticosteroids and/or immunosuppressants.

Methods: To this purpose we designed aninterventional, prospective, open label, single arm and multicenter clinical trial. Quality of life was evaluated by using the validated questionnaires EuroQol-5D (EQ-5D) and the 36 items version of the Inflammatory Bowel Disease Questionnaire (IBDQ-36). Questionnaires were administered at baseline, day 4 and weeks 1, 2 4 and 12 with standardized adalimumab treatment (160 mg – 80 mg – 40 mg eow).

The modified intention to treat (mITT) population was the primary population for analysis and consisted of those patients enrolled in the study who had received at least one dose of adalimumab.

Statistical analyses were performed by the t-test or the Wilcoxon signed rank test, as applicable.

Results: Eighty patients were included. At baseline, the median EQ-5D index score was 0.68. EQ-5D scores improved significantly versus baseline, at day 4 and weeks 1, 2, 4 and 12, with median changes of 0.05 ($p<0.01$), 0.05 ($p<0.001$), 0.11 ($p<0.001$), 0.10 ($p<0.001$) and 0.12 ($p<0.001$), respectively. Similarly, EQ-5D VAS median scores also improved significantly, compared to baseline (median score at baseline: 55.00), at day 4 and thereafter, with median changes of 6.00, 5.00, 10.00, 10.00 and 13.00, respectively ($p<0.001$ at all time-points).

The comparison, versus baseline, of the IBDQ-36 overall score (median score at baseline: 143.50) at day 4 and weeks 1, 2, 4 and 12, also yielded statistically significant differences, with median improvements of 14.0, 18.0, 30.0, 42.0 and 32.0 respectively ($p<0.001$ at all time-points). Restoration of normal health (IBDQ-36 score >209) was obtained in 11% of patients at day 4 and increased to 31% at week 12.

Conclusions: Adalimumab produces rapid improvement of quality of life since day 4 in patients with moderate-to-severe Crohn's disease.

P424
Association between infliximab trough levels, clinical remission, mucosal healing and quality of life in patients with inflammatory bowel disease on maintenance therapy

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Background: Adequate infliximab (IFX) trough levels (TL) are associated with clinical remission (CR) and mucosal healing (MH). We aimed to investigate the association between ITX TL and quality of life (QoL) in inflammatory bowel disease (IBD) patients.

Methods: We carried out a prospective cohort study in IBD patients in IFX maintenance therapy. IFX levels were determined using a quantitative rapid test immediately before drug infusion. Disease activity indices (MAYO/HBI), endoscopic scores (MAYO/SES-CD) were obtained. QoL was assessed using the Inflammatory Bowel Disease Questionnaire (IBDq). The study was approved by the Institutional Review Board and informed consent was obtained from all patients.

Results: Seventy-one consecutive subjects were included in the study (59 with Crohn's disease and 17 with ulcerative colitis). Drug levels were considered satisfactory (TL≥3μg/mL) in 29 patients (39.4%) and unsatisfactory (TL<3μg/mL) in 43 (60.6%). Satisfactory TL were associated with higher rates of clinical remission (85.7% x 27.9%, $p<0.001$) and mucosal healing (85.7% x 18.6%, $p<0.001$). Higher TL were also associated with improved IBDQ scores (183±32 x 161±28, $p=0.006$), particularly regarding bowel symptoms (59.6±9.3 x 52.3±8.5, $p=0.001$), systemic function (27.3±5.6 x 22.7±5.2, $p=0.001$) and social function (30.8±5.7 x 26.7±7.4, $p=0.015$).

Conclusions: Satisfactory IFX levels were associated with higher rates of CR, MH and improved QoL in IBD patients on maintenance therapy.

P425
Biosimilar infliximab in real-life Crohn's disease treatment in anti-TNF-alpha naïve and non-naïve patients in comparison to biologic originator: a comparative observational cohort study

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Background: Recently we have shown, that biosimilar infliximab (I) in the treatment of Crohn's disease (CD) patients, is equivalent to biologic originator (R) in terms of efficacy and safety. However data comparing response in anti-TNF naïve and non-naive patients with CD are still limited and controversial.

The aim of the study was to assess the efficacy, tolerability, and safety of biosimilar infliximab in comparison to biologics originator in anti-TNF-alpha naïve and switch CD patients.

Methods: This was a retrospective, one center study enrolled a cohort of 168 consecutive adult CD patients. The patients received either R (73) or I (95) on the basis of the same inclusion criteria (CDAI >300 or active perianal fistula). According to local national regulations, treatment was stopped after one year. Assessments included treatment-emergent adverse events (TEAEs) and disease-specific clinical response and remission after induction therapy, one year of treatment and during 12 months of follow-up.

Results: Both group were comparable according to age, sex, duration and type of disease, concomitant medications and smoking. 47 patients from R group and 68 from I were anti-TNF-alpha naïve. We did not observe differences between anti-TNF-alpha naïve and non-naïve patients in respect to clinical response and remission rate after induction and 1 year of treatment (R – 80.9% vs. 73.1% respectively; I – 79.4% vs. 74.1%). The relapse rate during 1 year follow-up was significantly higher in anti-TNF non-naïve patients