DOP078

Are IBD specialists aware of biosimilar monoclonal antibodies? Results from a survey among ECCO members

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Background: Monoclonal antibodies (mAb) are effective therapies in immune mediated inflammatory diseases (IMID), including inflammatory bowel disease (IBD). High cost for healthcare systems is a main limitation for the use of mAb in these conditions. Recently, 2 infliximab biosimilar mAb have been approved by regulatory agencies for all IMID indications, based on a randomized controlled trial (RCT) in rheumatoid arthritis, showing equivalence to the original mAb. No data are available for other indications. Current knowledge on the efficacy, safety and use of biosimilar mAb among gastroenterologists is unknown. We developed a web survey aimed at IBD specialists to evaluate their awareness of biosimilar mAb and readiness to use these therapies.
Methods: A 15-question anonymous web survey was conducted with the logistic support of ECCO. Randomly selected ECCO members were invited by to participate. Information on gender, job position, country and mAb experience were collected.
Results: Of 272 responders, 69% worked in a University Hospital, 33% as consultants, 88% autonomously prescribe mAb for >2 years. Two thirds were aware that biosimilar mAbs are not the same molecules as their originators (69%) and agreed that biosimilars should carry distinct International Nonproprietary Names. Most responders regarded cost-sparing (89%) as the main advantage of biosimilars, immunogenicity (69%) as their main concern, and estimated that post-marketing pharmacovigilance, well-designed RCT and further study of risk profile were needed (54%, 66%, 63% resp.). For prescription, 85% disagreed with automatic replacement of the originator with a biosimilar by a pharmacist, although 18% would support substitution for new prescriptions. Most clinicians thought that medical societies should promote information about biosimilars (median 66%), collaborate with health institutions to develop rules (78%) and guidelines (57%) on the use of biosimilars, and create multispecialty safety registries (80%). Most responders (73%) thought that patient organizations should be involved in these processes. Only 6% of responders thought that the originator and biosimilar mAb were interchangeable, although 28% would replace scheduled originator therapy with a biosimilar. If equivalence was shown by RCTs in IBD, 49% of responders thought a biosimilar should be first choice because of costs, although 27% thought the savings would be marginal. Most (63%) felt little or not confident in the use of biosimilar mAb.
Conclusions: IBD specialists are generally informed on biosimilars, but think they are not interchangeable with the originator, unless strong evidence is shown about similarity for each indication. Most clinicians do not feel confident on the use of biosimilars in clinical practice.

DOP079

Correcting iron deficiency anaemia in IBD: A pivotal phase 3 study of a novel oral ferric iron

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Background: Iron deficiency anaemia (IDA) is common in inflammatory bowel disease (IBD). Traditional oral ferrous (Fe2+) salts, are often poorly tolerated and may adversely affect IBD. Ferric (Fe3+) iron salts are well tolerated but poorly absorbed due to insoluble chelate formation in the gut. ST10 is a novel Fe3+ iron that remains in an absorbable state.
The aim of this study was to demonstrate the efficacy of oral ST10 over placebo in the treatment of IDA in subjects with quiescent IBD who have failed to respond to, or been intolerant to, oral ferrous salts. The primary endpoint was change in Hb from baseline to Week 12. Secondary endpoints included safety, disease activity and quality of life [Clintrials.Gov: NCT01340872/01352221].
Methods: Double blind randomised controlled trial of 120 IBD subjects with IDA (Hb 9.5–12.0 g/dL female, 9.5–13.0 g/dL male; and ferritin <30 μg/L). Subjects were randomised to receive oral 30 mg ST10 twice a day for 12 weeks or identical placebo. At the study end all available subjects were enrolled in a 52 week open label study. The study was approved by the relevant Ethics Committee and informed consent was obtained from all subjects.
Results: 128 subjects were randomised. Baseline Hb, age and gender were comparable in both groups. The pre-specified analysis plan included the first 120 subjects randomised (60 ST10, 60 Placebo; 67 CD, 53 UC). 101 (87% ST10, 82% Placebo) completed at least 12 weeks treatment. Mean Hb improved by 2.3 g/dL from 10.9 to 13.2 g/dL in the ST10 group and remained at 11.1 g/dL in the Placebo group. Difference between estimated means was 1.0 g/dL at 4 weeks, 1.8 g/dL at 8 weeks and 2.2 g/dL at 12 weeks, [$p < 0.0001$ for all 3 analyses, ANCOVA]. Hb increased to normal values in 65% of ST10 group and 10% of Placebo subjects.
Adverse events (AEs) were recorded in 58% of ST10 and 72% of the Placebo subjects. Gastrointestinal AEs were observed in 38% and 40%, respectively. In the ST10 group the most common AEs were abdominal pain (10%), diarrhoea (7%), constipation (6%) and nasopharyngitis (4%). Study medication discontinuation due to AEs in 8 ST10 and 5 Placebo subjects. There was 1 serious AE in the ST10 and 2 in the Placebo group. AE data and IBD activity scores suggested that ST10 did not increase IBD symptoms.
Conclusions: At 12 weeks of treatment ST10 gave a highly statistically significant, and clinically relevant rise in Hb of 2.2 g/dL and increase of 1.0 g/dL by 4 weeks. Over the study period ST10 was well-tolerated (87% completing 12 weeks of treatment) and did not exacerbate IBD symptoms.
ST10 may provide an alternative to IV iron in anaemic patients intolerant or unsuitable to be treated with existing oral iron therapies.

DOP080

Increasing colectomy rates over time in ulcerative colitis and the impact of thiopurines: A nationwide cohort study

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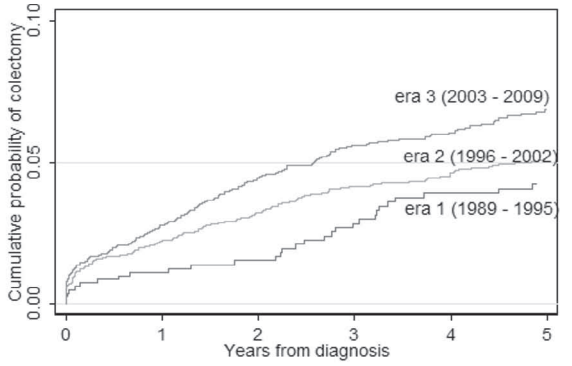
Background: The efficacy of thiopurines for the treatment of ulcerative colitis (UC) is well established but whether they alter the long-term need for colectomy remains unknown. Our aim was to determine the changing trends in colectomy over time using the Clinical Practice Research Datalink (CPRD).
Methods: We conducted a nationwide cohort study using electronic primary care records in the UK. We identified incident cases of UC between 1989 and 2009 in the CPRD which contains prescribing and clinical data for 8% of the UK population and is a validated research database. We divided the cohort according to year of diagnosis: era 1–1989 to 1995, era 2–1996 to 2002, era 3–2003 to 2009. We performed survival analysis using the Kaplan–Meier method to obtain the 5 year rates for total colectomy and thiopurine (azathioprine and mercaptopurine) prescribing from our cohort. Log-rank testing was used to compare survival between groups.

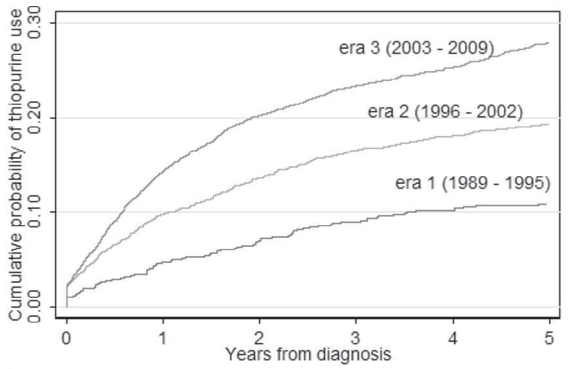
Results: Overall, 8673 patient met our inclusion criteria of which 479 went on to have a total colectomy during follow up. 52% of patients were male and the median age of the cohort was 46 years. The overall 5 year colectomy rate over the whole period of follow up was 5.9% (95% CI: 5.4–6.5%). Colectomy was more common in males (62.2% vs 37.8%, $p < 0.001$). The 5 year colectomy rate was 4.2%, 5.1% and 6.9% for era 1, era 2 and era 3 respectively ($p = 0.001$ via Log-rank testing) (Figure 1). The 5 year probability of receiving a thiopurine was 10.9%, 19.3% and 27.9% for era 1, era 2 and era 3 respectively ($p < 0.001$, via Log-rank testing) (Figure 2). Furthermore, the proportion of early thiopurine users within the first year of diagnosis increased by era and was 4.6%, 9.6% and 13.4% (χ^2 $p < 0.001$).



Number at risk

era = 1	821	749	698	649	606	573
era = 2	2848	2568	2402	2235	2097	1980
era = 3	5004	3922	3014	2259	1619	1044

Figure 1. Colectomy by era.



Number at risk

era = 1	821	719	658	609	566	532
era = 2	2848	2365	2137	1947	1800	1681
era = 3	5004	3486	2564	1874	1320	834

Figure 2. Thiopurine by era.

Conclusions: Rates of colectomy in the UK have increased by era of diagnosis despite the earlier and increasing use thiopurines over the same time period. This is in contrast to findings in Crohn's disease and to that of other studies in UC. Further study is proposed to explain these trends.

DOP081

Long-term natural history of postoperative recurrence in patients on preventive treatment with azathioprine

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Background: The postoperative recurrence (POR) in Crohn's disease (CD) occurs in >75% within the first year after intestinal resection if no preventive treatment is started. Nowadays, azathioprine (AZA) is the most prescribed drug to prevent POR, but its long-term efficacy is unknown and no recommendations about POR monitoiring beyond the first year after surgery are available.

Aims: To evaluate the long-term clinical and endoscopic outcomes of CD after intestinal resection and early preventive therapy with AZA.

Methods: From an specific database in which all patients with CD who underwent resection with anastomosis at our institution since 1998 were prospectively included and followed, we identified those who initiated AZA (associated or not with metronidazole or 5-ASA) within the first month after surgery and with at least a follow-up of 3 years. Endoscopic recurrence (ER) was defined as a Rutgeerts score >1 and clinical recurrence (CR) as the development of symptoms that required changes in the treatment for CD. Surgical recurrence (SR) was considered as the need for surgery. We defined a Combined Outcome as any combination of the following events: rescue with biological agents, CR or SR.

Results: 189 patients were included of whom 57% male, 64% active smokers at the time of surgery, 54% penetrating behaviour. 58% of patients had ER after a median of 22 months (IQR 11.5–44.5). The cumulative probability of ER was 35%, 48% and 59%, the probability of CR was 18%, 27 and 34% and for SR was 3% 10% and 16%, at 3, 5 and 10 years, respectively. Only active smoking after surgery was associated with POR. The risk for the combined outcome was 21%, 23% and 46% at 3, 5 and 10 years. In patients without ER at the first endoscopic control, the probability at 3, 5 and 10 years of CR was 14%, 22% and 27%; for SR 6%, 9% and 9%; and for the combined outcome of 13%, 26% and 38%, respectively. In the log-rank analysis, the cumulative probability of CR or SR was significantly higher among those patients with early ER (at the first control after surgery – $p = 0.044$ and $p = 0.05$).

Conclusions: The use of AZA after surgical resection in Crohn's disease is associated with a low rate of CR and SR, probably because of early introduction of rescue therapy with biological in those patients with advanced endoscopic lesions. Patients without early ER, although at lower risk have a slow but steady increase in the development of ER and CR upon time, suggesting that periodical assessment of POR should be kept indefinitely.

DOP Session 10 – Clinical practice

DOP082

Identified areas of need to enhance evidence-based inflammatory bowel disease management and patient care

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Background: The continual publication of data impacts the practice of evidence-based medicine in inflammatory bowel disease (IBD) management. Acting on evidence to make treatment decisions is the goal, yet many busy clinicians cannot achieve it. In September 2013, a group of 6 global gastroenterology leaders (GLs) conducted a systematic clinical appraisal of the medical literature and compared data to clinical practice patterns of gastroenterologists. The goal was