group can be rescued with co-therapy. These data demonstrate that co-therapy is a safe and effective treatment option in the DGH setting.

**Competing interests** None declared.

### PWE-251

**DISTRICT GENERAL HOSPITAL EXPERIENCE OF OPTIMISING TREATMENT OUTCOME ON THIOPURINES BY CO-PRESCRIPTION OF ALLOPURINOL IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

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S Cherian,* A Gera, V Saxena, A Loganayagam. Department of Gastroenterology, Queen Elizabeth Hospital NHS Trust, London, UK

**Introduction** Numerous patients, especially those with elevated thiopurine methyltransferase (TPMT) activity, selectively methylate thiopurine drugs, generating high levels of methylated metabolites and low thioguanine nucleotides. This pattern of metabolism is related to hepatotoxicity and non-response to therapy. Co-prescription of thiopurines (TP) (at 25% of standard dose) with allopurinol (xanthine oxidase inhibitor) seems to avoid this problem, optimising both metabolite profile and clinical response. British experience on the use of this combination therapy (CT) remains limited. In this study we report a district general hospital (DGH) experience for the indications of toxicity (mainly hepatic) and very high TPMT activity in patients with inflammatory bowel disease (IBD).

**Methods** Retrospective notes review of patients at a district general hospital treated with CT using 25% dose of TP and 100 mg allopurinol was undertaken. Particular attention was paid to whether CT overcame the specific problem that prevented thiopurine monotherapy.

**Results** 15 patients (age 24–77 yrs, male=6, Crohn’s=6, ulcerative colitis=9) were identified. All 15 patients were on an oral five amino salicylic acid preparation and 12 patients had previously been on a TP. Two patients with fibrotic stricture and one patient with hepatic steatosis were excluded from the analysis. Of those patients receiving co-prescription for side effects (four hepatotoxicity and five others: rash, nausea, headache, fatigue), 78% were able to tolerate CT with complete resolution of liver function abnormality where relevant. Clinical remission was achieved in 100% of the patients who tolerated CT. In the three patients where CT was commenced for very high TPMT activity, 1 (33%) developed non-specific side effects (headache, nausea) leading to discontinuation of therapy and 2 (67%) achieved clinical remission.

**Conclusion** CT with low-dose TP and allopurinol avoids hepatotoxicity and improves chances for clinical remission. CT may also prevent other side effects. CT should be fully utilised in a DGH for hepatotoxicity and other side effects. Using CT as first line in those with high TPMT activity remains questionable and requires further scrutiny in a prospective study.

**Competing interests** None declared.

### PWE-252

**TRENDS IN IMAGING AND IMPACT OF DIAGNOSTIC MEDICAL RADIATION IN INFLAMMATORY BOWEL DISEASE**

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S Chatu,* A Poullis, R Holmes, R Greenhalgh, R Pollok. 1Department of Gastroenterology, St George’s Hospital, London, UK; 2Department of Radiology, St George’s Hospital, London, UK

**Introduction** Increasing use of diagnostic imaging in inflammatory bowel disease has led to concerns about the malignant potential of ionising radiation in a cohort that is already predisposed to malignancy. The aim was to quantify radiation exposure in inflammatory bowel disease patients referred from primary care, determine predictors of high exposure and evaluate temporal changes in imaging at a single centre.

**Methods** Patients with a diagnosis of Crohn’s disease (CD) or ulcerative colitis (UC) were prospectively recruited from clinic between January 2011 and June 2011. Demographic and clinical data were obtained by scrutinising medical records. The number and type of imaging procedures was obtained from the radiology database which was first set up in 1990, we only included those diagnosed after the database was initiated. The effective dose of radiation from each test was estimated from published standardised tables. Cumulative effective dose (CED) was calculated for each subject by summing the effective doses of radiation from diagnosis until end of study period which was June 2011. Cox regression analysis was performed to assess for factors associated with potentially harmful levels of ionising radiation defined as total CED >50 mSv.

**Results** The cohort included 415 patients. Median disease duration for Crohn’s disease and ulcerative colitis was 8.3 and 7.7 years. Median total CED was 7.2 mSv (IQR 3.0–22.7) in Crohn’s disease and 2.9 mSv (IQR 0.5–8.9) in ulcerative colitis patients. A total of 32 patients (8%) received a CED >50 mSv. Multivariate analysis revealed a history of IBD related surgery had a HR of 7.7. During the study period use of abdominal CT increased by 350%.

**Conclusion** About 1 in 10 patients were exposed to potentially harmful levels of ionising radiation therefore strategies to reduce radiation exposure are needed. While there was an increased uptake of both MRI and small bowel ultrasound over the past 20 years use of CT also increased substantially.

**Competing interests** None declared.

### PWE-253

**ADALIMUMAB IMPROVES HEALTH-RELATED QUALITY OF LIFE FOR 52 WEEKS IN PATIENTS WITH ULCERATIVE COLITIS**

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1W J Sandborn, 2G Van Assche, 3R B Thakkar, 4A Lazar, 4M Kron, 3M Yang, 5S P Patel,* 3J Cho, 3P M Mulani. 1UCSD, La Jolla, California, USA; 2U Hosp Gastuisberg, Leuven, Belgium; 3Abbott, Abbott Park, Illinois, USA; 4Abbott, Ludwigshafen, Germany; 5Abbott, Maidenhead, UK

**Introduction** We investigated effects of adalimumab (ADA) maintenance therapy on health-related quality of life (HRQOL) through 52 weeks (wks) in patients (pts) with ulcerative colitis (UC).

**Methods** 494 pts with moderate to severe UC (Mayo score, 6–12 points; endoscopic subscore, 2–3 points; anti–tumour necrosis factor [anti-TNF]–naive and anti-TNF–experienced [40.5%]) who had failed conventional therapy were enrolled in a 52-wk, randomised, double-blind, placebo (PBO)-controlled maintenance trial. ADA-treated pts received induction therapy (160/80 mg @ Wks 0/2) and 40-mg every-other-week (eow) maintenance therapy. Pts with inadequate response could switch to open-label eow therapy after Wk 12 and subsequently to weekly therapy. HRQOL was measured by Inflammatory Bowel Disease Questionnaire (IBDQ). Intent-to-treat population was analysed. IBDQ response rates were compared between treatment groups using Cochran-Mantel-Haenszel test stratified for prior anti-TNF use whereas χ² test was used in anti-TNF-naive pts. Non-responder imputation was used for response variables. For change of IBDQ scores, ANCOVA model with treatment and prior anti-TNF status as factors and baseline value as covariate was used. Missing values were imputed through last observation carried forward (LOCF).

**Results** Significantly more ADA-treated pts were IBDQ responders (increase in IBDQ score ≥16 points from baseline) throughout Wks
8, 32, and 52 compared with PBO. Mean changes from baseline IBDQ scores were consistently greater for ADA- vs PBO-treated pts (Abstract PWE-253 table 1). In anti-TNF–naive pts, improvements from baseline for IBDQ were 34±38 and 22±57 at Wk 8 (p<0.002), 33±43 and 24±43 at Wk 52 (p=0.03), and 33±44 and 25±42 at Wk 52 (p=0.02) for ADA and PBO, respectively. IBDQ responder rates were 68% and 52% at Wk 8 (p=0.004), 42% and 27% at Wk 52 (p=0.006), 32% and 21% at Wk 52 (p=0.040) for ADA and PBO, respectively, among anti-TNF–naive pts.

Abstract PWE-253 Table 1 Improvement in IBDQ

<table>
<thead>
<tr>
<th></th>
<th>PBO, (N=246)</th>
<th>ADA, (N=248)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBDQ at baseline (mean± SD)</td>
<td>123±33</td>
<td>128±29</td>
</tr>
<tr>
<td>IBDQ (mean±SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>20±36</td>
<td>29±36*</td>
</tr>
<tr>
<td>Week 32</td>
<td>20±41</td>
<td>28±41*</td>
</tr>
<tr>
<td>Week 52</td>
<td>19±41</td>
<td>27±42*</td>
</tr>
<tr>
<td>IBDQ response, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 8</td>
<td>112 (45.5)</td>
<td>144 (58.1)†</td>
</tr>
<tr>
<td>Week 32</td>
<td>54 (22.0)</td>
<td>86 (34.7)†</td>
</tr>
<tr>
<td>Week 52</td>
<td>40 (16.3)</td>
<td>65 (26.2)†</td>
</tr>
<tr>
<td>Weeks 8, 32, and 52</td>
<td>30 (12.2)</td>
<td>58 (23.4)†</td>
</tr>
</tbody>
</table>

*p<0.05, p Values from ANCOVA with treatment and prior anti-TNF status as factors and baseline value as covariate.
†p<0.05, p Values from Cochran-Mantel-Haenszel test stratified for prior anti-TNF use.

Conclusion For pts with moderate to severe UC who failed conventional therapy, ADA was more effective than PBO for inducing and maintaining improvements in HROQL, as measured by IBDQ through 52 wks.


PWE-254 IMPACT OF INDUCTION DOSING ON MAINTENANCE OUTCOME WITH ADAлимумаб IN CROHN'S DISEASE
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1 J-F Colombel, 2 P J Rutgeerts, 3 W J Sandborn, 4 W Reinisch, 5 E V Loftus Jr, 6 J Tang, 7 P F Pollack, 8 M Yang, 9 P M Patel, 10 B Huang, 11 J Chao, 12 M Mulani. 1Centre Hospitalier Universitaire de Lille, Lille, France; 2University Hospital of Gasthuisberg, Leuven, Belgium; 3University of California, San Diego, La Jolla, California, USA; 4Medical University of Vienna, Vienna, Austria; 5Mayo Clinic, Rochester, Minnesota, USA; 6Analysis Group Inc, Boston, Massachusetts, USA; 7Abbott Laboratories, Abbott Park, Illinois, USA; 8Abbott Laboratories Ltd, Maidenhead, Berkshire, UK

Introduction Two induction regimens of adalimumab are used in Crohn’s disease (CD): 160/80 mg or 80/40 mg at Weeks 0/2. We compared long-term efficacy for patients who received 160/80 mg vs 80/40 mg as induction therapy followed by eow maintenance therapy.

Methods Data were from two randomised, double-blinded, placebo-controlled efficacy and safety trials in moderate to severe CD. EXTEND, a 52-week study in patients with mucosal ulceration, used the 160-/80-mg induction regimen. CHARM, a 56-week study for maintenance of clinical remission, used the 80-/40-mg induction regimen. All patients who started with induction dose and were randomised to eow plus dropouts prior to Week-4 randomisation were included. Missing Crohn’s Disease Activity Index (CDAI) scores were imputed with both non-responder imputation (NRI) and last observation carried forward (LOCF). Remission (CDAI <150) and hospitalisation were compared between induction regimens. To incorporate the correlation between visits for a patient, a logistic regression with the patient-level random intercept using all the time points after Week 4 was constructed to compare likelihood of remission, controlling for baseline CDAI, fistula, prior use of an anti–tumour necrosis factor therapy, concomitant medications, CD duration, and other factors.

Results 70 patients in the 160-/80-mg group were compared with 336 patients in the 80-/40-mg group. Baseline characteristics were similar except for greater rates of rectal/anal CD in the 160-/80-mg group and greater use of concomitant steroids in the 80-/40-mg group. Compared with the 80-/40-mg group, the 160-/80-mg group had a greater percentage of time in remission from Week 0—52 (30% vs 25%; p<0.05, NRI), significantly fewer hospitalisations per patient (0.09 vs 0.25; p<0.05), and significantly fewer CD-related hospitalisations (0.07 vs 0.18; p<0.05). Patients in the 160-/80-mg group were significantly more likely to be in remission during Weeks 4 to 52 than were patients in the 80-/40-mg group after adjusting for baseline characteristics (adjusted OR 4.8; p<0.001). LOCF results for remission analysis were consistently similar. The 160-/80-mg regimen did not appear to lead to a higher rate of AEs.

Conclusion The 160-/80-mg induction regimen of adalimumab was associated with a greater likelihood of remission, more time in remission, and fewer hospitalisations during eow maintenance therapy compared with the 80-/40-mg regimen.


PWE-255 5-ASA ENHANCES DUOX2 EXPRESSION IN ACTIVE ULCERATIVE COLITIS: A RISK FOR COLORECTAL CANCER?
doi:10.1136/gutjnl-2012-302514d.255

1 T Macfa, 2 A Parker, 3 A Nijhuis, 4 T Boitsova, 5 S Patel, 6 J Jeffery, 7 Poulson, 8 J Lindsay, 9 A Silver. 1Centre for Digestive Diseases, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK; 2Digestive Diseases Clinical Academic Unit, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK

Introduction Colonic DUOX2 expression produces hydrogen peroxide, a reactive oxygen species (ROS), which is up-regulated in active ulcerative colitis (UC). Overproduction of hydrogen peroxide amplifies ROS-induced genetic damage and causes cellular transformation which may explain the increased colorectal cancer (CRC) risk associated with chronic UC. Mesoalazine (5-ASA) has been shown to be chemo-preventative for UC associated CRC and scavenges ROS. Here, we aimed to identify and investigate the effect of 5-ASA on DUOX2 expression using human rectal cancer cell lines and mucosal tissue biopsies.

Methods Mucosal biopsies were taken from 35 patients with UC and 24 patients with normal colons for in vivo experiments, and 24 patients with UC and 14 patients with normal colons for ex vivo experiments. Total RNA was extracted and quantitative real-time qPCR used to calculate expression of DUOX2. Cytometric bead array technology was used on ex vivo culture supernatants to measure cytokine profiles. In situ hybridisation for DUOX2 expression was performed on sections from eight matched pairs of non-inflamed/inflamed biopsies and five matched pairs of non-inflamed/inflamed dysplasia biopsies from UC patients. Human rectal cancer cells were