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CHANGING PATTERNS OF ANTIDEPRESSANT MEDICATION USE AMONGST INFLAMMATORY BOWEL DISEASE PATIENTS: A UK POPULATION-BASED STUDY

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Introduction Concern has been raised about long-term use of antidepressant medications (ADM) by the Royal College of Psychiatrists (RCPsych) in the general population.¹ Anxiety and depression, for which these medications are often used, is more common in Inflammatory Bowel Disease (IBD). However, little is known about patterns of ADM prescribing in this condition.

Aim To examine trends in prevalence, incidence and duration of ADM prescribing episodes among IBD patients in the UK compared to the general population and their use in keeping with national recommendations.

Methods Using Clinical Practice Research Datalink, a nationally representative research database, we identified IBD cases diagnosed from 2004 to 2016. A non-IBD comparison group was matched for age and sex. We selected medical record codes for the 8 most commonly used ADM, excluding tricyclics. We identified patients with an ADM code in that calendar year (prevalence) and the first prescription among non-prevalent users (incidence). We calculated the yearly median duration of prescribing episodes (days) and proportions on an ADM episode for more than 2 years.

Results We identified 12,397 cases of ulcerative colitis (UC), 5,297 cases of Crohn's disease (CD) and 46,481 individuals in the comparison group. Prevalence of ADM use was higher in IBD patients from 2004–16 than in people without. Between 2004–16 ADM prevalence use increased from 100 to 145/1000 person years (PY) for CD and 88 to 142/1000 PY for UC. ADM initiation rates remained stable for CD and UC at 25 to 24/1000 PY and 19 to 21/1000 PY respectively. Over time there was an increase in the median episode duration (211 to 234 days, coefficient 0.02, 95% CI -0.08–0.11).

In the latter study period, proportion of patients prescribed an ADM episode lasting at least two years was higher in IBD patients compared to controls (figure 1). Fifty-three percent of IBD patients received two or more ADM episodes.

Conclusion ADM initiation in IBD patients has remained stable. There is however a rising prevalence of ADM use and

Abstract P114 Figure 1 ADM episode of more than two years: IBD vs control

prescription duration. A greater proportion receives long-term prescriptions among IBD patients compared to the general population. These findings underscore the need to reassess ADM requirement and support cessation amongst IBD patients where indicated, in line with national recommendations.¹

REFERENCE

1. RCPsych Position statement on antidepressants and depression, accessed 01.12.2019 <https://www.rcpsych.ac.uk/improving-care/campaigning-for-better-mental-health/policy/position-statements/position-statements-2019>

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LOW GRADE DYSPLASIA PROGNOSIS IN THE 21ST CENTURY – A LARGE MULTI-CENTRE RETROSPECTIVE COHORT STUDY

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Introduction Recent advances in ulcerative colitis (UC) endoscopic surveillance such as high-definition imaging and greater chromoendoscopy (CE) use have led to an increase in detection and resection of visible dysplasia. An updated study of prognosis of low grade dysplasia (LGD) is needed to address uncertainty as to the accuracy of progression rates based on historical studies.

Methods This retrospective cohort study involved four UK IBD centres. Hospital pathology databases were searched between 1 January 2001 and 30 December 2018 to identify adult patients with UC who had their first LGD diagnosis diagnosed within the extent of colitis. Only patients followed up with at least one colonoscopy or colectomy by 30 August 2019 were included. The study end point was time to high grade dysplasia or cancer, i.e. advanced neoplasia (AN), or end of follow-up. Kaplan-Meier and Cox

	Cumulative incidence of advanced neoplasia % (number at risk)			
	At 1 year	At 2 years	At 5 years	At 10 years
Endoscopically resected visible LGD	2% (343)	3% (316)	6% (196)	14% (52)
Unresected visible LGD	19% (60)	25% (33)	38% (10)	38% (4)
Invisible LGD	10% (48)	24% (32)	36% (16)	45% (5)

Abstract P115 Figure 1 Kaplan-Meier plot of cumulative incidence of advanced neoplasia of LGD according to morphology and endoscopic resection

proportional hazards model survival analyses were performed.

Results 460 patients met the inclusion criteria and were followed up for a median of 4.1 years (2,2201 patient-years). 77% of patients had CE surveillance. Complete endoscopic resection was achieved in 94% and 64% of the polypoid and non-polypoid LGD respectively. Incidence rate of AN per 100 patient-years was 1.0 (95% CI 0.6–1.7) after endoscopic resection of polypoid LGD, 2.5 (95% CI 1.3–4.4) after resection of non-polypoid LGD resection and 8.9 (95% CI 6.0–12.6) if the LGD was unresected. Figure 1 demonstrates the cumulative incidence of AN according to LGD visibility and resectability. On multivariate analysis, predictors of AN progression were visible LGD of 1 cm diameter or more [Hazard ratio (HR) 2.5; 95% CI 1.4–4.45; $p=0.002$], multifocality [HR 1.8; 95% CI 1.1–3.2; $p=0.046$] and incomplete endoscopic resection, including invisible dysplasia [HR 5.8; 95% CI 3.3–10.1; $p<0.001$].

Conclusions This is the largest study this century to examine prognosis of LGD based on endoscopic features. Incidence of AN is low if visible LGD is endoscopically resected but large size, multifocality and co-existent invisible LGD increase this risk and should be considered when decision-making.

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EFFECTS OF FILGOTINIB ON CIRCULATING CYTOKINES AND WHOLE-BLOOD GENES/PATHWAYS IN PATIENTS WITH ACTIVE CROHN'S DISEASE

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Introduction A Phase 2 study of filgotinib (FIL), a Janus Kinase (JAK) 1-selective inhibitor, in moderate-to-severe Crohn's disease (CD; FITZROY) demonstrated significantly higher clinical remission rates compared to placebo at 10 weeks (Vermeire S. Lancet. 2017;389(10066):266–275), and an early decrease in systemic and mucosal inflammation biomarkers, which was more pronounced in endoscopic responders (Roblin X. ECCO, Vienna, Austria, 2018). We investigated the baseline (BL) correlation of whole-blood transcriptome pathway activities with clinical disease indices and circulating cytokines. The effect of FIL on changes in disease-related pathways in responders and nonresponders was also explored.

Methods PAXgene blood samples were collected from 104 patients with CD at BL and Week 10 (W10). RNA was sequenced (Illumina HiSeq 2500) after globin depletion (ThermoFisher GlobinClear). Differential gene expression analysis

was performed using limma R package and hallmark pathway activity scores were calculated using single sample gene set enrichment analysis. All correlations were performed using the Spearman method.

Results At BL, pathways with activity scores positively correlated with Simple Endoscopic Score for Crohn's disease (SES-CD) were immune (IL-6/JAK/STAT3, inflammatory response), metabolic, and reactive oxygen species (ROS). These were also positively correlated with markers of systemic inflammation (CRP, SAA, IL-6, and OSM) and epithelial turnover (IL-22, C4M2, and C3M). Ten weeks of FIL treatment led to significant decreases of these pathways in endoscopic responders (50% reduction in SES-CD), whereas there were no significant changes following placebo treatment. While interferon (IFN) response pathway scores showed weak correlation ($\rho < 0.2$) with SES-CD at BL, they were significantly reduced by FIL treatment, particularly in FIL responders.

Conclusions In whole blood, inflammation, metabolic and ROS pathways were reduced by FIL in endoscopic responders at W10, while reductions in IFN response pathways were observed in all patients regardless of endoscopic response.

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FILGOTINIB REDUCES MARKERS OF JAK1 SIGNALING IN CROHN'S DISEASE: CONCORDANCE WITH ENDOSCOPY AND HISTOPATHOLOGY

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Introduction Filgotinib (FIL) is a JAK1 inhibitor under phase 3 clinical evaluation for treatment of IBD. We conducted a post hoc analysis in patients (pts) with moderately to severely active Crohn's disease (CD) to assess the effect of FIL on markers of JAK1 signaling (STAT1/3 phosphorylation [pSTAT1/3]) within intestinal mucosa and their correlation to histologic/endoscopic indices (NCT02048618).

Methods Baseline (BL) and Week 10 (W10) biopsies were collected from predefined bowel segments. Within-subject matched biopsies (FIL, $n=42$; placebo [PBO], $n=18$) were scored for histologic and endoscopic disease activity. Machine learning (Visiopharmv.2019.06) was used to quantify %pSTAT1 and %pSTAT3 positive nuclei within epithelium (Ep) and non-Ep regions. Basal pSTAT levels from 182 non-diseased

Abstract P117 Table 1

pSTAT	BL MDA	W10 change	Ep			Non-Ep		
			FIL	PBO	P	FIL	PBO	P
pSTAT1	Low	Worsen	−0.168	−0.348	<0.05	−0.173	−0.394	<0.05
	High	Improve	0.436	0.286	NS	0.390	0.327	NS
pSTAT3	Low	Worsen	−0.115	−0.375	<0.005	−0.109	−0.382	<0.005
	High	Improve	0.449	0.241	<0.05	0.442	0.232	<0.05