were labelled as true positive (CRC within 0 to 6 months of the procedure), false negative (CRC within 6 to 36 months) and true negative (CRC beyond 36 months). The PCCRC-3 yr rate was calculated as: $\frac{\text{false negatives}}{\text{true positive} + \text{false negative}} \times 100\%$.

The PCCRC-3 yr rate was calculated for each year from 2006 to 2012. In addition, the rate in each colonoscopy provider was calculated, and organisations grouped using quintiles. PCCRC rates were calculated in relation to patient and tumour characteristics.

Results Between 2006 and 2012 1 08 908 colonoscopies followed by a diagnosis of CRC were identified. Of these, 93 240 (86%) were labelled true positive, 7781 (7%) were false negatives, and 7887 (7%) were true negative tests. There was a significant reduction in PCCRC-3 yr rates, from 8.6% in 2006 to 7.5% in 2012 (χ^2 for trend $p < 0.01$). There was variation in unadjusted, mean PCCRC-3 yr rate between NHS Trusts from 5% (SD $\pm 2\%$) in the highest performing quintile to 11% (SD $\pm 2\%$) in the lowest. PCCRCs were significantly associated with female sex, right-sided colonic lesions, inflammatory bowel disease and diverticular disease diagnosis, mucinous CRC and in individuals with metachronous CRC.

Conclusion There has been a significant reduction in PCCRC-3 yr rates from 2006 to 2012, likely to be related to improvements in colonoscopic quality: particularly improved caecal intubation and bowel preparation resulting in improved lesion recognition and removal. There appears to be unwarranted variation of PCCRC-3 yr rates across NHS trusts. Reasons for this variation need to be explored and subject to quality improvement projects. Evidence from this study can be used to help target those at highest risk of PCCRC.

REFERENCES

1. Morris EJA, et al. *Gut* 2014;**64**:1248–56.
2. Beintaris I, et al. *UEG J* 2017;**5**:P0436.

OWE-034 EVALUATION OF A NEW CARE PATHWAY TO REDUCE HOSPITAL ADMISSIONS FOR PRIMARY CONSTIPATION

Sandra Blythin*, Zoe Crook, Julie McAteer. *University Hospital Aintree, Liverpool, UK*

10.1136/gutjnl-2018-BSGAbstracts.368

Introduction HES data revealed 301 acute hospital admissions over 1 year in a single trust were assigned a primary diagnosis of constipation. This study evaluates a new patient pathway focused on reducing hospital admissions due to constipation, with the opportunity for rapid access to a new acute constipation clinic (ACC)

Methods 216 of the 301 patients were admitted to the trust via the Accident and Emergency Department (AED). The average length of stay was calculated as 3.3 days, totalling 713 bed days. This equates to £2 85 120 per annum, based on a local tariff of approximately £400 per day.

To reduce admissions/costs related to constipation within our Trust a pathway was proposed by the specialist physiotherapy clinicians. These patients would be managed and treated in the ACC.

Clinicians led a bid to an in-hospital initiative, resulting in funding of £16 000 for a 12 month study. This secured a staff member for 14.25 hours per week to develop, implement, organise and audit the pathway.

The pathway was formalised, see below, including the development of information leaflets for patients. Changes to practice and patient flow were introduced within AED for patients presenting with primary constipation. Administration staff were trained to liaise between AED and the ACC. Data was collected prospectively.

Abstract OWE-034 Figure 1 AED/ACC constipation pathway

Results Over the year, 70 patients were referred to the ACC using the new pathway, thereby avoiding hospital admission. This equates to a saving of 231 bed days per annum at the estimated cost of £92 400. Data showed that a number of patients were regular attenders at AED, 9 patients had more than 5 previous admissions with constipation.

Conclusions The study has confirmed the benefits of introducing a patient care pathway for patients presenting to the AED with primary constipation.

The introduction of this pathway provides AED staff with a safe, suitable and efficient treatment pathway for patients with constipation, reducing hospital admissions and bed stays.

The pathway allows patients to manage their symptoms in their own home with support from specialist clinicians, enhancing patient dignity. Although the majority of patients were discharged after this acute episode, the information gathered in the ACC identified patients requiring referral to the functional bowel clinic for ongoing, long term management. Further audit of this patient group will hopefully demonstrate a reduction in future AED attendances and admissions due to constipation.

ADTU-07 5-AMINOSALICYLIC ACID TARGETS COLORECTAL CANCER STEMNESS IN VITRO

^{1,2}Steven Dixon*, ¹Eleanor Mortenson, ²Tom Creed, ¹Ann C Williams. ¹University Of Bristol, Bristol, UK; ²UH Bristol NHS Foundation Trust, Bristol, UK

10.1136/gutjnl-2018-BSGAbstracts.369

Introduction The mechanism by which 5-aminosalicylic acid (5-ASA) reduces colorectal cancer risk in ulcerative colitis is not fully understood and appears to involve multiple targets. Although previously reported to target wnt signalling, the

functional consequence of inhibition is not fully understood. Using a 3-dimensional (3D) organoid model we report that 5-ASA can prevent the formation of adenoma and carcinoma derived spheroids and propose that it does so through targeting the cancer stem cells.

Methods Human colorectal cancer (CRC) and adenoma (CA) cell lines were seeded into Matrigel (Corning, USA), treated with 5-ASA (Sigma Life Sciences, UK) in culture medium and imaged at multiple timepoints. Z-stacks through the Matrigel hemispheres were analysed using an in-house MatLab (Mathworks, USA) programme to estimate organoid area. In parallel cells were also grown in T25 flasks and treated with 5-ASA and expression of β -catenin targets assessed by western blotting. Wnt/ β -catenin activity was assayed using a TOPflash TCF-luciferase construct in 24-well plates.

Results All cell lines tested formed organoids in Matrigel. 5-ASA slowed the growth of CRC and CA cell organoids in all lines tested at physiologically relevant concentrations (5 and 10 mM) when treatment was initiated 7 days after seeding into Matrigel. Importantly, treatment with 5-ASA within 24 hours of seeding at low doses (2 mM) prevented any organoid growth (figure 1). In these cultures, Wnt/ β -catenin signalling, active in the intestinal crypt stem compartment and constitutively active in the majority of CRC, was reduced in CRC cells by 24% (10 mM) – 38% (20 mM) and CA cells by 22% (10 mM) – 44% (20 mM) by treatment with 5-ASA. Furthermore expression of the colonic stem cell marker leucine-rich G-coupled receptor-5 (LGR5) and Wnt-targets c-Myc, Axin-2 and dephosphorylated β -catenin was suppressed in both CRC and CA cell lines by treatment with 5-ASA.

Abstract ADTU-07 Figure 1 Growth curve of AA/C1/SB/10c cells following treatment with 5-ASA within 24 hours of seeding into matrigel

Conclusions Here we demonstrate that 5-ASA impairs growth of CRC and CA in a 3D model. That 5-ASA arrests the growth of organoid if treated at the time of seeding suggests that 5-ASA may be affecting cell stemness. This is likely to be due to – at least in-part – reduced Wnt/ β -catenin activity. Further work is being undertaken to elucidate the mechanism by which of 5-ASA could target cancer stemness to inform on potential clinical trials of 5-ASA as a prophylactic agent for patients at high risk of CRC.

ADTU-08 INCIDENCE AND MANAGEMENT OF IMMUNOTHERAPY-INDUCED COLITIS IN A TERTIARY IBD CENTRE – CLINICAL PRACTICE DATA

T Gupta*, V Cheung, L Boddy, E Harrogate, I Liew, R Rudra, M Payne, M Middleton, O Brain. Oxford University Hospitals NHS Foundation Trust, Oxford, UK

10.1136/gutjnl-2018-BSGAbstracts.370

Introduction Checkpoint inhibitors are a novel anti-cancer therapy that are standard of care in metastatic melanoma, non-small cell lung and renal cancer.¹ CTLA-4 inhibitors (e.g Ipilimumab) and PD-1 inhibitors (Nivolumab, Pembrolizumab) can be used separately or in combination for melanoma, whereas singlet therapy is currently the norm for others. Their immune inhibition is non-specific, leading to a number of immune-related adverse events (irAEs) including colitis, hepatitis and pancreatitis.² Combination therapy is known to cause more irAEs than single-agent PD-1 inhibition. There are limited real-world clinical data describing the incidence and management of these GI irAEs.

Aims 1) To determine the incidence of GI irAEs in a tertiary oncology centre. 2) To analyse the management and outcome of GI irAEs within a tertiary oncology and IBD centre.

Methods Retrospective single-centre review. Melanoma, renal and lung cancer patients receiving Ipilimumab $\pm$ Nivolumab $\pm$ Pembrolizumab between Dec 2011 and June 2017 were identified from the oncology prescribing database. The electronic patient record was used to determine the incidence of GI side effects. Investigations, treatment, and outcome data were collated.

Results 272 patients who received immunotherapy were identified. There was a higher incidence of diarrhoea and hepatitis in those receiving simultaneous or sequential dual therapy versus monotherapy (Figure 1). The incidence of diarrhoea for dual therapy (n=18/29,62%) was in excess of that described in trial data (44%).³ Colitis requiring infliximab or colectomy was exclusively associated with ipilimumab therapy, with dual immunotherapy more likely to require infliximab (13%) versus monotherapy (4%). Colitis was generally associated with a raised CRP and low albumin. There was significant variability in symptoms, time of onset, and in management decisions.

Abstract ADTU-08 Figure 1 Patient outcomes (n=272)

Conclusions Dual therapy with CTLA-4 and PD-1 inhibitors may result in a higher incidence of colitis than described in clinical trials. Although guidelines exist,² there is no clear biological threshold for timing of therapy initiation and