

Results The most important clinical factor influencing patient outcome was the colorectal cancer itself, and hence there was no significant difference between five year OS (55%), TTP (62%) and PFS (52%). As expected the disease was most likely to recur in subjects with more advanced tumours (Duke's C $p = 0.04$) and male sex. However, irrespective of the tumour stages Duke's A-C, the most significant risk factor for tumour recurrence was the presence of anti-CEA CD4⁺ T cell responses, the majority of which were suppressed by Tregs ($p = 0.002$). The magnitude of these responses was greater in the group with disease recurrence ($p = 0.004$). Pre-operative responses to other antigens, including the tumour antigen 5T4, did not reflect outcome.

Conclusion The presence of pre-operative anti-CEA immune responses identifies patients most likely to experience CRC recurrence during the 5 year follow-up period. This relationship holds true irrespective of the tumour stage. This information might be used to direct adjuvant treatment strategies.

Disclosure of Interest None Declared.

PWE-152 SELECTIVE LOSS OF ONCOFOETAL ANTIGEN 5T4-SPECIFIC T CELL RESPONSE CORRELATES WITH PROGRESSION OF COLORECTAL CANCER

doi:10.1136/gutjnl-2013-304907.440

¹M Scurr, ²M Davies, ³S Phillips, ⁴R Hargest, ⁵A Christian, ⁶T Hockey, ⁷G Williams, ⁸A Gallimore, ⁹A Godkin. ¹*Institute of Infection and Immunity, Cardiff University;* ²*Department of Surgery;* ³*Department of Histopathology, Cardiff and Vale University Health Board, Cardiff, UK*

Introduction The human oncofoetal antigen 5T4 is expressed on many human carcinomas, including colorectal cancer (CRC) cells, but has limited expression on normal tissues making it an ideal target for cancer immunotherapy. Here, a significant loss of T cell response to 5T4 in patients with more advanced CRC has been identified.

Methods Lymphocyte samples obtained from HLA-typed CRC patients and healthy donor controls were cultured for two weeks with pools of overlapping 20mer 5T4 peptides, spanning the entire protein, before subsequent analysis for antigen specificity, as measured by the highly sensitive IFN- γ /IL-10 ELISPOT assay.

Results Positive 5T4-specific lines were identified in 79% (15/19) of CRC patients and all (11/11) healthy donors tested. Intriguingly, CRC patients respond to significantly fewer candidate epitopes and generate a lower magnitude of IFN- γ responses to 5T4. Furthermore this response diminishes with tumour advancement despite similar responses to the recall antigen PPD. The mechanism of loss of T cell response is independent of HLA-DR type or patient age, but depletion experiments indicate suppression by Foxp3⁺ regulatory CD4⁺ T cells. In addition, analysis of peripheral blood and tumour-infiltrating lymphocytes in the same cohort of patients revealed a marked suppressive phenotype in comparison to healthy age-matched controls.

Conclusion Effective anti-tumour immunotherapy will be reliant upon overcoming such regulation of tumour-specific T cell responses. These data support a rationale for re-stimulating 5T4-specific immune responses in CRC patients, and reducing tumour-induced immunosuppression to enhance immunotherapy.

Disclosure of Interest None Declared.

PWE-153 ASSOCIATION BETWEEN CONSTIPATION AND COLORECTAL CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES

doi:10.1136/gutjnl-2013-304907.441

¹A M Power, ²N J Talley, ³A C Ford. ¹*Leeds Gastroenterology Institute, St. James's University Hospital, Leeds, Leeds, UK;* ²*Faculty of Health, University of Newcastle, Callaghan, Australia*

Introduction Constipation is common in the community, and may affect survival adversely. An association between constipation and development of colorectal cancer (CRC) could be one possible explanation for this association. We performed a systematic review and meta-analysis examining this issue.

Methods We searched MEDLINE, EMBASE, and EMBASE Classic (through July 2012). Eligible studies were cross-sectional surveys, cohort studies, or case-control studies reporting the association between constipation and CRC. For cross-sectional surveys and cohort studies, we recorded number of subjects with CRC according to constipation status, and for case-control studies number of subjects with constipation according to CRC status. Study quality was assessed according to published criteria. Data were pooled using a random effects model, and the association between CRC and constipation was summarised using an odds ratio (OR) with a 95% confidence interval (CI).

Results The search strategy identified 2282 citations, of which 28 were eligible. In eight cross-sectional surveys, presence of constipation as the primary indication for colonoscopy was associated with a lower prevalence of CRC (OR 0.56; 95% CI 0.36–0.89). There was a trend towards a reduction in odds of CRC in constipation in three cohort studies (OR = 0.80; 95% CI 0.61–1.04). The prevalence of constipation in CRC was significantly higher than in controls without CRC in 17 case-control studies (OR = 1.68; 95% CI 1.29–2.18), but with significant heterogeneity, and possible publication bias.

Conclusion Prospective cross-sectional surveys and cohort studies demonstrate no increase in prevalence of CRC in patients or individuals with constipation. The significant association observed in case-control studies may relate to recall bias.

Disclosure of Interest None Declared.

PWE-154 IRON DEFICIENCY ANAEMIA AS AN INDICATOR OF MALIGNANCY - THE IDIOM STUDY

doi:10.1136/gutjnl-2013-304907.442

¹A Castro-Silva, ²Z A Sheppard, ³S L Surgenor, ⁴E J Williams, ⁵J A Snook. ¹*Gastroenterology Unit, Poole Hospital NHS Foundation Trust, Poole;* ²*Clinical Research Unit, Bournemouth University, Bournemouth, UK*

Introduction Iron deficiency anaemia (IDA) is common. It is of particular importance because about 10% of subjects with IDA over the age of 50 will have an underlying gastro-intestinal (GI) malignancy, often in the absence of other clinical pointers to the diagnosis. IDA is therefore an accepted indication for examination of the GI tract, generally through bidirectional endoscopy.

Investigation of IDA is labour-intensive however, and most examinations will not reveal significant pathology. The aim of this study was to determine whether simple and objective clinical variables can identify sub-groups of subjects with IDA who are at clinically useful extremes of risk for underlying malignancy – arbitrarily defined as < 1% for low risk and > 20% for high risk.

Methods A retrospective study of 720 subjects referred to a single IDA clinic between 2004 and 2012. All had confirmed iron deficiency, minor or no localising symptoms, and subsequent GI tract investigation. Recorded information included age, sex, haemoglobin concentration (Hb), mean cell volume (MCV), iron studies, and final diagnosis.

Results A total of 68 (9.4%) of the study population had a GI malignancy. In the model generated by logistic regression analysis, age (> 70 v < 71), sex (M v F) and Hb quartile were all predictive of the probability of underlying malignancy. The effects of these variables were cumulative.

Percentage of cases of GI malignancy in each subgroup (cases/number in subgroup):