	Schizophrenia (n=22)	Patients without schizophrenia (n=1453)	p value
Discontinuation due to side effects	4.5% (1)	13% (189)	p=0.34
Discontinuation due to non-compliance	0% (0)	4.9% (72)	p=0.62
Overall Sustained Viral Response (SVR)	81.8% (18)	54.2% (788)	p=0.09
SVR in Genotype 1	33.3% (2/6)	32.8% (199/555)	p=0.25
SVR in Genotype 2&3	100% (16/16)	82% (589/714)	p=<0.01

Abstract PWE-149 Figure

Introduction Treating hepatitis C with pegylated interferon alpha may induce or exacerbate psychiatric illness including depression, mania and aggressive behaviour. There is limited data regarding treatment in the context of chronic schizophrenia. We sought to establish the safety and efficacy of treatment of patients with a diagnosis of schizophrenia amongst patients attending treatment centres in Greater Glasgow

Methods Patient and treatment data collected on the Scottish hepatitis C database were retrospectively analysed according to the presence or absence of a diagnosis of schizophrenia. Combination antiviral therapy was defined as Interferon (pegylated or standard) and Ribavirin. Treatment outcomes including sustained viral response (SVR) rates, reasons for treatment termination and adverse events were documented

Results 5497 patients were recorded on the database, of whom 64 (1.2%) had a diagnosis of schizophrenia. Patients with and without schizophrenia were of similar age at diagnosis [median 34 (IQR 31–40) vs 36 (IQR 29–41) years, p = 0.85]. Patients with schizophrenia had higher rates of current or previous intravenous drug use [50/64 (78.1%) vs 3015/5433 (55.5%), p < 0.01] and prior alcohol excess > 21 units/week [25/64 (39%) vs 1211/5433 (22.2%), p = 0.02)]. More patients with schizophrenia had a diagnosis of cirrhosis [13/64 (20.3%) vs 589/5419 (10.86%), p = 0.02]. Of those patients who had attended at least one clinic appointment 1639/4415 (37.1%) of patients without schizophrenia commenced treatment versus 26/61 (42.6%) of patients with schizophrenia (p = 0.21). Patients with schizophrenia took almost three times as long to commence treatment after initial referral [median 1123 (IQR 531–2130) vs 421 (IQR 209–1086) days, p < 0.01], despite similar times from referral to first attendance [median 65 (IQR 36–141) vs 62 (IQR 35–130) days, p = 0.92] The treatment outcomes were as follows:

Conclusion Patients with stable schizophrenia are good candidates for hepatitis C treatment

Disclosure of Interest None Declared.

Neoplasia and cancer pathogenesis

PWE-150 "THE EARLY GROWTH RESPONSE GENES INDUCE APOPTOSIS IN COLON CANCER CELLS"

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Introduction The Egr familly (Early Growth Respone Genes) of zinc finger transcription factors, which consists of four members; Egr-1, –2, –3 and –4, have been proved to have dynamic functions in the regulation of cell growth and the immune responses.Moreover, in a number of malignancies-which is a cell growth and immune related process- it seems that Egr1 and 2 induce apoptosis leading to the inhibition of the tumour growth. The present study was designed to answer the question whether colon cancer cells undergo apoptosis when the EGR genes are exogenously introduced and if the presence of a mutant p53 can affect this apoptotic pathway.

Methods Two cell lines deriving from human colon cancer; one p53 negative (DLD1) and another p53 positive (HCT116) were transfected with Egr-1, –2 and –3 and a fluorescent protein which was the marker of the transfection. The transfected cells were incubated for 48 hours. Flow cytometry was used to create a pure population of transfected cells and 24hours later these cells were examined in the fluoroscopic microscope and compared with the controls.

Results We found that all three Egr members can suppress tumour cell growth suggesting that the function of Egr in the control of cell growth is not associated with the function of p53. In addition to the growth arrest, the transfected cells changed morphology to round shape indicating of senescence.

Conclusion This may suggest that Egr molecules are important to control the unwanted growth in response to malignant transformation. Our results not only demonstrated an important function of Egr molecules and also indicate the therapeutic potential for the treatment of tumour.

Disclosure of Interest None Declared.

PWE-151 CELL-MEDIATED IMMUNE RECOGNITION OF CEA IS ASSOCIATED WITH EARLY TUMOUR RECURRENCE FOLLOWING RESECTION OF COLORECTAL CANCER

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Introduction Colorectal cancer (CRC) is one of the commonest malignancies in men and women. Clinical staging is used to predict prognosis after resection. The interaction of the cancer with the adaptive cellular immune response plays an important role in disease pathogenesis, but this relationship may be compromised by a population of regulatory Foxp3$^+$ CD4$^+$ T cells (Tregs). Here, the 5 year post-operative clinical outcome was correlated with pre-operatively measured anti-tumour immune responses.

Methods Eighty patients with non-metastatic CRC, undergoing a resection with curative intent, were recruited over 24 months. CD4$^+$ T cell responses to tumour associated antigens (CEA and 5T4) were compared to control antigens (PPD and HA). The influence of immune regulation was measured by repeating the assays after *in vitro* depletion of Tregs. Clinical databases were interrogated for details, including morbidity and mortality data, and the five year overall survival (OS), time to progression (TTP), and progression free survival (PFS) was calculated. These parameters were compared to the original details of pre-operative anti-tumour immune responses.

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

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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-g/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

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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 colonoscopywas 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 Conclusions: 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

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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):