Recurrent Disease Relapse After Withdrawal of Dendritic Cells Imprint Pro-inflammatory Gut – relapse, 43.1% (19/44) required steroids and 88.6% (39/44) was lost when multivariate analysis was undertaken. Following CD (perianal OR 0.87 CI 0.09 – 7.01 p=0.03), but there was no association with disease location, phenotype, presence of perianal disease or those with a smoking history.

Conclusions Ustekinumab is effective in the treatment of moderate-severe CD in a treatment refractory RW cohort. In keeping with trial data, prior anti-TNF exposure was a negative predictor of remission and concomitant IM use did not alter clinical or biological outcomes.

P104 FREQUENT DISEASE RELAPSE AFTER WITHDRAWAL OF INFlixIMAB IN IBD PATIENT WITH SUSTAINED REMISSION
Hannah Gordon*, Jennifer Murray, Falguni Tailor, Sean Goh, James O Lindsay. Royal London Hospital, Whitechapel, UK

Introduction In the UK, NICE guidance recommends annual review of biologics, with withdrawal of therapy in all patients in remission. This study retrospectively evaluates disease course following withdrawal of infliximab in IBD patients with sustained remission.

Primary Outcome Relapse free survival.

Secondary Outcomes Identification of predictors of relapse and evaluation of response to future therapy.

Methods IBD patients from Royal London Hospital who ceased infliximab due to sustained remission were identified. The following information was obtained from electronic patient records: demographics, Montreal classification, immunomodulator use, clinician determined relapse, objective evaluation of disease activity within 3 months prior to treatment cessation and 6/12/18/24 months following cessation (CRP>5, calprotectin>50, endoscopic, radiological), steroid use at relapse, subsequent biologic use and outcome Analysis was undertaken for total IBD, CD and UC. Survival analysis and logistical regression was calculated using SPSS®.

Results 75 patients were identified. CD:UC = 43:32; F:M = 34:41, median age = 31.3 years (IQR 41.15–40.75), median duration of follow up = 21.1 months (IQR 11.1–44.2), Asian:Black:Caucasian:Unknown = 16:3:47:9. The median relapse free survival for CD was 12.4 months (IQR 10.4–14.4) and for UC was 18.2 months (IQR 10.5–25.9). Relapse rates for patients who had completed follow up for each time point are presented in table 1:

In univariate analysis, perianal disease and L3 disease were negatively associated with relapse at 1 year for patients with CD (perianal OR 0.87 CI 0.09–0.81 p=0.03 and L3 OR 0.18 (comparator L1) CI 0.04–0.87 p=0.03). However significance was lost when multivariate analysis was undertaken. Following relapse, 43.1% (19/44) required steroids and 88.6% (39/44) restarted a biologic, 69.2% (30/44) restarting infliximab. Of those who restarted infliximab, 56.7% (17/30) responded to standard therapy, with 10% (3/30) requiring dose escalation. 33.3% (10/30) required alternative therapy.

Conclusion Within 24 months of cessation 76.5% patients relapsed. The majority of these restarted a biologic. However, only 56.7% patients who restarted infliximab responded to standard dose. With additional costs of newer biologics and morbidity of disease flare and steroid use, routine withdrawal of TNF antagonists should only occur after careful consideration.

P105 DENDRITIC CELLS IMPRINT PRO-INFLAMMATORY α4β7 +CLA+ T CELLS WITH POTENTIAL FOR GUT AND SKIN HOMING
1,2Hannah Gordon*, 1Inva Hoti, 1Katherine Wichmann, 1,2Theodore Saunders, 1Martha Wildemann, 1Eve Hornsby, 1Neil E McCarthy, 1,2James O Lindsay, 1Andrew J Stagg. 1Centre for Immunobiology, the Blizzard Institute, Queen Mary University of London, London, UK; 2Barts Health NHS Trust, London, UK

Background Integrin α4β7 induced on T cells during activation in intestinal lymphoid enables selective homing to the intestinal mucosa. Retinoic acid (RA) produced by the activating dendritic cell (DC) induces α4β7 and also inhibits the fucosyltransferase FUCT-VII that otherwise generates the selectin ligand CLA for skin homing. Therefore, antigen experienced T cells are generally either gut tropic (α4β7 +CL-A-) or skin tropic (α4β7-CLA+). We hypothesised the existence of additional ‘dual tropic’ (α4β7+CLA+) T cells, generated in the gut but with capacity to traffic to skin; such cells could explain skin inflammation in inflammatory bowel disease (IBD). Here, we report the generation of dual tropic cells in vitro and characterise the population in blood.

Methods Using flow cytometry, expression of α4β7 and CLA was assessed on ex vivo T-cells in whole blood and on proliferating cells generated by stimulation of naïve CD4+ T cells with monoclonal antibodies (anti-CD3/28/2), or with allogeneic colonic or monocyte-derived DC (moDC). Cultures were in the presence or absence of serum, monoclonal antibodies, RA receptor (RARα) antagonist, or conditioned media. Expression of FUCT-VII was assessed by qRT-PCR.

Results T-cells activated with antibodies expressed β7 but not CLA. Inhibition of RARα signalling and removal of serum reduced β7 expression and induced both CLA and FUCT-VII expression, suggesting endogenous RARα signalling shapes homing phenotype in these cultures. In contrast, activation with DC (colonic or RA-generating moDC), generated CLA+ T cells, including a population which co-expressed β7. Conditioned medium from DC stimulated cultures did not induce CLA on antibody-activated cells.

Activation by DC or in the presence of the RARα antagonist both led to increased expression of FUCT-VII. However,
the impact of activation by DC on homing profile was not identical to RAR blockade: DC-activated T cells expressed significantly higher levels of integrins α4, β7 and β1.

Dual tropic β7+CLA+ cells were present in blood at low frequency amongst antigen experienced T-cells in from both healthy donors and patients with active IBD. This population were enriched for cells producing pro-inflammatory cytokines (IFNγ, IL-17, TNFα) compared with β7-CLA-, β7+CLA- and β7-CLA+ cells.

Conclusion DC derived signals promote CLA expression to generate dual tropic T-cells in vitro, likely in part by attenuating RARα signalling. Dual tropic cells were also identified in blood. The pro-inflammatory nature of this population supports a possible role in intestinal or cutaneous IBD.

Introduction

The management of ASC needs early characterisation of factors predictive of outcome to allow appropriate patient counselling and stratification for second-line therapy or surgery. Travis et al (1996) predicted colectomy rates during same admission on basis of Day 3 stool frequency and CRP. Dinesen et al (2010) suggested that the number of additional Truelove and Witts’ (TW) criteria (fever, tachycardia, anaemia or CRP elevation) on admission predict colectomy rates. Following this Corte et al (2015) shown that UCEIS at baseline predict adverse outcomes (need for rescue therapy, Colectomy and readmissions). We compared the predictive accuracy of TW criteria on admission with a validated endoscopic scoring system (UCEIS), and with accepted Day 3 criteria.

Methods

Cases of ASC were retrospectively evaluated. Number of TW criteria, UCEIS, inpatient medical therapy, same admission outcome and follow up were recorded. Pre-specified end-points included rescue therapy, colectomy during same admission and colectomy within 1 year of follow up.

Results

Consecutive 131 admissions (117 patients) between 2015–9 were analysed. All satisfied modified TW definition of ASUC. Sixty-eight patients (58%) were female, index presentation 38 (29%), median age at presentation 40 years (16–76), median disease duration 1 year (1–43), median follow up 23 months (1–49). Seventy-one (54%) received rescue therapy (ciclosporin 35/71 and anti-TNF 36/71). Colectomy rates were 15% (19/131) during same admission and 26% (30/117) within 1 year of follow up. Outcomes were stratified...