P015 T H A L I D O M I D E IN LUMINAL AND FISTULISING CROHN’S DISEASE RESISTANT TO STANDARD THERAPIES

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Background and Aim: Thalidomide has been shown to be an effective treatment in Crohn’s disease (CD). We retrospectively assessed the efficacy and tolerability of thalidomide in refractory CD patients.

Methods: Twenty-five patients with CD (eight luminal, 11 fistulising, 4 luminal and fistulising, 2 perianal ulcerating) refractory to standard therapy, including infliximab, were treated for a mean of 32 weeks. All patients had active luminal disease with a Crohn’s Disease Activity Index (CDAI) >200 and/or draining fistulising disease. Thalidomide was started at a dose of 30mg or 100mg at night and increased stepwise if tolerated. Retrospective "estimated" CDAIs were assessed at baseline and at end of follow-up.

Clinical response was defined as symptomatic improvement and a reduction in the 'estimated' CDAI of >100 points, >50% reduction in draining fistulas or clinical improvement in perianal ulcers. Clinical remission was defined as symptom resolution and an 'estimated' CDAI <150, complete fistula closure, or complete ulcer healing.

Results: Six of eight patients treated for luminal disease responded to thalidomide at a median follow-up of 12 months (3 clinical responses, 3 clinical remissions). The median reduction in ‘estimated’ CDAI was 212 points (p<0.005). Nine of eleven patients with active fistulising disease responded to thalidomide (3 remissions). The four patients treated for both luminal and fistulising disease had fistula response. Three of them had a response in luminal disease activity. One of two patients with ulcerating perianal disease responded. Three of seven steroid-dependent patients discontinued steroids. Twelve patients discontinued treatment because of adverse effects (3 sedation; 2 abdominal pain; 1 leucopenia; 6 neuropathy).

Conclusion: Thalidomide is an effective short to medium term treatment in selected patients with refractory luminal and fistulising CD. Its long term use is limited by toxicity.

P016 RECURRENT PROLONGED ANTIGEN ENCOUNTERS ARE NECESSARY FOR 6-MP INDUCED CLONAL DELETION OF ANTIGEN-SPECIFIC MEMORY T-CELLS IN VIVO


Introduction: We previously demonstrated that the delayed onset of effect of Azathioprine/6-MP may be due to their inability to suppress effector functions of activated T-cells. However, the mechanism of their eventual effect remained obscure.

Aim: To test the effect of 6-MP on T-cell Ag-specific responses.

Methods: Balb/C mice were immunized simultaneously with HEL/IFA and Ovalbumin/IFA. After a 4 week interval, one group was treated daily with i.p. 6-MP and the other with vehicle only. Both groups continued to receive bi-weekly i.p immunizations with HEL antigen only. Mice were sacrificed after 4 or 20 weeks of treatment. Proliferation of CD4+ splenocytes to HEL, Ovalbumin, or medium was determined by CFSE dilution.

Results: CD4+ memory response to HEL and Ovalbumin was similar among mice sacrificed after 4 weeks, regardless of 6-MP treatment. However, after 20 weeks, the CD4+ memory response to HEL was markedly decreased in 6-MP treated mice compared to mice treated with vehicle only (% proliferation 7.6±6.3 vs. 23±7.5, P<0.01). Importantly, the memory response to Ovalbumin was not different between 6-MP treated or un-treated mice (% proliferation 22±3.9 vs. 29±6.8, P=NS). Intriguingly, the spleen weight of the 20 weeks 6-MP treated mice was lower than the spleen weight of untreated mice (115±9.9g vs. 150±12g, P<0.05), and the total number of splenocytes was reduced (35±1.2×10^6 vs. 58±4.4×10^6 cells, P<0.01).

Conclusions: These data suggest that the onset of suppression of inflammation by 6-MP, is associated with deletion of T-cell memory towards repeatedly encountered cognate antigens and may thus allow to manipulate these responses.

P017 SUSPECTED ACUTE ILEITIS: A PROSPECTIVE DIAGNOSTIC PROTOCOL


Introduction and Aim: Suspected acute ileitis (SAI) is an ill-defined clinical condition with multiple possible causes. Diagnostic workup of patients presenting in the Emergency Room with suspected acute ileitis has rarely been standardized. We tried to evaluate the incidence of SAI in our setting, describe its causes, and suggest a protocol to evaluate and follow such patients.

Methods and Materials: We defined SAI as a clinically compatible picture (abdominal pain, diarrhea, fever ... ) with at least one confirmatory imaging technique (CT or ultrasound). We prospectively studied all patients seen in the Medical Emergency Room of our hospital from March 2005 to September 2006, finally discharged with a presumptive diagnosis of SAI. We evaluated such patients according to a preestablished protocol, including ileocolonoscopy.

Results: We prospectively analyzed 42 cases (73,1% female). Mean age was 33±15 years. Infectious causes explained 45.2% of the cases; the most frequent microorganism was Yersinia spp (19% of total). Gynaecologic diseases were the cause of 14.3% of the total cases initially diagnosed as SAI, representing a 19% of female cases. The final diagnosis in 16.7% was Crohn's disease. Only 9.5% of cases remained undiagnosed after completing the protocol. Predominant extraabdominal symptom was fever (47,6%). The most prevalent epidemiological risk factor was the ingestion of raw fish (26,2%).

Conclusions: The incidence of SAI is 0.03% of the total patients assisted in the Emergency Room. A protocolized study of this ill-defined condition, leads to a definitive diagnosis in more than 80% of the cases. The most common cause of ileitis in our setting is infection. Approximately 20% of female cases finally correspond to gynaecologic diseases. Although AI is by definition an acute presentation, in more than 15% of cases an inflammatory bowel disease is finally diagnosed. Disclaimer: part of this series of patients was presented at the UEGW 2006.

P018 CERTOLIZUMAB PEGOL IS EFFECTIVE IN PATIENTS REGARDLESS OF CRP LEVEL AND DISEASE DURATION: DATA FROM PRECISE 2


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Introduction: Certolizumab pegol, a PEgylated Fab' fragment of humanised anti-tumour necrosis factor (TNF) monoclonal antibody, is in advanced development for the treatment of Crohn's disease (CD). The PRECiSE 2 trial showed that certolizumab pegol rapidly induced and maintained response and remission in patients with active CD (CD Activity Index (CDAI) score 220—450 points). Patients received induction treatment (certolizumab pegol 400mg, Weeks 0, 2, 4) and responders (patients with at least 100-point decrease in CDAI) were randomised to certolizumab pegol 400mg or placebo 4-weekly, Weeks 8—24.

Methods: Efficacy data from PRECiSE 2 were analysed according to C-reactive protein (CRP) plasma concentration and disease duration.

Results: At Week 6, 64% of patients (428/668) responded to induction treatment. Of these 428 patients, 213 had a baseline serum CRP concentration of at least 10mg/L. Maintenance of response at Week 26 in this cohort was 62% and 34% in the certolizumab pegol and placebo groups, respectively (p<0.001). These response rates were very similar to overall response rates; 63% vs 36% (p<0.001). Trends were similar for maintenance of remission (CDAI score equal or less than 150). Week 26 response and remission rates were significantly greater with certolizumab pegol than with placebo irrespective of disease duration. Maintenance of response and remission at Week 26 with certolizumab pegol was inversely correlated with time since CD diagnosis. In patients recently diagnosed (1 year or less), 89.5% maintained a response at Week 26 compared with 57.3% of patients diagnosed for at least 5 years. A similar pattern was observed for remission (68.4% vs 44.3%, respectively).

Conclusions: Certolizumab pegol was significantly better than placebo in maintaining response and remission in patients with CD, for all patients and those with a high CRP concentration, and regardless of disease duration. However, these data suggest better outcomes in patients treated soon after diagnosis.

P019 SUBCUTANEOUS CERTOLIZUMAB PEGOL IS EFFECTIVE IN PATIENTS WITH PRIOR INFLIXIMAB EXPOSURE, OR CONCOMITANT IMMUNOSUPPRESSANT OR GLUCOCORTICOID TREATMENT: DATA FROM PRECISE 2


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Cortolizumab pegol, a PEgylated Fab' of a humanised anti-tumour necrosis