Methods: Since 1991, incident IBD cases in the South-Limburg (SL) area, The Netherlands, are included in our population-based IBD-SL cohort. The natural disease course was compared between adult-onset UC (i.e. <60 years of age at diagnosis) and elderly-onset UC (i.e. $\geqslant$60 years of age at diagnosis) in terms of progression of disease extent, use of immunosuppressive or anti-TNFα agents, hospitalisation and colectomy. Also long-term response to immunosuppressive and anti-TNFα treatment was assessed. Data were analysed with a Kaplan–Meier survival curve, and hazard ratios (HR) of age at diagnosis were calculated using a Cox regression model, while correcting for confounders.
Results: In total, 373 UC patients with elderly-onset (EO) and 1288 with adult-onset (AO) were included. Median follow-up was 7.1 years (IQR 3.7–13.5) and 9.0 years (IQR 4.6–15.2), respectively. The proportion of elderly in newly-diagnosed UC patients increased over time (9.2% to 17.4%, r2 = 0.51, p < 0.01). In elderly, more left-sided disease (56.7% vs. 45.3%, p < 0.01) and less rectal disease (26.3% vs. 36.4%, p < 0.01) were observed at diagnosis. The risk of hospitalisation was higher in EO patients (HR 1.38; 95% CI 1.10–1.73), while the risk of more hospitalisations (HR 1.10; 95% CI 0.75–1.60), the risk of colectomy (HR 0.96; 95% CI 0.61–1.51), and the risk of progression of disease extent (HR 1.00; 95% CI 0.74–1.35) did not differ between groups. EO patients were less likely to receive immunosuppressive (HR 0.66; 95% CI 0.50–0.87) or anti-TNFα treatment (HR 0.42; 95% CI 0.25–0.72) (Figure).
Risk of treatment failure was comparable (HR 1.10; 95% CI 0.69–1.74 and HR 1.38; 95% CI 0.58–3.24, respectively) between groups.
Conclusions: In this population-based UC cohort, elderly-onset UC behaved differently compared to adult-onset UC, reflected by a reduced use of immunosuppressive and anti-TNFα treatment, without consequent increased need for multiple hospitalisations or colectomy.

OP006

Personalized thiopurine dosing based on TPMT genotyping reduces leucopenia occurrence and results in cost-savings in IBD patients. Results from a randomized trial in the Netherlands

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Background: More than 20% of inflammatory bowel diseases (IBD) patients discontinue thiopurine therapy due to severe adverse drug reactions among which leucopenia is one of the most serious. Thiopurine S-methyltransferase (TPMT) pharmacogenetics has been proven effective for optimizing azathioprine/mercaptopurine safety. Nevertheless, TPMT screening is used in clinical practice on a very limited scale. The aim of our study was to assess whether pre-treatment TPMT genotype-based dosing reduces the occurrence of leucopenia and whether this strategy is cost-effective.
Methods: We performed a randomized trial in thiopurine naïve IBD patients starting on thiopurine treatment [the Dutch "Thiopurine response Optimization by Pharmacogenetic testing in Inflammatory bowel disease Clinics" (TOPIC) study (ClinicalTrials.gov: NCT00521950)]. Patients were randomly assigned to pre-treatment screening for three common variants in TPMT (TPMT*2, *3A and *3C) or standard thiopurine treatment. Patients heterozygous for a TPMT variant received 50% of the standard thiopurine dose, patients homozygous for the tested variants 0–10%. We compared pre-treatment genotyped patients with patients receiving standard dose for the occurrence of leucopenia (leucocyte count $<3.0\times10^9$/l) in the first 20 weeks after treatment initiation. For the cost-effectiveness analysis we only included complete cases (patients with outcome (EQ-5D) and self-reported costs data).
Results: Seven hundred sixty-nine patients met the inclusion criteria. Of them 74 patients (9.6%) carried a TPMT variant, and 58 (7.5%) developed leucopenia. Overall, the occurrence of leucopenia did not differ between the intervention and control group (7.2% vs. 7.8%). However, among carriers of a genetic variant the occurrence of leucopenia was significantly reduced in those receiving a TPMT guided dose compared to the control group (2.6% versus 22.9%, OR 0.09, 95% CI=0.01–0.75). Treatment efficacy appeared to be similar across both study arms (delta EQ-5D (mean $\pm$ standard deviation) 0.014$\pm$0.080 versus 0.016$\pm$0.071). The average costs (direct medical costs and indirect costs) were lower for patients who received a genotype-guided dose advise (n = 238) than for those that received standard dose (n = 216): €4433 versus €6150, p = 0.023.
Conclusions: Ten percent of IBD patients have an increased risk of thiopurine-induced leucopenia due to low TPMT activity. Prior-to-treat TPMT screening of IBD patients reduces the risk of leucopenia and produces substantial cost-savings over the initial 20 weeks. This study strongly implies that personalized treatment by pharmacogenetic testing for TPMT should be advocated as standard care for IBD patients.

OP007

Anti-MAdCAM monoclonal antibody PF-00547659 does not affect immune surveillance in the central nervous system of anti-TNF and immunosuppressant experienced Crohn's disease patients who are anti-TNF inadequate responders: Results from the TOSCA study

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Background: Therapy that inhibits white blood cell (WBC) trafficking from the bloodstream to the gut has shown promising results in the treatment of inflammatory bowel disease. Its use, however, has been limited by the risk of progressive multifocal leukoencephalopathy (PML) in patients treated with the nonselective anti-α 4 integrin antibody natalizumab. PML is an opportunistic infection caused by the highly prevalent JC virus that attacks the central nervous system (CNS) in immunocompromised hosts. Reduced CNS immune surveillance