population. Our aim was to evaluate the rate of infliximab-related IAE in elderly IBD patients.

Methods: All adult patients in the ENEIDA registry (a large, prospectively maintained database of the Spanish Working Group in IBD–GETECCU) who received a first course of infliximab treatment were identified. Patients were selected in two cohorts regarding the age at the beginning of infliximab treatment: over 60 years, and between 18 and 50 years of age. The rates of IAE recorded in the ENEIDA database (infusion reactions, delayed hypersensitivity, oedema, allergy, anaphylaxis, psoriasis, lupus-like syndrome) were compared, as well as the rate of secondary loss of response (SLR).

Results: We included 939 (12%) patients who started infliximab over 60 years and 6844 (88%) patients below 50 years. The rate of IAE (15% vs. 15%, ns) and treatment withdrawal due to IAE (13% vs. 12%, ns) was similar in both groups. Neither differences were observed according to IAE: infusion reactions (8.3% vs. 8.2%), late hypersensitivity (1.4% vs. 1.2%), paradoxical psoriasis (0.9% vs. 1.4%) and drug-induced lupus erythematosus (0.7% vs. 0.6%). Patients below 50 years were significantly more often treated with concomitant immunosuppressants (57% vs. 48.1% >60 years, $p < 0.05$). In the multi-variate analysis, combination with immunosuppressants (OR 0.741; 95% CI 0.64–8.5, $p < 0.05$) and female sex (OR 1.8; 95% CI 1.6–2.1, $p < 0.05$) were the only independent predictors to develop IAE. The rate of SLR was also similar in both study groups (20% vs. 21%). Combination therapy with immunosuppressants was the unique risk factor to develop SLR (OR 0.85; CI 95% 0.73 to 0.98, $p = 0.021$).

Conclusions: Elderly IBD patients who start treatment with infliximab have a similar risk of developing IAE and SLR than younger patients. From this point of view, elderly would benefit from combination therapy.

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Lupus-like reactions in patients with inflammatory bowel disease treated with anti-TNFs are rare but insidious adverse events: data from a large single-centre cohort

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Background: The occurrence of lupus-like reactions (LLRs) may complicate the management of patients with inflammatory bowel disease (IBD) treated with anti-TNFs. However, very few data on the incidence, predictors, and clinical outcomes of LLRs have been reported. We aimed to describe all these features in a large cohort of IBD patients treated with anti-TNF drugs

Methods: All records of consecutive patients who started a treatment with an anti-TNF from January 2006 to June 2018 were retrospectively reviewed. Patients were defined as having LLR by the presence of immunologic abnormalities (positivity for ANA and/or anti-ds-DNA), along with clinical features that included at least two of the following: arthralgia, fatigue, fever, cutaneous manifestations, or serositis, which had a clear temporal association with exposure to the anti-TNFs, and resolved without recurrence once the drug was discontinued. Univariable and multiple Cox proportional hazard models were used to estimate the association between all variables at baseline and occurrence of LLRs.

Results: In total, 760 patients (1059 total treatments with anti-TNFs) were included. Participants contributed a total of 2863.5 person-years of follow-up, during which 16 cases of LLRs (2.1% of patients) were reported, with an incidence rate of 5.6 per 1000 person-years. Female gender and being former smokers were more prevalent in the LLR group (75.0% vs. 44.1%, $p = 0.02$; and 18.8% vs. 5.4%, $p = 0.037$, respectively), with a hazard ratio of 3.86 (95% CI: 1.21–12.38; $p = 0.023$) and 4.42 (95% CI: 1.20–16.24; $p = 0.025$), respectively, at Cox regression analysis adjusted for possible confounders. LLRs occurred after a mean of 12.0 ± 9.7 months of therapy with anti-TNFs. Antinuclear antibodies were universally positive, and 10 out 16 (62.5%) patients had also anti-ds-DNA. Arthropathy was the most frequent symptom (87.5%), followed by fatigue (81.2%), and fever (31.2%). Three cases presented with a concomitant autoimmune hepatitis-like syndrome. The diagnosis of LLR was further confirmed by a re-challenge with the culprit agent in half of the cases. All LLRs resolved following discontinuation of the drug after a mean of 8.1 ± 4.2 weeks, even if 10 patients required corticosteroids for the control of symptoms. Five patients (31.2%) were switched to a second anti-TNFs, and one of them developed a second LLR.

Conclusions: In this very large cohort of patients treated with anti-TNFs, LLRs were rare adverse events, more common in women and former smokers. Clinical features are non-specific and insidious. All LLRs resolved following discontinuation of the drug, but the use of corticosteroids was required in most of the cases.

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Effectiveness and safety of the sequential use of a second and third anti-TNF agent in patients with inflammatory bowel disease: results from the ENEIDA registry

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Background: The aim of the present study was to investigate the efficacy and safety of the sequential use of a second and a third anti-TNF agent after failing or developing intolerance to an anti-TNF drug.

Methods: Patients diagnosed with Crohn's disease (CD) or ulcerative colitis (UC) from ENEIDA registry (a prospectively maintained registry from GETECCU) who switched to another anti-TNF drug after failure or intolerance to a previous anti-TNF, were included. Efficacy, loss of response, and safety of the second and third anti-TNF were evaluated by logistic regression, Kaplan–Meier and Cox regression analyses.

Results: In total, 1122 patients that switched to a second anti-TNF were included (50% men, mean age at diagnosis 31 years, 73% CD). The reasons for withdrawal the first anti-TNF were: primary failure (22%), secondary failure (51%), and intolerance (27%). Remission was achieved with the second anti-TNF drug in 45% of patients in the short-term. The rate of remission was similar between CD and UC patients (46% vs. 41%, $p = 0.06$). There was no difference in remission rates according to the sequence of the anti-TNF administration: infliximab–adalimumab or adalimumab–infliximab (42% vs. 48%, $p = 0.07$). The factors associated with a lower probability of achieving remission after a second anti-TNF were: combo therapy (OR = 0.5 95% CI = 0.4–0.8), to withdraw the first anti-TNF due to a primary failure (vs. intolerance; OR = 0.6, 95% CI = 0.4–0.9), and to withdraw the first anti-TNF due to secondary failure (vs. intolerance) (OR 0.6, 95% CI = 0.5–0.9). The cumulative incidence of loss of response after achieving remission with the second anti-TNF (median follow-up of 19 months) was 45%: 23% at 1 year and 62% at 5 years. The incidence of loss of response to the second anti-TNF was 19% per patient-year of follow-up. The factors associated with a higher risk of loss of response were: UC vs. CD (HR = 1.6; 95% CI = 1.1–2.1, $p = 0.005$) and combo therapy (HR = 2.4; 95% CI = 1.8–3, $p < 0.0001$). Adverse events occurred in 15% of the patients who switched to a second anti-TNF (10% stopped the treatment). Seventy-one patients switched to a third anti-TNF and 55% achieved remission. The incidence of loss of response to a third anti-TNF was 22% per patient-year (median follow-up of 9 months). Seven patients (11%) had adverse events, but only one discontinued the therapy.

Conclusions: Almost half of the patients who switched to a second anti-TNF achieved remission; however, a high proportion of them subsequently lost response. Factors associated with loss of response were type of inflammatory bowel disease and combo therapy. Approximately 50% of patients who received a third anti-TNF achieved remission; however, again, a high proportion of them lost response subsequently.

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Comparison of infliximab serum levels between venous and capillary blood in paediatric IBD patients using novel blood sampling technology

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