clinical trial were provided by AbbVie. AbbVie participated in the interpretation of data, drafting, review, and approval of the abstract.
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THU0364 IMMUNOGENICITY OF ANTI-TNF DRUGS AND CLINICAL RESPONSE IN PATIENTS WITH SPONDYLOARTHRITIS

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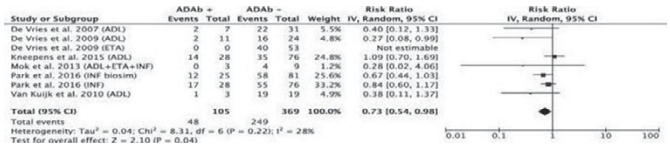
Background: Antidrug antibodies (ADAb) seem to be associated with a loss of response in immune-mediated inflammatory diseases (1) and in psoriatic arthritis (2).
Objectives: To assess the effect of ADAb on clinical response in patients with spondyloarthritis (SpA) treated with anti-TNF drugs.
Methods: We conducted a systematic literature review of controlled trials and observational studies assessing the effect of ADAb on response to anti-TNF drugs (Adalimumab (ADL), Certolizumab (CTZ), Etanercept (ETA), Golimumab (GOL) and Infliximab (INF)) in patients with axial or peripheral SpA. Databases analysed were PubMed, the Cochrane library, and ACR/EULAR meeting abstracts, until January 2017. A meta-analysis was performed using the inverse variance approach and statistical heterogeneity was assessed with the Cochran Q-test and I^2 values. A statistical threshold of 5% was considered as significant.
Results: Over 1,387 publications screened, 7 studies were selected for meta-analysis (3–9). These studies were observational studies (n=6) or controlled trial (n=1); involved patients with axial or peripheral SpA (n=6) or psoriatic arthritis (n=1); included treatments with ADL (n=4), ETA (n=1), INF and INF biosimilar (n=2), or various anti-TNF drugs (n=1). ADAb rates varied between anti-TNF drugs: 0% for ETA, 13.6–31.4% for ADL, 0–28.9% for INF. Patients with ADAb were less often responders than patients without ADAb in 6 studies, more often responders in one study, while the risk ratio (RR) for response was not assessable in one study due to the absence of ADAb. The weighted pooled RR (95% CI) for response to anti-TNF drugs was 0.73 (0.54–0.98) in ADAb+ in comparison with ADAb- patients (p=0.04) (see figure). There were trends towards more infusion reactions and lower serum drug levels in patients with ADAb (data not shown).



Conclusions: According to the results of this meta-analysis, ADAb positivity is associated with a lower rate of response to anti-TNF agents in patients with SpA.
References:
[1] The immunogenicity of anti-TNF therapy in immune-mediated inflammatory diseases: a systematic review of the literature with a meta-analysis, Garcês.S and al, ARD 2014; 72:1947–1955.
[2] The comparative immunogenicity of biologic therapy and it's clinical releavance in psoriatic arthritis: a systematic review of the literature, Balsa.A and al, ACR 2016, Abstract number 1691.
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THU0365 DO EXTRA-ARTICULAR MANIFESTATIONS AFFECT THE CHOICE OF BIOLOGIC THERAPY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS? A MULTICENTRE REAL-LIFE ANALYSIS

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Background: Extra-articular manifestations (EAMs), such as uveitis, inflammatory bowel diseases (IBD) and psoriasis (PsO), frequently complicate the disease course of patients with axial spondyloarthritis (axSpA), although prevalence data on this regard are still controversial. The occurrence of EAMs might also contribute to the decision of introducing a biologic therapy and even influence the choice between the available TNF inhibitors (TNFis).
Objectives: The aim of this study is to retrospectively evaluate the prevalence of EAMs in a multicentre cohort of axSpA patients treated with TNFi, investigating how these influenced the choice of treatment.
Methods: Clinical data from axSpA patients treated with a TNFi between May 2003 and May 2016 where obtained from a multicentre registry. Prevalence of EAMs (uveitis, IBD and PsO) was calculated at the time of TNFi prescription, evaluating their distribution according to drug subgroup.
Results: The study included 503 patients with axSpA (172 [34.2%] women, mean age [±SD] 40.5 [±13.2] years, mean disease duration 9.7 [±14.7] years), receiving a total of 675 lines of treatment (I-line n=503, II-line n=118, ≥ III-line n=54) with a TNFi (272 infliximab [IFX], 173 adalimumab [ADA], 89 golimumab [GOL], 141 etanercept [ETN]). At the time of TNFi introduction, 28.6% patients claimed at least one EAM (IBD 11.3%, uveitis 10.9%, and PsO 8.8%). The baseline presence of at least one EAM was associated with a more frequent prescription of an anti-TNF monoclonal antibody rather than etanercept (34.1% versus 21.9%, respectively; p=0.005). In detail, EAMs were found in 41.6, 36.9, 29.8, and 21.9% patients treated with GOL, ADA, IFX, or ETN, respectively. The prevalence of IBD was significantly higher (p=0.004) in patients treated with ADA (12.7%), IFX (14.3%), or GOL (11.2%) compared with ETN (4.9%). Uveitis was numerically more frequent in GOL (20.2%) and ADA (13.3%) rather than IFX (9.5%) and ETN (9.9%) groups. Finally, PsO prevalence was similar in patients treated with ADA (10.9%) and GOL (10.1%), and numerically lower in the ETN (7.1%) and IFX (5.9%) groups.
Conclusions: In our cohort of axSpA patients treated with TNFis, EAMs were highly represented. The presence of extra-articular involvement has been carefully taken into account when a TNFi was required to better control the disease. In particular, IBD and uveitis drove more frequently the choice toward an anti-TNF monoclonal antibody instead of the receptor.
Disclosure of Interest: None declared
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THU0366 GASTROINTESTINAL INFECTIONS IN PATIENTS WITH SPONDYLOARTHRITIS TREATED WITH ANTI-TNF DRUGS: RESULTS OF GISEA REGISTER

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Background: Tumour necrosis factor (TNF) plays a pivotal role in controlling intracellular of bacterial infection. The BSR Biologics Register (BSRBR) has reported an increase in the occurrence of listeria and salmonella infections in anti-TNF-treated rheumatoid arthritis patients in comparison with those patients treated with non-biological DMARDs.
Objectives: The aim of this study was to determine the incidence of gastrointestinal infection in the anti-TNF-treated spondyloarthritis (SpA) patients in the GISEA registry, and identify the factors associated with its development.
Methods: The prospective GISEA registry was designed to collect real-world clinical data concerning patients with RA or SpA treated with biological drugs. The baseline information includes demographics, disease duration, HAQ-DI, DAS-28, BASDAI, BASFI and BASMI scores, steroid use, smoking history and comorbidities.
Results: Of the 3321 anti-TNF-treated SpA patients in the registry (1731 males, 52.2%; mean age 47±13 years; median disease duration three years, interquartile range [IQR] 0–8), 1065 (32%) were treated with infliximab (IFN), 1052 (32%) with adalimumab (ADA), and 1204 (36%) with etanercept (ETN). Two thousand, one hundred and five patients (63.4%) had a median of one comorbidity (IQR 0–2], the most frequent being hypertension (701), thyroid diseases (281), diabetes mellitus (207), cardiopathy (189), and osteoporosis (145). In combination with the biological drug, 919 patients (27.7%) received steroids and 2451 (79.9%) at least one DMARD. The median follow-up was three months (IQR 1–2 years). Twenty-two patients 0.7% experienced bacterial gastrointestinal infections, the most frequent being due to listeria, klebsilla and salmonella. The crude incidence rate was 2.5 per 1000 patient-years (95% CI 1.6–3.7). Univariate analysis showed that female gender (OR 3.9, 95% CI 1.5–10.0; p=0.004) and comorbidities (OR 3.4, 95% CI 1.0–3.5; p=0.049) were associated with a high risk of gastrointestinal infections, and that the use of IFN rather than ETN and ADA (p=0.712 and p=0.238) was not associated with a higher risk of gastrointestinal infections.

Furthermore, univariate models showed that age (p=0.738), disease duration p=0.090, previous DMARDs (p=0.616), and HAQ (p=0.674) and BASFI (scores p=0.850) were not statistically significant predictors of gastrointestinal infections.
Conclusions: The incidence rate of gastrointestinal infections in SpA patients treated with anti-TNF drugs is not increased. Being female and having comorbidities are predictive factors of gastrointestinal infections.
Disclosure of Interest: None declared
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THU0367 THE INFLUENCES OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON SERUM VEGF AND BMP-2 LEVELS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: VEGF has been found abnormal in patients with SpA and related to disease activity [1,2]. BMP-2 has a function of promoting the osteophyte formation, and may be involved in the integration process of AS spine [3,4]. VEGF and BMP-2 interact with each other, participating in the formation of osteoblast [5]. COX-2 works together with the expressions of BMP2 and VEGF is an important factor of heterotopic ossification [6].
Objectives: To investigate the serum levels of VEGF and BMP-2 in axSPA treated with NSAIDs and their possible relationship with disease activity.
Methods: 120 patients with axSPA were randomized administered with imrecoxib or celecoxib respectively for 3 months. Serum VEGF and BMP-2 were detected. ESR, CRP, BASDAI, BASFI and SPARCC were measured.
Results: A statistically significant change was found in ESR, BASDAI, patients global assessment of disease activity, Schober test and SPARCC following treatment with imrecoxib or celecoxib (P <0.05). There were no statistically significant differences between the two groups. (P >0.05). There was statistically significant difference in serum VEGF levels before and after treatment (240.89±17.68 pg/ml vs 187.00±11.42 pg/ml, P<0.05), but no difference in BMP-2 (231.74±104.44 vs 226.80±116.26 pg/ml, P>0.05). A significant correlation was found between VEGF level and ESR, CRP, BASFI, tragus-up-wall distance and finger to floor distance, lumbar side flexion,Schober test and intermalleoar distance (r=0.628, 0.542, 0.238, 0.299, 0.353, -0.369, -0.373, -0.359, -0.274, P<0.05).And the BMP-2 levels were correlated with CRP and lumbar side flexion (r =0.213, -0.190, P<0.05). Serum VEGF levels were significantly increased in HLA-B27-positive patients than in HLA-B27-negative ones (P<0.05).
Conclusions: NSAIDs can not only improve symptoms and function, but also reduce sacroiliitis possibly by affecting the levels of VEGF and BMP. Imrecoxib and celecoxib have the same efficacy.The response to treatment was correlated with the expression of HLA-B27.
References:
[1] Appel H,Janssen L,Listing J,Heydrich R,Rudwaleit M,Sieper J.Serum levels of biomarkers of bone and cartilage destruction and new bone formation in different cohorts of patients with axial spondyloarthritis with and without tumor necrosis factor-alpha blocker treatment.Arthritis Res Ther;2008:10:R125.
[2] Liu KG,He QH,Tan JW,Liao GJ.Expression of TNF-alpha, VEGF, and MMP-3 mRNAs in synovial tissues and their roles in fibroblast-mediated osteogenesis in ankylosing spondylitis.Genet Mol Res;2015:14:6852–6858.
[3] Poddubnyy D,Conrad K,Haibel H,Syrbe U,Appel H,Braun J,et al. Elevated serum level of the vascular endothelial growth factor predicts radiographic spinal progression in patients with axial spondyloarthritis.Ann Rheum Dis;2014:73:2137–2143.
[4] Chen MH,Chen HA,Chen WS,Chen MH,Tsai CY,Chou CT.Upregulation of BMP-2 expression in peripheral blood mononuclear cells by proinflammatory cytokines and radiographic progression in ankylosing spondylitis.Mod Rheumatol;2015:25:913–918.
[5] Minamizaki T,Yoshiko Y,Kozai K,Aubin JE,Maeda N.EP2 and EP4 receptors differentially mediate MAPK pathways underlying anabolic actions of prostaglandin E2 on bone formation in rat calvaria cell cultures.Bone;2009:44:1177–1185.
[6] Pape HC,Marcucio R,Humphrey C,Colnot C,Knobe M,Harvey EJ.Trauma-induced inflammation and fracture healing. J Orthop Trauma. 2010 2010–09–01;24:522–5.
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Disclosure of Interest: None declared
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THU0368 CLINICAL AND IMAGING CHARACTERISTICS OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS REPORTING FLARE SYMPTOMS IMMEDIATELY PRIOR TO NEXT DOSE IN ROUTINE TNFI THERAPY

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Background: Tumour necrosis factor inhibitors (TNFi) are highly efficacious in axial spondyloarthritis (axSpA) with significant clinical responses mirrored in resolution of MRI determined bone marrow oedema (BMO) lesions representative of active inflammation in the sacroiliac joints (SIJ) and spine. However, symptom flare suggesting loss of response is common with many patients reporting deterioration days or weeks prior to the next dose. We hypothesised that intermittent suppression of inflammation with longer acting TNFis such as adalimumab or infliximab may be associated with a greater likelihood of recurrence of MRI determined BMO lesions than shorter acting agents such as etanercept.
Objectives: To explore the relationship between symptom flare immediately prior to next treatment dose and recurrence of MRI determined BMO lesions with different TNFi in axSpA.
Methods: Proof-of-concept, single centre study. Eligible participants were adults with axSpA established on adalimumab, etanercept or infliximab describing loss of response immediately prior to next treatment dose. Loss of response was defined as subjective “flare” or “wearing off” of drug effect before the expected duration of treatment effect. Participants attended at three points: Baseline: first day of treatment cycle (day of drug dose); Endpoint 1: 3–4 days after dose; and Endpoint 2: within 48 hours of next dose. ASDAS-CRP and whole spine and SIJ MR imaging utilising 3T MRI scanner were performed at each visit. Images were scored according to the semi-quantitative Leeds MRI scoring system by two observers blinded to participant identity and date of scan.
Results: 38 participants (16 adalimumab; 12 etanercept; 10 infliximab) with a total 113 MRI scans were analysed. 71% (n=27) male; 60% (n=23) HLA-B27+ with no differences between the groups; 73.7% (n=28) fulfilled mNYC for AS; the remainder were classified as nr-axSpA. 58% (n=22) had at least 1 Grade 1 BMO lesion at baseline with lesions more commonly seen with longer acting drugs (5/12 in etanercept group; 9/16 in adalimumab group; 8/10 in infliximab group) and 11 (50%) had at least 1 Grade ≥2 lesion (Table 2). There was a trend towards number and severity of BMO lesions fluctuating through the treatment cycle (Figure 1) mimicking subjective loss of response, also reflected on the ASDAS-CRP (Table 1) but this did not reach statistical significance.

Table 1. Median (range) ASDAS-CRP by drug and visit

	Baseline	Endpoint 1	Endpoint 2
Etanercept	2.94 (1.5–4.4)	2.46 (1.8–4.0)	3.18 (1.1–4.2)
Adalimumab	2.97 (1.7–5.5)	2.17 (1.0–7.9)	2.79 (1.4–5.3)
Infliximab	3.3 (3.0–4.7)	2.93 (1.0–4.5)	3.31 (2.8–4.8)

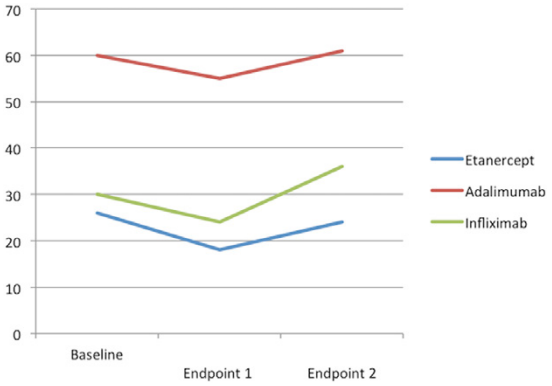

Figure 1. Total number of BMO lesions (grade 1 and ≥2).

Conclusions: This small proof-of-concept study shows subtle fluctuations on MRI changes of BMO and ASDAS-CRP corresponding to time of subjective “flare” before next scheduled TNFi dose in subjects with axSpA. Although these changes may be more common with the longer acting TNFi our data are not confirmatory. Larger studies are required to explore this concept further as these observations are potentially relevant for disease progression since cycles of inflammation and its subsequent suppression could theoretically increase the risk of new bone formation.
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