opportunity to study effectiveness and safety of bDMARDs, including bsDMARDs in AS.

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THU0362 EFFECT OF BIOTECHNOLOGICAL DRUGS ON EXTRA-ARTICULAR MANIFESTATIONS OF ANKYLOSING SPONDYLITIS: SYSTEMATIC REVIEW

A.L.R. Pinto [1], C.V. Pessoa [1,2], L.S. Inês [1,3]. *[1]Faculty of Health Sciences, University of Beira Interior, Covilhã; [2]Rheumatology, Local Health Unit of Guarda, Guarda; [3]Rheumatology, Coimbra Hospital and Universitary Centre, Coimbra, Portugal*

Background: Treatment with biotechnological agents (infliximab, etanercept, adalimumab, golimumab and certolizumab pegol) in ankylosing spondylitis (AS) is effective. However, evidence regarding the potential efficacy of these anti-TNF drugs in the extra-articular manifestations of ankylosing spondylitis, namely in uveitis (UV), inflammatory bowel disease (IBD) and dactylitis is scarce.

Objectives: To analyze evidence on efficacy of anti-TNF drugs approved for AS treatment in UV, IBD and dactylitis associated with AS.

Methods: A systematic literature review was performed using the PubMed and Cochrane Library databases. Randomized controlled trials (RCT), meta-analyzes and observational studies (OS) reporting efficacy of anti-TNF agents in extra-articular manifestations of AS were included.

Results: Fifty studies were included (seventeen RCTs, six meta-analyses and twenty seven observational studies). From the RCT we extracted the results presented in Table 1 for uveitis and in Table 2 for IBD. None reported results for dactylitis. Of the meta-analyzes included, only one presents results. These one shows that the incidence of uveitis is lower in patients taking etanercept than placebo (incidence of 8.6 and 19.3 per 100 patients per year, respectively; p value =0.03). In OS comparing different drugs, in one the risk of developing uveitis was 1.9 times higher in patients under etanercept compared to those under adalimumab (p value =0.0223) and a risk similar to those under infliximab and those under adalimumab. In another we have a percentage of patients with uveitis, during the course of the study, under etanercept of 8.0% and under infliximab of 4.0%. In the OS, the percentage of patients with UV events with infliximab was in a range of 0.0%>3.1% with a follow-up interval between 2 years and 5 years; with etanercept was 0.9%>29.6% and a follow-up time interval between 12 weeks to 7 years; with adalimumab there is only one study with duration of 2 years reporting 3.9% UV events. Regarding IBD reported in OS, there was 3.7%>7.7% patients with events under treatment with etanercept over a follow-up time of 3.2–7 years; with adalimumab only a 2-year study reported IBD in 0.6% of cases. We did not find results regarding for other extra-articular manifestations or anti-TNF drugs.

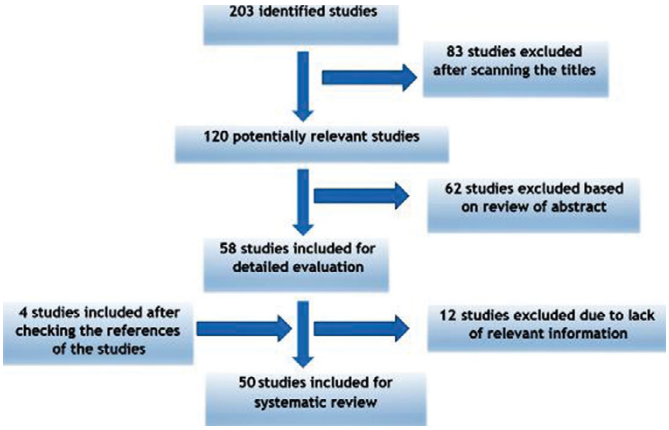
Table 1. Percentage of patients with events of uveitis on Randomized Controlled Trials

Uveitis	Randomized Controlled Trials	
	% patients with events under therapy	% patients with events under placebo
Infliximab	2,9	8,6
Etanercept	1,1	3,5
Adalimumab	No results	No results
Golimumab	No results	No results
Certolizumab pegol	0,9	2,8

Table 2. Percentage of patients with events of inflammatory bowel disease on Randomized Controlled Trials

Inflammatory Bowel Disease	Randomized Controlled Trials	
	% patients with events under therapy	% patients with events under placebo
Infliximab	No results	No results
Etanercept	1,1	0,7
Adalimumab	1,0	0,0
Golimumab	No results	No results
Certolizumab pegol	0,0	0,9

Conclusions: Efficacy of anti-TNF drugs on extra-articular manifestations of AS is under-reported in RCTs. Available data suggests possible efficacy of infliximab, adalimumab and certolizumab in UV, and of certolizumab in IBD. No evidence is available about anti-TNF efficacy in AS-associated dactylitis. Future studies with anti-TNF drugs should better report on extra-articular manifestations in AS.



Disclosure of Interest: None declared

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THU0363 IMPACT OF ADALIMUMAB ON CLINICAL OUTCOMES, HEALTHCARE RESOURCE UTILIZATION AND SICK LEAVES IN ANKYLOSING SPONDYLITIS PATIENTS IN CENTRAL AND EASTERN EUROPE

D. Opris-Belinski [1], S. Erdes [2], S. Grazio [3], L. Šenolt [4], M. Hojnik [5], O. Nagy [6], L. Iosub [7], S. Szántó [8]. *[1]Rheumatology, Sf. Maria Clinical Hospital, Carol Davila University of Medicine, Bucharest, Romania; [2]V. A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; [3]Univ. Dpt. of Rheumatology, Clinical Hospital Centre Sisters of Mercy, Croatia, Zagreb, Croatia; [4]Dpt. of Rheumatology, 1st Faculty of Medicine, Charles Univ, Institute of Rheumatology, Prague, Czech Republic; [5]AbbVie, Global Medical Affairs, Ljubliana, Slovenia; [6]AbbVie, Global Medical Affairs, Budapest, Hungary; [7]AbbVie, Global Medical Affairs, Bucharest, Romania; [8]Rheumatology, Faculty of Medicine, Univ. of Debrecen, Debrecen, Hungary*

Background: Ankylosing spondylitis (AS) represents a considerable socioeconomic burden due to early disease onset, development of functional disability and life-time costs. The impact of originator adalimumab on the extent of outpatient attendance, hospitalizations and sick leave in relation to clinical outcomes is not known in Central and Eastern Europe (CEE).

Objectives: To evaluate disease activity, physical function, selected health care resource utilization and sick leaves in patients treated with adalimumab in clinical practice in CEE countries.

Methods: This was a 52-week multi-center post-marketing observational study conducted in 5 countries in CEE. Eligible AS patients were prescribed originator adalimumab according to the local practice; 5 study visits (V) were performed approx. 3 months apart. Disease activity was measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Index ($ASDAS_{CRP}$), treatment response as BASDAI50 and $\triangle ASDAS \geq -2$ (at study end), physical function by Bath Ankylosing Spondylitis Functional Index (BASFI). Data on AS related healthcare resource utilization and sick leave during the study was recorded prospectively through a systematic interview with the patient at each study visit. For pre-and post-treatment comparison, the same sort of data were recorded retrospectively at baseline visit for the 3-month period preceding adalimumab therapy, verified against chart review, then multiplied by 4 to match the prospective follow-up duration. Descriptive statistics were used; last observation carried forward data are presented herein.

Results: 452 patients were enrolled, 360 completed the study. Mean age was 42.9 (±12.1) yrs; 68.7% were male and 62.7% were employed at baseline. Average disease duration was 7.7 (±8.7) yrs. Mean BASDAI and ASDAS decreased from 6.3 (±2.1) and 4.0 (±1.1) at baseline to 2.3 (±2.0) and 1.9 (±1.1) at study end, respectively; mean BASFI from 6.2 (±2.3) to 2.6 (±2.3). BASDAI and ASDAS based treatment response was seen at study end in 72.3% and 58.9% of patients, respectively. The mean number of hospital admissions and inpatient days decreased from 2.8 (±3.9) to 0.9 (±2.8) and from 23.0 (±40.8) to 3.9 (±17.7), respectively (pre- and post-treatment). The mean number of sick leaves and sick leave days decreased from 3.2 (±8.8) to 1.1 (±5.6) and from 32.2 (±69.2) to 5.1 (±24.5), respectively (employed patients only, n=282). The reduction of hospital admissions/days, sick leaves and sick leave days were higher in treatment responders compared to non-responders. No new safety signal was detected.

Conclusions: Treatment with adalimumab in routine clinical practice in 5 CEE countries resulted in clinically meaningful improvements in disease activity and physical function as well as reduced healthcare resource utilization and sick leaves.

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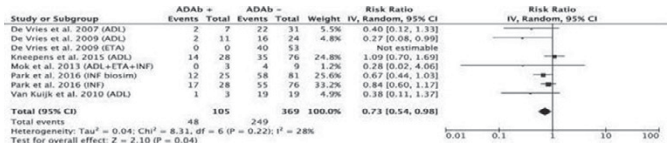
THU0364 IMMUNOGENICITY OF ANTI-TNF DRUGS AND CLINICAL RESPONSE IN PATIENTS WITH SPONDYLOARTHRITIS

D. Geiger[1], Y. Degboe[1], T. Barnetche[2], A. Cantagrel[1], A. Ruyssen-Witrand[1], A. Constantin[1]. *[1]Rheumatology, Centre de Rhumatologie, CHU Purpan, Place du Dr Baylac, Toulouse Cedex 9; [2]Rheumatology, Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France*

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.
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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

E.G. Favalli[1], S. D'Angelo[2], A. Carletto[3], A. Becciolini[1], F. Martinis[3], G. Tramontano[2], M.G. Raimondo[4], M. Biggioggero[4], A. Marchesoni[1], M. Rossini[3], I. Olivieri[2]. *[1]Department of Rheumatology, Gaetano Pini Institute, Milano; [2]Rheumatology Institute of Lucania (IRel) - Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Potenza; [3]UOC Reumatologia, Dipartimento di Medicina, AOUI, Verona; [4]Department of Clinical Sciences and Community Health, Division of Rheumatology, University of Milan and Gaetano Pini Institute, Milano, Italy*

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

F. Atzeni[1], V. Panetta[2], M. Sebastiani[3], F. Salaffi[4], A. Carletto[5], R. Foti[6], F. Iannone[7], G. Elisa[8], M. Govoni[9], A. Marchesoni[10], E.G. Favalli[10], R. Gorla[11], R. Ramonda[12], P. Sarzi-Puttini[13], G. Ferraccioli[8], G. Lapadula[7] on behalf of GISEA group. *[1]Rheumatology Unit, University Hospital L. Sacco, Milan, Italy, Milan; [2]L'altrastatistica Consultancy & Training, Biostatistics Office, Rome; [3]University Hospital of Modena, Modena; [4]Polytechnic University of Marche, C. Urbani Hospital, Jesi; [5]Rheumatology Unit, University of Verona, Verona; [6]Rheumatology Unit, Vittorio-Emanuele University Hospital of Catania, Catania; [7]University of Bari, Bari; [8]Division of Rheumatology, Institute of Rheumatology, Catholic University of the Sacred Heart, Rome; [9]Department of Medical Sciences, UOC of Rheumatology, Santa Anna University Hospital, Ferrara; [10]G. Pini Orthopedic Institute, Milan, Milan; [11]Rheumatology and Immunology Unit, Spedali Civili, Brescia; [12]University of Padua, Padua; [13]Rheumatology Unit, University Hospital L.Sacco, Milan, Italy*

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.