each biologic-treated patient with RA (n=53,214) by sex, age, and geographical region. A patient could participate to several of these exposure cohorts. For each patient, follow-up under a cohort ended either with an outcome event (GI perforation identified in the NPR as an ICD10 code from a predefined list) or with the first of any of the following censoring events: emigration from Sweden, death, transition to another cohort, discontinuation of treatment (+90/+180 days lag time) or end of study period. Crude incidence rates were tabulated for each cohort and adjusted hazard ratios (HR) and 95% confidence intervals were estimated in multivariable Cox regressions, controlling for baseline differences. The final adjusted model included the following covariates: sex, age, line of biologic treatment, disease characteristics, co-medication at treatment start, co-morbidities and a history of GI perforation.

Results: We found 31 GI perforations among 18 604 person-years (pyr) exposed to TNFi, and 31 GI perforations among 10 947 pyr exposed to non-TNFi, corresponding to crude incidence rates of 1.67 and 2.83 per 1000 pyr, respectively. The crude incidence rate among the biologics-naïve was 2.54 while among the general population comparators it was 0.94. The rate of GI perforations remained higher in patients with RA compared to the general population after adjustment for patient characteristics, HR of 1.78 (95% CI: 1.44 to 2.17), whereas the seemingly increased rate among bionaïve and non-TNFi users vs TNFi was largely explained by differences in age and disease history at start of follow-up, with adjusted HRs of 1.10 (0.68–1.78) for TNFi vs bionaïve and 1.10 (0.63–1.91) for TNFi vs non-TNFi, respectively.

Conclusions: Although patients with RA had a higher rate of GI perforations than matched general population comparators, no significant differences in risk remained between bionaïve, TNFi or non-TNFi treated RA patients after adjusting for baseline patient characteristics.

Disclosure of Interest: None declared

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OP0232 FEMALE GENDER AND POSITIVE RHEUMATOID FACTOR PREDICT LOW SERUM INFLIXIMAB LEVELS AND POSITIVE ANTI-DRUG ANTIBODIES, WHICH ASSOCIATE WITH TREATMENT FAILURE ON INFLIXIMAB IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS. REPORT FROM THE SWEFOT TRIAL POPULATION

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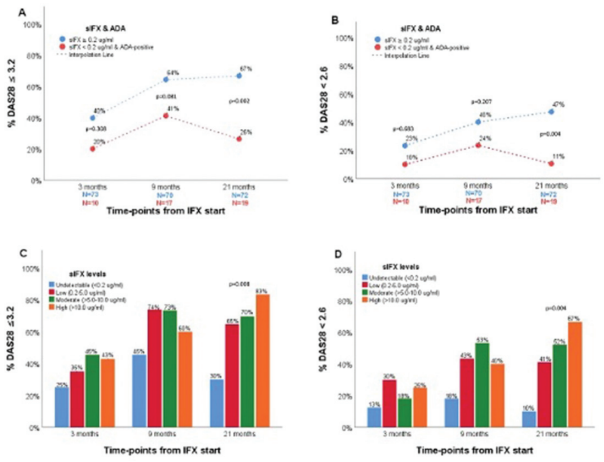
Background: Tumour necrosis factor (TNF) inhibitors, with infliximab (IFX) first on the market, have revolutionised treatment of patients with rheumatoid arthritis (RA). However, in a substantial proportion of patients, they lose efficiency, and up to 44% of patients have been found to develop anti-drug antibodies (ADA), leading to low serum IFX (sIFX) levels. Despite this, sIFX measurement is still rarely used for clinical decision making, and standardised clinical threshold titre levels have not been clearly defined.

Objectives: In an early RA trial adding IFX to methotrexate (MTX) in patients not achieving low disease activity (LDA=DAS28≤3.2) after 3 months monotherapy, we studied whether sIFX or ADA were associated with treatment outcome, and whether easily available baseline parameters predicted ADA development.

Methods: Of IFX-treated SWEFOT patients (n=128), 101 had available serum samples at follow-up, which were analysed for sIFX levels at 3, 9 and 21 months (routine ELISA). Samples with undetectable sIFX (<0.2 μg/ml) were analysed further for ADA using direct ELISA with plate-bound TNF. Primary and secondary outcome measures were LDA and remission (DAS28 <2.6) at 21 months. Clinical and demographic characteristics of patients at start of IFX therapy (baseline) were tested as potential predictors of ADA development, using uni- and multivariate logistic regression.

Results: At 3, 9 and 21 months from IFX add-on to MTX, 15%, 23% and 28% of patients, respectively, had undetectable sIFX, and 34% were ever ADA-positive. Significantly higher proportion of patients achieved LDA among those with detectable sIFX, versus undetectable sIFX and positive ADA (67% vs 26%, p=0.002, figure 1A), with similar difference for remission (47% vs 11%, p=0.004, figure 1B). When sIFX levels were further stratified into <0.2, 0.2–5.0, 5.0–10.0 and >10 μg/ml, there was a significant trend across the groups in achievement of LDA (30%, 65%, 70% and 83% respectively, p=0.008, figure 1C) or remission (10%; 41%, 52% and 67%, respectively, p=0.004, figure 1D). Women had undetectable sIFX at 21 months more often than men (35% vs 7%, p=0.006). In multivariate logistic regression analysis, the following baseline characteristics were significant predictors of ever ADA-positivity: female gender, RF-positivity, higher tender joint count, erythrocyte sedimentation rate and lower health assessment questionnaire score (data not shown).



Abstract OP0232 – Figure 1 Clinical outcome of patients at 3, 9 and 21 months stratified for sIFX and ADA status at the same time points. Proportion of patients in LDA (A) and remission (B) among patient with detectable sIFX level (blue dots) and ADA positive patients with undetectable sIFX levels (red dots). Proportion of patients in LDA (C) and remission (D) among four strata of patients according to sIFX levels undetectable (<0.2 μg/ml) – blue bars, low (0.2–5.0 μg/ml) – red bars, moderate (>5.0–10.0 μg/ml) – green bars, and high (>10.0 μg/ml) – orange bars.

Conclusions: In early RA patients receiving add-on IFX therapy, ADA-positivity or lower serum IFX levels were associated with a higher risk of not reaching treatment targets, that is LDA or remission. RF positivity and female gender, factors known to be associated with worse clinical outcomes, predicted development of ADA.

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OP0233 LONG-TERM SAFETY OF ADALIMUMAB IN ADULT PATIENTS FROM GLOBAL CLINICAL TRIALS ACROSS MULTIPLE INDICATIONS: AN UPDATED ANALYSIS IN 29,987 PATIENTS REPRESENTING 56,951 PATIENT-YEARS

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Background: Adalimumab is an anti–tumour necrosis factor-α (TNF-α) agent indicated for the treatment of immune-mediated diseases. The long-term safety of adalimumab was previously reported in 23 458 patients representing up to 12 years of clinical trial exposure in rheumatoid arthritis (RA), juvenile idiopathic arthritis, ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis (Ps), and Crohn's disease (CD).

Objectives: Here we report an updated analysis examining the long-term safety of adalimumab in adult patients with RA, AS, non-radiographic axial spondyloarthritis (nr-axSpA), peripheral SpA (pSpA), PsA, Ps, hidradenitis suppurativa (HS), CD, ulcerative colitis (UC), and non-infectious uveitis (UV).

Methods: Here we report an updated analysis examining the long-term safety of adalimumab in adult patients with RA, AS, non-radiographic axial spondyloarthritis (nr-axSpA), peripheral SpA (pSpA), PsA, Ps, hidradenitis suppurativa (HS), CD, ulcerative colitis (UC), and non-infectious uveitis (UV).

Results: This analysis included 29 987 patients, representing 56 951 patient-years of exposure (table 2). The majority of adalimumab exposure was in RA studies. The most frequently reported SAE of interest was infection (highest incidences in CD, RA, UV, and UC). Overall and for most of the adalimumab populations (AS, PsA, Ps, UC, CD, and RA), the observed number of deaths was below what would be expected in an age- and sex–adjusted population (table 1). For HS, nr-axSpA, pSpA, and UV studies, the small size of these trials precluded accurate assessment of the standardised mortality ratio, and the 95% CIs all included 1.0.

Abstract OP0233 – Table 1 Standardised mortality ratios across indications

Indication	SMR	95% CI
RA (n=15,511)	0.74	0.63–0.87
AS (n=2026)	0.14	0.00–0.77
nr-axSpA (n=863)	1.22	0.14–4.40
pSpA (n=165)	1.84	0.21–6.65
PsA (n=837)	0.34	0.04–1.24
Ps (n=3732)	0.34	0.15–0.64
HS (n=733)	1.50	0.40–3.84
CD (n=3896)	0.44	0.14–1.02
UC (n=1739)	0.37	0.12–0.87
UV (n=464)	1.23	0.45–2.68
Total (n=29,986)	0.65	0.57–0.74

AS, ankylosing spondylitis; CD, Crohn's disease; HS, hidradenitis suppurativa; nr-axSpA, non-radiographic axial SpA; Ps, plaque psoriasis; PsA, psoriatic arthritis; pSpA, peripheral SpA; RA, rheumatoid arthritis; SMR, standardised mortality ratio; SpA, spondyloarthritis; UC, ulcerative colitis; UV, uveitis.

Abstract OP0233 – Table 2 Incidence rates of serious adverse events of interest*

Characteristic	RA	AS	nr-axSpA	pSpA	PsA	Ps	HS	CD	UC	UV	Total†
n	15,512	2026	863	165	837	3732	733	3896	1739	464	29,987
Exposure, PYs	24,922	2120	709	391	998	5479	1198	4359	3407	1151	56,951
Serious infection	4.6	1.8	2.5	1.0	2.8	1.8	2.8	6.9	3.5	4.1	3.7
Tuberculosis	0.3	0.1	0.1	0.3	0.2	0.2	0	0.2	<0.1	0.4	0.2
Active	0.3	0.1	0.1	0	0.2	0.2	0	0.1	<0.1	0.2	0.2
Latent	<0.1	0	0	0.3	0	0	0	<0.1	0	0.3	<0.1
Opportunistic infection‡	<0.1	0	0.1	0	0	0	0	<0.1	<0.1	0.4	<0.1
Demyelinating disorder	<0.1	<0.1	0	0	0	0	0	0.1	<0.1	0.3	<0.1
Lupus-like syndrome	<0.1	<0.1	0.1	0	0	0	0	<0.1	<0.1	<0.1	<0.1
CHF	0.2	<0.1	0	0	0	0.1	0.2	0	<0.1	<0.1	0.2
Ps new onset/worsening	<0.1	<0.1	0	0	0.1	<0.1	<0.1	<0.1	<0.1	0	<0.1
Malignancy§	0.7	0.2	0.1	0.3	0.2	0.5	0.5	0.4	0.6	0.7	0.6
Lymphoma	0.1	<0.1	0	0	0.2	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
NMSC	0.2	0.2	0	0	0.1	0.1	<0.1	<0.1	<0.1	0.2	0.1
Melanoma	<0.1	<0.1	0	0	0	0.2	0	0	<0.1	0	<0.1
Sarcoidosis	<0.1	<0.1	0	0	0	0	0	0	0	<0.1	<0.1
Any AE leading to death	0.7	<0.1	0.3	1.0	0.3	0.2	0.5	0.1	0.1	0.6	0.5

AE, adverse event; AS, ankylosing spondylitis; CD, Crohn's disease; CHF, congestive heart failure; HS, hidradenitis suppurativa; NMSC, non-melanoma skin cancer; nr-axSpA, non-radiographic axial SpA; Ps, plaque psoriasis; PsA, psoriatic arthritis; pSpA, peripheral SpA; PY, patient-year; RA, rheumatoid arthritis; SpA, spondyloarthritis; UC, ulcerative colitis; UV, uveitis.
*Rates in events/100 PYs.
†Total includes the 10 populations shown plus 20 patients with Behcet's disease (35.5 PY).
‡Excludes oral candidiasis and tuberculosis.
§Excludes lymphoma, hepatosplenic T-cell lymphoma, leukemia, NMSC, and melanoma.

Conclusions: This analysis of data from clinical trials of adalimumab demonstrated an overall safety profile consistent with previous findings and with the TNF inhibitor class. No new safety signals or tolerability issues with adalimumab treatment were identified and, for most indications, the mortality rate was below what would be expected in an age- and sex–adjusted population. Efficacy and safety data continue to support the well-established benefits of adalimumab for the approved indications.

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Clinical and therapeutic aspects of vasculitis

OP0234 INFLIXIMAB THERAPY IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic inflammatory disease that predominantly affects the aorta and its main branches. Glucocorticoids (GCs) are the cornerstones of the initial treatment of TAK. However, most patients relapse with steroid withdrawal.

Objectives: To evaluate the efficacy and safety of infliximab (IFX) in Korean patients with active TAK.

Methods: Patients with active TAK were enrolled in a single-centre prospective open label trial. Active disease was defined according to the National Institutes of Health (NIH) criteria. Concomitant GCs were tapered to prednisone ≤10 mg/day or equivalent at 2 weeks prior to the initiation of IFX. Patients received intravenous infusions of IFX, at a starting dose of 5 mg/kg at weeks 0, 2, 6, and then every 8 weeks, up to week 46, and were followed up to week 54. At week 30, patients with partial remission received increased dose of IFX by 1.5 mg/kg, and patients who failed with IFX terminated the study. At week 38 and 46, patients with symptom of active disease or high serum level of erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), were instructed to increase the IFX dose by 1.5 mg/kg, up to 9.5 mg/kg, at each point. All the patients underwent Positron Emission Tomography-Computed Tomography (PET-CT) at baseline and week 30. The primary efficacy end point was the achievement of partial or complete remission at week 30.

Results: Twelve patients with TAK were enrolled and treated with IFX; 1 patient with study violation was excluded from analysis. At week 30, 3 patients (27.3%) achieved complete remission and 6 patients (54.5%) achieved partial remission. Statistically significant improvements were seen at week 30 for all of major secondary measures, including change from baseline in Indian Takayasu Clinical Activity Score 2010 ITAS 2010 (median 11.0, interquartile range [IQR] 10.0–11.8; 6.0, IQR 5.0–9.0, p=0.004), ITAS.A (14.0, IQR 12.0–14.0; 7.0, IQR 6.0–10.5, p=0.003) and serum levels of ESR (56.0, IQR 44.0–82.5; 26.0, IQR 20.0–56.5, p=0.031) and CRP (1.3, IQR 0.7–2.6; 0.2, IQR 0.1–2.1, p=0.019). PET parameters were significantly reduced, including maximum standardised uptake value (3.50, IQR 3.10–3.84; 3.10, IQR 2.49–3.27, p=0.023), target-to-vein ratio (1.34, IQR 1.13–1.95; 1.31, IQR 1.05–1.45, p=0.032), and target-to-liver ratio (2.38, IQR 1.47–3.05; 1.92, 1.51–2.18, p=0.014) from baseline to week 30. Serum levels of pentraxin-3, soluble human leukocyte antigen-E (sHLA-E), interleukin-6 tended to decrease, while tumour necrosis factor-α level increased after IFX therapy. There were no serious adverse events (SAEs) or AEs necessitating discontinuation of IFX.

Conclusions: Treatment with IFX may lead to remission or improvement with lower glucocorticoid requirement in TAK (clinicaltrials.gov NCT02457585).

Disclosure of Interest: None declared

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