RTX-treated patients could not be established given the low number of patients consenting to 3 longitudinal biopsies it is conceivable that RTX is responsible for preserving exocrine function.

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Spondyloarthritis - treatment

OP0137

TUMOR NECROSIS FACTOR INHIBITORS SHOW A DELAYED EFFECT ON RADIOGRAPHIC SACROILIITIS PROGRESSION IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: 10-YEAR RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: Observational cohort studies have shown that there is low, but still detectable progression level in radiographic sacroiliitis, which might also have an impact on the function in patients with axial spondyloarthritis (axSpA). Recent data showed that tumor necrosis factor inhibitors (TNFi) might retard spinal progression when initiated earlier and taken longer in patients with axSpA. However, the question of whether they also have such an effect on radiographic progression in sacroiliac joints (SIJs) is still unclear.

Objectives: To investigate the longitudinal association between radiographic sacroiliitis progression and treatment with TNFi in patients with early axial SpA in a long-term inception cohort.

Methods: Based on the availability of at least two sets of SIJ radiographs, 301 patients (166 with nr-axSpA, symptom duration ≤5 years and 135 with r-axSpA, symptom duration ≤10 years) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in this analysis. These patients contributed with a total of 737 2-year radiographic intervals. Two trained and calibrated central readers scored the radiographs according to the modified New York criteria. If both scored an image as definite radiographic sacroiliitis, the patient was classified as having r-axSpA. The sacroiliac sum score was calculated as a mean of both readers. The association between previous as well as current TNFi use and radiographic sacroiliitis progression, which was defined as the change in the sacroiliitis sum score over 2 years, was analysed using longitudinal generalized estimating equations (GEE) analysis.

Results: At baseline, 9 (3.0%) patients were treated with a TNFi, and 87 (28.9%) patients received at least one TNFi during the entire follow-up period. A total of 141 of the radiographic intervals were covered with TNFi of any duration, while 109 of them were covered with a TNFi of at least 12 months. While receiving ≥12 months TNFi in the previous interval was associated with a lower progression of the sacroiliitis sum score compared to not receiving TNFi in the previous interval, this was not the case in patients who received TNFi ≥12 months in the current 2-year interval (Figure 1). The significant association between TNF ≥12 months in the previous interval and progression in the sacroiliitis sum score were confirmed in the adjusted multivariable longitudinal GEE analysis. In addition, a similar trend for the beneficial effects was observed in different models, which included other treatment definitions with TNFi in the previous 2-year interval (Table).

Conclusion: Treatment with TNFi was associated with retardation of radiographic sacroiliitis progression in patients with axSpA. This effect becomes evident between 2 and 4 years after treatment initiation.

Figure. A) Cumulative probability plot of the 2-year progression in the sacroiliitis sum score, stratified by receiving at least 12 months TNFi in the previous and current 2-year radiographic intervals. **B)** The change in sacroiliitis sum scores over two years in patients with axial spondyloarthritis treated vs non-treated with TNFi at least 12 months in the previous and current 2-year radiographic intervals.

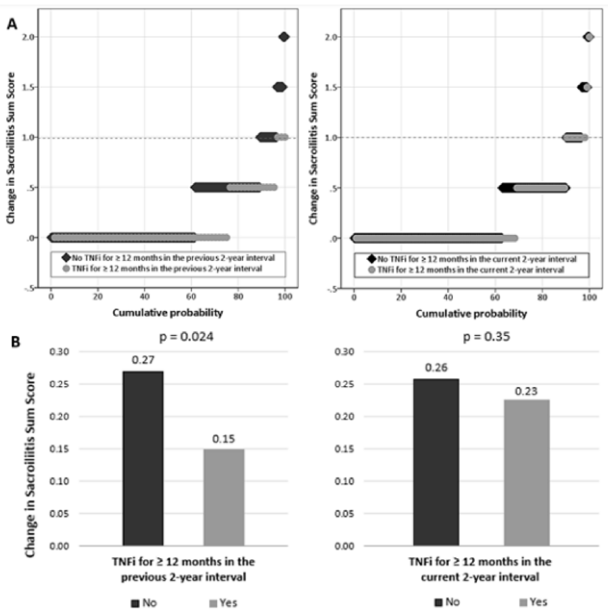

Table 1. The longitudinal GEE analysis of the association between progression in the sacroiliitis sum score and TNFi use.

TNFi treatment definition	Reference	β* (95% CI)
TNFi for ≥ 12 months in the previous 2-year interval	No TNFi for ≥ 12 months in the previous 2-year interval	**-0.09 (-0.18, -0.003)**
Any TNFi use in the previous 2-year interval	No TNFi use in the previous 2-year interval	-0.09 (-0.17, 0.002)
TNFi for ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the current 2-year interval	-0.03 (-0.11, 0.06)
Any TNFi use in the current 2-year interval	No TNFi use in the current 2-year interval	0.05 (-0.05, 0.14)
TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	-0.08 (-0.17, 0.004)

* Parameter estimates from the multivariable models adjusted for **sex**, **age** at the beginning of the current 2-year interval, **HLA-B27** positivity, **symptom duration** at the beginning of the current 2-year interval, time-averaged elevated **CRP**, time-averaged **BASDAI**, and time-averaged **NSAID intake score** in the current 2-year interval.

References:

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OP0138

FEASIBILITY OF PROGRESSIVE ANTI-TNF TAPERING IN AXIAL SPONDYLOARTHRITIS PATIENTS IN LOW DISEASE ACTIVITY: RESULTS FROM THE MULTICENTER NON-INFERIORITY PROSPECTIVE RANDOMIZED CONTROLLED TRIAL SPACING

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Background: Anti-TNF treatments (TNFi) have shown high efficacy in axial spondyloarthritis (ax-SpA) with inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs). However their effect remains predominantly symptomatic, and their long-term tolerance as well as significant societal cost justify investigation about a potential reduction in drug dosage, or –most feasible and comfortable for the patient– increase in intervals between doses.
Objectives: To assess if a progressive and monitored reduction of administered TNFi by increase of intervals between injections results in a comparable proportion of patients remaining after 12 months (m) in low disease activity state despite a decreased cumulative treatment dose received.
Methods: Non-inferiority randomized controlled trial, having included adult patients with ax-SpA fulfilling ASAS criteria, already treated by anti-TNF, and in stable low disease activity for at least 6 m (current and at least 6 m old BASDAI<4/10), who were randomized into 2 groups: either keeping on their usual treatment with stable doses ("unchanged" group), or progressive spacing of injections of their treatment ("spacing" group). Follow-up was done every 3 m during 12 m, with regular monitoring of disease activity and, in patients from the group "spacing", modification of the rhythm of injections according to disease activity and predefined standardized protocol (either increase or decrease (step-back) of intervals between injections). The primary endpoint was the difference of proportions of patients having a low disease activity state (BASDAI<4/10) after 12 m of follow-up between the 2 groups. It was estimated on the ITT population after multiple imputation. The 90% confidence interval associated was calculated using the Farrington-Manning method and the lower bound was compared to the non-inferiority margin of -20%. With an expected proportion of 85% patients remaining in low disease activity in the unchanged group, and α and β risks at respectively 5% and 90%, the required number of patients was calculated at 358, and thus 398 had to be included with a 10% expected proportion of patients with unavailable data.
Results: 398 patients were randomized in 23 French rheumatology units (197 and 201 in the spacing and unchanged groups respectively), and 389 included in analyses (9 did not receive the allocated treatment). Mean (SD) age was 44.3 (12.4) years, 71.2% were males. Mean (SD) BASDAI at inclusion was 1.45 (1.02). TNFi used were etanercept (35.7%), adalimumab (33.9%), infliximab (20.6%), golimumab (9.3%) and certolizumab (0.5%). For the 373 patients with complete follow-up (93.7%), 162/184 (88.0%) had a low disease activity in the "spacing" group vs. 173/189 (91.5%) in the "unchanged" group at 12 m. After multiple imputation for the 16 patients with missing data, the difference of proportion between the two groups was estimated to -4.18% [CI90% -10.0; 1.7], thus confirming the non-inferiority of the "spacing" procedure. In the "spacing" group at 12 m, 134/162 (82.7%) patients in low disease activity were still receiving a lowered TNFi dose.
Conclusion: In ax-SpA patients with BASDAI<4 for at least 6 months under TNFi, it is possible to increase intervals between injections while maintaining a low disease activity by adjusting treatment with quarterly monitoring of SpA activity.
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OP0139

A TIME-SHIFTED EFFECT OF TUMOR NECROSIS FACTOR INHIBITORS ON RADIOGRAPHIC SPINAL PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: LONG-TERM RESULTS FROM THE GERMAN SPONDYLOARTHRITIS INCEPTION COHORT

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Background: There are inconclusive data on the effect of tumor necrosis factor inhibitors (TNFi) on radiographic spinal progression in axial spondyloarthritis (axSpA). Although inflammation and new bone formation are linked in axSpA, TNFi failed to show inhibition of radiographic spinal progression over two years compared to historical cohorts in pivotal studies in radiographic axSpA. Subsequent observational studies suggested that a longer treatment duration, earlier treatment initiation and effective inflammation suppression might be required to achieve inhibition of radiographic progression.
Objectives: The aim of the current study was to evaluate the effect of TNFi on radiographic spinal progression in patients with early axSpA in a long-term inception cohort.
Methods: A total of 266 patients with early axSpA (with r-axSpA with symptom duration ≤10 years and nr-axSpA with symptom duration ≤5 years) from the German Spondyloarthritis Inception Cohort (GESPIC) with at least two sets of spinal radiographs obtained at least 2 years apart during a 10-year follow-up were included. These patients contributed with a total of 542 2-year radiographic intervals. Spinal radiographs were evaluated by three trained and calibrated readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The final mSASSS was calculated as a mean of three reader scores. The association between the current TNFi, previous TNFi and radiographic spinal progression defined as the absolute mSASSS change score over 2 years was analyzed using longitudinal generalized estimating equations (GEE) analysis.
Results: Only 9 patients were treated with a tumor necrosis factor inhibitor (TNFi) at baseline, and a total of 77 patients received TNFi during the entire follow-up period that gave 103 2-year intervals covered by TNFi of any duration, and 78 intervals covered by TNFi with treatment duration of at least 12 months. Radiographic spinal progression in axSpA patients receiving TNFi in the current 2-year interval was not different from progression in patients not treated with TNFi, while TNFi in the previous 2-year interval was associated with lower progression compared to patients without TNFi in this interval (Figure 1). The latter was also evident for patients who received TNFi in both previous and current 2-year intervals, i.e. patients treated with TNFi over 4 years. The longitudinal GEE analysis confirmed no significant association between current TNFi treatment and radiographic spinal progression but a significant association between TNFi in the previous 2-year interval (especially if this was continued also in the current interval giving 4 years in total) and the progression in the current one (Table 1).

Table 1. The association between the change of the mSASSS over two years and current and/or previous treatment with TNFi in the longitudinal generalized estimation equation analysis.

TNFi treatment definition			
TNFi for ≥12 months in the previous 2-year interval	TNFi for ≥12 months in the current 2-year interval	Reference	β* (95% CI)
	Yes	No TNFi for ≥12 months in the current 2-year interval	-0.19 (-0.56 to 0.18)
Yes		No TNFi for ≥12 months in the previous 2-year interval	**-0.56 (-0.95 to -0.17)**
Yes	Yes	No TNFi for ≥12 months in the current and previous 2-year intervals	**-0.59 (-1.03 to -0.15)**

*Parameter estimates from the multivariable models adjusted for sex, symptom duration at the beginning of the current 2-year interval, time-averaged ASDAS in the current 2-year interval, smoking in the current 2-year interval, classification as non-radiographic or radiographic axSpA, and mSASSS at the beginning of the current 2-year interval.

Conclusion: TNFi treatment exhibits a time-shifted inhibitory effect on radiographic spinal progression in axSpA that becomes evident only in the second 2-year interval after treatment initiation.