**Conclusions:** This is the first trial to report imaging data in both AS and nr-axSpA pts over 4 years. Limited spinal radiographic progression was observed in CZP-treated pts with lower progression between Wks96 and 204 compared with the first 96 wks. Limited change in radiographic sacroiliitis was observed. Early reductions in MRI inflammation were maintained to Wk204.

**References:**

[1] Landewé R. Ann Rheum Dis 2014;73:39–47.

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## OP0024 DRUG TROUGH LEVELS AND ANTIDRUG ANTIBODIES IN NONSELECTED ANKYLOSING SPONDYLITIS PATIENTS USING SELF-INJECTED ANTITNF DRUGS

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**Background:** Immunization to biological drugs can reduce the treatment efficacy and increase the risk of adverse events.

**Objectives:** To determine the drug trough concentrations and anti-drug antibody (ADAb) levels of self-injected TNF-inhibitors, in non-selected patients with ankylosing spondylitis (AS) attending the rheumatological outpatient clinic, and to study the patient related factors affecting the immunization to antiTNF drugs.

**Methods:** A total of 313 patients with AS were recruited. A blood sample, taken 1–2 days prior to next drug injection, was obtained from 273 patients. Trough concentration of the anti-TNF drugs were measured with capture-ELISA (Promonitor EIA, Progenica), the levels of ADAb with radioimmunoassay (Sanquin Laboratories, The Netherlands), and the serum TNF-blocking capacity by using an in-house reporter gene assay. The clinical activity of AS was assessed using the Bath AS Disease Activity Index (BASDAI), the Bath AS Functional Index (BASFI), and the Maastricht AS Entheses Score (MASES).

**Results:** ADAbs were observed in 21% of patients on adalimumab (n=99), in 0% of those on etanercept (n=83), in 3% of those on golimumab (n=79) and in 50% of those on certolizumab pegol (n=12). The BASDAI in ADAb positive patients was 1.4 (sd 1.4) and in the ADAb negative patients 2.0 (sd 1.8 p=0.060). Factors affecting the immunization to biological drug could be further analyzed in patients using adalimumab. Trough drug concentrations of adalimumab correlated with the presence of ADAb (r=-0.54, rp<0.0001). In adalimumab users higher BMI was associated with the presence ADAb (p=0.019, adjusted for gender, age, and the time of biological use). Of patients who used methotrexate (MTX) 12% were ADAb positive and of those who did not use MTX 28% were ADAb positive (p=0.048 adjusted for gender, age, weight, and the time of biological use). The use of sulphasalazine was not associated with lower number of ADAb positive patients. Of adalimumab users with ADAb+ the mean BASDAI was 1.2 (sd 1.4) and of those without ADAb 1.9 (sd 1.9) (p=0.091). Of adalimumab users the drug concentration was in the target range (5–10 mg/l) in only 33% of patients.

**Conclusions:** The disease activity of AS patients using self injected antiTNF drugs was low. The immunization to adalimumab was relatively common in nonselected AS patient population. However, no clear association was observed between the presense of ADAb and the disease activity.

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## OP0025 ANTIDRUG ANTIBODIES DETECTION IS STRONGLY INFLUENCED BY THE TYPE OF ASSAY USED

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**Background:** Direct comparison of immunogenicity data is hampered due to different assays used with different sensitivity for drug interference. This is the first study to compare detection of antidrug antibodies (ADA) with different assays in ankylosing spondylitis (AS) patients. Studying immunogenicity in AS patients with a drug tolerant assay may contribute to a better understanding of development of ADA.

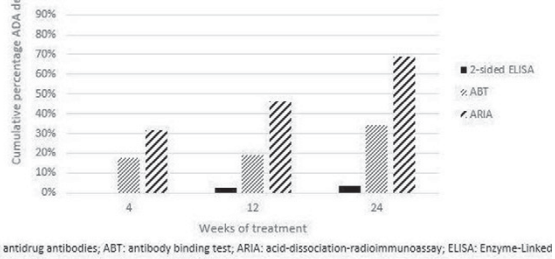
**Objectives:** To compare the detection of ADA in different assay techniques with differences in drug interference, acid-dissociation-radioimmunoassay (ARIA) antidrug binding test (ABT) and the more frequently used 2-sided Enzyme-linked Immuno Sorbent Assay (ELISA) in AS patients. Second, to study the relation of adalimumab drug levels with the detection of ADA.

**Methods:** In this study, the detection of the ADA in ARIA and ABT was compared with the detection of ADA in the 2-sided ELISA in 84 consecutive AS patient over a period of 24 weeks; at 4, 12 and 24 weeks of treatment. Adalimumab drug levels were measured using an ELISA. The assays were designed by Sanquin, Amsterdam. For the difference in drug levels we divided the patients in four different groups; all assays negative (group 0), only ARIA positive (group 1), ARIA and ABT positive, 2-sided ELISA negative (group 2) and all assays positive (group 3). We used last observation carried forward to imputate missing data.

**Results:** As shown in Figure 1, 26% of the patients tested positive for ADA in the ARIA compared to 14% in the ABT and no detection in the 2-sided ELISA at week 4. At weeks 12 and 24 respectively, cumulative 46% and 69% of patients, tested positive in the ARIA for ADA, compared to 19% and 35% in the ABT and 2% and 4% with the 2-sided ELISA.

Median adalimumab levels at week 24 in group 0, 1, 2 and 3 were 9.5 (5.3–13.3), 8.4 (5.3–11.0), 2.8 (0.9–4.3) and 0.002 (0.0–1.3) respectively. No significant differences were found in median adalimumab levels between patients with no ADA detection and patients tested positive in only the ARIA, respectively, 8.4 (5.3–11.0) and 9.5 (5.3–13.3) p=0.385. However, when both ARIA and ABT tested positive, drug levels significantly differed from patients with no ADA detection, 2.8

Figure 1. Cumulative percentages of ADA detection per assay type at different time points




ADA: antidrug antibodies; ABT: antibody binding test; ARIA: acid-dissociation-radioimmunoassay; ELISA: Enzyme-Linked Immuno Sorbent Assay

(0.9–4.3) and 9.5 (5.3–13.3), p=0.000. When patients tested positive in the ARIA, ABT and the 2-sided ELISA almost all patients had undetectable drug levels.
**Conclusions:** The fast majority of the AS patients develop ADA. The ARIA detects more ADA compared to the assays susceptible for drug interference, the ABT and the more frequently used 2-sided ELISA. Immunogenicity data should be interpreted with the knowledge of the assay and in context of drug levels.
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## OP0026 HIGH DRUG-FREE REMISSION IN EARLY PERIPHERAL SPONDYLOARTHRITIS AFTER INDUCTION THERAPY WITH GOLIMUMAB

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**Background:** In rheumatoid arthritis there is accumulating evidence for a so-called "window of opportunity" remission induction treatment at an early stage of the disease. Whether a similar concept also applies to Spondyloarthritis is currently unknown. Given the higher chance of obtaining remission or low disease activity with early aggressive (biologic) treatment in early axial SpA, one could speculate that there is at least also a possibility of a "window of opportunity" for drug-free remission in peripheral SpA (pSpA).
**Objectives:** To evaluate sustained drug-free clinical remission after induction therapy with golimumab in patients with active peripheral Spondyloarthritis in a very early stage of the disease.
**Methods:** CRESPA (Clinical REmission in peripheral SPondyloArthritis) is an ongoing monocentric study of golimumab treatment in pSpA patients. Eligible patients were $\geq$18 years and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for pSpA. All patients had a symptom duration $<$12 weeks. Patients were randomized 2:1 to receive golimumab 50 mg every 4 weeks or matching placebo for 24 weeks. The primary endpoint was the percentage of patients achieving clinical remission at week 24, defined as the absence of arthritis, enthesitis and dactylitis on clinical examination. If patients were in clinical remission at two consecutive visits (major evaluations at week 12, 24, 36 and 48) treatment was stopped.
These patients were prospectively followed to assess the percentage of patients in sustained drug-free clinical remission, compared to those experiencing a clinical relapse of arthritis, dactylitis or enthesitis. In case of clinical relapse patients were retreated with open-label golimumab in the extension part of this trial.
**Results:** In total 60 patients were randomized of whom 20 received placebo and 40 golimumab. Baseline demographics and disease characteristics were generally similar between the 2 groups. At week 24 a significantly higher percentage of patients receiving golimumab achieved clinical remission compared to patients receiving placebo (75% (30/40) versus 20% (4/20); $P<0.001$). At week 12 similar results were observed (70% (28/40) versus 15% (3/20); $P<0.001$). In 49 out of the 60 patients treatment could be stopped because they fulfilled sustained clinical remission at 2 major consecutive visits. All patients had at least a follow up of 12 months after discontinuation of treatment with a maximum of follow-up of 58 months. 53% (26/49) of these patients are still in drug-free sustained clinical remission and 47% (23/49) had a clinical relapse after withdrawal. The majority of relapsed patients experienced their flare within 6 months after discontinuation.
**Conclusions:** In patients with active, very early peripheral spondyloarthritis, treatment with golimumab led to high percentages of clinical remission at week 12 and 24. A remarkably high percentage of patients are still in sustained drug-free clinical remission after induction therapy with golimumab which indicates a window of opportunity for drug-free remission in this disease.
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## OP0027