

Treat-to-target dose reduction and withdrawal strategy of TNF inhibitors in Psoriatic Arthritis and Axial Spondyloarthritis: a randomized controlled non-inferiority trial



Michielsens CAJ^{1,2}, den Broeder N^{1,2}, van den Hoogen FHJ¹, Mahler EAM¹, Teerenstra S³, van der Heijde D⁴, Verhoef LM¹, den Broeder AA^{1,2}

1)Department of Rheumatology, Sint Maartenskliniek Nijmegen, the Netherlands 2)Department of Rheumatic diseases, Radboud Institute for Health Sciences, Radboudumc Nijmegen, the Netherlands 3)Department for Health Evidence, section Biostatistics, Radboud Institute for Health Sciences, Radboudumc Nijmegen, the Netherlands 4)Department of Rheumatology, Leiden University Medical Center, the Netherlands

BACKGROUND

- ❖ Tumor necrosis factor inhibitors (TNFi) are safe and effective for Psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).
- ❖ Disadvantages: higher infection rate, costs and injection side reactions.
- ❖ Treat-to-target (T2T) tapering might reduce these disadvantages, but no randomized controlled trials exist up-to-now.

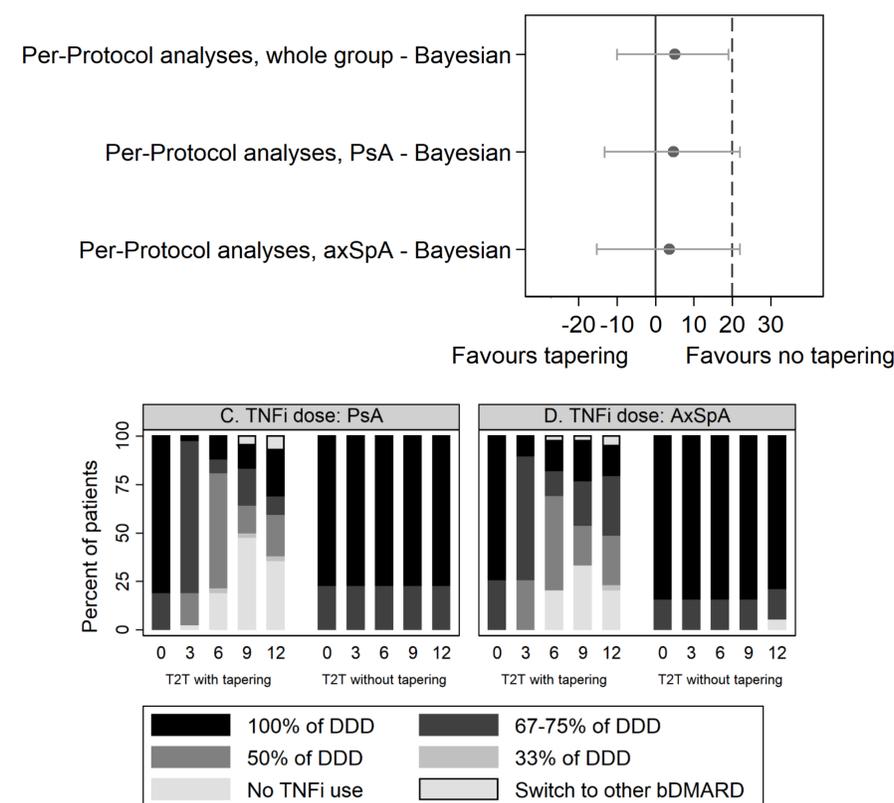
AIM

To investigate if a T2T strategy with tapering of TNFi is non-inferior, compared to a T2T strategy without tapering in PsA and axSpA patients with stable low disease activity.

METHODS

- ❖ Patients were randomized 2:1 in our monocentre to a T2T strategy with or without tapering and stratified for diagnosis (PsA or axSpA) and use of csDMARDs.
- ❖ Inclusion criteria:
 - ❖ Age ≥ 16 years;
 - ❖ Low disease activity (LDA) for ≥ 6 months (rheumatologist judgement, and either PASDAS ≤ 3.2 and mBSA $\leq 3\%$, or ASDAS < 2.1);
 - ❖ Stable TNFi ≥ 6 months and $> 50\%$ registered dose.
- ❖ Disease activity, medication use, adverse events were collected every three months.
- ❖ Primary outcome: difference in proportion of patients in LDA (PASDAS ≤ 3.2 or ASDAS < 2.1 and an absence of active extra-musculoskeletal symptoms) at 12 months.
- ❖ Prespecified non-inferiority margin of 20%.
- ❖ Bayesian analyses was performed for the primary outcome, with a diluted prior based on the DRESS trial in rheumatoid arthritis.¹

RESULTS



RESULTS - Disease outcomes

- ❖ Bayesian analysis for primary outcome (figure 1) showed non-inferiority of tapering strategy:
 - ❖ Proportion in LDA at month 12: 69% in tapering and 73% in non-tapering group
- ❖ Mean disease activity at 12 months:
 - ❖ PASDAS (for PsA): 2.29 (1.31) vs. 2.59 (1.43);
 - ❖ ASDAS (for axSpA): 1.82 (0.96) vs. 1.56 (0.73).

CONCLUSION

- T2T tapering strategy in spondyloarthritis:
 - ❖ Is non-inferior to a T2T strategy without tapering.
 - ❖ Leads to a substantial reduction in TNFi drug use.

RESULTS - Medication use and adverse events

- ❖ Mean TNFi use at 12 months (figure 2):
 - ❖ %DDD was 53% (95%CI [44%-63%]) for the tapering and 91% (95%CI [85%-97%]) for the no-tapering group.
- ❖ Concomitant medication use:
 - ❖ Cumulative incidence of NSAID in the tapering group compared to the no-tapering group was 44 (54%) vs. 10 (24%) (p=0.002). No difference was seen for glucocorticoid use.
- ❖ Occurrence of (serious) adverse events:
 - ❖ No difference in the occurrence of (serious) adverse events was seen. No deaths.

Baseline characteristic	T2T with tapering (N=81)	T2T without tapering (N=41)
Diagnosis, n (%)		
- Psoriatic arthritis	42 (52%)	22 (54%)
- Axial spondyloarthritis	39 (48%)	19 (46%)
Female, n (%)	28 (35%)	20 (49%)
Age at inclusion, years, mean (SD)	50 (14)	52 (15)
Disease duration at inclusion, years, median (IQR)	11 (5-21)	12 (5-21)
Duration of current bDMARD use, years, median (IQR)	2 (1-6)	2 (2-7)
Disease activity, mean (SD)		
- PASDAS - (64/64 PsA)	1.60 (1.26)	1.63 (0.98)
- ASDAS - (57/58 axSpA)	1.34 (0.87)	1.21 (0.61)
Current csDMARD use, n (%)	18 (22%)	10 (24%)
CASPAR Criteria, n (%)	34 (81%)	17 (77%)
ASAS Criteria, n (%)	35 (90%)	17 (89%)
Current NSAID use, n (%)	26 (32%)	14 (34%)

¹van Herwaarden N et al. Disease activity guided dose reduction and withdrawal of adalimumab or etanercept compared with usual care in rheumatoid arthritis: open label, randomised controlled, non-inferiority trial BMJ 2015.

