

Efficacy of bDMARDs in Early versus Established Disease in Axial Spondyloarthritis: A Meta-Analysis of Randomized Trials

Diego Benavent¹, Victoria Navarro-Compán², Dafne Capelusnik^{3, 4}, Sofia Ramiro ^{5, 6}

1. Rheumatology Department, Hospital Universitari de Bellvitge, Barcelona. 2. Rheumatology Department, Hospital La Paz, Madrid. 3. Maastricht University Care and Public Health Research Institute, Maastricht, The Netherlands. 4. Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. 5. Rheumatology, Leiden University Medical Center, Leiden, The Netherlands. 6. Rheumatology, Zuyderland Medical Centre, Heerlen, The Netherlands.

BACKGROUND

A consensus definition of ‘early axial spondyloarthritis (axSpA)’ for the research setting was recently developed under the auspices of ASAS, based on axial symptoms ≤ 2 years (1).

OBJECTIVE

We conducted a meta-analysis of all placebo-randomised controlled trials (RCTs) of approved bDMARDs and tsDMARDs in patients with axSpA, with the aim of investigating the influence of symptom duration on treatment response.

METHODS

- **Design:** Systematic review and meta-analysis, including RCTs sourced from systematic literature reviews for ASAS-EULAR management recommendations (2).
- **Eligibility criteria:** RCTs with adult axSpA patients, comparing b/tsDMARDs vs. placebo, focusing on early disease stages based on symptom duration thresholds (≥ 20% of patients in each category of the threshold).
- **Data:** Individual RCT data requested from Vivli, ClinicalStudyDataRequest, and Engagezone.
- **Population:** Patients were categorized based on symptom duration into early or established disease groups, stratified according to symptom duration thresholds (1, 2, 3, 4 and 5 years).
- **Outcomes:** Primary outcome was ASAS40 response; secondary outcomes included various ASAS and ASDAS metrics at the time of the primary endpoint of each RCT.
- **Analysis:** Treatment effects assessed with relative risk (RR) and RR ratio (RRR) per symptom duration threshold.
- **Meta-Analysis:** Random effects model performed across all RCTs.

RESULTS

- Eleven RCTs involving 3,272 axSpA patients were included in the analysis, with ASAS40 response included in seven studies.
- The patient cohort had a mean age of 37.9 years, a mean symptom duration of 9.3 years, and was predominantly male (59%) and HLA-B27 positive (78.8%).
- RCTs covered studies on golimumab (n=4), certolizumab (n=2), secukinumab (n=2), adalimumab (n=1), etanercept (n=1), and ixekizumab (n=1). No study with tsDMARDs was eligible. Only one had more than 20% patients over the 1-year threshold (not pooled).
- Analysis of the primary endpoint, ASAS40 response at 12-16 weeks, showed no significant difference between early and established disease across the symptom duration threshold (2 to 5 years).
- No statistically significant pooled RRRs were observed for any of the measured outcomes for early vs established disease according to the different thresholds.

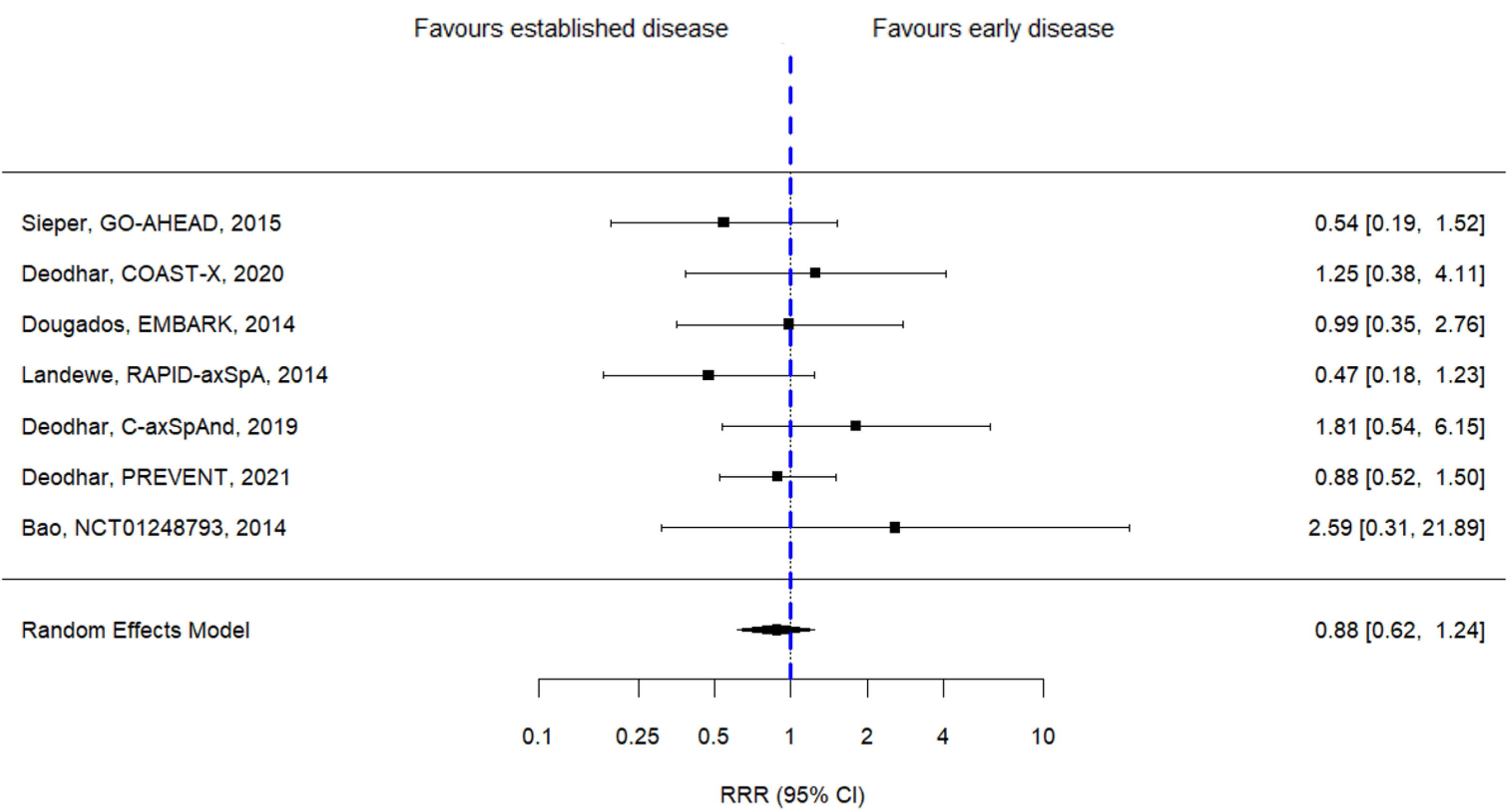


Figure 1. Relative risk ratio for ASAS40 at the timing of the primary endpoint for the bDMARD treatment vs placebo effect in patients with axSpA with early versus established disease, defined based on the 2-year symptom duration threshold

Table 1. Pooled relative risk ratio of bDMARDs vs PBO in early vs established disease for primary and secondary outcomes

Outcome	Threshold Symptom Duration (Years)	Pooled RRR (95% CI)	I ²
ASAS40			
	2	0.88 (0.62-1.24)	0
	3	1.14 (0.75- 1.75)	26.12%
	4	1.11 (0.80 -1.54)	0
	5	1.08 (0.78 – 1.49)	0
ASAS20			
	2	0.96 (0.77 – 1.20)	0
	3	1.09 (0.83 – 1.44)	36.6 %
	4	1.14 (0.92 – 1.40)	0
	5	1.15 (0.94 – 1.41)	0.41%
ASAS PR			
	2	1.10 (0.58- 2.09)	0
	3	1.30 (0.67 – 2.54)	0
	4	1.15 (0.58 – 2.30)	0
	5	1.32 (0.66 – 2.64)	0
ASAS 5/6			
	2	0.87 (0.61 – 1.24)	0
	3	0.86 (0.47 – 1.58)	53.5%
	4	0.95 (0.67 – 1.35)	0
	5	0.93 (0.66 – 1.31)	0
ASDAS LDA			
	2	0.96 (0.67 – 1.37)	16.77%
	3	0.98 (0.72 – 1.33)	0
	4	0.96 (0.68 – 1.36)	0
	5	0.92 (0.66 – 1.29)	0
ASDAS ID			
	2	1.21 (0.70 – 2.07)	0
	3	1.13 (0.60 – 2.56)	0
	4	0.93 (0.43 – 2.02)	0
	5	0.90 (0.33 – 2.51)	24.46%
ASDAS CII			
	2	1.03 (0.76 – 1.39)	0
	3	0.90 (0.64 – 1.24)	19.20%
	4	0.83 (0.64 – 1.10)	0
	5	0.84 (0.64 – 1.11)	0
ASDAS MI			
	2	0.84 (0.43 – 1.64)	8.47%
	3	0.92 (0.49 – 1.72)	0
	4	0.57 (0.29 – 1.13)	0
	5	0.65 (0.32 – 1.30)	0

ASAS: Assessment of SpondyloArthritis international Society; PR: Partial Remission; LDA: Low Disease activity; ID: Inactive Disease; CII: Clinical Important Improvement; MI: Major Improvement

CONCLUSIONS

- In this meta-analysis of RCTs, **no significant difference** has been found in the effect of **bDMARDs vs PBO** in **early** compared to **established axSpA**, defined according to several thresholds of symptom duration (between 2 and 5 years).
- Treating patients earlier or later in the disease course translates into the achievement of comparable short-term clinical outcomes.

