

# Prednisolone plus a disease-modifying antirheumatic drug improved outcomes in early rheumatoid arthritis

Svensson B, Boonen A, Albertsson K, et al. Low-dose prednisolone in addition to the initial disease-modifying antirheumatic drug in patients with early active rheumatoid arthritis reduces joint destruction and increases the remission rate: a two-year randomized trial. *Arthritis Rheum.* 2005;52:3360-70.

**Clinical impact ratings:** Rheumatology ★★★★★☆☆

## QUESTION

In patients with early rheumatoid arthritis (RA), does adding low-dose prednisolone to the first use of a disease-modifying antirheumatic drug (DMARD) improve outcomes?

## METHODS

**Design:** Randomized controlled trial.

**Allocation:** Concealed.\*

**Blinding:** Blinded (outcome assessors).\*

**Follow-up period:** 2 years.

**Setting:** 6 centers in southern Sweden.

**Patients:** 259 patients 18 to 80 years of age (mean age 55 y, 64% women) who were starting treatment with a first DMARD for active RA  $\leq 1$  year in duration. Patients with previous DMARD or glucocorticoid treatment, low bone mineral density (BMD), or a history of fragility fracture were excluded.

**Intervention:** Prednisolone, 7.5 mg daily for 2 years ( $n = 124$ ), or no prednisolone ( $n = 135$ ). The choice of DMARD (mainly methotrexate or sulfasalazine) was at the attending physician's discretion. All patients also received calcium, 1000 mg daily.

**Outcomes:** Change in joint damage in the hands and feet assessed by radiography (erosion score [0 to 280], joint space narrowing score [0 to 168], and total of the 2 scores), Disease Activity Score in 28 joints (DAS28), functional disability (Stanford Health Assessment Questionnaire [HAQ], 0 to 3), and

Signals of Functional Impairment (SOFI) index (0 to 44); clinical remission (DAS28  $< 2.6$ ); and adverse events.

**Patient follow-up:** 87% for the primary endpoint (97% included in the intention-to-treat analysis of secondary outcomes).

## MAIN RESULTS

At 2 years, the prednisolone group had less increase in erosion score and total score than the no-prednisolone group (Table). Disease activity decreased more with prednisolone (Table) and remission rate was higher (56% vs 33%,  $P < 0.001$ ). The prednisolone group had greater improvements in functional disability and impairment (Table). Groups did not differ for adverse events.

## Prednisolone vs no prednisolone in addition to a first disease-modifying antirheumatic drug in early rheumatoid arthritis at 2 years†

Outcomes	Prednisolone Mean change from baseline	No prednisolone	Reduction in mean change (95% CI)
Erosion score	1.9	4.0	2.1 (0.7 to 3.5)
Joint space narrowing score	3.3	5.0	1.7 (-0.3 to 3.7)‡
Total joint damage score	5.2	9.1	3.9 (0.7 to 7.1)
	Mean score at 2 y		Reduction in mean score (CI)
Disease activity	2.7	3.2	0.5 (0.2 to 0.8)
Functional disability	0.5	0.7	0.2 (0.1 to 0.3)
Functional impairment	4.0	7.0	3.0 (1.6 to 4.4)

†CI defined in Glossary. Differences in means and CI calculated from data in article.

‡Not significant.

## CONCLUSION

In patients with early rheumatoid arthritis, the addition of low-dose prednisolone to the first use of a disease-modifying antirheumatic drug reduced joint damage and disease activity.

*Sources of funding:* Swedish Rheumatism Association; 80-Year Foundation of King Gustaf V; Ugglas Foundation; Börje Dahlins Foundation; Gorthon Foundation in Helingsborg; Stiftelsen för Rörelsehindrade I Skåne.

*For correspondence:* Dr. B. Svensson, University of Lund, Lund, Sweden. E-mail [bjoern.svensson@swipnet.se](mailto:bjoern.svensson@swipnet.se).

\*See Glossary.

## COMMENTARY

Prevention of irreversible joint damage, functional decline, and reduced survival is the main goal in the treatment of RA, but the optimal strategy for achieving these objectives remains uncertain. Recent research supports the concept of the "window of opportunity" in RA treatment: early intervention using "disease-modifying" treatments immediately, close monitoring, and treatment adjustments to suppress disease activity and achieve remission. Ideally, RA treatment trials should target recently diagnosed, treatment-naïve patients with active disease, using a blinded, randomized design and multidimensional evaluation of disease (clinical and joint-imaging variables plus measures of functional status and quality of life). These outcomes must be measured using well-validated assessment tools, over as long a period as possible.

The well-executed study by Svensson and colleagues meets most of these requirements. However, the study was not blinded (except for the radiographic scoring) or long-term (although 2 y is adequate), and quality of life was not assessed. The exclusion of the 5% of patients with highly active disease and the 11% with osteoporosis is a reminder that not all patients with RA are candidates for low-dose prednisolone.

The authors' meticulous assessment of 250 randomized patients

strongly supports previous results (1) indicating that low-dose prednisolone is a very beneficial adjunctive treatment in patients with early RA. Treated patients had better disease control and function, and less radiographic damage. Differences were apparent at 3 months and persisted thereafter.

However, several caveats exist. First, a more intensive antiosteoporotic treatment is warranted, as well as special attention to cardiovascular risk factors that may be aggravated by prednisolone. Second, the optimal duration of prednisolone treatment is unknown. Third, while most study patients were treated with a single DMARD, current data support more aggressive initial treatment (2), with or without antitumor necrosis factor- $\alpha$  agents. Patients treated more intensively with drug combinations are likely to achieve still better outcomes.

*Ami Schattner, MD  
Hebrew University Hadassah Medical School  
Jerusalem, Israel*

## References

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