

# Combination disease-modifying antirheumatic drug therapy reduced work disability in early rheumatoid arthritis

Puolakka K, Kautiainen H, Möttönen T, et al. Impact of initial aggressive drug treatment with a combination of disease-modifying antirheumatic drugs on the development of work disability in early rheumatoid arthritis: a five-year randomized followup trial. *Arthritis Rheum.* 2004;50:55-62.

## QUESTION

In patients with early rheumatoid arthritis (RA), how does treatment with a combination of disease-modifying antirheumatic drugs (DMARDs) compare with a single DMARD for prevention of work disability?

## METHODS

**Design:** Randomized controlled trial (Finnish Rheumatoid Arthritis Combination Therapy trial).

**Allocation:** {Concealed}†.\*

**Blinding:** Blinded {outcome assessors}†.\*

**Follow-up period:** 5 years.

**Setting:** 18 hospitals in Finland.

**Patients:** 162 patients 18 to 65 years of age (mean age 45.5 y, 62% women) with RA of recent onset (< 2 y) and presence of active disease who had never received DMARDs and were still working or potentially employable.

**Intervention:** Combination therapy with DMARDs (simultaneous sulfasalazine, 500 to 1000 mg twice/d; methotrexate, 7.5 to 15

mg/wk; hydroxychloroquine, 300 mg/d; plus prednisolone, 5 to 10 mg/d) (combination-therapy group,  $n = 80$ ) or single therapy with a DMARD (initially sulfasalazine, 2 to 3 g/d, which was replaced with methotrexate 7.5 to 15 mg/wk if clinical response was < 25% at 6 mo) with or without prednisolone (single-therapy group,  $n = 82$ ). After 2 years, the drug treatment strategy was no longer restricted and patients with inadequate response to single DMARD therapy were allowed to switch to combination DMARD therapy.

**Outcomes:** Cumulative duration of all work disability (sick leaves plus RA-related disability pensions) was obtained from social insurance registers or case records.

**Patient follow-up:** 97.5%.

## MAIN RESULTS

The combination-therapy group had a lower median cumulative duration of all work disability days per patient-observation year than the single-therapy group (12.4 vs 32.2 d,  $P = 0.008$ ) and a lower median cumulative

duration of sick leaves (work disability periods  $\leq 300$  d) per patient-observation year than the single-therapy group (11.7 vs 30.0 d,  $P = 0.002$ ). Groups did not differ for median number of days on RA-related disability pension per patient-observation year (0 vs 0 d,  $P = 0.23$ ).

## CONCLUSION

In patients with early rheumatoid arthritis, aggressive initial treatment with a combination of DMARDs reduced the number of days of sick leave and overall work disability at 5 years more than therapy with a single DMARD.

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\*See Glossary.

†Information provided by author.

## COMMENTARY

The natural history of RA is characterized by poor outcome, with progressive joint damage and function loss in most patients. Therefore, the goal of treatment is not only to control pain, but also to reduce joint damage and disability.

Work disability is a frequent and serious outcome of RA that can translate into less income for the patient and less productivity for society. Patients who have more serious disease, as represented by greater functional limitation, are substantially more likely to become work disabled than are those with milder disease (1).

Evidence exists that early sustained suppression of disease activity in RA is essential to prevent joint damage. Previous studies have shown that aggressive initial drug therapy with a combination of such antirheumatic drugs as methotrexate, hydroxychloroquine, and sulfasalazine in early RA lead to slower progression of joint damage than therapy with a single antirheumatic drug over the first 2 years (2). In accordance with this benefit there has been a recent shift from single-drug therapy to combination therapy or early aggressive management. This well-done study by Puolakka and colleagues highlights that not only does early aggressive combination DMARD therapy have a beneficial effect on joint damage, it has a favorable influence on work disability. The benefits began to accrue in the first year and continued to accumulate in subsequent years.

2 related findings are notable. First, the rate of accumulation of work disability days in the single-therapy group did not decrease after half the group switched to combination therapy, indicating that initial treatment was very important. Second, only work disability measured as

sick leave days was significantly reduced in the combination-therapy group. Although fewer patients in the combination-therapy group had permanent disability, the difference did not differ significantly from that of the single-therapy group, suggesting that more powerful treatment is needed to achieve this outcome.

Some important limitations of the study are worth mentioning. First, the number of unemployed persons at baseline differed markedly between the 2 groups, with a probable bias favoring a positive finding in the combination-therapy group; however, in subgroup analyses of employed patients only, combination-therapy group patients still had fewer sick leave days. Second, small sample size may have limited the ability to detect a difference in permanent disability.

Overall the message is persuasive. Work disability, a frequent occurrence in patients with RA, is reduced by initial aggressive drug treatment. This study provides further evidence that aggressive management of RA should begin promptly after diagnosis.

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## References

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