Concise report

A simple model that suggests possible cost savings when modified-release prednisone 5 mg/day is added to current treatment in patients with active rheumatoid arthritis

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Abstract

Objective. The effects of a 12-week treatment with modified-release prednisone (MR-pred) on the costs of drug treatment of RA were modelled.

Methods. With the results of a recent randomized trial as source data, we expressed the effect of treatment (MR-pred vs placebo) on the decrease in the proportion of RA patients meeting disease activity thresholds for reimbursement of biologic treatment.

Results. The results showed 11–13% more patients on MR-pred than on placebo dropped below reimbursement thresholds for the Netherlands, Belgium and the UK. Assuming 1 year of biologics cost €15,000 and MR-pred costs €1/day, €396 are saved in each patient delaying biologic treatment by 12 weeks.

Conclusion. Despite a considerably higher cost than conventional prednisone, MR-pred is a cost-effective option for RA patients not on glucocorticoids who are eligible for therapy with biologic agents.

Key words: rheumatoid arthritis, treatment, glucocorticoids, cost of treatment, economic model.

Introduction

The prognosis of RA has improved through the application of early treat-to-target strategies with innovative combinations of traditional antirheumatic drugs and a rapid switch to biologic agents [1, 2]. However, the high cost of biologic agents is straining health care budgets, consequently reimbursement is restricted.

There has been a change of opinion about the use of glucocorticoids in RA, partly because there is now a better understanding that the risks of low-dose oral administration are relatively low [3]. Recently a modified-release prednisone (MR-pred) preparation has become available. The evidence suggests that MR-pred has an even better side-effect profile and is also particularly useful in combating morning stiffness, as it can be given at night without significantly disturbing the normal diurnal rhythm of indigenous cortisol production.

Patients and methods

We used data from a 12-week placebo-controlled study to model the benefits on drug costs of starting MR-pred in patients who have a reimbursable indication for biologic treatment [4]. In the Netherlands, this indication is persistent disease activity (DAS28 > 3.2) despite treatment with at least two antirheumatic drugs. In Belgium and the UK, the threshold is DAS28 > 3.7 and > 5.1, respectively.

Results

The CAPRA-2 study [4] randomized 350 RA patients with active disease (mean DAS28 5.2; s.d. 0.8) despite disease-modifying antirheumatic therapy to MR-pred 5 mg/day (n = 231) or placebo (n = 119). After 12 weeks, DAS28 was reduced by a mean of 1.2 in the MR-pred group compared with 0.6 in the placebo group. Analysis according to the last observation carried forward suggests that 28% of patients in the MR-pred group and 15% in the...
placebo group had a DAS28 \( \leq 3.2 \) at the end of the study, a difference of 13\% (95\% CI 4\%, 21\%; CAPRA-2 study report). Thus had these patients been in routine clinical practice in the Netherlands, starting MR-pred would have delayed initiation of biologics by at least 3 months in 28\% of patients: a net effect of 13\% against the wait-and-see policy (or placebo), increasing to 28\% when biologics are started immediately.

In the context of Belgium and the UK, 97\% and 55\% of patients, respectively, would have had an indication for reimbursement. Table 1 shows that the effect of MR-pred is similar at different thresholds (difference between treatment groups: 13\% and 11\%, respectively).

Without any further extrapolation beyond 3 months (in other words, if response is completely lost and all patients with an initial indication for reimbursement subsequently go on to receive biologics), the conservative net estimate of 13\% results in 3.25\% (i.e. 13/4) fewer biologic prescriptions on a yearly basis. Assuming €15,000 as the mean drug cost for 1 year of biologic treatment and €1 as the daily cost for MR-pred, the net drug cost savings can be calculated to be €396, that is:

\[
\text{Cost savings for biologics: } 3.25\% \times 15,000 = €487.50 \\
\text{Cost of 3 months of MR-pred: } €91.25 \\
\text{€487.50 – €91.25 = €396}
\]

In addition, any retention of response beyond the 3-month time window will increase the savings. For example, if this level of response is maintained for 1 year, net savings approach €1600. In Table 2, a simple bivariate sensitivity analysis explores alternative scenarios both for 3 and 12 months of efficacy:

(i) Lower and upper 95\% confidence limits of the net estimate of 13\%.
(ii) Upper 95\% confidence limits of the absolute estimate of 28\% (assuming no wait-and-see policy is applied).
(iii) Assuming a biologic treatment cost of €10,000 and €20,000/year, respectively.
(iv) Assuming a cost for MR-pred of €0.50 and €1.50/day, respectively.

Although the net savings vary, the MR-pred strategy remains dominant.

**Table 1** Proportion of patients dropping below reimbursement thresholds of disease activity during the trial

<table>
<thead>
<tr>
<th>Percentage of patients at or below threshold</th>
<th>DAS28 threshold for reimbursement</th>
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<tbody>
<tr>
<td>UK: 5.1</td>
<td>BELGIUM: 3.7</td>
</tr>
<tr>
<td>MR-pred Placebo MR-pred Placebo MR-pred Placebo</td>
<td></td>
</tr>
<tr>
<td>Baseline 45 45 3 3 0 0</td>
<td></td>
</tr>
<tr>
<td>12 weeks 79 68 42 29 28 15</td>
<td></td>
</tr>
<tr>
<td>Improvement 34 23 39 26 28 15</td>
<td></td>
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<tr>
<td>Difference (MR pred – placebo) 11 13 13</td>
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</table>

**Table 2** Bivariate sensitivity analyses of the net cost savings (in €) when MR-pred 5 mg/day is introduced before biologic therapy

<table>
<thead>
<tr>
<th>Duration of effect of MR-pred</th>
<th>Net gain in %</th>
<th>Absolute gain in LDAS, %</th>
<th>Yearly cost of biologics (€)</th>
<th>Daily cost of MR-pred (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>4 13 21</td>
<td>28 34 34</td>
<td>10,000 15,000 20,000</td>
<td>0.50 1.00 1.50</td>
</tr>
<tr>
<td>12 months</td>
<td>59 396 696</td>
<td>959 3835 1184</td>
<td>234 396 559</td>
<td>442 473 551</td>
</tr>
</tbody>
</table>

LDAS: low disease activity state, i.e. DAS28 \( \leq 3.2 \).  
*Net gain: the proportion of patients in LDAS after MR-pred minus the proportion in LDAS after placebo.*  
*Base case assumptions.*  
*Absolute gain in LDAS: the proportion of patients in LDAS after MR-pred.*

**Discussion**

In this simple model, we demonstrate that administration of low-dose modified-release prednisolone can delay the start of biologic treatment with the potential for considerable cost savings. Of course, a delay of 12 weeks in the course of a lifetime with RA is of limited value. However, several studies have shown that (immediate release) glucocorticoids added to conventional disease-modifying treatment in step-down schedules or at low doses lead to better clinical and radiological outcomes that can persist for a long period of time without undue toxicity [5-8]. So it is highly likely that the benefits demonstrated in this short study will persist beyond the 12-week time frame, suggesting that in a substantial proportion of patients the administration of biologics can be completely prevented. If this is the case, cost savings multiply.
The question of whether similar results can be obtained with immediate-release prednisone cannot be answered directly because a state-of-the-art trial with modern end points has not been performed. In the CAPRA-1 trial, RA patients on chronic prednisone showed advantages of MR-pred over immediate-release formulations in certain aspects of disease activity, notably morning stiffness [9]. Open-label follow-up data showed further benefits in all aspects of disease activity, as well as in the control group that continued on immediate-release prednisone and was allowed to switch to MR-pred after 12 weeks [10]. Both findings suggest an advantage of MR-pred over immediate-release prednisone and effects that persist beyond 12 weeks.

This is a very limited study that does not purport to replace a full economic model that includes other direct and indirect costs, nor does it model the long-term consequences of the proposed strategies. However, as the cost of biologic treatment is by far the most important contributor to overall cost, we feel justified in presenting this limited calculation as an indication of the potential impact of even briefly postponing the initiation of biologic treatment. In conclusion, despite a considerably higher cost price than conventional prednisone, MR-pred at low doses may be a cost-effective option for RA patients not on glucocorticoids who are eligible for therapy with biologic agents.

**Rheumatology key messages**

- A dose of 5 mg/day of modified-release prednisone has relevant effects on RA disease activity.
- Treatment with modified-release prednisone may reduce the need for biologics in RA.
- Costs are reduced when RA patients receive modified-release prednisone before biologics.

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**References**