Quality of life and economic impact of switching from established infliximab therapy to adalimumab in patients with rheumatoid arthritis


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
This 32-week study evaluated the switching of treatments in patients with rheumatoid arthritis (RA), from established and responsive infliximab therapy (at least 12 weeks' therapy) to adalimumab. The mean infliximab dosage was 5 mg/kg every 8 weeks. When patients were switched to adalimumab they received 40 mg subcutaneously every other week. One-year extrapolation data were also presented.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis

Study population
Eligible individuals were those with RA and responders to at least 12 weeks' infliximab, but with ongoing, varying levels of disease activity. They had to be willing to self-administer subcutaneous adalimumab.

Setting
The setting was inpatient and outpatient care. The economic study was conducted in a University Hospital in Dublin, Ireland.

Dates to which data relate
There was no indication of the dates to which either the trial data or the unit costs related.

Link between effectiveness and cost data
The effectiveness and resource use data were derived from the same sample of patients as that included in the trial.

Study sample
Nineteen patients were enrolled in the study. Power calculations and sample size planning were not reported. A convenience sample appears to have been recruited. No study flowchart was shown.

Study design
This was a single-centre, within-group (also known as before-and-after) open study. Blinding would have been difficult, though not impossible, owing to the different routes of administration and timing of the drugs. There was no wash-out period between the drugs. The follow-up time was 32 weeks, and the switch to adalimumab occurred at week 16. There was no loss to follow-up.

Analysis of effectiveness
Physical function was assessed using the Health Assessment Questionnaire Disability Index (HAQ DI). Quality of life was evaluated using both the disease-specific Rheumatoid Arthritis Quality of Life (RAQoL) questionnaire and the generic Short Form 36 (SF-36), and was assessed at baseline, at the time of the switch (week 16) and at the final visit (week 32). Differences were assessed using Student's paired t-test. Disease activity was evaluated through the Disease Activity Score (DAS28). All participants were accounted for in the analysis.
**Effectiveness results**
The mean dose and number of patients receiving disease-modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, or corticosteroids, remained broadly stable throughout the study. No patients discontinued adalimumab therapy during the study period following the switch from infliximab.

No significant changes in functional or quality-of-life assessments were observed either before or after the switch from infliximab to adalimumab in the HAQ DI, RAQoL or SF-36.

Following the switch, a significant improvement was seen in the DAS28 for the entire study population: the mean DAS28 was 4.05 (standard error of the mean, SEM=0.267) at baseline, 3.94 (SEM=0.328) at the time of the switch and 3.01 (SEM=0.266) at the final visit, (p<0.005 versus both baseline and time of the switch).

There were no statistically significant changes in mean tender joint counts, swollen joint counts, or sedimentation rate from baseline through to the final adalimumab treatment.

At the final visit, the patients' general health assessment ratings had decreased from baseline and the time of the switch, although these changes were not statistically significant.

**Clinical conclusions**
This small open-label study showed that switching from infliximab to adalimumab was safe and well tolerated. Though there were no changes in functional assessments or in quality-of-life measures, there was a significant reduction in disease activity.

**Modelling**
In a post hoc analysis, the results of each treatment were extrapolated over a 54-week period in order "to reflect a more real-life economic evaluation".

**Measure of benefits used in the economic analysis**
There was no summary measure of benefit. In effect, a cost-consequences analysis was conducted.

**Direct costs**
The cost categories included health professional salaries, laboratory investigations, study drugs with infusion equipment and dispensing fees, and concomitant medication. Resource use was directly measured at each visit. Costs sources included the Irish Municipal Public and Civil Trade Union (salaries, mileage costs), the hospital (infliximab, infusion equipment), or the standard drug tariff to the Health Service Executive with the addition of the compulsory pharmacy dispensing fee for high-tech prescriptions (adalimumab), and the Monthly Index of Medical Specialties (for concomitant medications). No price year was reported.

**Statistical analysis of costs**
No statistical analyses of the costs were reported.

**Indirect Costs**
Patient-related loss of earnings was estimated using the average industrial wage in addition to the time spent at the visit and travelling to and from treatment. Resources use was evaluated at each visit and the source of the unit costs was the Irish Municipal Public and Civil Trade Union.

**Currency**
Euros (EUR).

**Sensitivity analysis**
No methods were reported.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.
Cost results
The costs were evaluated both before the switch, when patients received two cycles of infliximab, and following the switch, when they received adalimumab for 16 weeks.

The total costs were EUR 114,980 prior to switching therapy and EUR 131,550 after switching therapy. This resulted in an overall cost of EUR 16,570 to switch 19 patients from infliximab to adalimumab during the study period.

In a post hoc analysis where the results of each treatment were extrapolated over a 54-week period, the total annual costs were estimated to be EUR 483,684 for 19 patients receiving infliximab therapy and EUR 410,102 for 19 patients receiving adalimumab therapy.

This analysis showed a potential reduction of EUR 7,479 per year in health professional salary costs and EUR 22,234 in patient-related costs.

Following a switch from infliximab to adalimumab in 19 patients, estimated total savings were EUR 73,582 and estimated health care-related savings were EUR 51,48.

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors' conclusions
In this study, a switch from infliximab to adalimumab for patients with rheumatoid arthritis (RA) who had responded to infliximab was feasible and well-tolerated. Although adalimumab costs were higher during the study period, there are potential reductions in costs that could be attributed primarily to reductions in patient- and staff-related costs in a longer-term horizon.

CRD COMMENTARY - Selection of comparators
The authors made general comments about their choice of different TNF antagonists in RA patients, but did not state clearly why they chose these particular two members of the TNF family. You should therefore decide whether these comparators are relevant in your own setting, but should bear in mind the omission.

Validity of estimate of measure of effectiveness
Given the study design (single-centre, within-group and open-label) and, as the authors' acknowledged, the small sample size, it is difficult to infer whether the observed results were directly due to any of the interventions. The authors did not justify the choice of study design, nor did they report any power calculations. As the authors stated, improvements in disease activity parameters following the switch may reflect the timing of the data collection more than the increased efficacy with adalimumab. Also, the DAS28 was calculated for patients receiving infliximab at potentially the worst day of their infusion cycle.

Validity of estimate of measure of benefit
No summary measure of benefit was used. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field.

Validity of estimate of costs
The perspective was not explicitly stated but, as the authors reported both the direct medical cost of a single provider as well as the costs due to productivity losses, it can therefore be inferred that the perspective was societal. Nevertheless, the authors reported costs in a disaggregated fashion, so the reader can calculate the implication for their own perspective. Relevant cost categories appear to have been included. Most cost sources were adequately reported, and resource use was directly measured during the study. The 54-week extrapolation should be viewed with caution, and the reader should consider whether the authors' assumptions are reasonable in their own setting. Although most resource use data were stochastic, no statistical analysis was performed with the cost data. Discounting was not used but this was appropriate given the time horizon (less than 1 year). The price year was not explicitly reported and this will impede future reworking exercises.
Other issues
The authors compared their findings with those from other studies. Few generalisability issues were addressed in their discussion.

Implications of the study
There is a potential to reduce economic burden when switching from infliximab to adalimumab, especially in patients in whom ongoing disease activity has necessitated an increase in dosage or frequency of administration of their original anti-TNF therapy. Nevertheless, as the authors' stated, since this small study evaluated patients over a short treatment period, extrapolation of the data to a larger population of patients should be undertaken with caution. More research about the effects of switching from one TNF antagonist to another when a patient has responded to, and is tolerating the first treatment, is needed. A complete cost-effectiveness model of TNF antagonist therapy would require an evaluation of long-term disease outcomes. This study supports the soon-to-be published, updated National Institute for Health and Clinical Excellence guidelines, which recommend that, when selecting a TNF antagonist, rheumatologists should consider clinical evidence and experience, the impact of therapy on the patient's quality of life, and medication costs to determine which agent is best suited to an individual patient.

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