Concise report

Reduction of direct and indirect costs in patients with AS receiving etanercept: results from an open-label 36-week extension of the ASCEND study in four European countries

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Abstract

Objective. To characterize the impact of etanercept (ETN) in AS on cost, work productivity and quality of life (QoL).

Methods. A Phase 4, open-label, multi-centre (UK, Scandinavia) extension study in AS. Eligible subjects (n = 84) were treated for 36–52 weeks with ETN 50 mg s.c. once weekly. Analysis included direct costs (transformed out-patient and in-patient care elements), indirect costs (sick leave and lost working days), efficacy and QoL.

Results. Annualized direct and indirect costs decreased (55.5%, P < 0.008) during ETN treatment, as did out-patient and in-patient episodes (physiotherapist/physician visits, P = 0.012). Work productivity and QoL increased.

Conclusion. ETN therapy significantly reduces direct and indirect health-care costs and increases work ability and QoL in AS.


Key words: ankylosing spondylitis, biologic therapy, cost analysis, health economics.

Introduction

AS is a chronic inflammatory arthritis that primarily affects the spine. The prevalence of AS in Europe is 0.2–1.4% [1, 2]. Patients with AS experience reduced quality of life (QoL) and increased work disability and sick leave [3, 4]. In addition to the direct costs of AS (including visits to health-care providers, hospitalization, treatments, devices), the indirect costs associated with loss of productivity are high and represent the majority of costs in this patient group [1, 5, 6].

The original ASCEND study was a randomized, double-blind trial that reported increased effectiveness of etanercept (ETN) over SSZ treatment in AS [7]. This 36-week extension study collected health economic (HE) data, measuring in-patient and out-patient care visits, work status and QoL.

Materials and methods

This study was conducted in accordance with the International Conference on Harmonisation Guideline for Good Clinical Practice and local regulatory requirements and...
was approved by national authorities, review boards and ethics committees (Regionala etikprövningsnämnden i Stockholm; De Videnskabsetiske Komiteé for Københavns og Frederiksberg Kommuner; HYKS Meilahden sairaala ethics committee and Royal Free Hospital and Medical School REC). Patients gave written informed consent to participate.

Design
This open-label extension study was conducted in UK, Denmark, Finland and Sweden following the ASCEND study, a 16-week double-blind, randomized, active-comparator study. Cost evaluation included a 12-month recall at screening in the ASCEND study and a 12-week recall at Weeks 0, 12, 24 and 36 of the extension study.

Patients
A total of 84 subjects with AS were included in the extension study. To be eligible for inclusion, patients had to complete 16 weeks of treatment and the baseline HE questionnaire at screening in the ASCEND study [7].

Objective
The primary objective was to evaluate out-patient and in-patient care visits, work status and QoL in patients with AS receiving ETN by comparing study evaluations with the baseline evaluations in the ASCEND study.

Results
Patient population
A total of 84 subjects were enrolled, of which 58 subjects started with ETN (ETN-ETN group) and remaining 26 subjects previously received SSZ in the ASCEND study (SSZ-ETN group). All 84 subjects were included in the intention-to-treat (ITT) population. Of 84 subjects, 79 (94.0%) completed the study. The study population consisted of female and male AS subjects (84.5% males) aged 24–65 years [42.7 (10.5) years]. Fifty-one (60.7%) subjects were included in the UK, 18 (21.4%) in Denmark, 10 (11.9%) in Finland and 5 (6.0%) in Sweden. Subjects starting with ETN in the extension study (SSZ-ETN) were comparable with subjects of the ETN-ETN group with regard to baseline characteristics.

Withdrawal of study medication
A total of five (6.0%) subjects withdrew from the study. This premature discontinuation was due to subject request (one), lost to follow-up (one) and adverse event (three).

HE parameters
Health-care resource use decreased comparing 48 weeks before and during treatment (Fig. 1). At inclusion in the original ASCEND study, 46 subjects (54.8%) were employed full time, 12 (14.2%) employed part time and 26 (30.9%) unemployed. Nine subjects (10.7%) showed an increase in productivity. In patients treated with ETN for 52 weeks, there was an increase in full-time employment rate of 6.8% [from 36 (61.0%) to 40 subjects (67.8%)]. Overall, the mean number of sick days decreased significantly during treatment (from 37.4 to 15.1 days, P = 0.008). In addition the mean number of work days for employed subjects increased from 226 days (range 12–260 days) to 241 days (range 89–260 days) (P = 0.144).

The mean direct and indirect costs per country decreased significantly pre- and post-ETN treatment (P < 0.008). QoL increased for all subjects, with a mean of 0.3 for the ETN-ETN arm as measured by the EuroQol Group Score (EQ-5D; Table 1). After 36–52 weeks of ETN treatment, 72.2% achieved an Assesment of Spondyloarthritis (ASAS)-20 response and 62.7% achieved an ASAS-40 response. ASAS partial remission was shown as 45.8%.

Fig. 1 Out-patient and in-patient care visits 48 weeks pre- and post-treatment. *Significant difference.
Safety
Sixty-eight subjects (81.0%) reported at least one adverse event (AE). Four serious AEs occurred: Hodgkin’s disease (one), worsening of Crohn’s disease (one), abnormal liver function (one) and spinal fracture (one); of these, three serious AEs led to withdrawal from the study. No cases of demyelinating disorders, tuberculosis or ulcerative colitis were observed.

Discussion
Other studies of cost offsets of tumour necrosis factor (TNF)-α inhibitor therapy in AS have shown that treatment is associated with reduction in hospital admissions, improved working status and less days off work [8–12]. This study showed a significant decrease in annualized costs consisting of out-patient and in-patient care visit elements (direct costs) and lost work days and sick leave (indirect costs) pre- and post-ETN treatment, with a mean cost reduction of 55.5%. There was an increase in the number of work days and a higher rate of full employment (eight subjects re-started full-time employment) during ETN treatment.

The number of physiotherapy visits, previously reported to cause 32% of health-care costs for AS in the UK [13] decreased significantly; as well as the number of patients requiring out-patient visits to a physician. QoL increased in all patients.

Limitations
The study evaluated change in costs before and after the use of ETN among patients continuing ETN after a 16-week RCT. As this is a selected patient population of responders, results cannot be generalized for all AS patients starting ETN. However, the results are important, as they indicate possible long-term cost offsets for AS patients likely to be selected for continuous ETN use, and thus the patients who, from a payer’s perspective, constitute the largest investment of resources. Although the ASCEND study had a control group, the 16-week follow-up time was deemed too short to capture changes in resource use and changes in work ability. Therefore the patients in the extension study were pragmatically chosen as their own controls.

A relatively small number of subjects were included and generalization of the results is therefore limited. Cost data were based on patient recall of up to 12 months and was not validated further by other sources of data. The counting of the out-patient care visits might have been affected by the fact that this study was an extension of an RCT. However, the first 4 weeks of the RCT (three visits) were not covered in the patient questionnaires and time taken off work to attend for any visits were not included in the cost calculation.

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Rheumatology key messages
- AS is associated with reduced QoL and lost working days.
- Treatment of AS with ETN significantly improves QoL and work ability.
- Treatment of AS with ETN significantly reduces cost of in-patient and out-patient care.

Table 1: Summary of QoL outcomes

<table>
<thead>
<tr>
<th>QoL outcome</th>
<th>ETN-ETN group (n = 58)</th>
<th>SSZ-ETN group (n = 26)</th>
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<tbody>
<tr>
<td></td>
<td>Baseline (ASCEND study)</td>
<td>Week 0 (extension study)</td>
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<tr>
<td></td>
<td>0 weeks</td>
<td>16 weeks</td>
</tr>
<tr>
<td>EQ-5D score</td>
<td>0.5 (0.45, 0.60)</td>
<td>0.8 (0.72, 0.82)</td>
</tr>
<tr>
<td>ASQoL</td>
<td>11.4 (9.71, 12.99)</td>
<td>5.2 (3.44, 6.86)</td>
</tr>
<tr>
<td>HADS</td>
<td>12.7 (11.11, 14.32)</td>
<td>9.6 (7.96, 11.23)</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>31.4 (29.33, 33.41)</td>
<td>41.7 (38.93, 44.48)</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>33.5 (29.95, 37.05)</td>
<td>61.3 (55.31, 67.31)</td>
</tr>
<tr>
<td>General Health</td>
<td>43.7 (39.29, 48.04)</td>
<td>57.8 (52.85, 62.77)</td>
</tr>
<tr>
<td>MCS</td>
<td>47.1 (44.12, 50.07)</td>
<td>51.8 (49.26, 54.31)</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>64.9 (58.43, 71.31)</td>
<td>81.5 (76.27, 86.66)</td>
</tr>
<tr>
<td>Vitality</td>
<td>35.6 (30.87, 40.34)</td>
<td>55.1 (49.26, 60.91)</td>
</tr>
</tbody>
</table>

Values are presented as mean (95% CI). EQ-5D: EuroQol Group Score; HADS: Hospital Anxiety and Depression Scale; SF-36: Short Form 36 Health Survey; PCS: physical component score; MCS: mental component score.
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Disclosure statement: R.-M.L. is employed by Pfizer. M.E. is employed in Pfizer (Sweden) and has received restricted stock units and stock options in Pfizer. S.Q. is employed in Pfizer (Denmark). P.J.’s institution has received a grant and costs of the investigator meeting from the sponsor, as well as costs for a few scientific meetings or congress’ outside this work. A.J.K.O. has received support from (including attendance at conferences), undertakes clinical trials and acts as a consultant to Roche, Chugai, Schering-Plough/MSD, Abbott, Wyeth/Pfizer, BMS, GSK, Merck Sorono and UCB. A.R. was previously an employee of Pfizer. R.J.M. or members of his group have received research grant 154 support from or undertaking clinical trials with Roche, Chugai, Schering-Plough, MSD, Abbott, Wyeth, BMS and UCB Pharma. D.K. has shares/stock in Pfizer. A.G.R.L. has served as a consultant for MSD and UCB and has served on the speakers' bureau at MSD. All other authors have declared no conflicts of interest.

References