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EDITORIAL

Adalimumab: a new alternative biologic agent for chronic plaque psoriasis

ℜ• *Anthony D. Ormerod*

- Department of Medicine and Therapeutics, University of Aberdeen, Aberdeen AB25 2ZB, U.K.
  E-mail: a.d.ormerod@abdn.ac.uk

Methotrexate has been the primary conventional systemic therapy for psoriasis for 40 years and as such could be regarded as a gold standard maintenance therapy against which new interventions are measured. It is desirable for newer targeted therapies that are considerably more expensive to give better disease control and safety. This is best demonstrated in a randomized controlled trial (RCT).

The results of a phase III European multicentre trial comparing adalimumab, placebo and methotrexate are published in this issue.[1] An accompanying article examines the quality of life impacts derived from the same study.[2] Adalimumab has been licensed for use in severe rheumatoid arthritis in combination with methotrexate and in psoriatic arthritis, ankylosing spondylitis and Crohn's disease. A licence for psoriasis in Europe is anticipated in the first quarter of 2008. The trial, which has the acronym CHAMPION, is a landmark study for two reasons, firstly for its groundbreaking comparison of a biologic with conventional therapy in psoriasis and secondly for the impressive efficacy demonstrated.

Subjects in the study had to have Psoriasis Area and Severity Index (PASI) > 10, psoriasis of similar severity to that required by the British Association of Dermatologists guidelines for biologic interventions.[3] Practically for such a randomized comparison subjects also had to be naÃ¯ve to methotrexate, rather than having failed or having intolerance. Eighty-six per cent had received previous systemic therapy or phototherapy, and mean PASI was 19Â·7. Based on a Mantoux test response > 5 mm, 22 patients received prophylaxis for tuberculosis and no cases of tuberculosis were seen. The study was powered to demonstrate noninferiority of adalimumab to methotrexate. A previous RCT with methotrexate with similar dosing showed a 75% reduction in PASI score (PASI 75) in 60% of subjects over 16 weeks.[4] Methotrexate was dosed in a schedule consistent with its normal clinical use, while adalimumab routinely started with a loading dose of 80 mg. Methotrexate was increased at intervals,

according to tolerance. Although 93% achieved doses over 15 mg per week at week 12, incremental methotrexate dosing produced a slower start and responses might have caught up somewhat in a longer term follow up. Nevertheless, the dose of methotrexate was optimal and response to adalmumab was rapid with 56% improvement in PASI at week 4. By week 16 79Â·6% achieved PASI 75 and 51Â·9% PASI 90 with adalimumab compared with only 35Â·5% achieving PASI 75 and 13Â·6% achieving PASI 90 with methotrexate. Folate deficiency may stimulate the pathogenesis of psoriasis through accumulation of homocysteine. All patients received folic acid 5 mg per week and it is speculated that this may have accounted for an unexpected response of 18Â·9% PASI 75 in the placebo group. The possibility that folic acid itself may be beneficial in psoriasis certainly merits further investigation.

Two patients in the adalimumab group reported serious adverse events (one patient with pancreatitis and one patient with an enlargement of an ovarian cyst), while in the methotrexate group one patient reported hepatitis and 9Â·1% had elevated liver enzymes leading to a higher dropout rate in this group.

The quality of life study[2] examines the Dermatology Life Quality Index (DLQI) and the EuroQOL 5D outcomes in this trial. The latter measures general health while the former is a dermatology-specific instrument. Also reported are Patientâ€™s Global Assessment (PGA), pruritus and arthritis-associated pain. With adalimumab compared to placebo all scales were significantly improved and, compared with methotrexate, PGA, pruritus and joint pain were significantly improved. The DLQI was reduced by 9Â·1 points with adalimumab compared with 5Â·7 points with methotrexate. Adalimumab clearly results in clinically meaningful improvement in the limitations psoriasis causes in everyday life and the impact of its symptoms. These quality improvements are also vital in determining cost effectiveness and in making comparisons with other disease states for determination of renumeration.

Are the findings of these studies replicated elsewhere? A previous phase II dose-ranging study[5] compared weekly adalimumab 40 mg with administration every other week and showed a PASI 75 in 80% after 12 weeks with weekly administration but in only 53% of those treated every other week. However, a more recent large phase III study in the U.S.A. of 1212 patients receiving fortnightly treatment[6] similarly demonstrated PASI 75 in 71% at 19 weeks and sustained responses after a 6-month open-label extension. The weighted average proportion achieving PASI 75 for the three RCTs[1,5,6] combined is 68Â·3%, which compares very favourably with other currently available biologics. Adalimumab will be a welcome addition to the choice of biological agents with some added benefits of administration at fortnightly intervals by a self-administered pen. Adalimumab is currently under review as a single technology appraisal by the National Institute for Health and Clinical Excellence.

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