surrogate markers. There are some valid surrogate markers of disease progression which can be reliably used to monitor chronic conditions, and as treatment goals. However, the clinical utility of many surrogates is open to question and their validity is largely untested. Practitioners need to keep in mind that some widely used surrogate markers of disease have not been adequately validated for use in clinical situations. A disease may be associated with a surrogate marker, but this does not mean that treating the marker will improve the outcome of that disease.

## References

- Department of Health and Human Services. Food and Drug Administration. New drug, antibiotic, and biological drug product regulations: accelerated approval. Federal Register Vol 57 No 73. 1992. p. 13234-42.
- Fleming TR, DeMets DL. Surrogate end points in clinical trials: are we being misled? Ann Intern Med 1996;125:605-13.
- 3. Barnes D. How prescription drugs are developed. Aust Prescr 2006;29:159-61.
- Vogel R, Crick RP, Newson RB, Shipley M, Blackmore H, Bulpitt CJ. Association between intraocular pressure and loss of visual field in chronic simple glaucoma. Br J Ophthalmol 1990;74:3-6.
- Traver GA, Cline MG, Burrows B. Predictors of mortality in chronic obstructive pulmonary disease. Am Rev Respir Dis 1979;119:895-902.

- 6. Dolan S, Varkey B. Prognostic factors in chronic obstructive pulmonary disease. Curr Opin Pulm Med 2005;11:149-52.
- 7. Berger VW. Does the Prentice criterion validate surrogate endpoints? Stat Med 2004;23:1571-8.
- 8. Prentice RL. Surrogate endpoints in clinical trials: definition and operational criteria. Stat Med 1989;8:431-40.
- 9. Krumholz HM, Lee TH. Redefining quality implications of recent clinical trials. N Eng J Med 2008;358:2537-9.
- Kastelein JJ, Akdim F, Stroes ES, Zwinderman AH, Bots ML, Stalenhoef AF, et al. Simvastatin with or without ezetimibe in familial hypercholesterolemia. N Eng J Med 2008;358:1431-43.
- Kanis JA, Borgstrom F, De Laet C, Johansson H, Johnell O, Jonsson B, et al. Assessment of fracture risk. Osteoporos Int 2005;16:581-9.
- Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996;312:1254-9.

## **Further reading**

Rolan P. The contribution of clinical pharmacology surrogates and models to drug development – a critical appraisal. Br J Clin Pharmacol 1997;44:219-25.

Temple R. Are surrogate markers adequate to assess cardiovascular disease drugs? JAMA 1999;282:790-5.

Conflict of interest: none declared

## Treatments for severe psoriasis: update

In March 2009 it was announced that efalizumab would be withdrawn from the Australian market. This follows a review of the drug in Europe which found the benefits no longer outweigh the risk of harm. There are reports of progressive multifocal leucoencephalopathy arising in patients who have been treated with efalizumab for more than three years.<sup>1</sup> The drug has also been under review in the USA.<sup>2</sup>

## References

- European Medicines Agency. Questions and answers on the recommendation to suspend the marketing authorisation for Raptiva. 2009 Feb 19. www.emea.europa.eu/humandocs/PDFs/EPAR/raptiva/ RaptivaQ&A\_1552509en.pdf [cited 2009 Mar 13]
- US Food and Drug Administration Center for Drug Evaluation and Research. FDA Public Health Advisory. Updated safety information about Raptiva (efalizumab). 2009 Feb 19. www.fda.gov/cder/drug/advisory/efalizumab.htm [cited 2009 Mar 13]

Comment from Dr JR Sullivan and Dr V Preda, the authors of an article about treating severe psoriasis recently published in Australian Prescriber (Aust Prescr 2009;32:14–18):

For rare side effects it takes a number of years of post-marketing surveillance for a signal to appear. This can take longer for

therapies with only a single therapeutic indication such as efalizumab. This drug has only been used in 46 000 patients worldwide.

The tumour necrosis factor-alfa antagonists, infliximab and etanercept, for psoriasis have been used for a number of clinical indications over a much longer period. We have 15 years of patient safety data and over 1.4 million patient years and 630 000 patients with etanercept, and 15 years of patient safety data and 4.3 million patient years and 340 000 patients with infliximab. For these two drugs much more is known about their longer-term safety profiles.

The use of biologicals for the treatment of severe psoriasis needs to be considered in light of the safety profile of each drug and also in the context of the individual patient. Biologicals are not only used in severe psoriasis but also for a number of other disorders. Thus with regard to safety data we can benefit from the experience with these medications used in other specialties such as rheumatology and gastroenterology. From rheumatology we know to screen for tuberculosis before starting therapy to help prevent potentially serious infections. Although adverse effects are often grouped together as a class effect, it is important to consider each biological drug individually as they have their own unique pharmacological profiles.