12 was based on the cohort of patients for whom DLQI was available. In these patients 34.3% of patients achieved SPC on efalizumab, compared with 7.3% on placebo (Table 3).

In high-need patients, only 4/117 patients (3.4%) given placebo achieved SPC at week 12, compared with 73/221 (33.0%) on efalizumab (Figure 1).

Observed response rates at week 12 were lower in the prospective validation compared with the retrospective rates. However, the rate differences between active and placebo observed in the prospective study (27% for the total study group and 30% for the high need group) were similar to that seen in the retrospective analyses (29%).

Comparison of PASI-75 and SPC

The efficacy-only measure, PASI 75, was compared with the multidimensional SPC for pooled retrospective data from the three studies (ACD 2058, 2059, and 2390). This showed that 27.3% of patients treated with efalizumab achieved PASI 75 at week 12, while 39.4% of patients achieved SPC (Figure 2).

Discussion and conclusion

Efalizumab has been studied in more than 3500 patients. This extensive database offers an ideal source of information for assessing traditional measures of efficacy, and generating new measures of benefit to assess whether a patient's psoriasis is controlled. The SPC assessment moves away from an approach focused primarily on treatment difference in PASI 75 response in isolation, to an approach that would further characterize each patient's response to treatment, leading to a better understanding of the benefit:risk that should be expected in psoriasis treatment.

Using conventional, uni-dimensional assessment measures such as PASI 75 and DLQI, efalizumab has already been demonstrated to be significantly more effective than placebo. However, the use of these physician- or patient-assessed scales either alone, or independently of each other, does not accurately demonstrate the multidimensional effect that efalizumab has in safely controlling psoriasis. Studies indicate that there is a need to consider psoriasis and its treatment not just in terms of objective assessments of lesion severity, but also in terms of the impact of the disease on patients' lives [16,17]. The inclusion of the safety component in the SPC endpoint allows a simple benefit:risk assessment to be made, as the endpoint describes the proportion of patients who had benefit without major side effects.

We applied this new outcome measure – SPC – using week 12 data obtained from studies that had already been completed and analyzed using conventional uni-dimensional measures such as PASI, and evaluated SPC prospectively in a new study (IMP 24011) that had not been completed at the time SPC was described.

A favorable overall benefit:risk profile as determined by the SPC endpoint was confirmed in nearly 40% of all the patients treated with efalizumab for 12 weeks. Using SPC in both prospective and retrospective clinical trial analyses, efalizumab consistently demonstrated superiority over placebo, demonstrating that many patients achieve disease control without major safety issues, and at the same time experience an improved quality of life. Importantly, efalizumab was similarly effective in high-need patients. Also, even amongst those patients who did not manage to achieve SPC, approximately 9% achieved PASI 75 after 12 weeks of treatment with efalizumab 1.0 mg/kg, compared with less than 1% of patients on placebo.

Improvement in the management of psoriasis is particularly welcome as the impact of the disease, particularly among high-need patients, and shortcomings of current treatments are becoming more widely recognized. Current management of patients with moderate-to-severe plaque psoriasis involves systemic therapies, such as cyclosporin, methotrexate, acitretin and PUVA, which are associated with treatment-limiting systemic cumulative toxicities. The use of biological agents such as efalizumab that modulate the activation of T-cells and their migration into the dermal and epidermal tissues may provide more targeted therapy with an improved safety profile. Our findings, and those of prior trials of efalizumab, support this concept and demonstrate promising opportunities to improve therapy. The observations of substantial disease

Table 3: Prospective SPC results at week 12

Study IMP 24011[15]	Treatment Group	Safe Psoriasis Control (SPC)*
Total study group	Placebo (n = 165)	12 (7.3 %)
	Efalizumab 1.0 mg/kg/wk (n = 329)	113 (34.3 %)
High need group	Placebo (n = 117)	4 (3.4 %)
	Efalizumab 1.0 mg/kg/wk (n = 221)	73 (33.0 %)

* SPC is defined by PASI <= 8 and DLQI <= 6 and No SAEs and No Severe AEs related to Study Drug and not withdrawn