Prospective application

SPC was applied prospectively to week 12 data from studies that were completed after derivation of the endpoint. For this paper data analyses were performed on the ITT subject populations enrolled in an international randomized, double-blind, placebo-controlled, parallel-group, multicentre trial (IMP 24011, ClinicalTrial.gov registration number NCT00256139) consisting of an initial 12-week, double-blind treatment period. PASI 75 responders entered an observation period until relapse or up to 24 weeks, after which patients received 12 weeks of open-label re-treatment. Non-responders went directly to an extended treatment period of 12 weeks. The primary objective of the study was to evaluate the safety and efficacy of efalizumab 1.0 mg kg^{-1} given subcutaneously once weekly for 12 weeks compared with placebo in moderate-to-severe patients, and in a cohort of "high-need" patients for whom existing therapies were inadequate or unsuitable. An initial cohort of moderate-to-severe patients was recruited, on whom an interim analysis was performed showing efalizumab efficacy versus placebo. After this, only high-need patients were recruited.

High-need patients were defined as those patients who had failed treatment on, were intolerant of, or had contraindications to at least two currently available systemic therapies (e.g., photochemotherapy, cyclosporin, corticosteroids, methotrexate, oral retinoids, mycophenolate mofetil, thioguanine, hydroxyurea, sirolimus, azathioprine, 6-mercaptopurine).

SPC was analyzed for the first 12-week treatment period for which data are available.

Patients

Inclusion and exclusion criteria were similar for all studies included in the analysis, except for the high-need cohort, as already explained. Patients were required either to have received previous systemic treatment for psoriasis or to be a candidate for such treatment without prior history. All patients enrolled were 18 to 75 years old with at least a 6-month history of moderate-to-severe plaque psoriasis covering ≥10% of total body surface area (BSA), with a minimum PASI of 12.0 at screening.

The total number of all patients for the prospective analysis using study IMP 24011 was 793, of whom 526 were high-need patients.

Treatment

Study treatment efalizumab 1 mg/kg/week was administered via subcutaneous injection once weekly for 12 weeks. The first weekly dose of efalizumab was given at a conditioning dose of 0.7 mg kg^{-1}, followed by the full dose level of 1.0 mg kg^{-1}. No other systemic psoriasis therapy or phototherapy was allowed during the trial.

Assessment of benefit:risk

Conventional physician-assessed endpoint data such as PASI, and patient outcome measures such as DLQI, were collected for the 12-week timepoint. Safety was assessed in terms of the incidence, severity, and relationship to treatment of adverse events (including serious adverse events) and the incidence of treatment-emergent laboratory abnormalities. SPC for efalizumab was calculated from these 12-week data.

Results

Retrospective SPC analysis

Table 2 shows the SPC outcome data from the retrospective analyses. The results were similar between the studies. At 12 weeks, SPC was achieved by 46.3%, 37.1%, and 37.9% of efalizumab-treated patients for studies ACD 2058, ACD 2059, and ACD 2390, respectively. When pooled, 39.4% of patients achieved SPC at week 12, compared with 10.4% for placebo.

Prospective SPC analysis in study IMP 24011

In the study IMP 24011, DLQI was administrated to 494 of the 793 patients (165 randomized to placebo and 329 to efalizumab 1.0 mg/kg/wk), as appropriately validated translations of the questionnaire were not available for use in Greece, Israel, Portugal or Russia. Thus, determination of the percentages of patients achieving SPC at week

Table 2: Retrospective SPC results (Good control level) at week 12

Study	Treatment Group	Safe Psoriasis Control (SPC)*
ACD2058[14]	Placebo (n = 170)	18 (10.6 %)
	Efalizumab 1.0 mg/kg/wk (n = 162)	75 (46.3 %)
ACD2059[13]	Placebo (n = 122)	12 (9.8 %)
	Efalizumab 1.0 mg/kg/wk (n = 232)	86 (37.1 %)
ACD2390[12]	Placebo (n = 187)	20 (10.7 %)
	Efalizumab 1.0 mg/kg/wk (n = 369)	140 (37.9 %)
Pooled studies	Placebo (n = 479)	50 (10.4%)
	Efalizumab 1.0 mg/kg/wk (n = 763)	301 (39.4%)

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