# Long-term efficacy and safety of adalimumab in patients with moderate to severe psoriasis treated continuously over 3 years: Results from an open-label extension study for patients from REVEAL

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***Background:*** REVEAL was a 52-week phase III trial of adalimumab therapy for moderate to severe chronic plaque psoriasis. Patients from REVEAL could enter an open-label extension trial to receive adalimumab for approximately 3 years of total therapy.

***Objective:*** We sought to determine long-term efficacy and safety of continuous adalimumab therapy for patients from REVEAL.

***Methods:*** Efficacy and safety over greater than 3 years of treatment were analyzed for 4 groups of patients from REVEAL. Patients who received adalimumab continuously from baseline were grouped by their responses in REVEAL: (1) greater than or equal to 75% improvement in Psoriasis Area and Severity Index (PASI) score (PASI 75) at weeks 16 and 33 (sustained responders); (2) less than PASI 75 at week 16; and (3) greater than or equal to PASI 75 at week 16 with 50% to less than 75% improvement in PASI score at week 33. Results were also analyzed for patients who began adalimumab after 16 weeks of placebo therapy.

***Results:*** For patients with sustained PASI 75 responses during REVEAL, efficacy was generally well maintained over 3 years, with 75%/90%/100% improvement in PASI score response rates (last observation carried forward) of 83%/59%/33% after 100 weeks and 76%/50%/31% after 160 weeks of continuous therapy. Some patients with less than PASI 75 responses in REVEAL also achieved long-term PASI 75 responses. Efficacy in the placebo/adalimumab group was consistent with the ensemble of results from the other 3 groups. Adverse event rates were consistent with those during REVEAL.

***Limitations:*** The REVEAL study design prevented analyzing all patients from the adalimumab arm as one long-term cohort.

***Conclusion:*** Adalimumab efficacy was well maintained over more than 3 years of continuous therapy for patients with sustained initial PASI 75 responses. Maintenance was best at the PASI 100 level. (J Am Acad Dermatol 2012;66:241-51.)

***Key words:*** adalimumab; anti–tumor necrosis factor therapy; clinical trial; efficacy; long-term treatment; open-label; psoriasis; safety.

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Long-term efficacy and safety are important for optimal control of psoriasis, and may be relevant to the management of psoriasis-related comorbidities.[1-6] Biologic therapies have demonstrated efficacy in placebo-controlled studies of psoriasis that were typically less than 4 months long. Outcomes for time points well beyond the primary end point have also been reported.[7-12] The understanding of long-term efficacy provided by these trials is limited, however, because the protocols extended only to 1 year,[7,8,11] studied a dosage that is not currently recommended for long-term use,[9] or excluded patients with less than 75% improvement in Psoriasis Area and Severity Index (PASI) score (PASI 75) response.[10]

REVEAL is the largest placebo-controlled trial for psoriasis with adalimumab, a fully human, monoclonal anti–tumor necrosis factor antibody. The REVEAL study design had 3 periods—period A (weeks 0-16), period B (weeks 16-33), and period C (weeks 33-52)—and permitted only patients with at least a PASI 75 response at the end of one period to continue into the next.[13] At week 16, PASI 75 responses were observed in 71% of patients treated with adalimumab versus 7% with placebo. At week 33, PASI 75 responders from the adalimumab arm were rerandomized to receive adalimumab or placebo, to assess loss of adequate response at week 52.[13]

Patients from REVEAL had the option to subsequently receive long-term adalimumab therapy in an open-label extension (OLE) study. Patients who received adalimumab from REVEAL baseline could enter the OLE study as less than PASI 75 responders at week 16; as 50% improvement in PASI score (PASI 50) to less than PASI 75 responders at week 33; or upon completing or losing adequate response during period C. Patients who received placebo in period A could also enter the OLE study. The current report analyzed these 4 groups to describe long-term outcomes for all patients from REVEAL who received continuous adalimumab therapy. Special attention was given to patients who achieved sustained PASI 75 responses in REVEAL, as they represent the type of patients who are most likely to receive long-term therapy in clinical practice.

**CAPSULE SUMMARY**

- REVEAL, a 52-week trial of adalimumab for chronic plaque psoriasis, was followed by an open-label extension study, for a total of more than 3 years of uninterrupted treatment with adalimumab.
- Patients who achieved sustained 75% improvement in the Psoriasis Area and Severity Index score in REVEAL had good long-term maintenance of efficacy, especially at the 100% improvement in Psoriasis Area and Severity Index score level, with safety results that were comparable with those observed in REVEAL.
- A favorable long-term benefit-risk profile for psoriasis was observed with continuous adalimumab therapy over a period of greater than 3 years.

## METHODS

### Patients

**REVEAL and the OLE study.** REVEAL was a 52-week, double-blind, randomized, placebo-controlled study of adalimumab for patients with stable, chronic, moderate to severe plaque psoriasis. Study details for REVEAL have been reported elsewhere.[13] Patients who had initially enrolled in REVEAL or 3 other clinical trials of adalimumab for psoriasis[14-16] could potentially enroll in the first part (period O) of an OLE study (designated M03-658) to receive uninterrupted, open-label treatment with adalimumab at 40 mg subcutaneously every other week (eow) for a minimum of 108 weeks (or until dosage escalation; see below). Patients from REVEAL could enter period O of the OLE study upon: (1) having a less than PASI 75 response at week 16; (2) having a PASI 50 to less than PASI 75 response at week 33; (3) completion of week 52 in REVEAL; or (4) losing adequate response after week 33 (defined as <PASI 50 response relative to REVEAL baseline, with a ≥6-point increase in PASI score from week 33) (Fig 1). Patients with a less than PASI 50 response at week 33 could not enter the OLE study. Eligibility for OLE entry was determined at the final visit in REVEAL, with the first OLE injection of adalimumab to be given 0 to 10 days later. The most recent visit on or before the day of this injection was designated OLE week 0. Patients were allowed to continue treatment with medicated shampoos, bland emollients, and class VI or VII low-potency topical corticosteroids on the palms, soles, inframammary area, and groin only, with no treatment allowed within 24 hours of a study visit. Phototherapy and systemic therapies for psoriasis other than adalimumab were not allowed. OLE study visits during treatment with adalimumab at 40 mg eow were to occur every 12 weeks. From OLE week 24 onward, patients with less than PASI 50 response, relative to REVEAL baseline, could increase adalimumab dosing to 40 mg weekly.