tients in both the tacrolimus and vehicle groups responded to tacrolimus treatment of relapse. With regard to safety, patients treated during the stabilization phase with tacrolimus versus topical steroid were more likely to have cutaneous site reactions (18% vs 9%; \(P = .015\)) during the first 4 days of treatment; this was not seen during the rest of the treatment course.

CONCLUSIONS. Tacrolimus maintenance therapy increased the number of symptom-free days and the time to relapse, compared with vehicle alone.

REVIEWERS COMMENTS. AD is a disease characterized by intermittent flares and symptom-free periods. Maintenance, intermittent, topical corticosteroid dosing regimens have been successful in preventing relapse. The use of maintenance steroid-sparing therapies is desirable. This study indicates that maintenance therapy may prevent relapse occurrence and decrease the severity of disease and provides an interesting treatment option for patients with AD with frequent relapses. Also, in light of recent Food and Drug Administration warnings concerning topical calcineurin inhibitors, it is valuable to know that dosing could be reduced to 3 times weekly for maintenance. Overall, this well-designed study provides convincing support for maintenance therapy of AD with topical nonsteroidal calcineurin inhibitors. Similar results were seen in 3 other studies using 2 or 3 times per week dosing schedules for topical steroids and topical calcineurin inhibitors. These studies indicate that maintenance therapy is superior to as-needed use of topical medications for patients with moderate-to-severe AD.

Three Times Weekly Tacrolimus Ointment Reduces Relapse in Stabilized Atopic Dermatitis: A New Paradigm for Use


PURPOSE OF THE STUDY. To evaluate the safety and efficacy of intermittent topical tacrolimus as maintenance therapy in patients with moderate-to-severe atopic dermatitis.

STUDY POPULATION. Subjects 2 to 15 years of age with moderate-to-severe atopic dermatitis.

METHODS. Subjects underwent stabilization with either 0.05% aclometasone ointment or 0.03% tacrolimus in a double-blind fashion for 4 days, followed by twice-daily, open-label, 0.03% tacrolimus treatment for all subjects. Subjects who became “clear” or “almost clear” entered phase II (maintenance phase) and underwent double-blind, random assignment to either 0.03% tacrolimus or vehicle applied once daily, 3 times per week, for up to 40 weeks. Emollients were permitted, but corticosteroid use was prohibited; open-label tacrolimus use was permitted to treat relapses.

RESULTS. A total of 206 patients were randomly assigned, and 50 subjects completed the study. There were no significant differences between groups at baseline. Aclometasone-treated patients showed more improvement in the acute phase than did tacrolimus-treated patients, and there were no differences in application-site adverse events between groups. During maintenance, tacrolimus-treated patients had a significantly greater number of disease-free treatment days, compared with vehicle-treated patients (mean: 174 vs 107 days; \(P = .0008\)), and a longer time to first relapse (median: 116 vs 31 days; \(P < .04\)).

CONCLUSIONS. Long-term intermittent application of 0.03% tacrolimus to clinically normal-appearing but previously affected skin was significantly more effective than vehicle at maintaining disease stabilization in patients with moderate-to-severe atop dermatitis. The safety profile of intermittently applied tacrolimus was similar to that of vehicle.

REVIEWERS COMMENTS. Atopic dermatitis is a chronic relapsing disease. Prevention of relapse is aimed at skin hydration and avoidance of triggers. Adverse effects of topical steroids limit their long-term use and, although there are concerns that calcineurin inhibitors may carry an increased risk of malignancy, long-term data on the safety of topical calcineurin inhibitors contradict this notion. This study shows promise that intermittent application of 0.03% tacrolimus offers a novel, steroid-sparing approach to maintaining stabilization of atopic dermatitis that seems both safe and efficacious.

MAS063DP Is Effective Monotherapy for Mild to Moderate Atopic Dermatitis in Infants and Children: A Multicenter, Randomized, Vehicle-Controlled Study


PURPOSE OF THE STUDY. To examine the safety and efficacy of MAS063DP (Atopiclair [Graceway Pharmaceuticals, Bristol, TN]), a topical nonsteroidal antiinflammatory agent, in the management of mild-to-moderate atopic dermatitis in infants and children.
STUDY POPULATION. Infants and children (N = 142) between the ages of 6 months and 9 years with mild-to-moderate atopic dermatitis affecting ≥5% of body surface area and scores of ≥40 of 100 on a visual analog scale (VAS) for pruritus.

METHODS. Subjects were randomly assigned to apply MAS063DP or vehicle cream 3 times per day to affected areas, as well as those prone to flares, after a washout period. Assessments were made at baseline and days 3, 8, 15, 22, 29, and 43. The primary end point was the subject’s Investigator’s Global Assessment (IGA) score on day 22 (0 indicates clear skin and 5 indicates severe disease activity). Treatment success was defined as an IGA score of 0 or 1. Secondary end points included IGA scores at other time points, subject/caregiver assessment of pruritus as evaluated with the VAS and an ordinal scale of 0 to 3, onset and duration of itch relief, Eczema Area and Severity Index, subject/caregiver assessment of global response, and need for rescue medication during a flare.

RESULTS. For the primary end point of IGA score at day 22, there was a highly significant difference between the 2 groups (analysis of covariance, P < .0001) in favor of the treatment group. In intention-to-treat analysis, 53 (77%) of 69 subjects achieved treatment success, compared with none in the vehicle group. The mean treatment difference was −1.636 (95% confidence interval: −1.928 to −1.344) in favor of MAS063DP. The secondary end point of IGA scores at other time points demonstrated treatment success for 39.1% of the MAS063DP-treated subjects by day 8, 71% by day 15, and 78.2% by day 29. Treatment success in the vehicle-treated group did not exceed 7.1%. The difference was significant at all time points (Fisher’s exact test, P < .0001). Other secondary end points that demonstrated significant benefit in the treatment group versus the vehicle group included the VAS score, Eczema Area and Severity Index score, subject/caregiver assessment of global response from baseline, onset of itch relief and duration of action, and need for rescue medication (8.7% in the treatment group and 28.6% in the vehicle group). No serious adverse events were related to MAS063DP, although stinging (8.3%), burning (6.9%), and fever (6.9%) were common adverse events (the latter 2 occurring more frequently in the vehicle group). Rates of treatment discontinuation because of adverse events were 9.9% in the MAS063DP group and 16% in the vehicle group.

CONCLUSIONS. MAS063DP is safe and effective in the treatment of mild-to-moderate atopic dermatitis in infants and children.

REVIEWERS COMMENTS. Concerns about adverse effects of topical corticosteroids and calcineurin inhibitors elicit understandable parental apprehension. The results of this study show promise for an alternative therapy for mild-to-moderate atopic dermatitis in infants and children. Although this study did not monitor for the theoretical risk of systemic toxicity after prolonged use, no systemic adverse events have been reported in post-marketing surveillance.
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