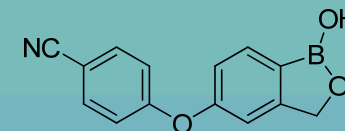


AN2728 Ointment, A Novel Oxaborole With Anti-Inflammatory Activity, Demonstrates Safety and Significant Efficacy in a Phase Ib Psoriasis Plaque Test

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Summary:

AN2728 is a novel, boron-containing, broad spectrum, anti-inflammatory compound, which inhibits the release of TNF- α , IL-12, IL-23, and other pro-inflammatory cytokines, currently in development for the topical treatment of plaque psoriasis and atopic dermatitis.

This study sought to evaluate the safety, anti-psoriatic activity, and dose-response relationship of AN2728 Ointment (0.5%, 2%, and 5%) in a psoriasis plaque test.

In this randomized, observer-blind study, 12 subjects had a psoriasis plaque treated with 6 test articles under occlusion over 12 days. Efficacy parameters included sonographic measurement of infiltrate thickness (mean and area under the curve [AUC]) and clinical assessment. Each parameter was measured at baseline, Day 8 and Day 12. Ointment vehicle was the negative control, whereas betamethasone cream and tacrolimus ointment were positive controls.

Primary efficacy endpoint: after 12 days of treatment, mean percent reductions in infiltrate thickness for AN2728 Ointment, 0.5%, 2%, and 5% were 26%, 35%, and 36%, respectively (all $P < 0.002$ vs. vehicle; **Figure 1**). Reductions in infiltrate thickness from baseline to Day 8 and Day 12 demonstrated a significant linear trend ($P < 0.0001$). Area under the curve (AUC) and clinical assessments paralleled the sonographic findings (**Figure 2** and **Figure 3**, respectively).

No adverse events, significant changes in laboratory values, or relevant changes in physical examinations were observed.

In summary, AN2728 ointment was well-tolerated and achieved the primary efficacy endpoint of the study, demonstrating a clear and relevant anti-psoriatic effect at all concentrations tested by sonographic and clinical efficacy parameters in the psoriasis plaque test.

Efficacy Results:

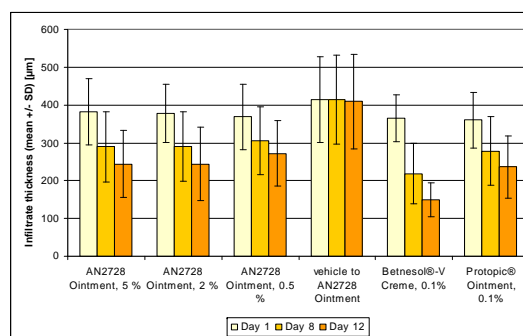


Figure 1: Mean infiltrate thickness of AN2728 Ointment, 5%, 2%, 0.5%, vehicle, and comparators (μm). The percent change in infiltrate thickness was -36% for the AN2728 Ointment, 5%, -35% for the AN2728 Ointment, 2%, and -26% for the AN2728 Ointment, 0.5% at the end of the study (all $P < 0.002$ vs. vehicle at corresponding timepoints).

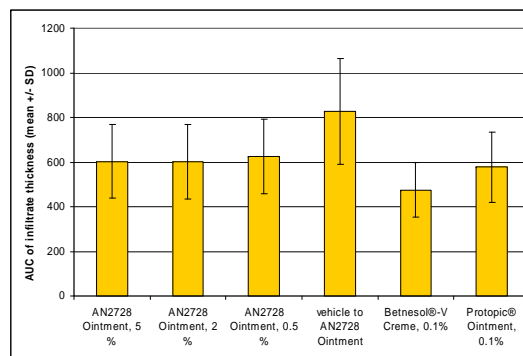


Figure 2: Area under the curve of infiltrate thickness (Arbitrary Units); $AUC = \frac{1}{2} * (INF_1 + 2 * INF_8 + INF_{12})$. The results of the mean AUC parallel the findings for the mean infiltrate thickness. A clearly higher mean AUC was noted for the corresponding ointment vehicle.

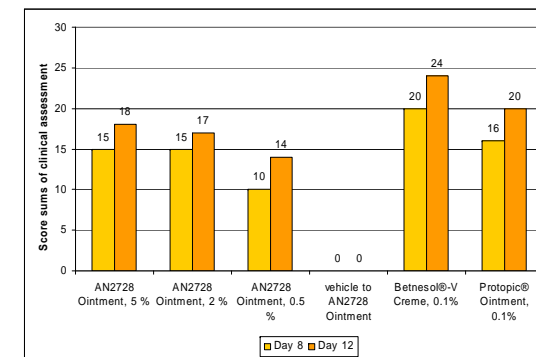


Figure 3: Score sums of clinical assessment. Sums were achieved by adding the individual clinical scores of all test fields for a given treatment (Scale: -1, worsened; 0 unchanged; 1, slight improvement; 2, clear improvement but not completely healed; 3, completely healed). These findings are consistent with those for mean infiltrate thickness.

Safety Results:

No adverse events were observed in this study. No significant changes in clinical laboratory values caused by treatment were seen and the final physical examination did not show relevant findings in any of the subjects.

Conclusion:

This Phase Ib study demonstrates a clear anti-psoriatic effect for AN2728 Ointment at multiple concentrations following 12 days of occlusive treatment. This effect was seen in both sonographic measurements of infiltrate thickness and clinical assessments. AN2728 was well-tolerated at all concentrations tested; no adverse events were observed. Based on these results, AN2728 Ointment has now entered Phase 2 clinical trials with patient self-application under non-occlusive conditions.