



AN2728, a novel oxaborole in development for treatment of psoriasis, demonstrates significant activity in a micro plaque study

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Summary

AN2728 is novel boron-containing oxaborole drug with a molecular weight of 251 amu and anti-inflammatory activity based on the inhibition of the release of pro-inflammatory cytokines including TNF- α , IFN- γ , IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, and IL-23. AN2728 also inhibits the release of the chemokine MCP-1 and PGE2. This activity is explained in part by the inhibition of phosphodiesterase-4 (PDE-4). The purpose of this study was to evaluate the antipsoriatic activity of AN2728. This single-center, randomized, vehicle-controlled, observer-blind study enrolled 12 subjects with psoriasis. Six test fields per subject were treated (two active formulations: AN2728 Ointment, 5%, AN2728 Cream, 5%; two vehicles, and two comparators). All fields were treated under occlusion 10 times over 12 days. Experimental measurements included sonography and clinical assessments with intra-individual comparison of the treatments. The primary endpoint for this study was the efficacy of the active study preparations compared to the corresponding vehicle using differences in infiltrate thickness. Secondary endpoints included descriptive statistics of sonographic measurements of infiltrate thickness, the AUC of the infiltrate thickness and clinical assessment scores for assessment of efficacy.

Efficacy Results

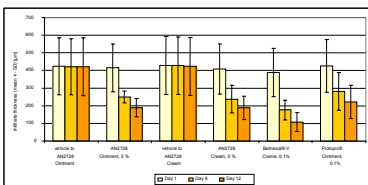


Figure 1: The mean infiltrate thickness of AN2728, vehicle and comparators (μm)
 $\text{dINF}_x = \text{INF}_x - \text{INF}_1$ where $x = (8, 12)$

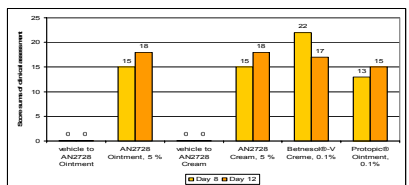


Figure 2: Score sums of clinical assessment using a 5-point score:

- 1 = worsened
- 0 = unchanged (no effect)
- 1 = slight improvement
- 2 = clear improvement but not completely healed
- 3 = completely healed

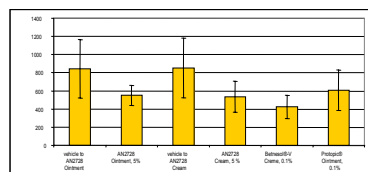


Figure 3: Area under the curve for the infiltrate thickness [arb. Units]
 $\text{AUC} = \frac{1}{2} \times (\text{INF}_1 + 2 \times \text{INF}_8 + \text{INF}_{12})$ where INF_1 = infiltrate thickness Day 1; INF_8 = infiltrate thickness Day 8 and INF_{12} = infiltrate thickness Day 12

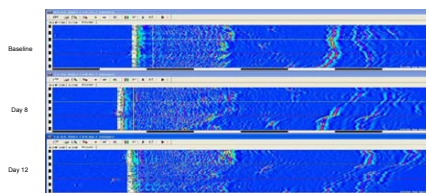


Figure 4: Sonography for Subject 008 (5% AN2728 Ointment)

Safety Results

The two AN2728 formulations were well tolerated. There were no application site reactions, other treatment-related adverse reactions or laboratory abnormalities.

Conclusions

The purpose of this proof of concept study was to assess the antipsoriatic efficacy of AN2728 Ointment, 5% and AN2728 Cream, 5% compared with their corresponding vehicles in subjects with stable psoriatic plaques. A clear antipsoriatic effect was found for both AN2728 formulations after 12 days of occlusive treatment on the basis of the sonographic and clinical measurements.

Significant differences in the mean infiltrate thickness to the vehicle were observed at all test points. This was also confirmed by the clinical assessment data. In this study all test articles were applied under occlusion. The effect of occlusion on the activity of drugs may vary between different classes of molecules. For this reason, this study has very limited ability to define relative potency of drugs from very different chemical classes. Based on the results of this trial, AN2728 is being advanced to clinical trials with patient self-application under non-occlusive conditions.