

A Randomized, Double-Blind, Vehicle-Controlled, Multicenter Study to Evaluate the Safety and Efficacy of Topically Applied AN0128 1% Cream for the Treatment of Mild to Moderate Atopic Dermatitis

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Background

AN0128 is a novel topical anti-inflammatory drug which blocks pro-inflammatory cytokines *in vitro* and in pre clinical studies demonstrates an excellent topical and systemic safety profile.
 See poster #E0429 for mechanism of action.

Introduction

Atopic dermatitis (AD) is a genetically determined, distinctive eczematous condition that usually occurs in people who have a personal or family history of asthma or seasonal or perennial allergic rhinitis. It affects 10% to 20% of infants in the United States¹ and is a common cause for pediatric healthcare visits². AD is the eighth most common disease in persons under 25 years of age, nonetheless, it continues to be frequently misdiagnosed, misunderstood, and ineffectively treated³.

Study Design

Eight centers enrolled 103 subjects over 18 years of age with mild to moderate atopic dermatitis (AD) and a body surface area of 3-10% to be randomized 2:1 to twice daily treatment for 4 weeks with either AN0128 Cream 1% or the vehicle cream. At baseline 67% of subjects were evaluated as moderate in severity. Evaluations were made at Baseline and on Days 3, 7, 14, 28, and 35. The ISGA score was assessed on the same schedule using a 6-point scale ranging from 0 (clear) to 5 (very severe). As the first clinical trial of this new therapy in the treatment of atopic dermatitis, this trial was considered exploratory in nature and thus there were no formal power calculations.

Table 1. ISGA Definition

Score	Grade	Definition
0	Clear	No inflammatory signs of AD
1	Almost clear	Just perceptible erythema, and just perceptible papulation/induration
2	Mild	Mild erythema, and mild papulation/induration
3	Moderate	Moderate erythema and moderate papulation/induration
4	Severe	Severe erythema and severe papulation/induration
5	Very Severe	Severe erythema and severe papulation/induration with oozing/crusting

Table 2. Demographics and Baseline Characteristics of Atopic Dermatitis

	Vehicle		AN0128		Total Subjects	
	N	%	N	%	N	%
Number of ITT Subjects	36		67		103	
Age (years)						
Median	14.6		17.5		16.5	
Mean	31.0		35.0		34.0	
Gender						
Male	14	38.9%	29	43.3%	43	41.7%
Femal	22	61.1%	38	56.7%	60	58.3%
Duration of AD (months)						
Median	155.1		209.8		195.3	
Mean	238.4		267.1		256.0	

Definition of Efficacy

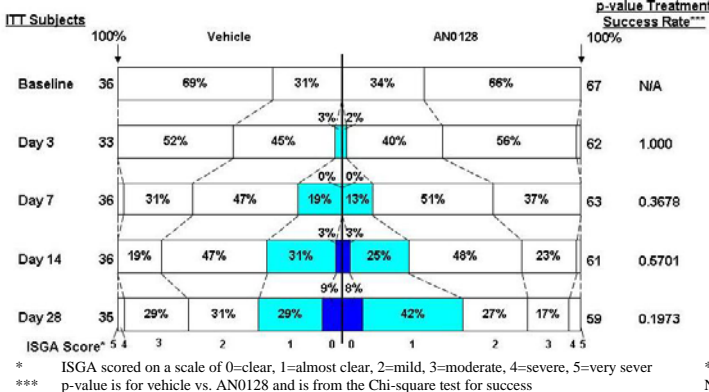
Investigator's Static Global Assessment (ISGA):

The ISGA, based on a 6-point scale ranging from 0 (Clear) to 5 (very severe), was assessed at each visit. The ISGA was dichotomized to success and failure with a score of 0 or 1 considered a success and scores of 2, 3, 4 and 5 considered a failure for the Week 2 and Week 4 evaluations.

Results

An intent to treat analysis of all subjects randomized, at the end of the treatment period showed that 51% (30/59) of the AN0128 treated subjects vs. 37% (13/35) of the vehicle treated group reached a level of clear or almost clear (p=0.19) based on a 6 point (clear, almost clear, mild, moderate, severe) investigator static global assessment (ISGA). In a modified intent to treat population of only those subjects who were of moderate severity at baseline 47%, (18/38) of the AN0128 treated group and 29% (7/24) of the vehicle group reached at least a two grade improvement in their ISGA (p=0.15). Both treatments were well tolerated with only rare application site reactions and no serious adverse events report.

Graph 1. AN0128 Clinical Results: ITT Population Baseline Mild and Moderate ISGA Going to Clear or Almost Clear ISGA (1 or 2 Grade Improvement)



Graph 2. AN0128 Clinical Results: ITT Population Baseline Moderate ISGA Going to Clear or Almost Clear ISGA (2 Grade Improvement, or Current Approval Standard)

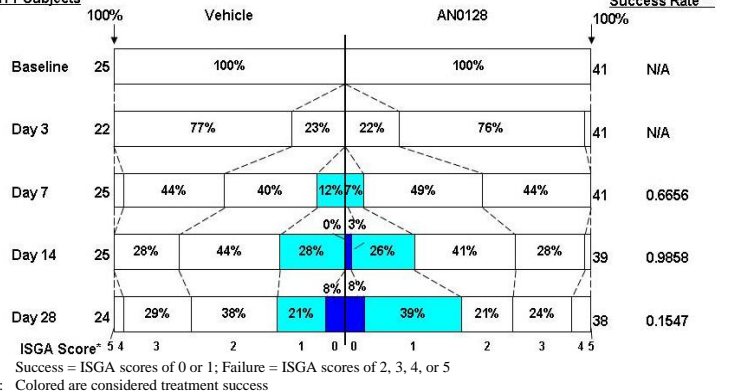


Table 3. Summary or Treatment Emergent Adverse Events

	Vehicle		AN0128		Total Subjects	
	N	%	N	%	N	%
Number of ITT Subjects	36		67		103	
Subjects with Any AEs	13	36.1%	27	40.3%	40	38.8%
Total Number of Reported AEs	17		38		55	
Total Number of Unique AEs	24		22		46	
Relationship of AEs to Study Drug						
Not Related	9	52.9%	19	50.0%	28	50.9%
Unlikely	5	29.4%	9	23.7%	14	25.5%
Possible	0	0.0%	7	18.4%	7	12.7%
Probable	3	17.6%	3	7.9%	6	10.9%
Definite	0	0.0%	0	0.0%	0	0.0%
Maximum Severity						
Mild	6	35.3%	19	50.0%	25	45.5%
Moderate	10	58.8%	18	47.4%	28	50.9%
Severe	1	5.9%	1	2.6%	2	3.6%
Subjects with Serious AEs	0	0.0%	0	0.0%	0	0.0%
Subjects Withdrawn from Study Drug due to AEs	1	2.8%	4	6.0%	5	4.9%

Table 4. Application Site Reactions

	Incidence				Frequency			
	Vehicle		AN0128		Vehicle		AN0128	
	N	%	N	%	N	%	N	%
Number of ITT Subjects	36		67		36		67	
Total Number of Reported Treatment Emergent AEs	17		38		17		38	38.8%
General Disorders and Administration Site Conditions								
Application Site Irritation	2	5.6%	0	0.0%	2	11.8%	0	0.0%
Application Site Pruritus	1	2.8%	1	1.5%	1	5.9%	1	2.6%
Application Site Swelling	0	0.0%	1	1.5%	0	0.0%	1	2.6%
Pyrexia	0	0.0%	1	1.5%	0	0.0%	1	2.6%

Conclusions

The results of this study indicate that AN0128 represents a potential new therapy for AD and this study provides the necessary data to power future trials.

- AN0128 had a strong trend towards superiority in terms of improvement in the ISGA.

References

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