

K. Beutner<sup>a</sup>, J. J. Leyden<sup>b</sup>, K. Kaidbey<sup>b</sup>, and K. Maples<sup>a</sup>,<sup>a</sup>Anacor Pharmaceuticals, 1060 E. Meadow Circle, Palo Alto, CA 94303; <sup>b</sup>Ivy Laboratories (KGL, Inc.), 505 Parkway, Broomall, PA 19008-4204**ABSTRACT**

AN0128 is a novel borinic acid ester with combined antimicrobial and anti-inflammatory activity. Its minimum inhibitory concentration *in vitro* against *S. aureus* *P. acnes* is 2 mcg/mL for both bacteria. At a concentration of 10 mcg/mL, AN0128 significantly inhibits the release of pro-inflammatory cytokines TNF-alpha, IL-1beta, IL-6, and IL-8 with no significant effect on Th1 and Th2 cytokine release. Systemic and dermal toxicology studies in rats and minipigs for up to 28 days of continuous dosing at concentrations exceeding 10 mg/mL revealed no organ toxicities that would prohibit clinical investigation of a 1% AN0128 Cream applied topically to skin. Clinical safety and antibacterial activity of 1% AN0128 Cream versus its vehicle was evaluated in a randomized, double-blind, parallel study of 50 normal subjects who presented with baseline *P. acne* colonization of the forehead of >6 log<sub>10</sub>/cm<sup>2</sup>. This poster will focus only on the clinical safety of 1% AN0128 Cream. Subjects applied the test agents bid for 28 consecutive days with daily clinical evaluations for local tolerance of the tested agents. Treatment emergent systemic adverse events were also monitored daily.

AN0128 Cream and its vehicle were well tolerated with no evidence of erythema or other skin irritation. There were no treatment emergent adverse events or serious adverse events associated with either test agent.

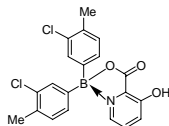
In this first in man study of 1% AN0128 Cream, this new chemical entity was safe with no clinical evidence of adverse systemic effects and excellent local tolerance at the site of topical application.

**INTRODUCTION**

AN0128 is a novel compound with combined antibacterial and anti-inflammatory activity that is currently being evaluated for clinical efficacy in atopic dermatitis trials. The anti-inflammatory activity, the antibacterial activity, and the preclinical toxicology of AN0128 are the subject of other posters being presented at this meeting (see list at right). Summarized here are the clinical safety data from the first Phase I study completed for AN0128. The purpose of the test investigation was to evaluate the safety and tolerance of the test product when applied twice daily for 4 weeks to the forehead of volunteers.

**AN0128**

3-hydroxypyridine-2-carboxyloxy-bis(3-chloro-4-methylphenyl)-borane)

**METHODS**

This study was a double-blind, randomized trial in which AN0128 Cream, 1% was compared to AN0128 Cream Vehicle in two parallel groups of subjects. Each group consisted of twenty five (25) normal, healthy adult males and females 18 years of age and older. Each volunteer was treated once daily under supervision by a technician at Ivy Laboratories in a standardized manner for 4 weeks. The topical test material was applied by the subjects (unsupervised) at home once daily at bedtime and twice on Saturdays and Sundays. At each visit, a sufficient amount of the test product (about 0.5 mL) was applied to the entire forehead area and rubbed in for about 30 seconds. Erythema, defined as abnormal redness of the skin, was assessed at post screening visits after both 2 and 4 weeks of application. Erythema was scored on a scale of 0-3.

**Erythema Scoring Scale**

Score	Grade	Guideline
0	None	No redness present
1	Mild	Faintly detectable erythema; very light pink
2	Moderate	Dull red, clearly distinguishable
3	Severe	Deep, dark red

**Inclusion Criteria:**

- Healthy, adult male and/or female volunteers 18 years of age and older with no past or present history of any significant internal disease (e.g. cardiovascular, pulmonary, renal, etc.)
- All females must have been using a highly effective method of contraception
- Subjects had to be willing to refrain from sunbathing or excessive sun exposure
- Subjects had to be compliant and able to return to Ivy Laboratories as instructed once daily for four weeks

**Exclusion Criteria:**

- Any volunteer who exhibited any skin disorders of an acute or chronic nature including psoriasis, eczema, etc.
- History of any significant internal disease
- Females who were pregnant, planning a pregnancy or breastfeeding
- Subjects who were known to be allergic to any of the test product(s) or any components in the test product(s)
- Past or present history of drug abuse
- AIDS or AIDS Related Complex
- Any subject not able to meet the study attendance requirements

**RESULTS AND CONCLUSIONS**

Erythema was not observed in any subject at any screening visit. AN0128 was safe and well tolerated at the site of topical application.

**RELATED POSTERS ON AN0128 BEING PRESENTED AT THIS MEETING**

AN0128, A Novel Borinic Acid Ester with *In Vitro* and *In Vivo* Anti-Inflammatory Activity. Emily Ip, Carole Bellinger-Kawahara, Yvonne Freund, Kirk Maples

Preclinical Toxicology of AN0128, A Novel Borinic Acid Ester with Combined Antimicrobial and Anti-Inflammatory Activity. Emily Ip, Conrad Wheeler, Kirk Maples

A Novel Borinic Acid Ester With Antibacterial Activity Against *Propionibacterium acnes*. Richard Kimura, Carole Bellinger-Kawahara, Kirk Maples

A Novel Borinic Acid Ester with Antibacterial Activity Against *Staphylococcus aureus*. Richard Kimura, Carole Bellinger-Kawahara, Kirk Maples

A Novel Synthetic Borinic Acid Ester with a Broad Spectrum of Antibacterial Activity. MRK Alley, Weimin Mao