

Evaluation of the Safety and Efficacy of a Novel Anti-Acne Nanoemulsion (NB-003) in a Randomized, Open-Label Parallel-Group, Single-Center Study

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ABSTRACT

Background: Anti-microbial agents that inhibit *Propionibacterium acnes* are one approach to treating acne vulgaris. NB-003 is a topical bactericidal oil-in-water emulsion with nanometer-sized droplets that concentrate in the pilosebaceous unit, the site of *P. acnes* infection. We evaluated the safety and effectiveness of NB-003 in reducing skin *P. acnes* levels in healthy subjects.

Method: Thirty-five (35) adult subjects with high forehead levels of *P. acnes* ($\geq 4 \log_{10}$ CFU/cm²) were enrolled in the study. Twenty-five (25) subjects were randomized to NB-003 (0.25%) while 10 subjects were randomized to 2.5% Benzoyl Peroxide (positive control). Subjects applied the product to the forehead twice daily (morning and afternoon) for 4 weeks. Quantitative forehead *P. acnes* cultures were obtained at screening, baseline, then at weeks 1, 2 and 4 of treatment. Safety was evaluated daily by questioning about adverse events and dermal irritation scoring.

Results: NB-003 was well tolerated with no reported adverse events. NB-003 produced a mean 0.46 log₁₀ reduction (SD=0.63) after 1 week with an increase to 0.66 log₁₀ reduction (SD=0.78) after 4 weeks.

Conclusions: NB-003 is well tolerated and demonstrates *in vivo* reduction in *P. acnes* similar to that reported for topical 2% erythromycin products. A confirmatory study of the anti-acne activity of NB-003 is underway.

BACKGROUND

Propionibacterium acnes is one of the primary factors involved in the pathogenesis of acne vulgaris. It is the predominant microorganism of the pilosebaceous glands of human skin, with up to 10⁷ viable organisms isolated from a single sebaceous unit.

NB-003 is a novel topical nanoemulsion composed of high energy nanometer-sized droplets (Figure 1) with bactericidal activity that traverse skin pores and hair follicles and diffuse laterally to the infected pilosebaceous gland. *In vitro* skin permeation studies demonstrated that NB-003 permeates into the pilosebaceous gland¹ (Figure 2).

Upon contact with the bacterium, NB-003 droplets are thermodynamically driven to fuse with the cell membrane causing disruption and cell lysis (Figure 3). This novel mechanism of action renders the emergence of drug resistance highly unlikely.

The effectiveness of acne treatments has been limited due to their relative inability to permeate into the pilosebaceous unit, the site of acne formation.

The objectives of this study were to evaluate the safety and efficacy NB-003 formulation in reducing skin *P. acnes* levels in healthy subjects with high levels of *P. acnes* ($\geq 4 \log_{10}$ CFU/cm²).

¹Pannu et al. Abstr. 616, 69th Society for Invest. Derm Ann. Meeting.

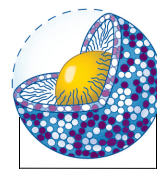


Figure 1. Nanoemulsion droplet

RESULTS

SAFETY AND TOLERABILITY

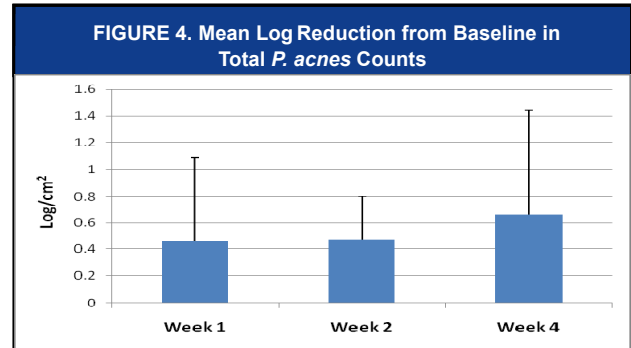
- There were no adverse events reported in either treatment group.
- 0.25% NB-003 was well tolerated. Two subjects had transient burning and stinging following NB-003 application. Two subjects had mild to moderate dryness with 2.5% BPO (Table 2).

Study Group	Subject	Dermal Score (study day)			
		Erythema	Dryness	Burning/Stinging	Itching
0.25% NB-003	1	0	0	2 (9)	0
	2	0	0	1 (14)	0
2.5% BPO	3	0	2 (13-29)	0	0
	4	0	1 (16), 2(15)	0	0

Dermal Scoring: 0=none, 1=mild, 2=moderate and 3=severe.

RESULTS

EFFICACY



- The positive BPO control (gold standard) performed as expected with a mean 2.14 log reduction (SD=0.73) at 4 weeks.
- The vehicle control produced no significant reduction in *P. acnes* counts (mean 0.09 log ± 0.21) at 4 weeks (separate study).
- 32% of the NB-003 treated subjects had a mean log reduction ≥ 0.67 at 4 weeks.

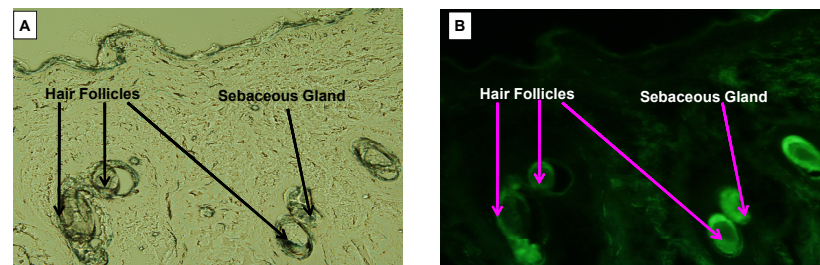
METHODS

- Thirty-five adult subjects with confirmed high levels of forehead *P. acnes* ($\geq 4 \log_{10}$ CFU/cm²) were randomized to 0.25% NB-003 BID or 2.5% benzoyl peroxide BID (Proactiv®, Repairing Lotion).
- 0.3 to 0.5mL of NB-003 was applied by cotton pad while 0.5 mL of BPO was applied by finger tips. Treatments were applied for a maximum of 28 days.
- Efficacy was assessed by quantitative forehead *P. acnes* cultures collected at screening, baseline and weeks 1, 2 and 4 of treatment. Safety, including dermal irritation, was evaluated by AE query at clinic visits.
- There were no differences in the baseline demographic parameters between the two treatment groups (Table 1).
- The mean number of treatments applied in the NB-003 and BPO groups was 53.0 and 51.6, respectively.

	0.25% NB-003 N=25	2.5% BPO N=10
Age		
Median	27.0	20.5
Min, Max	19, 52	18, 55
Sex		
Men	7 (28%)	4(40%)
Women	18 (72%)	6 (60%)
Race		
White	24 (96%)	8 (80%)

MECHANISM OF ACTION NB-003

Skin Model



Hamster Ear Model

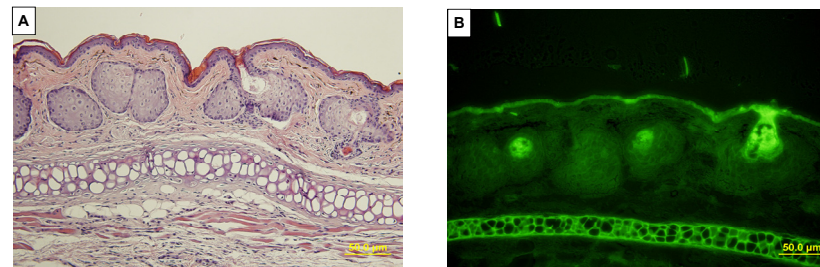


Figure 2. a) Skin/Hamster Ear cross-section b) Skin/Hamster Ear cross-section under fluorescence showing NB-003 preferentially distributing in the hair follicles and sebaceous glands.

MECHANISM OF ACTION NB-003

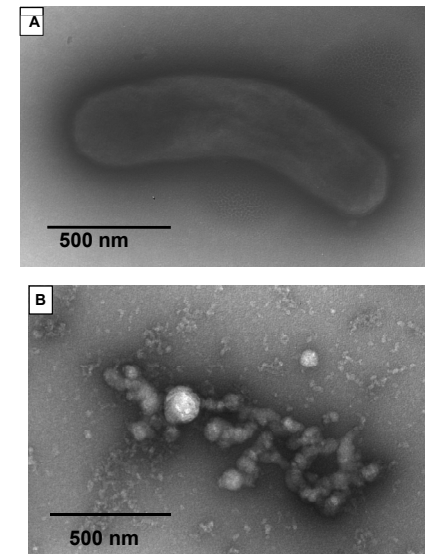
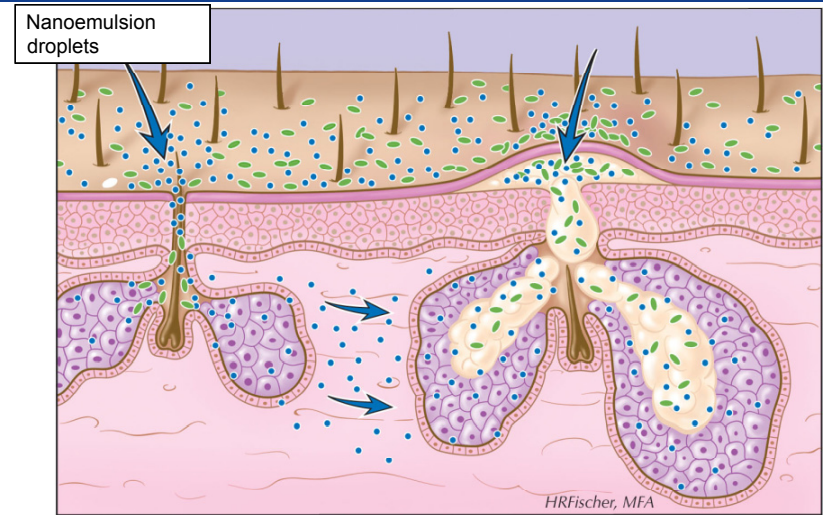


Figure 3. Scanning electron micrographs of *P. acnes* (a) before and (b) after one hour of NB-003 treatment.



CONCLUSIONS

- NB-003 permeates into the pilosebaceous unit in the hamster ear model.
- NB-003 is well tolerated and demonstrates *in vivo* reduction of *P. acnes* from the forehead similar to that reported for topical 2% erythromycin products.