Phase 2 Study of Efficacy and Safety of SB204 in the Treatment of Acne Vulgaris

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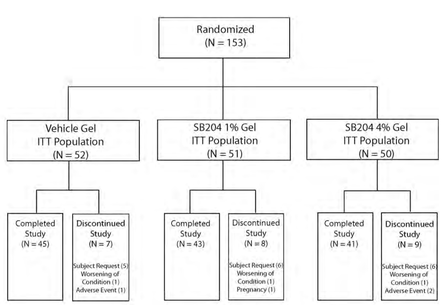
INTRODUCTION

Nitric oxide is an endogenous, short-acting molecule with anti-microbial and anti-inflammatory activity. Novan's nitric oxide-releasing drug, NVN1000, has demonstrated activity against *P. acnes*, anti-inflammatory activity, and inhibition of lipogenesis by insulin-stimulated immortal sebocytes. We report results of a Phase 2 clinical trial with an NVN1000 containing topical gel, SB204, in subjects with acne vulgaris.

STUDY DESIGN

The study (NCT01844752) was a Phase 2, multicenter, randomized, double-blinded, vehicle-controlled, parallel-group, 3-arm study. Patients were enrolled at 4 sites in Latin America. To be eligible for the study, subjects must have been 12 to 40 years of age, in good general health, and had acne vulgaris. Subjects must have had 20 to 40 inflammatory lesions, 25 to 70 non-inflammatory lesions, no greater than 2 nodules on the face, and have a Baseline Investigator's Global Assessment (IGA) score of 2 (mild), 3 (moderate), or 4 (severe). Subjects were randomized to treatment with SB204 1%, SB204 4%, or Vehicle in a 1:1:1 ratio and instructed to dose evenly over the entire face twice daily for 12 weeks. Subjects were not permitted to use any anti-acne topical or systemic treatments during the study.

A total of 153 subjects were randomized to the study. Subject disposition is detailed in the table below.

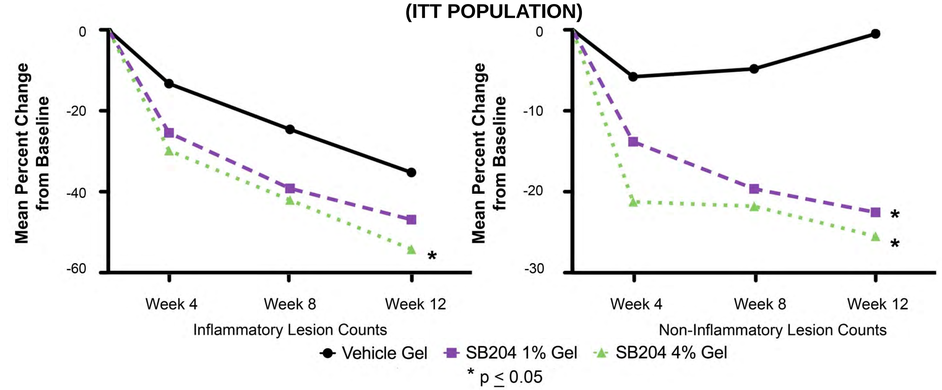


Demographics, lesion counts, and IGA scores were similar at Baseline across all treatment groups. The majority (79.1%) of subjects had a Baseline IGA score of "moderate".

BASELINE DEMOGRAPHICS

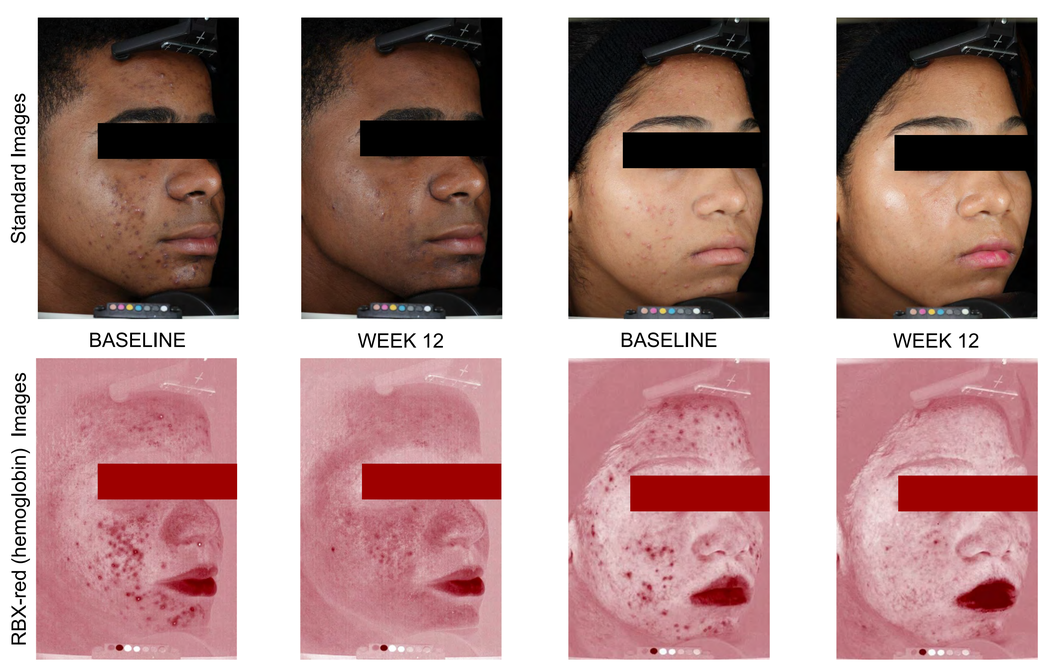
Characteristic	Vehicle (N = 52)	SB204 1%l (N = 51)	SB204 4% (N = 50)
Mean age (SD)	20.0 (5.57)	20.0 (5.39)	19.3 (4.30)
Age group; n (%)			
Age 12-17	21 (40.4%)	16 (31.4%)	14 (28.0%)
Age 18-29	27 (51.9%)	30 (58.8%)	35 (70.0%)
Age ≥ 30	4 (7.7%)	5 (9.8%)	1 (2.0%)
Sex; n (%)			
Male	25 (48.1%)	26 (51.0%)	26 (52.0%)
Female	27 (51.9%)	25 (49.0%)	24 (48.0%)

PERCENT CHANGE FROM BASELINE IN INFLAMMATORY AND NON-INFLAMMATORY LESION COUNTS (ITT POPULATION)



* $p \leq 0.05$

At Week 12, subjects treated with SB204 4% had a greater reduction in inflammatory lesion counts from Baseline compared to the Vehicle treated group (ANCOVA, $p<0.05$). Subjects treated with SB204 1% and 4% had a significantly greater reduction in non-inflammatory lesion counts from Baseline compared to the Vehicle treated group (ANCOVA, $p<0.05$). A dose response was observed with increasing concentration of SB204. Separation of the SB204 treatment group from vehicle as measured by reductions in the number of non-inflammatory and inflammatory lesions was observed as early as Week 4 in the SB204 4% treatment group. There were no statistically significant differences in the dichotomized IGA scores of 'success' (score of "clear/almost clear" and minimum 2 grade change between BL and Week 12) between Vehicle Gel and SB204 1% or SB204 4% Gel treatment groups. In the SB204 treatment groups, there was a decrease in the percentage of subjects with "moderate" or "severe" IGA scores.



TOLERABILITY/SAFETY

Overall, SB204 demonstrated good cutaneous tolerability at both concentrations tested. Among subjects who experienced events related to cutaneous tolerability, most were mild in severity. Tolerability at the Week 12 visit is shown below.

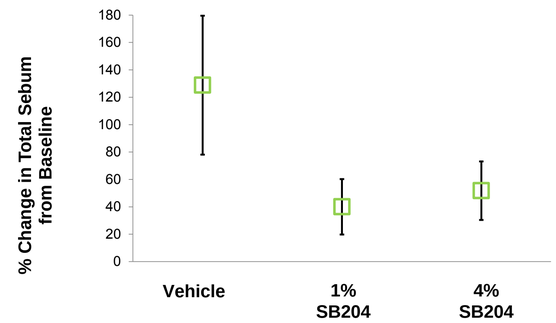
CUTANEOUS TOLERABILITY AT WEEK 12

	Vehicle Gel (N = 45)			SB204 1% (N = 43)			SB204 4% (N = 41)		
	Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
Erythema	4	0	0	4	2	0	6	1	0
Scaling	1	0	0	4	0	0	8	0	0
Dryness	4	0	0	1	0	0	5	0	0
Itching	4	0	0	3	0	0	10	0	0
Burning/Stinging	3	0	0	0	0	0	3	0	0

The adverse event (AE) and laboratory profile (methemoglobin, hemoglobin) were similar in SB204 and Vehicle treated subjects. A total of 10 subjects (19.2%) in the Vehicle treatment group and 20 subjects (19.8%) treated with SB204 reported at least 1 treatment-emergent AE (TEAE) over the course of the study. The most frequent TEAEs observed in this study were headache (11 subjects), dysmenorrhea (10 subjects), and nasopharyngitis (6 subjects). Most TEAEs were mild in severity and were considered unrelated to study drug.

SEBUM ANALYSIS

At the end of treatment, 80% less sebum was measured in sebutapes from subjects treated with SB204 compared to Vehicle (Figure below). Subjects treated with SB204 with a net decrease in total sebum (18/42) had mean reduction of inflammatory lesions of 60%. There was a dose dependent decrease in squalene (µg/tape) and the percent fatty acids in the SB204 treated subjects.



CONCLUSION

The higher dose of SB204 (4%) demonstrated a statistically significant difference in inflammatory lesion counts and both 1% and 4% were effective at decreasing non-inflammatory lesions in subjects with acne vulgaris treated for 12 weeks. Improvement in inflammatory and non-inflammatory lesion counts compared to vehicle was observed as early as 4 weeks of treatment in subjects treated with SB204 4%. Subjects treated with SB204 had 80% less sebum on the skin surface than those treated with Vehicle. Both concentrations of SB204 were well-tolerated; the safety profile in subjects treated with SB204 or Vehicle were comparable.

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