A Multicenter, Randomized, Evaluator-blinded, Vehicle-controlled, Parallel-Group Study Evaluating the Efficacy, Tolerability, and Safety of SB204 Gel Once or Twice Daily in the Treatment of Acne Vulgaris over 12 weeks

L Eichenfield, L Stein-Gold, J Quiring, C Enloe, MJ Rico

Presented by:
Lawrence F. Eichenfield, M.D.
Professor of Dermatology and Pediatrics
Chief, Pediatric and Adolescent Dermatology
University of California, San Diego and Rady Children's Hospital, San Diego

SB204—a First-in-Class Topical for Acne

SB204 is a novel nitric oxide–releasing therapy with multiple mechanisms of action

- Broad-spectrum antimicrobial activity
- Anti-inflammatory activity

SB204—a First-in-Class Topical for Acne

SB204 is a novel nitric oxide–releasing therapy

Broad-spectrum antimicrobial activity

- Nitrosative and oxidative stress results in numerous toxic effects on bacteria, including[1,2]:
  - Direct modification of membrane proteins
  - Lipid peroxidation
  - DNA cleavage
- No evidence of bacterial resistance to nitric oxide has been demonstrated to date[2,3]

1. Gautam P, Jain SK. *Indian J Biotechnol.* 2007;6(3):293-304.
2. Privett BJ et al. *Nitric Oxide.* 2012;26(3):169-173.
3. Qin M et al. *J Invest Dermatol.* 2015;135(11):2723-2731.

SB204—a First-in-Class Topical for Acne

SB204 is a novel nitric oxide–releasing therapy

Anti-inflammatory activity

- Nitric oxide targets the IL-1 and IL-17 components of the acne inflammatory pathway[3,4]
  - Inhibits activation of NLRP3 inflammasome by *P acnes*
  - Inhibits IL-1β production
  - Inhibits IL-1β–dependent Th17 cell differentiation

1. Qin M et al. *J Invest Dermatol.* 2015;135(11):2723-2731.
2. Niedbala W et al. *Proc Natl Acad Sci USA.* 2011;108(22):9220-9225.

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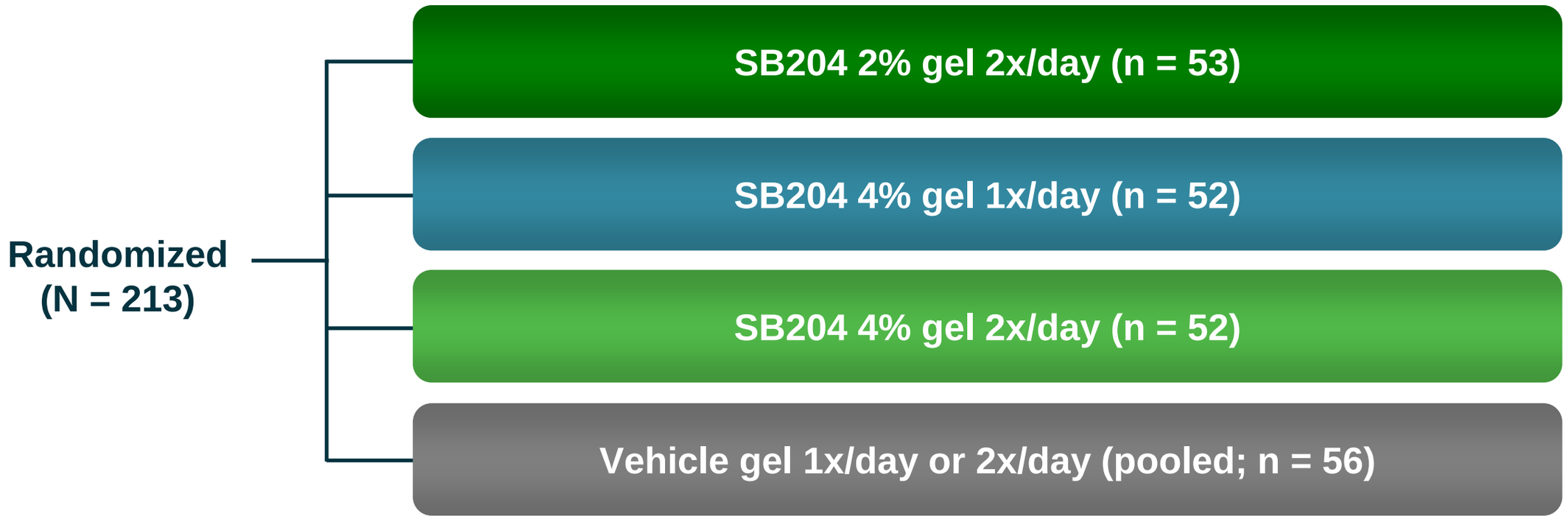
Study Design

- 12+ years of age
  - n= 213 randomized
- Moderate to severe acne (IGA)
- Inflammatory lesions: 20-40
- Non-inflammatory lesions: 25-70
- Vehicle-controlled, 2% and 4% gel
- 12 week study

Data on file, Novan, Inc.

Study Design



Co-primary endpoints	Secondary endpoints
⊙ Absolute change in inflammatory and noninflammatory lesion counts from baseline to week 12 ⊙ Success* on Investigator's Global Assessment (IGA) at week 12	⊙ Percent change in inflammatory and noninflammatory lesion counts from baseline to week 12 ⊙ Median time to improvement in lesion counts from baseline to week 12

*IGA success was defined as a score of clear or almost clear at week 12 and a minimum 2-grade change from baseline to week 12.. IGA Score 0 (Clear) – 4 (Severe)

Data on file, Novan, Inc.

Patient Demographics and Disposition

	SB204 2% gel 2x/day (n = 53)	SB204 4% gel 1x/day (n = 52)	SB204 4% gel 2x/day (n = 52)	Pooled vehicle gel (n = 56)
Gender, n (%)				
Male	27 (50.9%)	23 (44.2%)	22 (43.1%)	29 (51.8%)
Female	26 (49.1%)	29 (55.8%)	29 (56.9%)	27 (48.2%)
Age, years				
Mean	20.1	18.8	20.1	18.2
Min to max	13-39	13-33	12-38	12-37
Completed study, n (%)				
Yes	51 (96.2%)	48 (92.3%)	48 (92.3%)	44 (78.6%)
No	2 (3.8%)	4 (7.7%)	4 (7.7%)	12 (21.4%)
Reason for discontinuation, n (%)				
Adverse event	0	1 (1.9%)	0	0
Lack of efficacy	0	0	1(1.9%)	1 (1.8%)
Subject request	2 (3.8%)	2 (3.8%)	2(3.8%)	9 (16.1%)
Lost to follow-up	0	1 (1.9%)	1 (1.9%)	1 (1.8%)

Data on file, Novan, Inc.

Baseline Lesion Counts and IGA Scores

	SB204 2% gel 2x/day (n = 53)	SB204 4% gel 1x/day (n = 52)	SB204 4% gel 2x/day (n = 52)	Pooled vehicle gel (n = 56)
Noninflammatory lesion count				
Mean	38.5	38.1	38.5	38.9
Median	33	33	33	34.5
Min to max	25-69	25-68	25-70	25-69
Inflammatory lesion count				
Mean	27.5	27.1	26.2	27.9
Median	27	26	24	27
Min to max	20-40	20-40	20-40	20-40
IGA				
0 = Clear	0 (0%)	0 (0%)	0 (0%)	0 (0%)
1 = Almost clear	0 (0%)	0 (0%)	0 (0.0%)	0 (0%)
2 = Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)
3 = Moderate	47 (88.7%)	48 (92.3%)	46 (90.2%)	47 (83.9%)
4 = Severe	6 (11.3%)	4 (7.7%)	5 (9.8%)	9 (16.1%)

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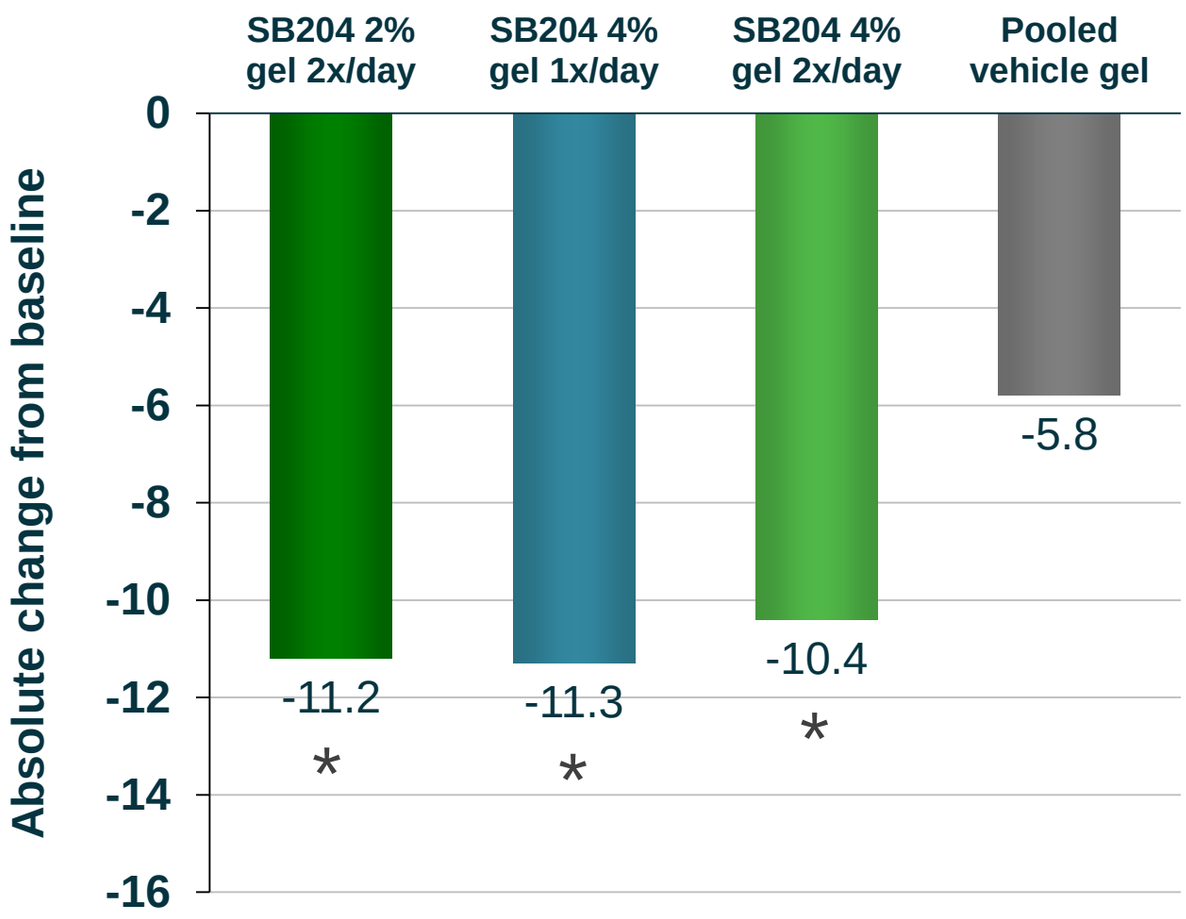
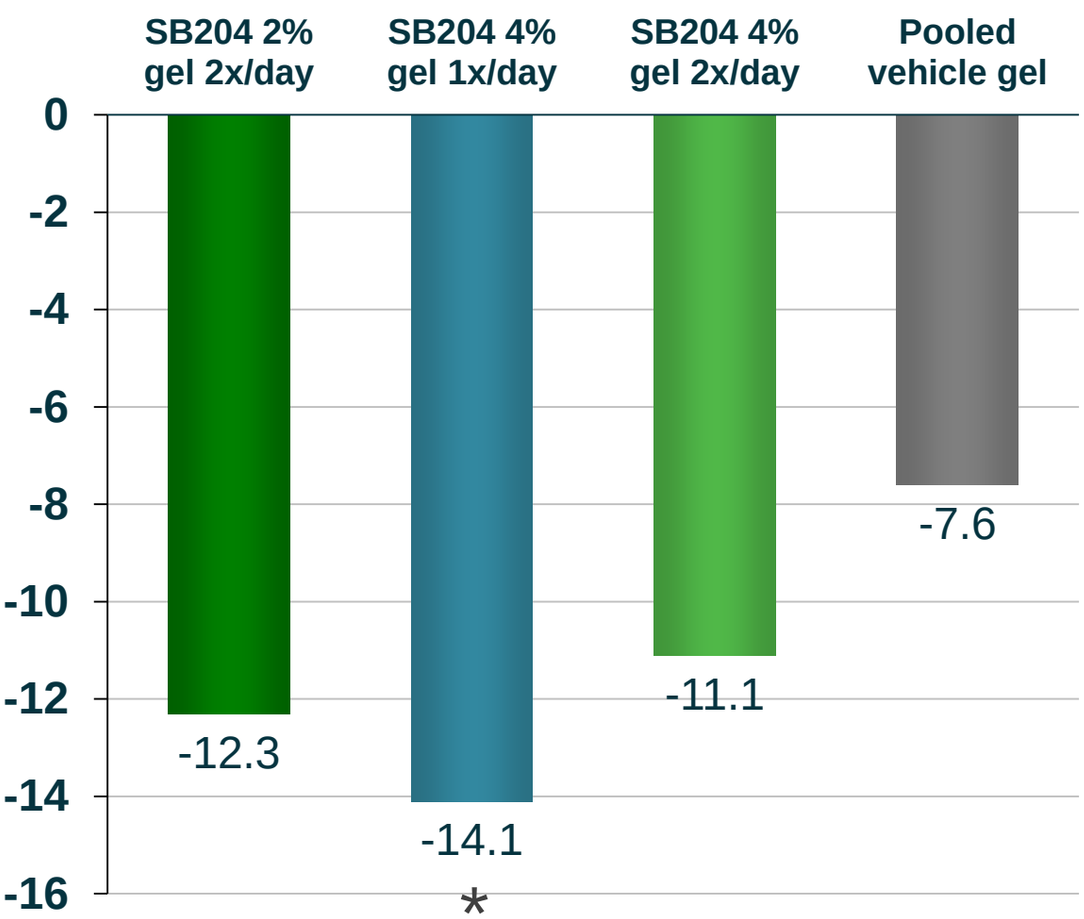
Primary Endpoint: Absolute Change in Lesion Counts From Baseline to Week 12

Inflammatory lesions



Noninflammatory lesions

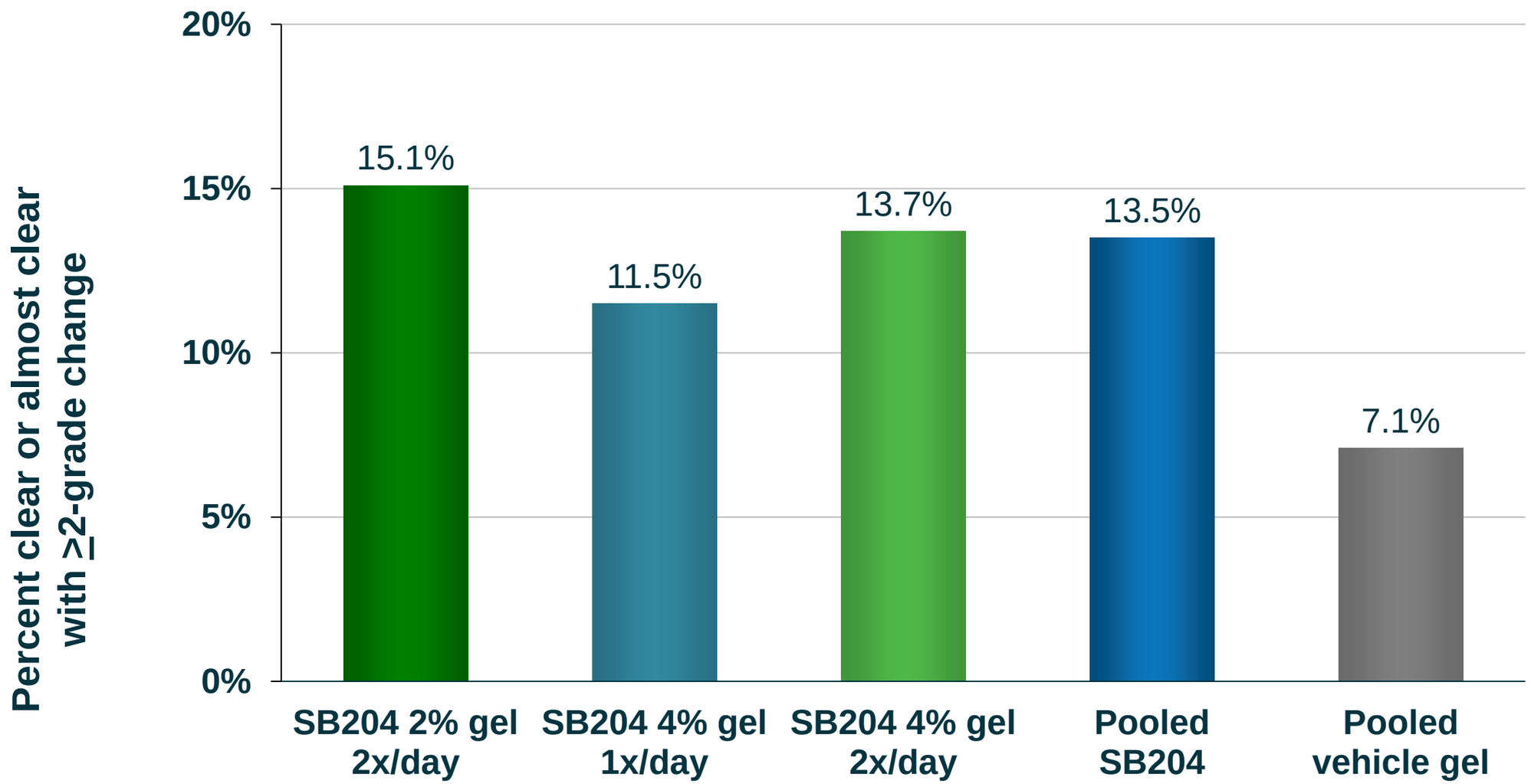


***P* ≤ .05**

Intent-to-treat population.
P values from contrasts comparing each SB204 gel group to vehicle gel group.

Data on file, Novan, Inc.

Primary Endpoint: IGA Success at Week 12



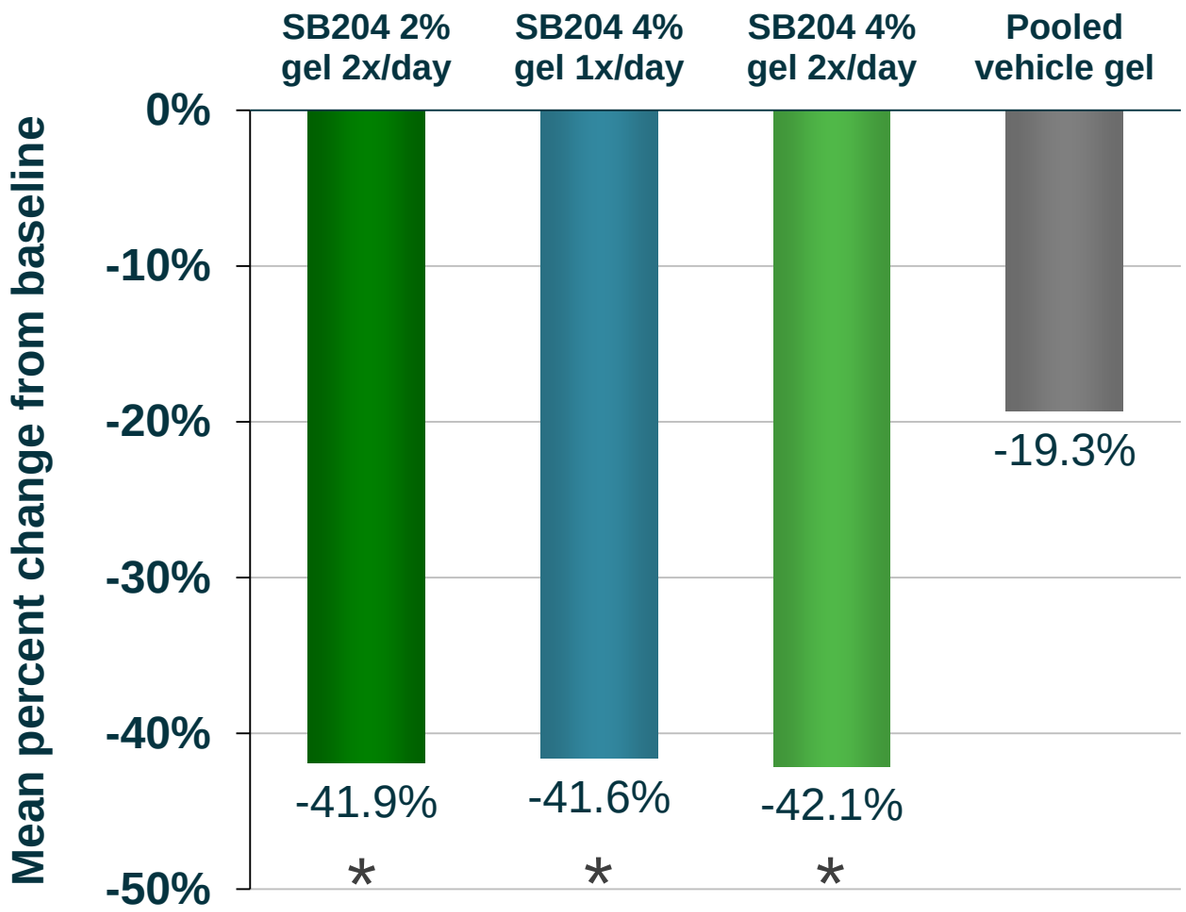
*IGA success was defined as a score of clear or almost clear at week 12 and a minimum 2-grade change from baseline to week 12. IGA Score: 0 (Clear) – 4 (Severe)

Intent-to-treat population.
"Pooled SB204" bar represents pooled SB204 treatment arms (n = 156) across all dose groups.

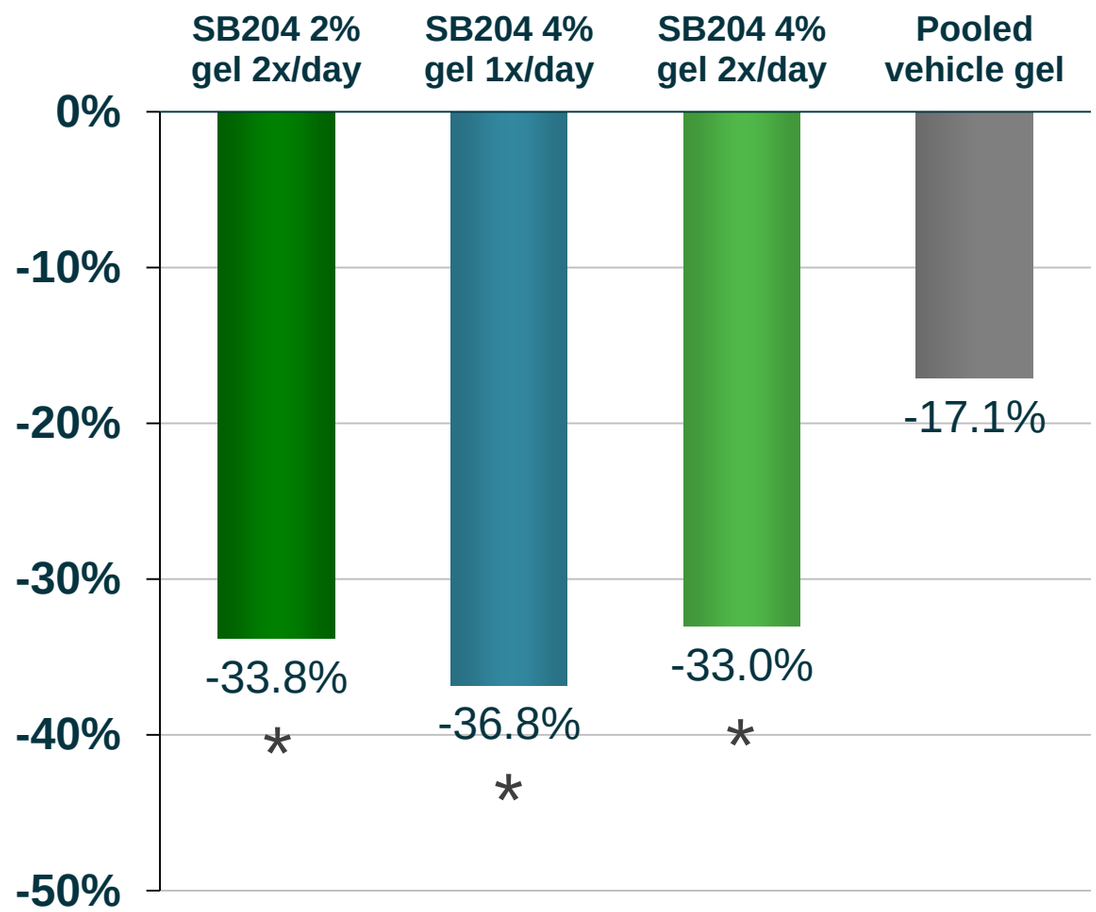
Data on file, Novan, Inc.

Secondary Endpoint: Mean Percent Change in Lesion Counts From Baseline to Week 12

Inflammatory lesions



Noninflammatory lesions



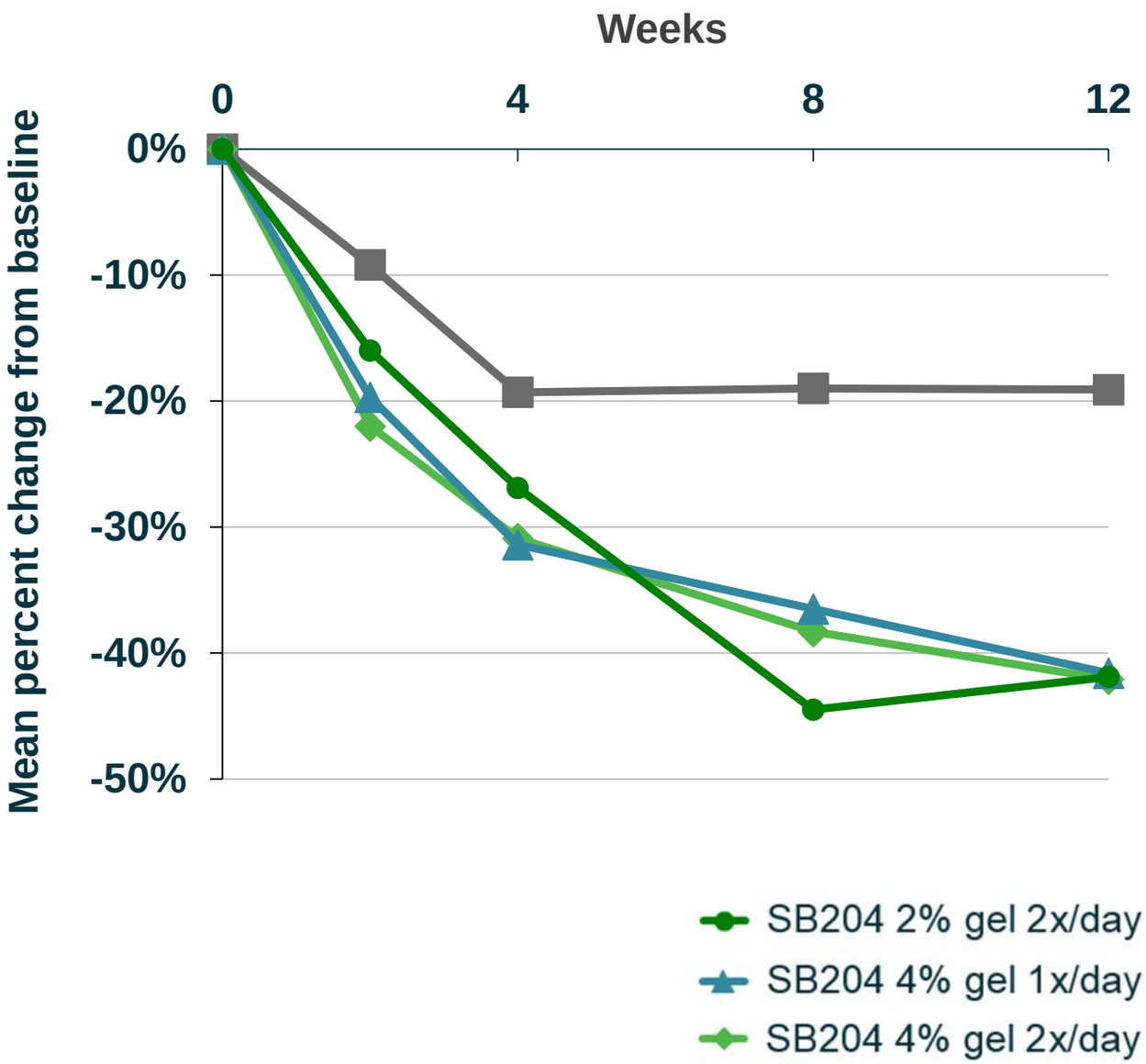
***P* ≤ .05**

Intent-to-treat population.
P values from contrasts comparing each SB204 gel group to vehicle gel group.

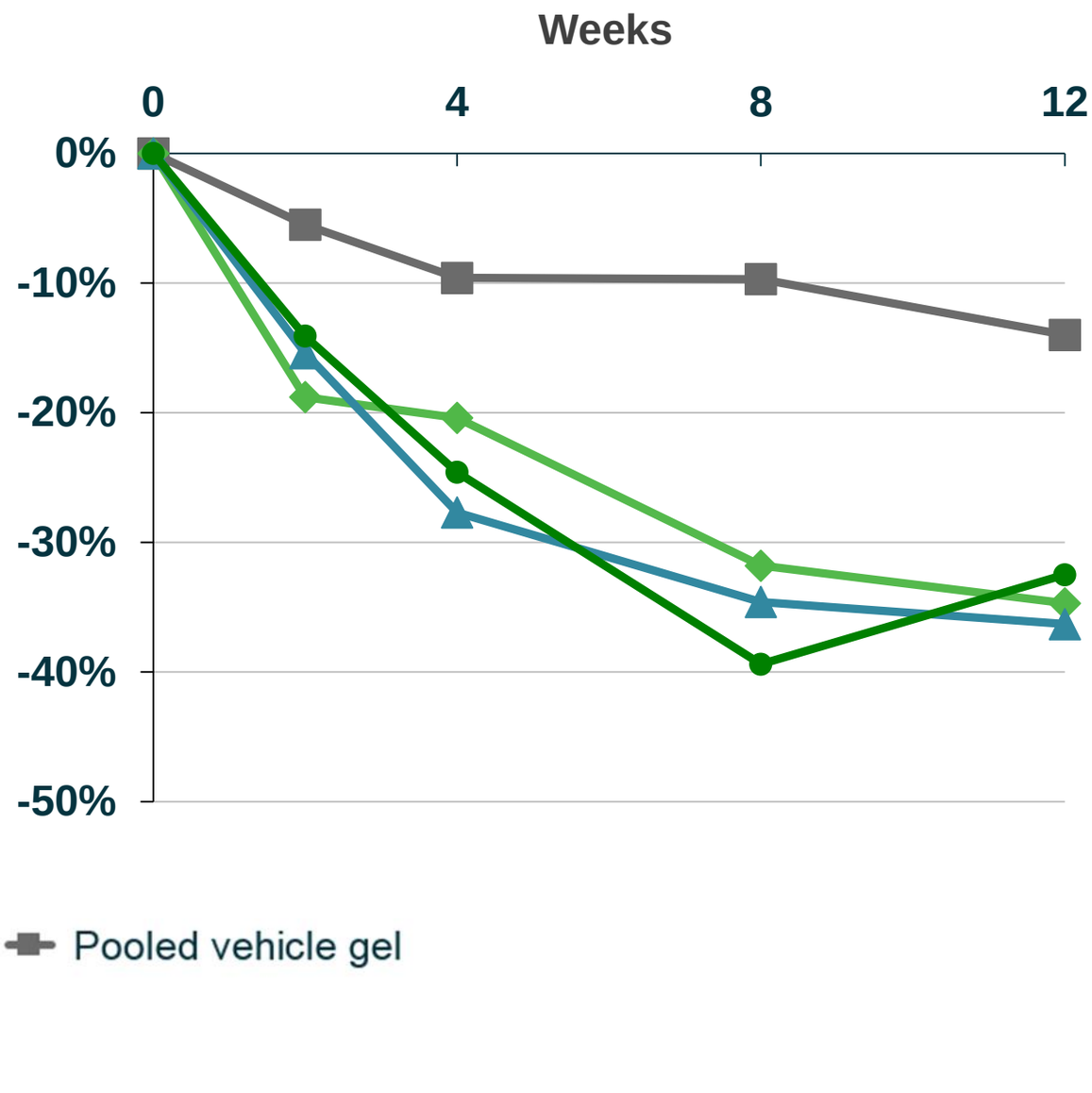
Data on file, Novan, Inc.

Secondary Endpoint: Mean Percent Change in Lesion Counts From Baseline to Week 12

Inflammatory lesions



Noninflammatory lesions



SB204 2% gel 2x/day
SB204 4% gel 1x/day
SB204 4% gel 2x/day
Pooled vehicle gel

Intent-to-treat population.
Missing values imputed using last observation carried forward.

Data on file, Novan, Inc.

Cutaneous Tolerability With SB204

	Baseline (before treatment)			Week 12 (end of treatment)		
n (%)	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema[a]	44 (28.2%)	8 (5.1%)	0 (0%)	35 (23.8%)	5 (3.4%)	0 (0.0%)
Dryness[a]	13 (8.3%)	0 (0.0%)	0 (0.0%)	20 (13.6%)	1 (0.7%)	0 (0.0%)
Scaling[a]	11 (7.1%)	1 (0.6%)	0 (0.0%)	16 (10.9%)	2 (1.4%)	0 (0.0%)
Itching[b]	14 (9.0%)	3 (1.9%)	0 (0.0%)	9 (6.1%)	4 (2.7%)	0 (0.0%)
Burning/stinging[b]	6 (3.8%)	0 (0.0%)	0 (0.0%)	19 (12.9%)	3 (2.0%)	0 (0.0%)

Pooled SB204 treatment arms (n = 156) across all dose groups.

[a]Physician observations

[b]Patient reported

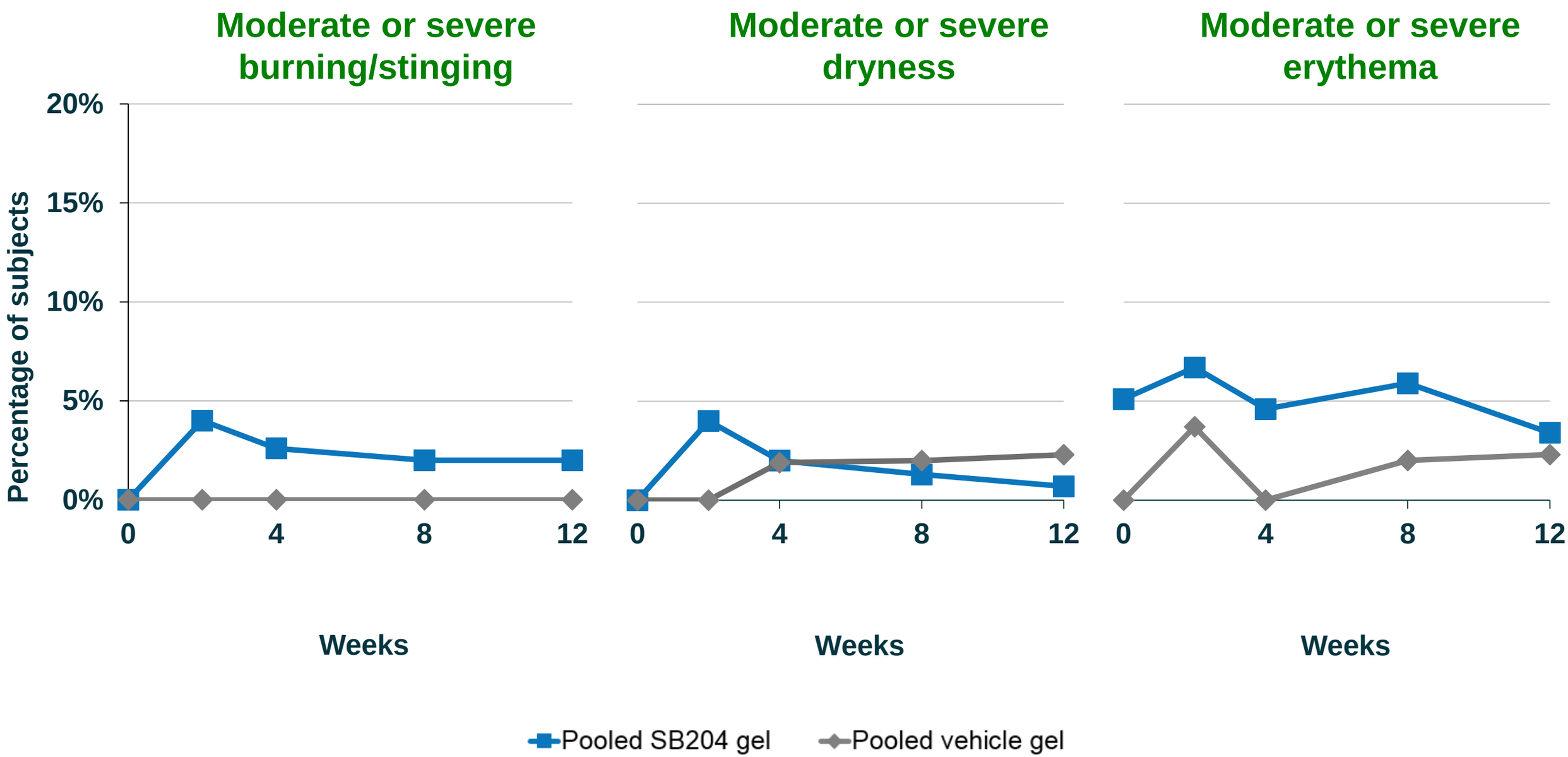
Tolerability scores were comparable for SB204 and vehicle gel

Safety population.

Data on file, Novan, Inc.

Cutaneous Tolerability From Baseline to Week 12

- Tolerability of SB204 was consistent across the study period and similar to that of vehicle gel



Safety population.

Data on file, Novan, Inc.

Treatment-Emergent and Application-Site Adverse Events

	Pooled SB204 gel (n = 156)	Pooled vehicle gel (n = 55)
General Disorders and Administration-Site Conditions	11 (7.1%)	2 (3.6%)
Dryness	4 (2.6%)	0
Erythema	2 (1.3%)	0
Hypersensitivity	1 (0.6%)	0
Irritation	1 (0.6%)	0
Pain	2 (1.3%)	0
Pruritus	3 (1.9%)	0
Other TEAE ≥3%		
Nasopharyngitis	6 (3.8%)	3 (5.5%)
Upper respiratory infection	5 (3.2%)	1 (1.8%)
Headache	1 (0.6%)	2 (3.6%)

Safety population.
TEAE, treatment-emergent adverse event.

Data on file, Novan, Inc.

Summary

- In a 12-week phase 2b study in subjects with moderate to severe acne, SB204 4% gel once daily:
  - Was significantly superior to vehicle gel in reducing both inflammatory and non-inflammatory lesion counts
  - Demonstrated a reduction in the percent inflammatory lesions by week 4
  - Had good cutaneous tolerability with no treatment-related serious adverse events reported
- Once-daily treatment with SB204, 4% was as effective as twice-daily treatment