Pharmacokinetics of SB204 in Subjects with Acne Vulgaris

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Introduction

• SB204, a nitric oxide releasing topical drug candidate, is in development for the treatment of acne vulgaris.
• The active ingredient in SB204 is NVN1000, a polyisoxazol macromolecule that stores nitric oxide on the polymer backbone.
• Three pharmacokinetic (PK) studies, NI-AC101, NI-AC103, and NI-AC104, were conducted with SB204 in subjects with moderate to severe acne.
  - SB204 was applied to 17% BSA: face, shoulders, upper back, and chest.
  - Subjects received a low nitrate diet during PK collection days.
• Major Exclusion Criteria:
  - Methemoglobin >2% at screening or baseline.
  - Subjects previously treated with NVN1000 Gel/SB204.

Methods

Studies assessed systemic exposure to:
• Hydrolyzed N-methyl-aminopropyltrimethoxysilane (hMAP3), a component of the NVN1000 parent polymer backbone. The lower limit of quantitation (LLOQ) for hMAP3 was 5.00 ng/mL.

Hydrolyzed MAP3 (hMAP3)

• Nitrate (NO), a marker for systemic nitric oxide exposure. The LLOQ for nitrate was 300 ng/mL.

Results

• In adults (n=66) and adolescents (n=18) with moderate to severe acne vulgaris treated topically with SB204 gel:
  - Plasma hMAP3 levels were below LLOQ (5.0 ng/mL) after single or repeat SB204 application at all timepoints and for all treatments, in all three (NI-AC101, NI-AC103, NI-AC104) studies.
  - Systemic exposure to nitrate was similar following administration of SB204 4% (NI-AC103, NI-AC104), SB204 8% (NI-AC101), and SB204 12% (NI-AC104) vehicle.
  - There were no noticeable differences in nitrate PK parameters in subjects at baseline and following repeat treatment with SB204 4% or 8% (NI-AC103, NI-AC101).

Plasma Nitrate (Single and Multi Dose)

Treatment Emergent Adverse Events (TEAEs)

• In all 84 treated subjects – no clinically significant changes in laboratory assessments including methemoglobin values, ECG results, and physical examinations were observed.
• One subject discontinued in NI-AC101 due to local application site adverse events.

Plasma Nitrate (Single Dose; Therapeutic and Supratherapeutic)

Conclusion

• Following single and repeat application of topical SB204 at doses between 4%-12% in adult or adolescent subjects with moderate to severe acne:
  - There was no detectable hMAP3 in any subject, at all timepoints, and for all treatments, in all three (NI-AC101, NI-AC103, NI-AC104) studies, including under maximal use conditions.
  - Plasma nitrate levels in subjects treated with SB204 4%, 8% and 12% (NI-AC101, NI-AC104) were bioequivalent with those after administration of vehicle. There were no noticeable differences in nitrate PK parameters at baseline and following treatment with SB204 (NI-AC103).
• All doses of SB204 administered in the studies were well tolerated and the adverse event profile was similar in active and vehicle treated subjects.

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