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A DOUBLE-BLIND, PLACEBO-CONTROLLED, RANDOMISED STUDY TO EVALUATE THE SAFETY AND REDUCTION OF EAR PAIN IN ADULTS WITH ACUTE OTITIS MEDIA

Study Treatment:	OP0201
Indication Studied:	Acute Otitis Media
Study Design:	Single-dose, double-blind, placebo-controlled, randomised, parallel-group, multicenter study
Sponsor:	Novus Therapeutics, Inc 19900 MacArthur Blvd, Suite 550 Irvine, CA 92612 (949) 238-8090
Protocol Number:	OP0201-C-004
IND Number:	106778
Clinical Development Phase:	1
Study Initiation Date:	07 Jan 2019
Study Completion Date:	30 Jan 2019
Coordinating Investigator:	Janak A. Patel, MD
Sponsor Signatory:	Janak A. Patel, MD 19900 MacArthur Blvd, Suite 550 Irvine, CA 92612 (949) 238-8090 jpatel@novustherapeutics.com
Version:	Final
Date of Report:	20 Aug 2019

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

CONFIDENTIAL

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2 SYNOPSIS

NAME OF THE SPONSOR: Novus Therapeutics, Inc.	
NAME OF FINISHED PRODUCT: OP0201	
NAME OF ACTIVE INGREDIENT: dipalmitoylphosphatidylcholine (DPPC) and cholesteryl palmitate (CP)	
Title of Study: A Double-blind, Placebo-controlled, Randomised Study to Evaluate the Safety and Reduction of Ear Pain in Adults with Acute Otitis Media	
Investigators: Dr. Antonio E. Blanco and Dr. Robert D. Eyzaguirre	
Study Centers: This study was conducted at 2 study centers in the United States.	
Publication(s) (reference): None	
Study Period: First subject first visit: 07 Jan 2019 Last subject last visit: 30 Jan 2019	**Phase of Development**: 1

Objectives:

The primary objective of this study was:

- To assess the safety of intranasal OP0201 20 mg compared to placebo

The exploratory objectives of this study were:

- To assess the effect of intranasal OP0201 20 mg compared to placebo on ear pain scores using the Visual Analog Scale (VAS)
- To assess the effect of intranasal OP0201 20 mg compared to placebo on ear pain scores using the Numeric Rating Scale (NRS-11)
- To assess impression of global change in symptoms as measured by Patient Global

Impression of Change (PGIC)

- To assess impression of global change in symptoms as measured by the Clinical Global Impressions Scale: Global Improvement (CGI-I)
- To assess the effect of intranasal OP0201 20 mg compared to placebo on acute otitis media (AOM) symptoms
- To assess the blinding efforts as measured by the Blinding Index (BI)
- To evaluate subject experience with the device as measured by the Device Experience Questionnaire-Subject
- To evaluate study staff experience with the device as measured by the Device Experience Questionnaire-Study Staff Administering the Treatment

Methodology: This was a single-dose, double-blind, placebo-controlled, randomised, parallel-group study to evaluate the safety and immediate (within 60 minutes [min]) reduction of ear pain caused by AOM in adults following a single dose of intranasal OP0201 20 mg or placebo.

All study-related procedures, including Screening, were performed on Day 1. Following Screening, but before any treatment-related procedures, eligible subjects were randomly assigned to 1 of the following treatment groups:

- Single intranasal dose of OP0201 20 mg (4 sprays per nostril for a total of 8 sprays)
- Single intranasal dose of placebo (4 sprays per nostril for a total of 8 sprays)

Prior to being dosed, all subjects were provided a training canister and were trained on the study treatment administration process. Study personnel administered the study treatment.

Ear pain was assessed in the left and the right ear separately at predose and at 10, 20, 30, and 60 min post dose using the VAS and the NRS-11. Global impression of change in symptoms was rated by the subject at 10, 20, 30, and 60 min post dose using the PGIC. The physician investigator rated global impression of change at 60 min post dose using the CGI-I. AOM symptoms (tinnitus, dizziness, vertigo, and feeling of fullness or muffled hearing in the ear) were also evaluated at predose and at 60 min post dose. The investigator recorded for each subject whether the symptom was present or absent.

Safety evaluations included vital signs measurements, otoscopy examination of the ear, nose, and throat (ENT), appearance of the tympanic membrane (TM), and adverse events (AEs). Vital signs (oral temperature, respiratory rate, pulse, and blood pressure [BP]) were measured (after 3 min of rest in the supine position) at predose and at 60 min post dose. An ENT examination (otoscopy of

the ear, nose, and oropharynx) was performed by the physician investigator (physician qualified to perform an otoscopic exam of the ears, nose, and oropharynx) at predose and at 60 min post dose. All spontaneously reported AEs were recorded. The appearance of the TM (contour, color, fluid, and translucency) was also evaluated using otoscopy by the physician investigator at predose and at 60 min post dose. The appearance of the TM was evaluated in both ears separately, regardless of whether AOM was bilateral or unilateral.

After the subject had completed all assessments, except the Device Experience Questionnaire, on Day 1, the BI was administered separately to the subject and physician investigator prior to the subject leaving the study center. The Device Experience Questionnaire was administered to the subject following the BI before the subject left the center.

Any study staff who administered treatment to subjects also completed the Device Experience Questionnaire. Study staff needed to complete the questionnaire once for the study, not for each subject treated, after all subjects to be treated by study staff had completed all Day 1 assessments.

Subjects received a follow-up safety call 1 week (wk) after treatment; reported AEs and concomitant medications were recorded. Subjects exited the study on Day 7 after completing this call.

Number of Subjects (Planned and Analyzed):

Planned: 24 subjects total, 12 subjects per arm
Actual: 24 subjects total, 12 subjects per arm
Completed: 24 subjects, 12 subjects per arm
Analyzed: 24 subjects, 12 subjects per arm

Diagnosis and Main Criteria for Inclusion:

Male and female subjects ≥ 18 years of age with a confirmed AOM diagnosis with moderate to severe bulging of the TM and recent (< 48 hours) onset of ear pain were eligible for enrollment if they met all inclusion criteria, none of the exclusion criteria, and signed an informed consent form. Subjects were required to have moderate to severe ear pain in affected ear(s), defined as a score of ≥ 5 (on a scale of 0-10) on the NRS-11 as evaluated by the subject at Screening.

Test Product, Dose, Mode of Administration, and Batch Number:

OP0201: OP0201 is a drug-device combination product for intranasal metered-dose inhaler delivery. The dry powder active ingredients (20:1 ratio DPPC and CP, respectively) are suspended in propellant (hydrofluoroalkane-134a [HFA-134a])
Dose: 20 mg (4 sprays per nostril, each 0.1 mL spray contained 2.5 mg OP0201)

Batch Number: 0002-058

Duration of Treatment: Duration of treatment, including Screening, was 1 day. Subjects exited the study after completing the follow-up safety call on Day 7.

Reference Therapy, Dose, Mode of Administration, and Batch Number:

Placebo: Propellant (HFA-134a) only
Dose: 0 mg (4 sprays per nostril, each 0.1 mL spray contained 0 mg OP0201)
Batch Number: 0002-060

Summary-Conclusions:

Subject Disposition:

A total of 24 eligible subjects were randomly assigned and received either OP0201 (12 subjects) or placebo (12 subjects); all 24 subjects completed the study.

Safety Results:

Overall, 8 (33.3%) subjects reported 10 treatment-emergent adverse events (TEAEs) during the study. A total of 6 (50%) subjects in the placebo group reported 8 TEAEs, and 2 (16.7%) subjects in the OP0201 group reported 2 TEAEs. Overall, the incidence of TEAEs was highest for respiratory, thoracic, and mediastinal disorders. Within this system organ class (SOC), TEAEs were reported by 4 subjects who received placebo and by 1 subject who received OP0201. Most of the TEAEs in this SOC were for mild nasal discomfort (2 subjects in placebo, 1 subject in OP0201). All reported TEAEs were of mild severity and considered to be treatment-related. All TEAEs resolved without sequelae and no subject discontinued the study due to a TEAE. No serious adverse event or death occurred during the study.

Vital signs, ENT, and otoscopy measurements were similar across both groups at each timepoint evaluated. No clinically meaningful changes from baseline were observed for BP, pulse rate, or respiration rate in either group, and most subjects had no shift from baseline to 60 min post dose for ENT and otoscopy findings. No clinically significant ENT changes were reported as TEAEs.

Conclusion:

The primary objective of the study was met. This study demonstrated that a single 20 mg dose of intranasal OP0201 has a favorable safety and tolerability profile when administrated to adults with AOM.

Date of Report: Final, 20 Aug 2019

