Post-Market Surveillance Study of the Preceptis Medical, Inc. Hummingbird TTS™ Tympanostomy Tube System

Protocol Date: 16 Feb 2021
Revision: 7.0

_____

Preceptis Medical, Inc.
10900 89th Av N, Suite #4
Maple Grove, MN 55369 USA
Telephone: 612-327-4795

INVESTIGATIONAL PLAN SUMMARY

1.0 BACKGROUND

1.1 Device Name

The Preceptis Medical, Inc. Hummingbird TTS™ Tympanostomy Tube System (H-TTS)

1.2 Device Description

The H-TTS is a disposable surgical tool designed to create an incision in the tympanic membrane and insert a ventilation tube (VT) in one pass down the ear canal, thereby reducing surgical trauma for the patient. The VT used with the HTTS is a standard, commercially available Armstrong-style ventilation tube. The H-TTS has received 510(k) clearance from the FDA under (i) general anesthesia in August 2014, (ii) for children under moderate sedation with local anesthesia in April 2015, and (iii) in-office in children 6-24 months old with local anesthesia in June 2020.

1.3 Study Sites

There will be 4 study sites: St. Cloud ENT, the Mayo Clinic, Children's Hospitals and Clinics of MN, and the University of Minnesota Children's Hospital. St. Cloud ENT will enroll patients prospectively. Data from the other three sites will be retrospectively procured from the previous multi-site moderate sedation study using data that was not previously submitted to FDA in support of the 510k application for use of the H-TTS in children under moderate sedation (K142282). This clinical data was procured after K142282 had already been submitted.

2.0 STUDY OBJECTIVE

The study is being initiated per section 522 of the Food and Drug Cosmetic Act (post-market surveillance). The objective of this study is continued commercial evaluation of the intraoperative safety and performance of the H-TTS for the placement of VT in patients undergoing a tympanostomy procedure under moderate sedation and local anesthetic.

3.0 STUDY DESIGN

3.1 Overview

The study will be a multi-site, prospective and retrospective, treatment-only post-market study of the H-TTS. The study will be performed in a commercial environment. Patients will already have a scheduled tympanostomy procedure with the H-TTS under moderate sedation and local anesthetic. A minimum of one hundred nine (109) subjects will be included in the study at 4 sites, one site prospectively (St. Cloud ENT) and three sites retrospectively (the Mayo Clinic, Children's Hospitals and Clinics of MN, and the University of Minnesota Children's Hospital).

3.2 Timeline

i. Expected enrollment completion date: Feb 2021
ii. Expected date for final report submission Mar 2021

3.3 Data oversight and analysis

Data will be collected via an electronic data capture system (EDC) maintained by NAMSA, a contract research organization (CRO).

Sample size:

The sample size was chosen to ensure an adequate precision in the estimation of the conversion rate. Based on an expected conversion rate of 15%, a sample size of 109 subjects will provide an upper, one-sided, Wilson 95% confidence bound that is no more than 6% greater than the estimated conversion rate with a probability of approximately 0.80.

Poolability of prospective and retrospective patients:

Subjects from the previous multi-site moderate sedation study who were not included in the previous 510k (K142282) data will be included in this data analysis if they met the following criteria: children 6 months through 5 years of age, who are candidates for placement of VT and required use of the H-TTS under moderate sedation and accompanying local anesthetic.

Poolability of the subjects prospectively enrolled in the 522 study and those retrospectively procured through the multi-site conscious sedation study will be tested using Fisher's Exact test. The proportion of subjects requiring conversion will be analyzed in a 2x2 table where the rows consist of the study from which the subjects information came and the columns are whether or not the subject required conversion. If the p-value for this comparison is greater than 0.15, the data will be considered poolable for the purposes of statistical analysis.

In addition to assessing poolability of the conversion rates between sites, additional comparisons between the sites providing retrospective data and the site providing prospective data will be completed. Specifically, subject age, which is the only common demographic, will be compared between the combined data from sites supplying retrospective data and the site providing prospective data. Age data will be compared using a two sample Wilcoxon test.

An ad hoc analysis based on the outcome of any procedure that was converted will also be attempted. The outcome of converted procedures will be classified as successful or unsuccessful and the differences in successful outcomes will be compared between the sites providing retrospective data and the site providing prospective data. A Fisher's Exact Test will be used for this comparison. This analysis is done only on converted cases therefore it should be noted that the sample size for this analysis may be extremely small.

Rates will be calculated for the outcome variables and detailed summaries for all adverse events will be provided. Statistical summaries will include number, mean, standard deviation and range for continuous parameters or frequency and percent for categorical parameters. No formal statistical hypothesis tests are planned.

Ad hoc analyses using logistic regression models will be used to assess the relationship between selected parameters and the outcome of conversion to general anesthesia. The pre-specified parameters will be assessed individually in univariable models with a subset of these parameters being used in the multi-variate model. The pre-specified parameters are age, sex, weight, type of anesthesia/sedation, number of ears treated, surgeon experience, surgery duration, patient movement, anatomy and lack of visualization. After each parameter has been modelled univariately (stage 1), those parameters with a p-value less than 0.20 will be included in a multivariable model and a stepwise selection process will be employed to determine if any parameters have a statistically significant association with conversion. The nominal p-value for retention in the final reduced model will be 0.05.

4.0 STUDY ENDPOINTS

4.1 The rate of conversion from moderate sedation to general anesthesia, along with surgeon experience, the patient and procedure characteristics associated with the decision to convert (age, sex, weight, type of anesthesia/sedation, number of ears treated, surgery duration (tympanostomy time for each ear), patient movement, anatomy, and lack of visualization). (Note: conversion to general anesthesia is **not** an adverse event, nor is it considered an additional risk to the patient.)

4.2 The rate of intra-operative and pre-discharge AEs and rates for each specific type of event.

5.0 ENROLLMENT

Prospective enrollment in the study will begin after receipt of Institutional Review Board (IRB) approval. A patient will be considered enrolled when the incision is made in the tympanic membrane and delivery of the VT is attempted with the H-TTS.

6.0 SAMPLE SIZE

This study will include a minimum of 109 treated patients.

7.0 PATIENT POPULATION

- Children 6 months through 5 years of age, who are candidates for placement of VT.
- Required use of the H-TTS under moderate sedation and accompanying local anesthetic.

8.0 SURGICAL PROCEDURE

The tympanostomy procedures will take place in a hospital or ambulatory surgery center. The choice of anesthesia drugs for moderate sedation will be up to the attending physicians. The H-TTS will be used to make the myringotomy incision and place the VT. Patients will receive moderate sedation and local anesthetic. Per standard sedation procedure, a patient may be converted to general anesthesia if deemed appropriate by the surgeon.

9.0 CONSENT AND HIPAA

Since all subjects will be children 6 months through 5 years of age, an IRB-approved parental consent document will be used for patients. The study will be explained to the parent or guardian prior to signing the consent document. Parents will also sign a HIPAA authorization form. Some sites may incorporate the required HIPAA language within the consent document.

The Consent document is located in **Attachment A**.

10.0 STUDY PROCEDURES FOR PROSPECTIVE PATIENTS

10.1 Summary of Study Procedures

Documentation of patient eligibility, anesthesia conversions, procedural and immediate post-operative adverse events will be collected via electronic data capture (EDC). Investigators will sign the CRFs via electronic signatures.

CRFs	Type of Form	Timing
#1	Enrollment/Procedure	Time of surgery
#2	Adverse events	Time of surgery until discharge

10.2 Enrollment/Surgical Procedure

Subjects will undergo evaluation at the time of referral or at the time of the procedure to confirm that they are candidates for VT placement using the H-TTS under moderate sedation and local anesthetic. The type of anesthesia and reason for conversion to general anesthesia, if needed, will be documented. Surgery duration will be defined for each ear as the time from when the H-TTS enters the ear until a VT is in place across the tympanic membrane.

10.3 Adverse Events

All adverse events (AE) that occur from when the H-TTS enters the ear through discharge will be reported. The event type, treatment, severity and relationship of the event to the procedure or to the study device will be assessed by the surgeon.

Anticipated adverse events and the definitions for serious adverse events are found in Attachment C. Common occurrences (e.g., minor bleeding, purulent discharge) during a tympanostomy procedure are not considered AEs.

10.4 Study Termination

The study will begin for each patient at the time the H-TTS is first used to attempt delivery of the VT and will end at discharge unless the patient experiences an intra-operative or immediate post-operative AE. The study, for those patients, will end when the AE resolves, or at the study termination, 30 days after the last patient is discharged. All unresolved AEs will be detailed in the final clinical report.

10.5 Stopping Rules/Safety Monitoring

If any perceived safety issues arise, the trial may be suspended and safety data will be analyzed. If the Sponsor and the Site Investigators agree that the study is safe to continue, the study may be resumed.

10.4 Protocol Modifications

The Investigator may not modify this protocol without written concurrence from the Sponsor.

10.5 Study Materials

Study materials will be provided by the Sponsor. Sites will be responsible for securing, storage, and handling of study materials according to site-specific institutional processes.

10.6 Parental Satisfaction Survey

Sites participating in this study may choose to utilize a parental satisfaction survey which is unique to their institution.

ATTACHMENT A

CONSENT DOCUMENT

ATTACHMENT B

CASE REPORT FORMS

ATTACHMENT C

ADVERSE EVENTS

ANTICIPATED INTRA-OPERATIVE ADVERSE EVENTS/DEFINITIONS

Anticipated AE	**Definition**
Acute tube extrusion	During the surgical procedure, a myringotomy incision is completed but the VT will not stay in the tympanic membrane.
Tube dislocation into the middle ear space	VT passes completely through the tympanic membrane, falls into the middle ear cavity and is unable to be retrieved.
Ossicular damage	Damage to the ossicular chain resulting in hearing loss.

SERIOUS ADVERSE EVENT DEFINITIONS

1. Event resulted in death
2. Event was life-threatening
3. Event required new hospitalization (> 24 hours stay)
4. Event required prolonged hospitalization (> additional 24 hours)
5. Event resulted in disability or permanent damage (e.g., permanent hearing loss)
6. Event required medical or surgical intervention to preclude permanent impairment of a body function, or prevent permanent damage to a body structure, due to the use of a medical device.