TAVT-119 (amlodipine besylate) gel, 0.1% and 0.2% strength
(Formerly referred to as DRGT-119)

Abbreviated Clinical Trial Summary

for Study DRGT119C01

A Randomized, Double-Blind, Adaptive Trial with an Open-Label Treatment Extension to Determine the Efficacy and Safety of Topical DRGT-119 0.1% and 0.2% Gels in Patients with Chronic Anal Fissure

Document Type:	Abbreviated Clinical Trial Summary
Sponsor Study Number:	DRGT119C01
EudraCT Number:	2019-000853-30
Clinical Trial Phase:	2
Date of Trial Summary:	05 April 2021
Version Number:	1.0
Sponsor:	Tavanta Therapeutics, Inc. 101 E. Baltimore Ave, # 602 Media, PA 19063 Tel: +1 833 776 8963 *(Formerly Druggability Technologies Holdings Ltd* *Level 2, Regional Business Centre University Heights* *Msida MSD 1751 Malta)*

Study Synopsis

Name of Sponsor/Company: Tavanta Therapeutics, Inc (formerly DRGT)	**Name of Study Treatment:** TAVT-119 Gel (previously referred to as DRGT-119)	**Name of Active Ingredient:** Amlodipine besylate
Title of Study: Randomized, Double-Blind, Adaptive Trial with an Open-Label Treatment Extension to Determine the Efficacy and Safety of Topical DRGT-119 0.1% and 0.2% Gels in Patients with Chronic Anal Fissure		
Publication (Reference): None		
Studied Period: 07 Aug 2019 to 10 Jun 2020		**Phase of Development:** 2

Objectives:

Primary Objectives

The primary objective of Part 1 of the study was:

- To demonstrate the efficacy of local application of varying strengths of TAVT-119 gels (0.1% and 0.2%) in patients with chronic anal fissure

The primary objective of Part 2 of the study was:

- To demonstrate the efficacy of a second cycle of TAVT-119 0.2% gel in patients with chronic anal fissure that did not heal after completion of Part 1 of the trial

Secondary Objectives

The secondary objective for both Part 1 and Part 2 of the study was:

- To obtain information on the safety and tolerability of varying strengths of TAVT-119 gels (0.1% [Part 1 only] and 0.2%) in patients with chronic anal fissure

Number of Subjects (Planned and Analyzed):

The number of subjects planned and analyzed are presented below.

- Planned for inclusion: 90 patients
- Randomized and dosed: 49 patients*
- Analyzed:
  - All 49 patients were included in the ITT Population
  - All 49 patients were included in the Safety Population
  - 41 patients (80.4%) were included in the Per-Protocol Population
  - 43 patients (84.3%) were included in the Open-Label Population

**: Due to the COVID-19 pandemic and the outcome of the pre-specified interim assessment for conditional powering of the primary efficacy endpoint (anal pressure), Tavanta decided to prematurely stop this study.*

Diagnosis and Main Criteria for Inclusion:

Male or female patients at least 18 years of age, fulfilling the criteria of an active chronic anal fissure for at least 6 weeks as defined in the inclusion criteria:

Part 1:

1. Male or non-pregnant, non-lactating female patients at least 18 years of age
2. Existing single, anal fissure for a minimum of 6 weeks as defined by the presence of a fibrous induration, exposed internal sphincter fibres, sentinel skin tag, or hypertrophic papilla

Name of Sponsor/Company: Tavanta Therapeutics, Inc (formerly DRGT)	**Name of Study Treatment:** TAVT-119 Gel (previously referred to as DRGT-119)	**Name of Active Ingredient:** Amlodipine besylate

3. Resting anal pressure is equal or higher than 80 mm Hg
4. Average anal pain during/after defecation over the past two weeks is moderate to severe (VAS score: 50-100 mm)
5. Presence of a midline anal fissure, dorsal or ventral
6. Pain during and after defecation lasting for more than 6 weeks
7. Increased anal pressure due to internal anal sphincter spasm
8. Females of childbearing potential who agree to use at least one form of contraception during the full duration of the study
9. Able to communicate adequately with the investigator and to comply with the requirements for the entire study
10. Capable of and freely willing to provide written informed consent prior to participating in the study
11. Patients were excluded if they had received any agent (prescription) that is intended to treat chronic anal fissure or act directly on the anal sphincter (including, but not limited to, topical GTN, CCBs or botulinum toxin) in the past 3 months prior to randomization

Part 2:

1. Completion of all study visits and study treatment in Part 1
2. Epithelization Grade recorded as none (0) or partial (1) by the Investigator at final V6 (Day 42) visit in Part 1.
3. Willingness to participate in an additional treatment period with 0.2% TAVT-119 gel.
4. Females of childbearing potential who agree to use at least one form of contraception during the full duration of the study
5. Able to communicate adequately with the investigator and to comply with the requirements for the entire study.

Summary – Conclusions:

Disposition Results

In total, 51 patients were randomized and 49 were dosed in Part 1 (n=16 for placebo, n=17 for 0.1% TAVT-119 Gel, and n=16 for 0.2% TAVT-119 Gel). Of the 51 randomized patients, 47 (92%) patients completed the 6-week randomized, double-blind treatment period of Part 1 of the study. A total of 43 patients continued into Part 2 of the study, with 39 of them completing the additional 6-week treatment.

Efficacy Results

Overall, although the primary efficacy endpoint of change in resting anal pressure at Day 42 was not different between treatment arms, statistically significant improvements were observed in the TAVT-119 treatment arms in clinically relevant secondary efficacy endpoints (anal pain and bleeding). Below is a brief summary of the primary and secondary endpoints.

Primary Endpoint:

During Part 1 of the study, resting anal pressure decreased over the 6-week treatment

Name of Sponsor/Company: Tavanta Therapeutics, Inc (formerly DRGT)	**Name of Study Treatment:** TAVT-119 Gel (previously referred to as DRGT-119)	**Name of Active Ingredient:** Amlodipine besylate

period in all treatment arms. At Day 42, the change from baseline in resting anal pressure was similar in all groups (mean changes of -42.3 mmHg in placebo, -43.5 mmHg in the TAVT-119 0.1% arm, and -36.1 mmHg in the TAVT-119 0.2% arm), [p > 0.05 for all active-to-placebo comparisons]).

Secondary Endpoints:

During Part 1 of the study, complete healing rates after 6-weeks of treatment were comparable between groups, with a trend of highest healing rate in patients receiving TAVT-119 0.2% for 12-weeks.

At the majority of timepoints during the study, patients treated with TAVT-119 Gel had reduced pain intensity and anal bleeding compared to those treated with placebo.

No obvious trends were observed in any of the subgroups for all secondary endpoints and the findings in the Per Protocol Population were consistent with the ITT Population.

Safety Results

During the study, TAVT-119 Gel appeared to be well tolerated. There were no serious AEs or discontinuation of the study drug due to tolerability.

No new safety signals emerged with longer treatment duration during the additional 6-week treatment with TAVT-119 Gel 0.2% in Part 2 of the study.

Conclusions

In summary, Study DRGT119C01 was the first clinical trial evaluating TAVT-119 Gel in patients with anal fissure. The study was prematurely discontinued due to the COVID-19 pandemic and the outcome of the pre-specified interim assessment for conditional powering of the primary efficacy endpoint (anal pressure).

Both strengths of TAVT-119 Gel (0.1% and 0.2%) were well tolerated, as there were no serious adverse events and no clinically meaningful differences in safety parameters between the active and placebo arms.

While the primary efficacy endpoint of change in resting anal pressure at Day 42 was not different between treatment arms and placebo, statistically significant improvements were observed in anal pain and bleeding after TAVT-119 treatment compared to placebo. The treatment differences for anal pain and bleeding in the TAVT-119 active arms vs. placebo arm were greater for the 0.2% strength than for the 0.1% strength.

Date of Report: 05 April 2021