# Proof of Concept Study to Evaluate the Efficacy of a Novel Thermosetting Bioadhesive 2% Clindamycin Phosphate Vaginal Gel in the Treatment of Bacterial Vaginosis

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## Objectives

The objective of the study was to test the efficacy and safety of a novel single dose of a thermosetting bioadhesive 2% clindamycin phosphate vaginal gel for the treatment of bacterial vaginosis (BV) in a single center, single arm, open-label study. The gel has unique properties that result in increased viscosity when transitioning from room temperature to body temperature. The gel erodes slowly which allows for sustained release of active pharmaceutical ingredients. The gel also adheres to the vaginal epithelium. All these properties should increase the duration of action and potentially improve the effectiveness of clindamycin relative to existing vaginal products.[1]

## Methods

The gel, containing 2.0% clindamycin phosphate as the free base, is composed of Poloxamer 407, xanthan gum, citric acid, sodium citrate, and benzyl alcohol in purified water; the gel was packaged in pre-filled vaginal applicators (5.0 g) (HTI Plastics, Lincoln, NE, USA). The gel was prepared under current Good Manufacturing Practices at Sterling Pharmaceutical Services, Dupo, IL, USA.

The clinical study was conducted at a single-site (OBGYN Associates of Montgomery, Montgomery, AL, USA). Clindamycin phosphate, the active ingredient in the vaginal gel, is an approved drug indicated for vaginal treatment of BV and the excipients are all used in other vaginal products. These aspects allowed conduct of the study without IRB approval. All patients were consented prior to treatment. Patient information was collected and a pelvic examination was performed to establish eligibility. Caucasian and African American women ($n$ = 30) between the ages of 17 and 51 were enrolled. If all study requirements were met and the patient consented for enrollment; a single dose clindamycin phosphate 2% vaginal gel was provided (Visit 1). Subjects met the inclusion criteria if all four Amsel criteria were observed [15]: 1) off-white (milky or gray), thin, homogeneous discharge with minimal or absent pruritus and inflammation of the vulva and vagina, 2) vaginal secretion pH of > 4.5, 3) the presence of clue cells > 20% of the total epithelial cells on microscopic examination of the saline wet mount, and 4) a fishy odor (i.e., a positive whiff test) of the vaginal discharge with addition of a drop of 10% KOH. A microscopic evaluation of the vaginal smear was performed in the last ten subjects and scored as per the Nugent method [16]. The Nugent scoring was based upon microscopic examination of the Gram stained vaginal smears for quantification of specific bacterial morphotypes. Women returned to the clinic approximately Day 7 – 14 following single administration of the vaginal gel (Visit 2). Following pelvic examination, the tests listed above were repeated. The subjects were questioned about the comfort level after the initial treatment and then re-examined. The subjects returned to the clinic for a final visit (Visit 3) 21 – 30 days following drug administration. The tests listed above were repeated following pelvic examination. The subjects were again questioned about the comfort level after the initial treatment.

The primary efficacy endpoint of the study was clinical cure, which includes the clinical response of subjects at Visit 2. Clinical cure was defined as resolution of the clinical findings from the Visit 1. Subjects must have all of the following: 1) resolution of abnormal vaginal discharge, 2) negative whiff test, and 3) presence of clue cells at less than 20 percent of the total epithelial cells on microscopic examination of the saline wet mount. Secondary efficacy endpoints were proportions of subjects with bacteriologic cure (Nugent scores <4) and therapeutic cure (a composite endpoint of clinical cure plus a Nugent score <4).

## Results

Of the 30 patients, 2 were unevaluable (1 never returned to the clinic and 1 patient was subsequently diagnosed with an STI) at Visit 2 (TOC). Therefore, these 2 subjects were excluded from cure rate calculations. Of the evaluable 28 patients, 24 (86%) were successfully treated (clinical cure) with one dose of 2% clindamycin gel at TOC visit. Of the 10 patients evaluated for Nugent scoring, 9 subjects were evaluable for clinical response. Additionally, two subjects did not have a gram stain at Visit 2. After a single dose of 2% clindamycin gel, 4/7 (57%), and 4/7 (57%) had a bacteriologic and therapeutic response, respectively. Twenty-four (24) subjects successfully completed the Visit 3 (Day 21 to Day 30). Twenty-two (22) of 24 subjects (92%) showed continued clinical cure following the single dose of 2% clindamycin gel. Of the 9 subjects evaluated at Visit 3, the bacteriologic cure was observed in 7 of 9 (78%) women; therapeutic cure was also observed of 6 of 9 (67%) women. These results are summarized in Table 1. There were no reports of adverse reactions, including local reactions to the vaginal gel product over the course of the study.

**Table 1.** *Summary of clinical, bacteriologic, and therapeutic cure*

| Study Visit | Clinical Cure | Bacteriologic Cure | Therapeutic Cure |
|---|---|---|---|
| Visit 2 | 24 of 28 (86%) | 4 of 7 (57%) | 4 of 7 (57%) |
| Visit 3 | 23 of 24 (96%) | 7 of 9 (78%) | 6 of 9 (67%) |

## Conclusions

Overall, the Clinical Cure rate in a total of 28 evaluable patients was 86% (24 of 28) at Day 7-14 (TOC) and 92% (22 of 24) at Day 21-30 follow up visit. These data support the expanded clinical evaluation of 2% clindamycin gel in a placebo-controlled, double blind efficacy and safety study. The novel gel may provide potential advantages over existing vaginal treatments for BV in terms of cure rate and acceptability.

## References

1. P. Mondal, H.H. Alur, T.P. Johnston, Evaluation of TRI-726 as a drug delivery matrix, *Drug Dev. Indust. Pharm.* (2011), doi: 10:3109/03639045.2011.555913.

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