Journal of Investigative Medicine High Impact Case Reports
Volume 10: 1–3

DOI: 10.1177/23247096221123144
journals.sagepub.com/home/hic
SAGE

Treatment of Recurrent Vulvovaginal Candidiasis With Ibrexafungerp

Leah M. Grant, MD[1] and Robert Orenstein, DO[1]

Abstract

Recurrent vulvovaginal candidiasis is a common disorder which causes significant morbidity among women worldwide, and treatment options are limited. Ibrexafungerp is a novel antifungal agent which was approved in 2021 for treatment of vulvovaginal candidiasis. We present a case of recurrent vulvovaginal candidiasis successfully treated with ibrexafungerp.

Keywords

ibrexafungerp, vulvovaginal candidiasis, fluconazole-resistant *Candida albicans*

Introduction

Vulvovaginal candidiasis is a common disorder encountered in primary care and gynecologic practices. Epidemiologic studies are difficult to perform as many women self-treat using over-the-counter therapies, though one Internet panel survey of more than 7000 women in 6 countries reported at least 29% to 49% had experienced an episode of vulvovaginal candidiasis by the age of 50. Of those women, 14% to 28% reported having recurrent vulvovaginal candidiasis (more than 4 episodes per 12-month period).[1] Most cases of vulvovaginal candidiasis are caused by *Candida albicans*, and vaginitis due to fluconazole-resistant strains has become increasingly recognized.[2] In June 2021, the novel oral glucan synthase inhibitor ibrexafungerp was approved by the FDA (Food and Drug Administration) for treatment of recurrent vulvovaginal candidiasis. This antifungal agent is active against many azole-resistant and echinocandin-resistant strains of *Candida.* We describe a case of successful use of ibrexafungerp in a patient with recurrent vulvovaginal candidiasis due to fluconazole-resistant *Candida albicans.*

Case Report

A healthy 42-year-old gravida 2 para 2 woman presented to an internal medicine clinic with a complaint of recurrent vulvovaginal candidiasis for 2 years. Initially, the patient used over-the-counter topical agents with some success. After several months of self-treatment, she presented to her physician's office and was diagnosed and treated for bacterial vaginosis with a course of oral antibiotic therapy. Following this, she developed a vaginal yeast infection and was prescribed a course of oral fluconazole. Her symptoms did not resolve; thus, she was also prescribed terconazole, which was ineffective.

The patient was then referred to a gynecology clinic due to persistent symptoms including profuse vaginal discharge and vulvar irritation. She tried additional therapies without resolution of her symptoms, including nystatin-triamcinolone cream, probiotics, supplements, dietary changes, hypoallergenic soaps, multiple courses of fluconazole, and boric acid suppositories. Testing for diabetes, HIV, gonorrhea, and chlamydia was negative. A vaginal swab culture was performed and grew *Candida albicans* susceptible to amphotericin, caspofungin, itraconazole, posaconazole, and resistant to fluconazole with a minimum inhibitory concentration of 16 mic/mL. She was then referred to an infectious diseases clinic for assistance. Her antifungal therapy was switched to itraconazole 200 mg daily for 3 days followed by weekly dosing, but the patient's symptoms recurred within the first week, thus she reverted to daily fluconazole. She continued on daily fluconazole with use of topical therapies.

In February 2021, an expanded access request was sent to Scynexis pharmaceutical company for a trial of the investigational new drug ibrexafungerp, which was undergoing phase 3 trial for treatment of refractory vulvovaginal candidiasis. The request was granted by the FDA, and the patient started on ibrexafungerp 375 mg twice daily for 3 days,

[1]Mayo Clinic, Phoenix, AZ, USA

Received June 22, 2022. Revised July 29, 2022. Accepted August 7, 2022.

Corresponding Author:
Leah M. Grant, MD, Division of Infectious Diseases, Mayo Clinic, 5777 East Mayo Blvd., Phoenix, AZ 85054, USA.
Email: leahmgrant1@gmail.com

followed by 375 mg twice daily on day 14, as this was the dosing regimen supplied by the pharmaceutical company. At follow-up with gynecology on day 7 of this regimen, the patient had no evidence of disease. Unfortunately, the patient's symptoms recurred prior to day 14 of this regimen. Thus, her dosing regimen was increased to 375 mg twice daily for 7 days, then twice daily every 72 hours. Her basic labs were checked 2 weeks after starting this regimen and were normal. The patient reported side effects of fatigue and nausea related to ibrexafungerp, as well as thinning of her nails (similar to when she was on fluconazole).

Her dose was increased to 500 mg twice daily every 3 days in June 2021 in an attempt to prevent breakthrough symptoms. She ultimately had her intrauterine device (IUD) removed in September 2021. Vaginal cultures were obtained and were negative for *Candida*. Her dose frequency was decreased to 500 mg twice daily every 28 days, and she has not had further symptoms of vulvovaginal candidiasis.

Discussion

Recurrent vulvovaginal candidiasis can lead to significant emotional distress and physical discomfort in patients, as well as frustration at the paucity of available treatment options. Fluconazole as well as topical agents remain the mainstay of therapy of vulvovaginal candidiasis, with an extended duration of therapy for recurrent episodes.[3] Suppressive regimens, including induction (fluconazole 150 mg every 72 hours for 3 doses) followed by once-weekly dosing of fluconazole 150 mg, may prevent recurrent episodes of vulvovaginal candidiasis in many women,[4] though this strategy was ineffective for our patient. Prolonged or repeated courses of fluconazole can lead to the development of infections with fluconazole-resistant *Candida albicans*. Current treatment options for fluconazole-resistant *C albicans* include additional azoles such as ketoconazole and itraconazole, though cross-resistance is common. Ketoconazole and itraconazole can be used as maintenance therapy once patients' symptoms are in remission, and periodic monitoring of liver enzymes is required. Unfortunately, *C. albicans* can develop resistance to these agents as well, and until now, no other treatment options were available.[2]

Ibrexafungerp is a novel glucan synthase inhibitor which has been formulated for both intravenous and oral administration. The compound has activity against many azole-resistant and echinocandin-resistant strains of *Candida.* Ibrexafungerp demonstrates fungicidal activity in a concentration-dependent fashion against *Candida* sp., and in vitro activity was unchanged by azole resistance. In addition to *Candida* spp., ibrexafungerp demonstrates potent in vitro activity against many *Aspergillus* species. Similar to echinocandins, it was largely ineffective against agents of mucormycosis, as well as *Fusarium* spp. and *Scedosporium*.[5]

Ibrexafungerp is highly bioavailable, and in phase 2 and 3 trials, the medication was generally well-tolerated. The most common side effects in phase 3 trials (545 patients) included diarrhea (16.7%) and nausea (11.8%); symptoms used lasted 1 to 2 days. Out of 575 patients, 1 patient discontinued treatment due to gastrointestinal side effects; there were no serious adverse effects. Among phase 1 studies, 2 patients experienced an elevation of ALT (alanine transaminase) and AST (aspartate transaminase) requiring discontinuation of the medication. It was noted that one of these patients admitted to also taking acetaminophen and drinking alcohol.[6]

Phase 3 clinical trials have shown ibrexafungerp to be effective at inducing a complete clinical response with sustained symptom resolution as compared with placebo in patients with acute vulvovaginal candidiasis. A phase 3 trial consisting of 320 participants comparing ibrexafungerp with placebo in patients with recurrent vulvovaginal candidiasis is currently in progress.[6] In June 2021, the FDA approved the use of ibrexafungerp for treatment of postmenarchal females with vulvovaginal candidiasis. The recommended dosage is 300 mg (150 mg twice daily for 1 day).

Our patient was treated with a suppressive regimen of ibrexafungerp, which ultimately, along with IUD removal, resulted in resolution of her vulvovaginitis symptoms. While we agree with our patient that her IUD removal was likely what ultimately led to resolution of her symptoms, this case demonstrates that ibrexafungerp is a safe and effective treatment option for women suffering from recurrent vulvovaginal candidiasis. The cost of ibrexafungerp will likely be prohibitive for many patients, as the current price as of this writing is $500 for 4 tablets. Savings offers are available via the company website. Ibrexafungerp represents a promising option for women with recurrent vulvovaginitis, especially for those with infections due to fluconazole-resistant strains of *C. albicans*.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ORCID iD

Leah M. Grant https://orcid.org/0000-0002-1262-7703

References

1. Blostein F, Levin-Sparenberg E, Wagner J, et al. Recurrent vulvovaginal candidiasis. *Ann Epidemiol*. 2017;27:575-582. e3. doi:10.1016/j.annepidem.2017.08.010.
2. Sobel JD, Sobel R. Current treatment options for vulvovaginal candidiasis caused by azole-resistant Candida species. *Expert Opin Pharmacother*. 2018;19(9):971-977. doi:10.1080/14656566.2018.1476490.
3. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48:503-535. doi:10.1086/596757.
4. Sobel JD, Wiesenfeld HC, Martens M, et al. Maintenance fluconazole therapy for recurrent vulvovaginal candidiasis. *N Engl J Med*. 2004;351:876-883. doi:10.1056/NEJMoa033114.
5. Davis MR, Donnelley MA, Thompson GR. Ibrexafungerp: a novel oral glucan synthase inhibitor. *Med Mycol*. 2020;58:579-592. doi:10.1093/mmy/myz083.
6. Scynexis, Inc. Investigator's Brochure: Ibrexafungerp. Jersey City, NJ: Scynexis, Inc; 2020.