Oral VT-1161 is Highly Effective and Safe in Patients with Recurrent Vulvovaginal Candidiasis - Results of REVIVE, a Multicenter Phase 2b Study

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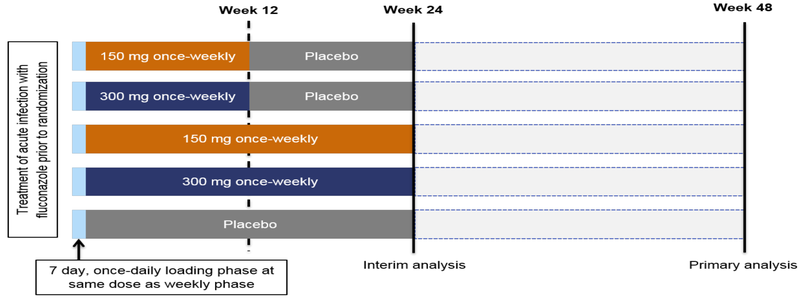
Background

VT-1161 is being developed for the treatment of recurrent vulvovaginal candidiasis (RVVC). Vulvovaginal candidiasis (VVC) is a common disorder, with 75% of all women having at least one acute episode in their lifetime, and an estimated 5-8% suffering from RVVC. While the physical symptoms are distressing, it is often the emotional and psychological consequences of the recurrent infections that have a significant impact on the patient. VT-1161 is a novel, oral, selective inhibitor of fungal CYP51 that is highly potent against Candida species associated with RVVC.

Methods

215 generally healthy RVVC patients ≥18 and <65 years of age presenting with acute VVC were enrolled at 32 US sites. Eligible subjects had a history of RVVC, defined as 3 or more episodes of acute VVC in the past 12 months. Subjects had a composite signs (erythema, edema and excoriation) and symptoms (itching, burning, and irritation) score of ≥ 3. *Candida* infection was confirmed by a positive KOH test. Following treatment of the acute infection with oral fluconazole (150 mg every 72 hours for a total of 3 doses), subjects were randomized to one of five treatment arms, schematically presented below. Patients were followed for a total of 48 weeks.



Results

The study met its primary endpoint of the proportion of subjects with one or more culture-verified acute VVC episodes through 48 weeks. In the per protocol (PP) analysis, which includes subjects who met all inclusion/exclusion criteria that could affect treatment evaluation, received ≥80% of planned doses of study drug, and had no major protocol violations), the recurrence rate in the placebo arm was 65.6%. In marked contrast, the proportion of subjects with one or more culture-verified AVVC episodes ranged from 0% to 10.7% in the four VT-1161 arms of the study with all arms achieving statistical significance vs. placebo (Table 1).

Table 1. Primary Efficacy Endpoint – One or More Culture-Verified Acute VVC Episodes Through Week 48 (PP Analysis)

	150 mg/ 12 Week	150 mg/ 24 Week	300 mg/ 12 Week	300 mg/ 24 Week	Placebo
Number of Patients (PP)	30	28	31	31	32
Culture-Verified Acute VVC Infection	3.3%*	10.7%*	0%*	0%*	65.6%
Median Time to Recurrence	Not reached*	Not reached*	Not reached*	Not reached*	28.0 weeks

*p<0.0001 vs. placebo

In the intent-to-treat population, defined as all randomized subjects, the proportion of subjects with one or more culture-verified acute VVC episodes through 48 weeks ranged from 0-7% in the VT-1161 treated arms compared to 52.2% in the placebo arm (p<0.0001 for all active arms compared to placebo).

VT-1161 was well tolerated with a favorable safety profile. The incidence of treatment-emergent adverse events was lower in all of the VT-1161 arms compared to placebo (Table 2). There was also no evidence of an adverse effect of VT-1161 on liver function.

Table 2. Adverse Events Through Week 48 (Safety Population)

	150 mg/ 12 Week	150 mg/ 24 Week	300 mg/ 12 Week	300 mg/ 24 Week	Placebo
Number of Patients	42	43	43	41	46
TEAE	63.4%	73.8%	71.4%	68.3%	77.8%
Related TEAE	4.9%	11.9%	11.9%	9.8%	11.1%
SAE	2.4%	0%	2.4%	4.9%	2.2%
Related SAE	0%	0%	0%	0%	0%
Discontinued Study Due to AE	0%	0%	0%	0%	0%

AE, Adverse Event; TEAE, treatment emergent adverse event; SAE, serious adverse event

Conclusions

- Oral VT-1161 demonstrated unprecedented efficacy in RVVC patients, with as low as 0% recurrence rates through 48 weeks
- VT-1161 was safe and well tolerated in all dosing arms, with an adverse event profile similar to placebo
- VT-1161 had no apparent effect on blood chemistry, hematology or urinalysis parameters
- These results suggest that VT-1161 may be a promising agent to treat RVVC, a condition associated with a very high burden of disease and for which there are no approved therapies