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Efficacy and safety of oteseconazole versus fluconazole for severe vulvovaginal candidiasis: a post-hoc analysis based on reproductive tract infection history

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Background

Vulvovaginal candidiasis (VVC) is among the most common fungal infections of the female genital tract, affecting 70–75% of women at least once and resulting in recurrent episodes in up to 40–50%. VVC is primarily caused by overgrowth of Candida species—C. albicans being most prevalent, but non-albicans species are increasingly reported. Symptoms include vulvar itching, burning, soreness, and non-offensive, curdy vaginal discharge.

Fluconazole, an oral triazole antifungal, remains the standard first-line therapy for acute, severe, and recurrent VVC. However, its repeated/prolonged use is associated with increasing treatment failures, especially in non-albicans Candida infections, highlighting the need for alternative treatments.

Oteseconazole is a novel, oral azole antifungal with over 2,000-fold selectivity for fungal CYP51, resulting in potent antifungal activity and reduced systemic toxicity. Recent trials have demonstrated oteseconazole's efficacy in preventing and treating recurrent and severe VVC, including superior activity in challenging patient populations.

Table 1. Baseline characteristics

	Patients with history of reproductive tract infections		Patients without history of reproductive tract infections	
	Oteseconazole (N = 47)	Fluconazole (N = 60)	Oteseconazole (N = 113)	Fluconazole (N = 99)
Age (year)				
Mean (SD)	30.7 (8.96)	31.9 (6.94)	29.6 (7.52)	30.8 (7.79)
Median (IQR)	30.0 (23.0, 35.0)	32.0 (26.5, 36.0)	28.0 (24.0, 33.0)	30.0 (24.0, 37.0)
Weight (kg)				
Mean (SD)	55.00 (7.377)	55.87 (7.952)	57.20 (9.878)	55.46 (9.210)
Median (IQR)	55.00 (49.00, 58.00)	55.00 (50.50, 60.00)	55.00 (51.00, 62.50)	55.00 (49.00, 61.00)
BMI (kg/m^2)				
Mean (SD)	20.755 (2.5507)	21.389 (2.7937)	21.636 (3.8044)	21.562 (3.3652)
Median (IQR)	20.370 (19.050, 22.310)	20.725 (19.245, 22.435)	20.900 (19.050, 23.050)	20.830 (19.350, 23.230)
Composite VSS score				
Mean (SD)	8.4 (1.67)	8.7 (1.98)	8.7 (1.78)	8.3 (1.73)
Median (IQR)	8.0 (7.0, 9.0)	8.0 (7.0, 10.0)	8.0 (7.0, 10.0)	8.0 (7.0, 9.0)
Candida species, n (%)				
Candida albicans	39 (83.0)	49 (81.7)	89 (78.8)	72 (72.7)
Candida glabrata	6 (12.8)	9 (15.0)	16 (14.2)	18 (18.2)
Candida tropicalis	1 (2.1)	0	4 (3.5)	3 (3.0)
Candida krusei	1 (2.1)	0	0	2 (2.0)
Candida spherical	0	1 (1.7)	2 (1.8)	1 (1.0)
Candida parapsilosis	0	0	1 (0.9)	2 (2.0)
Kodamaea ohmeri	0	0	0	1 (1.0)
Candida dubliniensis	0	0	1 (0.9)	0
Saccharomyces cerevisiae	0	1 (1.7)	0	0
Candida lusitaniae	0	0	0	1 (1.0)
Oteseconazole susceptibility testing, n (%)[a]				
Sensitive	45 (95.7)	59 (98.3)	110 (97.3)	95 (95.0)
Resistant	1 (2.1)	1 (1.7)	2 (1.8)	2 (2.0)
Dose-dependently sensitive	0	0	0	0
Wild strain	0	0	1 (0.9)	1 (1.0)
Unknown	1 (2.1)	0	0	2 (2.0)
Fluconazole susceptibility testing, n (%)[a]				
Sensitive	31 (66.0)	42 (70.0)	85 (75.2)	75 (75.0)
Resistant	10 (21.3)	4 (6.7)	5 (4.4)	13 (13.0)
Dose-dependently sensitive	6 (12.8)	14 (23.3)	22 (19.5)	11 (11.0)
Wild strain	0	0	1 (0.9)	1 (1.0)
Unknown	0	0	0	0

[a]Percentages in the fluconazole group of the without other reproductive tract infections subgroup were calculated with 100 as the denominator (99 patients yielded 100 results; one patient had two findings: *Candida parapsilosis* and *Kodamaea ohmeri*). For all other subgroups, denominators were the numbers of subjects indicated in the table header.

Table 2. Treatment-emergent adverse events

Treatment-emergent adverse event (TEAE)	Patients with history of reproductive tract infections		Patients without history of reproductive tract infections	
	Oteseconazole (N = 47)	Fluconazole (N = 60)	Oteseconazole (N = 113)	Fluconazole (N = 101)
Any TEAER	28 (59.6)	22 (36.7)	54 (47.8)	47 (46.5)
Urinary tract infection	5 (10.6)	4 (6.7)	8 (7.1)	3 (3.0)
Bacterial vulvovaginitis	4 (8.5)	4 (6.7)	3 (2.7)	8 (7.9)
Bacterial vaginosis	0	2 (3.3)	2 (1.8)	8 (7.9)
Nausea	3 (6.4)	3 (5.0)	2 (1.8)	2 (2.0)
Dizziness	4 (8.5)	1 (1.7)	2 (1.8)	2 (2.0)

TEAEs with an incidence greater than 5% are reported.

Results

Among patients with a history of reproductive tract infections, 47 received oteseconazole and 60 received fluconazole. For those without such a history, 113 were treated with oteseconazole and 99 with fluconazole. Table 1 summarizes the baseline characteristics across the four subgroups.

By Day 28, oteseconazole showed a higher therapeutic cure rate of 61.70% in patients with a history of reproductive tract infections, compared to 45.00% for fluconazole. In patients without a history of reproductive tract infections, oteseconazole achieved a therapeutic cure rate of 69.03% versus 46.46% for fluconazole. Oteseconazole consistently outperformed fluconazole in clinical and mycological cure rates, irrespective of reproductive tract infection history. Therapeutic, clinical, and mycological cure rates for oteseconazole exceeded those of fluconazole as early as Day 14 (Figure 1).

Conflicts of interest

The author has no conflicts of interest to declare.

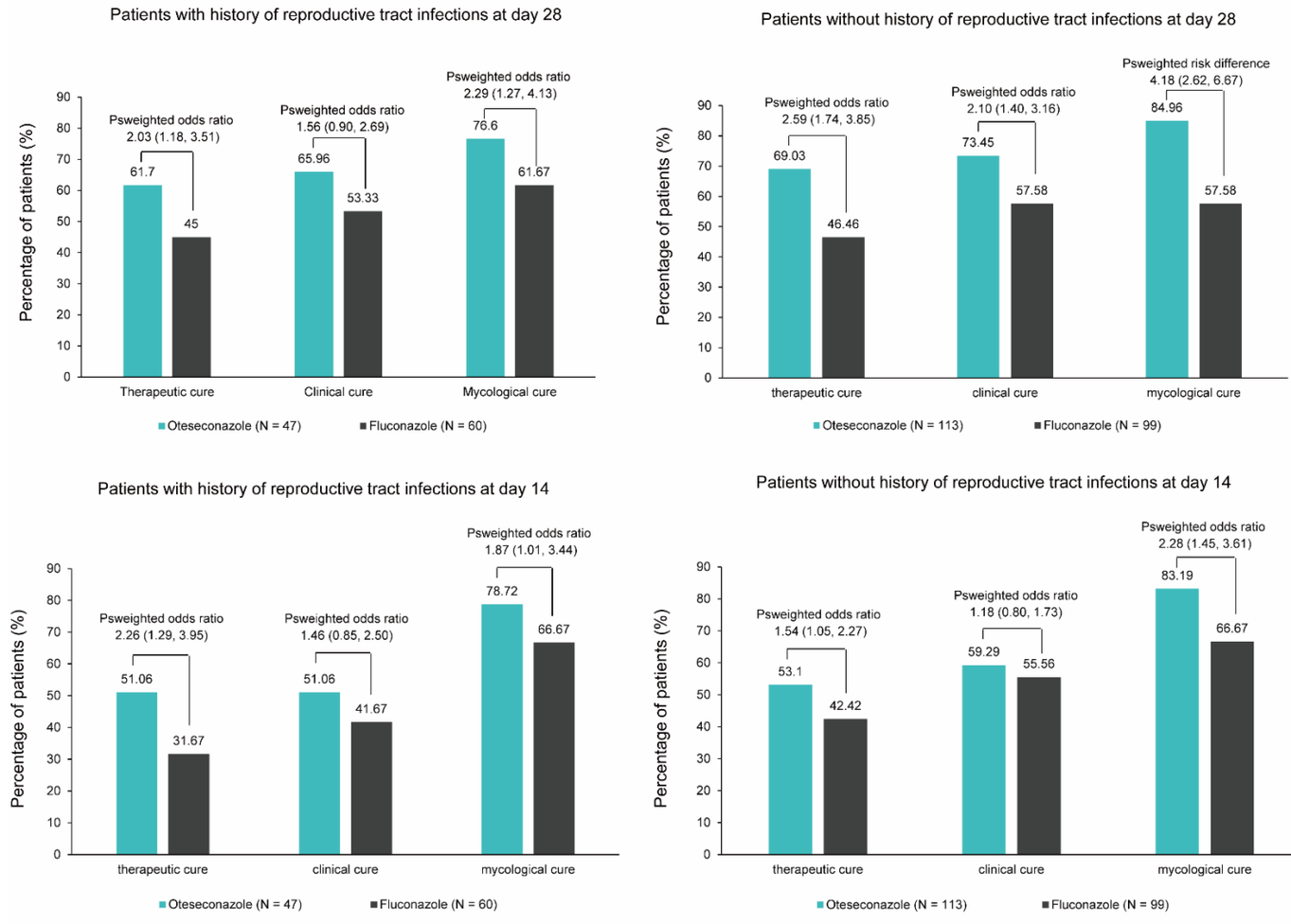
Methods

A randomized, double-blind, phase III trial enrolled women aged 18 to 75 years with severe VVC, defined as a vulvovaginal signs and symptoms (VSS) score of ≥7 and mycologically confirmed Candida infection.

Participants were randomized in a 1:1 ratio to receive either oteseconazole (600 mg on Day 1 and 450 mg on Day 2) or fluconazole (150 mg on Day 1 and Day 4). Matching placebos were used to maintain blinding, and rescue therapy with clotrimazole vaginal tablets was permitted in cases where symptoms persisted or worsened with confirmed infection.

A post hoc analysis utilizing propensity score weighting (Psweighted) compared the efficacy of oteseconazole and fluconazole in subgroups defined by history of reproductive tract infections. Study endpoints included therapeutic cure (combined clinical and mycological cure), clinical cure, mycological cure, rates of rescue therapy use, and safety as assessed by treatment-emergent adverse events (TEAEs).

Figure 1. Efficacy of oteseconazole versus fluconazole for severe vulvovaginal candidiasis: subgroup analysis by reproductive tract infection history



Results

No patients had their treatment interrupted or discontinued due to adverse events. In patients with a history of reproductive tract infections, TEAEs were more frequent with oteseconazole (59.6%) than fluconazole (36.7%). The higher incidence of TEAEs observed in the oteseconazole subgroups was mainly attributable to non-serious adverse events, including urinary tract infection and bacterial vulvovaginitis. In those without such history, overall TEAE rates were similar (47.8% vs. 46.5%), with bacterial infections more common on fluconazole and urinary tract infection slightly higher on oteseconazole (Table 2).

Conclusions

Oteseconazole demonstrated superior efficacy and comparable safety versus fluconazole in women with severe vulvovaginal candidiasis, regardless of a history of reproductive tract infections. Oteseconazole represents a promising alternative for the effective management of severe VVC.

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