#RES-104: Impact of Age on Efficacy and Safety of Oteseconazole in Patients with Severe Vulvovaginal Candidiasis: A Post-hoc Analysis of a Randomized, Double-Blind, Phase 3 Trial

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Background

- Oteseconazole, also known as VT-1161, is a novel oral antifungal agent with a tetrazole moiety and can inhibit fungal CYP51 with high specificity.[1]
- A randomised, double-blind, phase 3 trial showed the significant benefit of oteseconazole over fluconazole in patients with severe vulvovaginal candidiasis (VVC).[2]
- However, whether the effect of oteseconazole on VVC varies by age remains unknown.
- This study was aimed to assess the impact of age on efficacy and safety of oteseconazole versus fluconazole in patients with severe VVC.

Methods

- We conducted a post-hoc analysis on data from a multicentre, randomized, double-blind, phase 3 trial (NCT04956419). The study design of this phase 3 trial is shown in Figure 1.
- Endpoints, including the therapeutic cure (i.e., clinical and mycological cure) rate at days 14 and 28, the change from baseline to days 14 and 28 in the vulvovaginal signs and symptoms (VSS) score, the proportion of patients receiving rescue therapy, and safety, were assessed by age at baseline (<35 and ≥35 years).
- Inverse probability of treatment weighting (IPTW) analysis based on propensity scores was performed for binary outcomes using logistic regression, and ANCOVA model adjusting baseline VSS score was used for continuous outcomes.

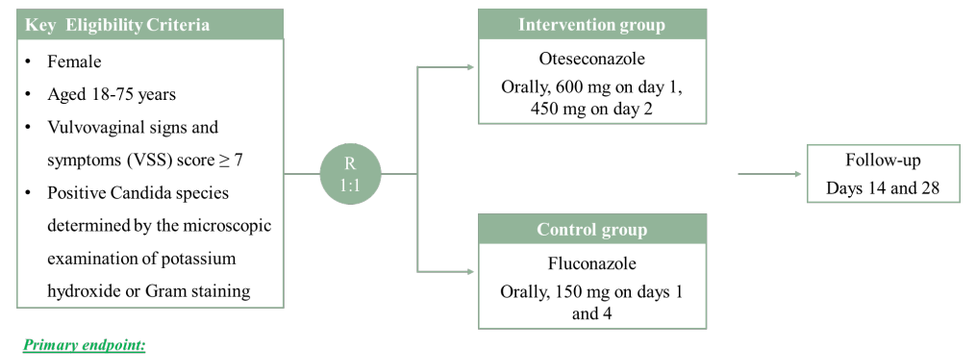

Figure 1. Study Design

Results

Patient characteristics

- In this analysis, 121 patients aged <35 years and 39 patients aged ≥35 years were included in the oteseconazole group, and the number was respective 109 and 52 in the fluconazole group.
- The detailed patient characteristics are listed in Table 1.

Table 1. Baseline characteristics

	Aged < 35 years		Aged ≥ 35 years	
	Oteseconazole (*n* = 121)	Fluconazole (*n* = 108)	Oteseconazole (*n* = 39)	Fluconazole (*n* = 51)
Age (year), mean (SD)	26.4 (4.47)	27.1 (4.49)	40.7 (6.54)	39.9 (4.35)
Ethnicity, n (%)				
Han	114 (94.2)	104 (96.3)	38 (97.4)	45 (88.2)
Other	7 (5.8)	4 (3.7)	1 (2.6)	6 (11.8)
Weight (kg), mean (SD)	55.5 (8.60)	54.6 (8.32)	59.9 (10.45)	57.7 (9.28)
BMI (kg/m^2), mean (SD)	20.9 (3.42)	20.8 (2.82)	22.9 (3.36)	22.9 (3.39)
Composite VSS score, mean (SD)	8.6 (1.71)	8.3 (1.76)	8.9 (1.85)	8.7 (1.95)
Candida speciesa, n (%)*				
Candida albicans	99 (81.8)	84 (77.8)	29 (74.4)	37 (72.5)
Candida glabrata	14 (11.6)	18 (16.7)	8 (20.5)	9 (17.6)
Candida tropicalis	5 (4.1)	1 (0.9)	0	2 (3.9)
Candida krusei	1 (0.8)	0	0	2 (3.9)
Candida spherical	1 (0.8)	2 (1.9)	1 (2.6)	0
Candida parapsilosis	1 (0.8)	1 (0.9)	0	1 (2.0)
Kodamaea ohmeri	0	0	0	1 (2.0)
Candida dubliniensis	0	0	1 (2.6)	0
Saccharomyces cerevisiae	0	1 (0.9)	0	0
Candida lusitaniae	0	1 (0.9)	0	0
Susceptibility testing, n (%)#				
Oteseconazole				
Sensitive	117 (96.7)	106 (98.1)	38 (97.4)	48 (92.3)
Resistant	3 (2.5)	1 (0.9)	0	2 (3.8)
Dose-dependently sensitive	0	0	0	0
Wild strain	0	1 (0.9)	1 (2.6)	0
Unknown	1 (0.8)	0	0	2 (3.8)
Fluconazole				
Sensitive	85 (70.2)	77 (71.3)	31 (79.5)	40 (76.9)
Resistant	12 (9.9)	10 (9.3)	3 (7.7)	7 (13.5)
Dose-dependently sensitive	24 (19.8)	20 (18.5)	4 (10.3)	5 (9.6)
Wild strain	0	1 (0.9)	1 (2.6)	0
Unknown	0	0	0	0

*Based on mycological culture of vaginal secretion. Vaginal secretion fungal culture. #One patient with fluconazole in aged ≥35 years subgroup presented with two strains (Candida parapsilosis and Kodamaea ohmeri). BMI, body mass index; SD, standard deviation; VSS, vulvovaginal signs and symptoms.

Efficacy

- At day 28, oteseconazole showed higher therapeutic cure rates than fluconazole in both age subgroups (<35 years: 65.29% vs. 45.37%, PSweighted OR 2.28 [95%CI 1.56-3.32]; ≥35 years: 71.79% vs. 47.06%, PSweighted OR 3.16 [95%CI 1.70-5.87]).
- Similar improved findings were observed across other efficacy endpoints, including assessments at day 14 (Table 2).
- Fewer patients in the oteseconazole group received antifungal rescue therapy in both age subgroups (<35 years: 4.13% vs. 12.96%, PSweighted OR 0.31 [95%CI 0.15-0.65]; ≥35 years: 2.56% vs. 17.65%, PSweighted OR 0.12 [95%CI 0.03-0.50]).

Table 2. Summary of efficacy results by age

	<35 years		≥35 years		*P* value*
	Oteseconazole (*n* = 121)	Fluconazole (*n* = 108)	Oteseconazole (*n* = 39)	Fluconazole (*n* = 51)	
At day 28#					
Therapeutic Cure					0.6570
No. (%)	79 (65.29)	49 (45.37)	28 (71.79)	24 (47.06)	
Risk difference (95% CI)	20.03 (11.11, 28.95)		27.10 (13.23, 40.96)		
Odds Ratio (95% CI)	2.28 (1.56, 3.32)		3.16 (1.70, 5.87)		
Clinical Cure					0.4740
No. (%)	85 (70.25)	62 (57.41)	29 (74.36)	27 (52.94)	
Risk difference (95% CI)	13.19 (4.45, 21.92)		22.76 (9.06, 36.46)		
Odds Ratio (95% CI)	1.78 (1.21, 2.61)		2.73 (1.45, 5.14)		
Mycological Cure					0.7008
No. (%)	98 (80.99)	62 (57.41)	34 (87.18)	32 (62.75)	
Risk difference (95% CI)	23.96 (15.77, 32.15)		25.36 (13.14, 37.58)		
Odds Ratio (95% CI)	3.20 (2.10, 4.88)		4.17 (1.97, 8.82)		
Change from baseline in VSS score					0.1230
Mean (SD)	-8.2 (1.90)	-7.1 (2.49)	-8.4 (2.19)	-8.0 (2.52)	
LSMean difference (95% CI)	-0.9 (-1.35, -0.46)		-0.3 (-0.81, 0.15)		
At day 14#					
Therapeutic Cure					0.4435
No. (%)	66 (54.55)	41 (37.96)	18 (46.15)	20 (39.22)	
Risk difference (95% CI)	17.45 (8.45, 26.45)		9.71 (-4.67, 24.10)		
Odds Ratio (95% CI)	2.03 (1.40, 2.95)		1.49 (0.82, 2.70)		
Clinical Cure					0.3660
No. (%)	71 (58.68)	53 (49.07)	20 (51.28)	27 (52.94)	
Risk difference (95% CI)	10.10 (1.02, 19.18)		0.72 (-13.90, 15.34)		
Odds Ratio (95% CI)	1.50 (1.04, 2.18)		1.03 (0.57, 1.85)		
Mycological Cure					0.9790
No. (%)	99 (81.82)	72 (66.67)	32 (82.05)	34 (66.67)	
Risk difference (95% CI)	14.78 (6.85, 22.71)		15.94 (3.41, 28.47)		
Odds Ratio (95% CI)	2.19 (1.42, 3.37)		2.37 (1.18, 4.76)		
Change from baseline in VSS score					0.7934
Mean (SD)	-7.8 (2.14)	-7.3 (2.15)	-7.9 (2.46)	-7.7 (2.69)	
LSMean difference (95% CI)	-0.2 (-0.59, 0.13)		-0.2 (-0.74, 0.43)		

#All risk difference (95% CI), odds Ratio (95% CI) and LSmean difference (95% CI) were analyzed with inverse probability of weighting (IPTW) based on propensity scores. *Treatment-subgroup interaction P value. CI, confidence interval; LSMean, least squares mean; VSS, vulvovaginal signs and symptoms.

Safety

- Regarding safety, 64 (52.9%) of 121 patients aged <35 years in the oteseconazole group and 44 (40.4%) of 109 such patients in the fluconazole group had at least one adverse event (AE); while among patients aged ≥35 years, AEs occurred in 18 (46.2%) of 39 patients and 25 (48.1%) of 52 patients, respectively (Table 3).
- No treatment-related serious AEs were observed.

Table 3. Treatment-emergent adverse events with an incidence of >3% in any subgroup

	<35 years		≥35 years	
	Oteseconazole (*n* = 121)	Fluconazole (*n* = 109)	Oteseconazole (*n* = 39)	Fluconazole (*n* = 52)
Any	58 (47.9)	34 (31.2)	18 (46.2)	25 (48.1)
Urinary tract infection	9 (7.4)	7 (6.4)	4 (10.3)	0
Bacterial vulvovaginitis	5 (4.1)	6 (5.5)	2 (5.1)	6 (11.5)
Bacterial vaginosis	1 (0.8)	5 (4.6)	1 (2.6)	5 (9.6)
Nausea	4 (3.3)	3 (2.8)	1 (2.6)	2 (3.8)
Upper respiratory infection	4 (3.3)	4 (3.7)	1 (2.6)	0
Dizziness	5 (4.1)	3 (2.8)	1 (2.6)	0
Headache	5 (4.1)	1 (0.9)	1 (2.6)	0
Anaemia	1 (0.8)	1 (0.9)	0	3 (5.8)
Asthenia	1 (0.8)	0	0	3 (5.8)
Abdominal pain	1 (0.8)	1 (0.9)	2 (5.1)	0
Dry mouth	0	0	2 (5.1)	0

Conclusions

- Oteseconazole demonstrated superior efficacy (higher rates of therapeutic, clinical, and mycological cure), a reduced need for rescue therapy, and a manageable safety profile versus fluconazole in patients with SVVC, regardless of age.

Reference: [1] Hoy SM. Drugs. 2022;82(9):1017-1023. [2] Wang X, et al. Antimicrob Agents Chemother. 2024;68(1):e0077823.

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