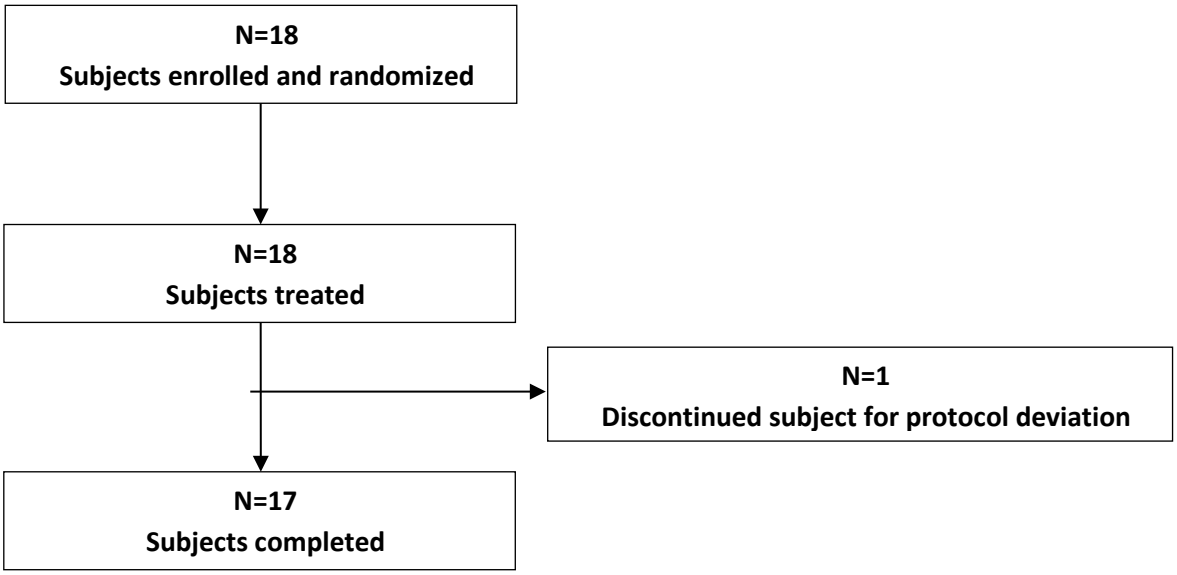
Participant flow



All 18 treated subjects were included in the safety set as follows:

- 17 subjects received at least one dose of Lorazepam IBSA 2.5 mg orodispersible film (T) under fasting conditions
- 17 subjects received at least one dose of Tavor® 2.5 mg tablets (R1) under fasting conditions
- 18 subjects received at least one dose of Tavor® 2.5 mg orodispersible tablets (R2) under fasting conditions

Baseline characteristics

Demographic data	Safety set N=18	PK set N=17
Sex		
Female - n (%)	9 (50.0)	9 (52.9)
Male – n (%)	9 (50.0)	8 (47.1)
Age (years)		
Mean ± SD	39.1±11.6	38.3±11.5
Median (range)	40.5 (20-55)	40.0 (20-55)
Body weight (kg)		
Mean ± SD	70.31±13.76	70.84±13.99
Median (range)	69.90 (48.2-95.0)	70.00 (48.2-95.0)
Height (cm)		
Mean ± SD	169.9±9.6	170.1±9.9
Median (range)	167.0 (154-183)	166.0 (154-183)
Body Mass Index (kg/m^2)		
Mean ± SD	24.14±2.95	24.29±2.97
Median (range)	24.55 (20.2-29.7)	25.00 (20.2-29.7)
Race		
White – n (%)	16 (88.9)	15 (88.2)
Black or African American – n (%)	1 (5.6)	1 (5.9)
Other, Mestizo – n (%)	1 (5.6)	1 (5.9)

Outcome measures

Primary outcome

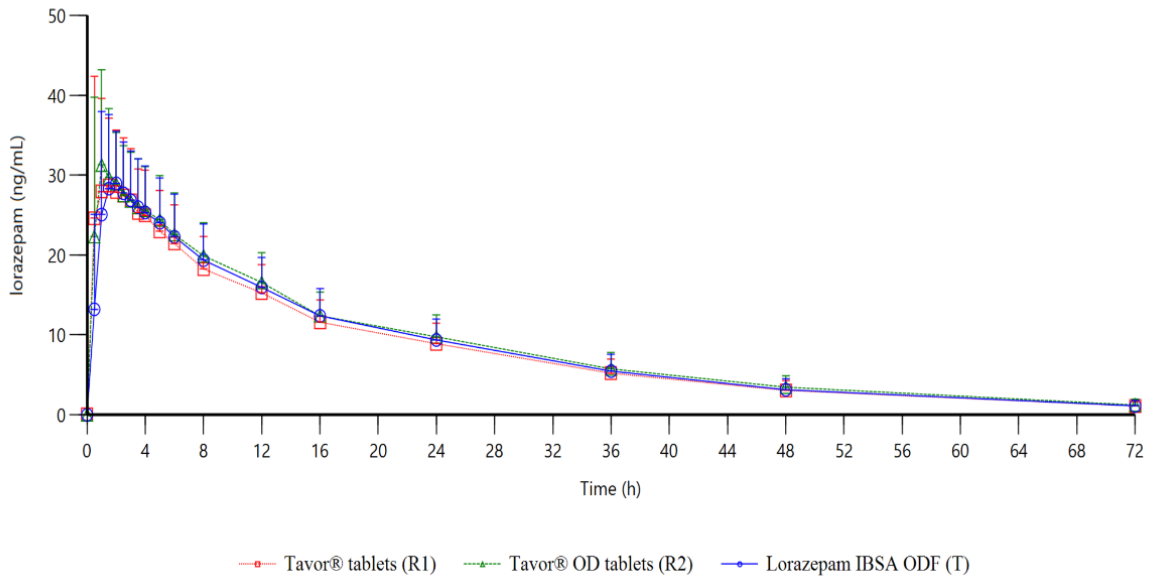
Results of the statistical comparison of lorazepam pharmacokinetic parameters between T vs. R1 and T vs. R2 administered under fasting conditions are presented in the table below:

Treatment comparison	**T vs. R1**		**T vs. R2**	
Parameter	**PE%**	**90% CI**	**PE%**	**90% CI**
C_{max}	95.32%	85.53 – 106.23	96.97%	88.51 – 106.23
AUC_{0-t}	102.54%	100.66 – 104.45	97.34%	94.59 – 100.17
$AUC_{0-\infty}$	102.37%	100.31 – 104.46	97.08%	93.91 – 100.35

T: Lorazepam IBSA orodispersible film; R1: Tavor® tablets; R2: Tavor® orodispersible tablets.
PE: Point Estimate, calculated as ratio of geometric means; CI: confidence interval; N=17.

Secondary outcome

Mean lorazepam plasma concentration-time profiles for T, R1 and R2 are shown in the figure below:



Descriptive statistics of lorazepam plasma pharmacokinetic parameters are presented in the table below:

Pharmacokinetic parameters	T	R1	R2
C_{max} (ng/mL)	32.900±8.466	35.294±12.680	34.476±11.116
AUC_{0-t} (ng/mL×h)	589.615±159.624	573.170±144.266	607.479±166.125
$AUC_{0-\infty}$ (ng/mL×h)	615.615±176.591	599.115±158.479	636.489±186.050
t_{max} (h)	1.5 (0.5–3.5)	1 (0.5–3.5)	1 (0.5–3)
$t_{½}$ (h)	15.150±2.129	15.598±1.801	15.481±2.395
λ_z (1/h)	0.046±0.008	0.045±0.006	0.046±0.008

T: Lorazepam IBSA orodispersible film; R1: Tavor® tablets; R2: Tavor® orodispersible tablets.
Values are arithmetic means ± SD, except for t_{max}: median (min-max). N=17

Lorazepam relative bioavailability (F_{rel}), calculated as ratio of AUC_{0-t}, is summarized below:

Pharmacokinetic set	T / R1	T / R2
F_{rel} (%)	102.539±5.016	97.401±6.395

T: Lorazepam IBSA orodispersible film; R1: Tavor® tablets; R2: Tavor® orodispersible tablets.
Values are arithmetic means ± SD. N=17

Adverse events

Number of treatment-emergent adverse events (TEAEs) and number and percentage of subjects with TEAEs by treatment, system organ class (SOC) and preferred term (PT) after single dose of Lorazepam IBSA orodispersible film (T), Tavor® tablets (R1) and Tavor® orodispersible tablets (R2). Safety set

SOC	**T N=17**		**R1 N=17**		**R2 N=18**		**Overall N=18**	
PT	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs – all SOCs	18	15 (88.2)	22	16 (94.1)	21	17 (94.4)	61	18 (100.0)
Nervous system disorders	15	15 (88.2)	16	16 (94.1)	19	17 (94.4)	50	18 (100.0)
Somnolence	15	15 (88.2)	16	16 (94.1)	17	17 (94.4)	48	18 (100.0)
Dizziness	0	0 (0.0)	0	0 (0.0)	2	2 (11.1)	2	2 (11.1)
Eye disorders	1	1 (5.9)	3	3 (17.6)	2	2 (11.1)	6	4 (22.2)
Diplopia	0	0 (0.0)	3	3 (17.6)	1	1 (5.6)	4	3 (16.7)
Vision blurred	1	1 (5.9)	0	0 (0.0)	1	1 (5.6)	2	1 (5.6)
Ear and labyrinth disorders	1	1 (5.9)	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Ear pain	1	1 (5.9)	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Investigations	0	0 (0.0)	3	1 (5.9)	0	0 (0.0)	3	1 (5.6)
ALT increased	0	0 (0.0)	1	1 (5.9)	0	0 (0.0)	1	1 (5.6)
AST increased	0	0 (0.0)	1	1 (5.9)	0	0 (0.0)	1	1 (5.6)
White blood cell count increased	0	0 (0.0)	1	1 (5.9)	0	0 (0.0)	1	1 (5.6)
Metabolism and nutrition disorders	1	1 (5.9)	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)
Decreased appetite	1	1 (5.9)	0	0 (0.0)	0	0 (0.0)	1	1 (5.6)

Number of TEAEs and number of subjects with TEAEs after single dose of Lorazepam IBSA orodispersible film (T), Tavor® tablets (R1) and Tavor® orodispersible tablets (R2). Safety set

Category	**T N=17**		**R1 N=17**		**R2 N=18**		**Overall N=18**	
	n AEs	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs	18	15 (88.2)	22	16 (94.1)	21	17 (94.4)	61	18 (100.0)
Related	17	15 (88.2)	19	16 (94.1)	20	17 (94.4)	56	18 (100.0)
Not related	1	1 (5.9)	3	1 (5.9)	1	1 (5.6)	5	3 (16.7)
Leading to discontinuation	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)
SAEs	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)	0	0 (0.0)