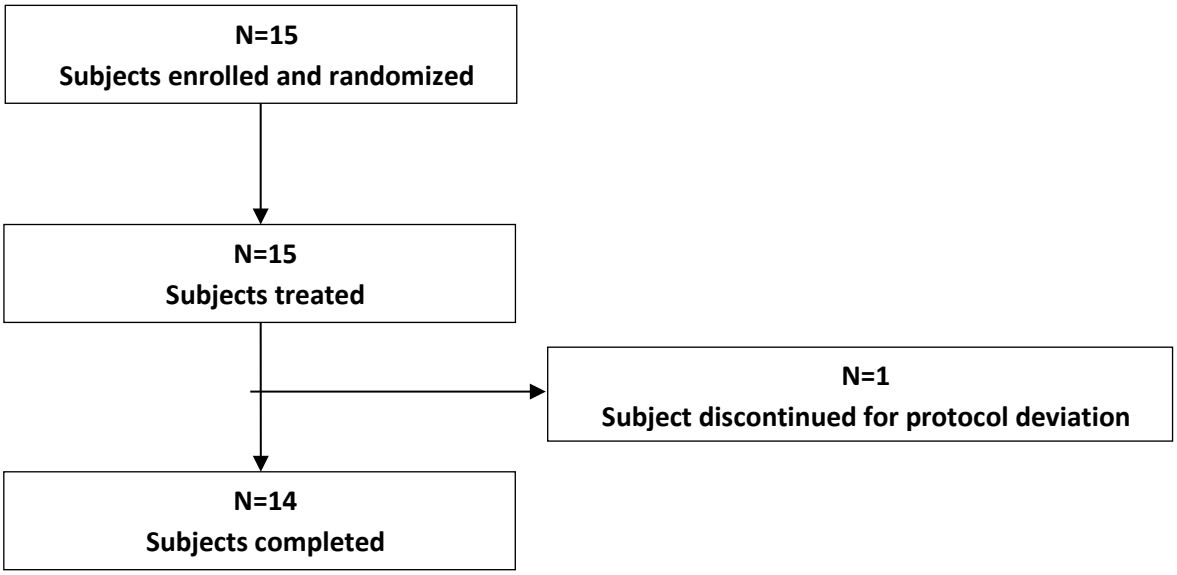
Participant flow



In detail:

- 14 subjects (93.3%) received all study treatments (i.e., IBSA tadalafil 20 mg orodispersible film under fed conditions [T_{fed}], IBSA tadalafil 20 mg orodispersible film under fasting conditions [T_{fast}] and Cialis® 20 mg film-coated tablet under fed conditions [R_{fed}]), were included in the pharmacokinetic set and considered for the statistical comparisons of the pharmacokinetic parameters.
- 1 subject (6.7%) received T_{fast}, underwent all blood samplings for the study period and then was withdrawn from the study. Tadalafil concentrations and pharmacokinetic parameters were listed and summarized for all 15 subjects for this treatment.

Baseline characteristics

Demographic data	Safety set N=15	Pharmacokinetic set N=14
Age (years)		
Mean ± SD	34.0±7.3	34.6±7.2
Median (range)	34.0 (24-45)	35.0 (24-45)
Body weight (kg)		
Mean ± SD	77.66±8.57	77.45±8.85
Median (range)	75.50 (67.8-95.0)	74.70 (67.8-95.0)
Height (cm)		
Mean ± SD	176.7±6.2	177.1±6.2
Median (range)	177.0 (168-187)	178.0 (168-187)
Body Mass Index (kg/m^2)		
Mean ± SD	24.87±2.42	24.67±2.39
Median (range)	24.50 (21.2-29.3)	24.45 (21.2-29.3)
Race		
White – n (%)	15 (100.0)	14 (100.0)

Outcome measures

Primary outcome

Results of the statistical comparison of the tadalafil pharmacokinetic parameters between T_{fed} and R_{fed} are presented in the table below.

Treatment comparison	Parameter	PE%	90% CI
T_{fed} vs. R_{fed}	**C_{max}**	86.07%	76.20 – 97.22
	AUC_{0-8}	54.57%	45.05 – 66.10
	AUC_{0-72}	100.06%	91.20 – 109.78
	$AUC_{0-\infty}$	101.13%	92.45 – 110.62

T_{fed}: test product under fed conditions; R_{fed}: reference product under fed conditions; PE: Point Estimate, calculated as ratio of geometric means; CI: confidence interval; N=14

The difference between t_{max} values of T_{fed} and R_{fed} (median values: 5.5 h versus 3 h) was statistically significant (Wilcoxon test p-value=0.0005).

Secondary outcome

Results of the statistical comparison of the tadalafil pharmacokinetic parameters between T_{fed} and T_{fast} are presented in the table below:

Treatment comparison	Parameter	PE%	90% CI
T_{fed} vs. T_{fast}	**C_{max}**	101.64%	87.26 – 118.38
	AUC_{0-8}	63.20%	52.97 – 75.41
	AUC_{0-72}	111.40%	98.62 – 125.84
	$AUC_{0-\infty}$	113.66%	100.74 – 128.24

T_{fed}: test product under fed conditions; T_{fast}: test product under fasting conditions; PE: Point Estimate, calculated as ratio of geometric means; CI: confidence interval; N=14

The difference between t_{max} values of T_{fed} and T_{fast} (median values: 5.5 h versus 3 h) was statistically significant (Wilcoxon test p-value=0.0005).

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

Pharmacokinetic parameters	T_{fed} N=14	T_{fast} N=15	R_{fed} N=14
C_{max} (ng/mL)	351.579±88.912	341.326±82.167	405.894±103.195
AUC_{0-8} (ng/mL×h)	1297.835±444.855	2011.464±509.178	2320.353±635.758
AUC_{0-72} (ng/mL×h)	10341.032±2474.944	9229.271±3443.079	10498.018±3203.642
$AUC_{0-\infty}$ (ng/mL×h)	11765.640±3164.852	10336.872±4351.766	11897.633±4121.415
t_{max} (h)	5.5 (5.5–12)	3 (1.5–6)	3 (1.5–6)
$t_{½}$ (h)	21.408±5.035	20.005±5.358	21.311±5.926
λ_z (1/h)	0.034±0.008	0.037±0.011	0.035±0.009

T_{fed}: test product under fed conditions; T_{fast}: test product under fasting conditions; R_{fed}: reference product under fed conditions; values are arithmetic means ± SD, except for t_{max}: median (min-max)

Tadalafil relative bioavailability (F_{rel}) in plasma, calculated as ratio of AUC_{0-72}, is summarized below:

Pharmacokinetic set	T_{fed} / R_{fed} N=14	T_{fed} / T_{fast} N=14
F_{rel} (%)	102.468±23.724	114.202±28.406

T_{fed}: test product under fed conditions; T_{fast}: test product under fasting conditions; R_{fed}: reference product under fed conditions; values are arithmetic means ± SD

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 T_{fed}, T_{fast} and R_{fed} are presented in the table below. Safety set

SOC	**T_{fed} N=14**		**T_{fast} N=15**		**R_{fed} N=14**		**Overall N=15**	
PT	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs – all SOCs	4	3 (21.4)	6	4 (26.7)	3	2 (14.3)	13	6 (40.0)
Musculoskeletal and connective tissue disorders	1	1 (7.1)	2	2 (13.3)	2	2 (14.3)	5	4 (26.7)
Myalgia	1	1 (7.1)	0	0 (0.0)	2	2 (14.3)	3	3 (20.0)
Back pain	0	0 (0.0)	2	2 (13.3)	0	0 (0.0)	2	2 (13.3)
General disorders and administration site conditions	2	1 (7.1)	2	2 (13.3)	0	0 (0.0)	4	2 (13.3)
Influenza like illness	2	1 (7.1)	1	1 (6.7)	0	0 (0.0)	3	2 (13.3)
Pyrexia	0	0 (0.0)	1	1 (6.7)	0	0 (0.0)	1	1 (6.7)
Nervous system disorders	1	1 (7.1)	1	1 (6.7)	1	1 (7.1)	3	2 (13.3)
Headache	1	1 (7.1)	0	0 (0.0)	1	1 (7.1)	2	1 (6.7)
Presyncope	0	0 (0.0)	1	1 (6.7)	0	0 (0.0)	1	1 (6.7)
Infections and infestations	0	0 (0.0)	1	1 (6.7)	0	0 (0.0)	1	1 (6.7)
Pharyngitis bacterial	0	0 (0.0)	1	1 (6.7)	0	0 (0.0)	1	1 (6.7)

T_{fed}: test product under fed conditions; T_{fast}: test product under fasting conditions; R_{fed}: reference product under fed conditions

Number of TEAEs and number of subjects with TEAEs after single dose of T_{fed}, T_{fast} and R_{fed} are presented in the table below. Safety set

Category	**T_{fed} N=14**		**T_{fast} N=15**		**R_{fed} N=14**		**Overall N=15**	
	n AEs	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**	**n AEs**	**n (%) subjects**
All TEAEs	4	3 (21.4)	6	4 (26.7)	3	2 (14.3)	13	6 (40.0)
Related	2	2 (14.3)	2	2 (13.3)	3	2 (14.3)	7	4 (26.7)
Not related	2	1 (7.1)	4	2 (13.3)	0	0 (0.0)	6	3 (20.0)
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)