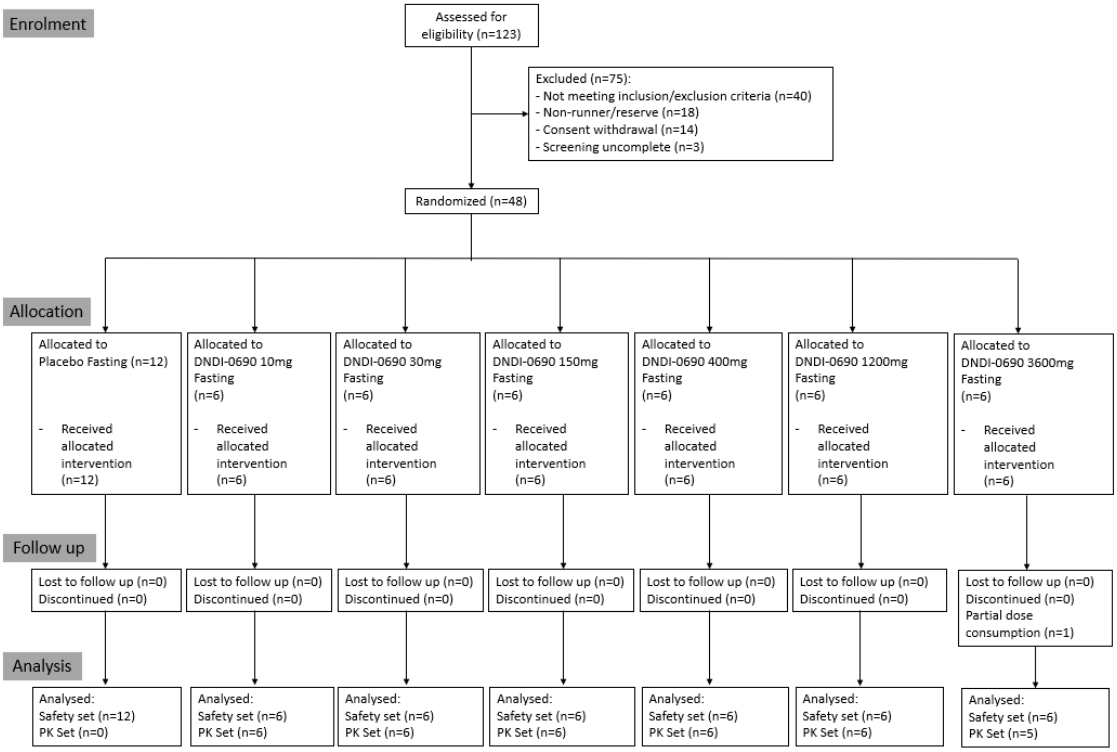
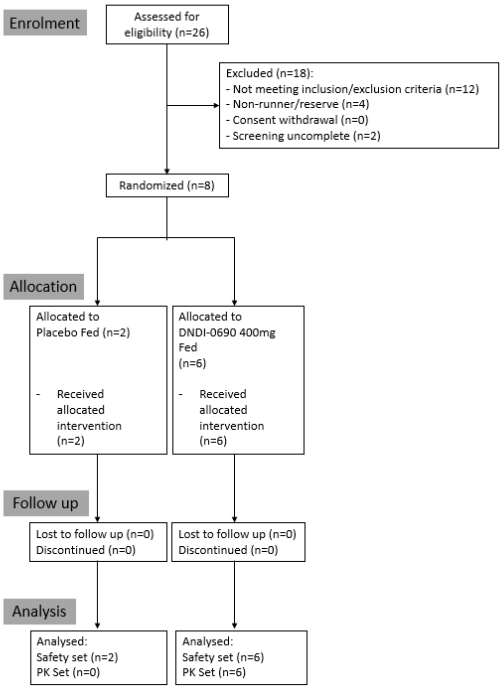
Participant Flow

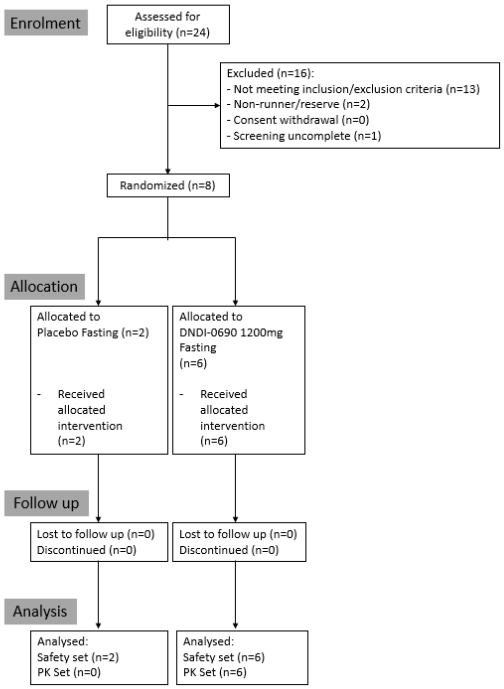
Males Fasting



Males Fed



Females Fasting



Baseline Characteristics

Table 1 Demographic Characteristics (Safety Set)

		All Males Fasted		All Males Fed		All Females Fasted	
		All Placebo N = 12 n (%)	All Active N = 36 n (%)	Placebo N = 2 n (%)	400 mg DNDI-0690 N = 6 n (%)	Placebo N = 2 n (%)	1200 mg DNDI-0690 N = 6 n (%)
Age (years)	Mean	40.0	34.8	36.5	36.7	51.5	54.7
	SD	9.9	11.1	23.3	11.8	3.5	4.3
	Median	42.5	36.0	36.5	40.5	51.5	56.0
	Min	24	18	20	21	49	48
	Max	54	54	53	48	54	59
	n	12	36	2	6	2	6
Sex n (%)	Male	12 (100)	36 (100)	2 (100)	6 (100)	0	0
	Female	0	0	0	0	2 (100)	6 (100)
Race n (%)	White	10 (83.3)	34 (94.4)	2 (100)	6 (100)	2 (100)	6 (100)
	Black or African American	1 (8.3)	1 (2.8)	0	0	0	0
	Asian	1 (8.3)	1 (2.8)	0	0	0	0
Ethnicity n (%)	Hispanic or Latino	0	1 (2.8)	0	1 (16.7)	0	0
	Not Hispanic or Latino	12 (100)	35 (97.2)	2 (100)	5 (83.3)	2 (100)	6 (100)
Height (cm)	Mean	179.1	177.1	179.5	175.0	158.0	164.0
	SD	7.9	7.6	6.4	7.4	4.2	6.4
	Median	177.0	177.5	179.5	174.5	158.0	163.5
	Min	170	158	175	165	155	157
	Max	194	193	184	185	161	174
	n	12	36	2	6	2	6
Weight (kg)	Mean	84.76	79.49	80.80	74.40	58.50	65.00
	SD	12.42	8.71	8.20	17.43	6.36	10.93
	Median	85.50	79.20	80.80	70.20	58.50	64.10
	Min	65.4	61.6	75.0	51.5	54.0	49.2
	Max	112.0	99.0	86.6	96.3	63.0	78.6
	n	12	36	2	6	2	6
BMI (kg/m²)	Mean	26.38	25.33	25.05	24.15	23.40	24.03
	SD	2.91	2.13	0.78	4.70	1.27	2.46
	Median	26.70	25.30	25.05	23.30	23.40	24.15
	Min	20.9	21.1	24.5	18.9	22.5	20.0
	Max	29.8	29.6	25.6	29.9	24.3	27.0
	n	12	36	2	6	2	6

ALL PLACEBO is all placebo subjects pooled over Cohorts 1 to 6 and ALL ACTIVE is all active subjects pooled over Cohorts 1 to 6.

Outcome measures

Table 2 Overall Summary of TEAEs by Severity (Safety Set)

	All Males Fasted								All Females Fasted	
			Active Dose Level of DNDI-0690							
	All Placebo (N = 12) n (%)	All Active (N = 36) n (%)	10 mg (N = 6) n (%)	30 mg (N = 6) n (%)	150 mg (N = 6) n (%)	400 mg (N = 6) n (%)	1200 mg (N = 6) n (%)	3600 mg (N = 6) n (%)	Placebo (N = 2) n (%)	1200 mg DNDi-0690 (N= 6) n (%)
Number (%) of subjects reporting at least 1 TEAE	3 (25.0)	7 (19.4)	0	2 (33.3)	1 (16.7)	2 (33.3)	1 (16.7)	1 (16.7)	1 (50.0)	4 (66.7)
Number (%) of subjects reporting at least 1 mild TEAE	3 (25.0)	7 (19.4)	0	2 (33.3)	1 (16.7)	2 (33.3)	1 (16.7)	1 (16.7)	1 (50.0)	4 (66.7)
Number (%) of subjects reporting at least 1 moderate TEAE	0	0	0	0	0	0	0	0	0	1 (16.7)
Number (%) of subjects reporting at least 1 severe TEAE	0	0	0	0	0		0	0	0	0
Number (%) of subjects reporting at least 1 life-threatening TEAE	0	0	0	0	0	0	0	0	0	0
Number (%) of subjects reporting at least 1 TEAE leading to death	0	0	0	0	0	0	0	0	0	0
Number (%) of subjects reporting at least 1 serious TEAE	0	0	0	0	0	0	0	0	0	0
Total number of TEAEs	3	9	0	4	1	2	1	1	1	5
Total number of mild TEAEs	3	9	0	4	1	2	1	1	1	4
Total number of moderate TEAEs	0	0	0	0	0	0	0	0	0	1
Total number of severe TEAEs	0	0	0	0	0	0	0	0	0	0
Total number of life-threatening TEAEs	0	0	0	0	0	0	0	0	0	0
Total number of TEAEs leading to death	0	0	0	0	0	0	0	0	0	0
Total number of serious TEAEs	0	0	0	0	0	0	0	0	0	0

ALL PLACEBO is all placebo subjects and ALL ACTIVE is all active subjects pooled over Cohorts 1 to 6

No TEAEs were recorded for male subjects receiving DNDI-0690 (or placebo) in the fed state.

Table 3 Summary of Plasma Pharmacokinetic Parameters of DNDI-0690 following a Single Oral Dose of 10, 30, 150, 400, 1200 and 3600 mg in Healthy Male Participants in the Fasted State: Pharmacokinetic Population

Regimen Dose level No. of Subjects Parameter	A 10 mg N=6	B 30 mg N=6	C 150 mg N=6	D 400 mg N=6	E 1200 mg N=6	F 3600 mg N=5
T_{max} (h) [a]	1.500 (1.00-2.50)	3.500 (2.50-4.00)	3.525 (3.00-4.02)	4.000 (2.50-9.00)	4.000 (3.00-4.08)	3.000 (2.00-4.03)
C_{max} (ng/mL) [b]	173 (26.7)	496 (29.1)	775 (25.7)	1120 (24.2)	1670 (25.2)	2560 (20.7)
$AUC_{(0\text{-}inf)}$ (ng.h/mL) [b]	1650 (77.9)	5280 (62.0)	7730 (78.6)	13900 (67.7)	25200 (63.8)	47800 (26.7)
$T_{1/2}$ (h) [a]	5.650 (3.32, 12.27)	6.062 (2.92, 10.26)	4.547 (2.55,7.40)	6.145 (3.68,9.69)	8.341 (6.28, 13.38)	12.144 (10.34,15.93)

[a] Median (range: min, max), [b] Geometric Mean (Geometric CV%) NC: not calculated

Table 4 Plasma Pharmacokinetic Parameters of DNDI-0690 following a Single Oral Dose of 400 mg in Healthy Male Subjects in the Fasted and Fed States: Pharmacokinetic Population

Regimen Dose level Prandial Status No. of Subjects Parameter	D 400 mg Fasted N=6	G 400 mg Fed N=6
T_{max} (h) [a]	4.000 (2.50-9.00)	4.000 (4.00-6.00)
C_{max} (ng/mL) [b]	1120 (24.2)	1960 (34.9)
$AUC_{(0\text{-}inf)}$ (ng.h/mL) [b]	13900 (67.7)	23200 (68.6)
$T_{1/2}$ (h) [a]	6.145 (3.68, 9.69)	5.157 (2.49, 10.43)

[a] Median (range: min, max) [b] Geometric Mean (Geometric CV%)

Table 5 Summary of Plasma Pharmacokinetic Parameters for DNDI-0690 Following Single Oral Doses of DNDI-0690 at 1200 mg to Healthy Female and Male Participants in the Fasted State: Pharmacokinetic Population

Regimen Dose level Sex No. of Subjects Parameter	E 1200 mg Males N=6	H 1200 mg Females N=6
T_{max} (h) [a]	4.000 (3.00-4.08)	4.000 (2.50-4.00)
C_{max} (ng/mL) [b]	1670 (25.2)	2260 (13.7)
$AUC_{(0\text{-}inf)}$ (ng.h/mL) [b]	25200 (63.8)	40600 (19.3)
$T_{1/2}$ (h) [a]	8.341 (6.28, 13.38)	9.925 (9.17, 11.18)
CLr (mL/min) [b]	0.0282 (41.0)	0.0530 (39.3)

[a] Median (range: min, max), [b] Geometric Mean (Geometric CV%)

Adverse events

Table 6 Incidence of Adverse Events: Safety Population (All males fasted)

System Organ Class	Preferred Term	All Placebo (N = 12)		All Active (N = 36)		Active Dose Level of DNDI-0690											
						10 mg (N = 6)		30 mg (N = 6)		150 mg (N = 6)		400 mg (N = 6)		1200 mg (N = 6)		3600 mg (N = 6)	
		n (%)	Event n	n (%)	Event n	n (%)	Event n	n (%)	Event n	n (%)	Event n	n (%)	Event n	n (%)	Event n	n (%)	Event n
Subjects reporting TEAEs (all SOCs/PTs)		**3 (25.0)**	**3**	**7 (19.4)**	**9**	**0**	**0**	**2 (33.3)**	**4**	**1 (16.7)**	**1**	**2 (33.3)**	**2**	**1 (16.7)**	**1**	**1 (16.7)**	**1**
Gastrointestinal Disorder	All	0	0	3 (8.3)	4	0	0	2 (33.3)	3	1 (16.7)	1	0	0	0	0	0	0
	Flatulence	0	0	2 (5.6)	2	0	0	2 (33.3)	2	0	0	0	0	0	0	0	0
	Abdominal Pain	0	0	1 (2.8)	1	0	0	0	0	1 (16.7)	1	0	0	0	0	0	0
	Diarrhoea	0	0	1 (2.8)	1	0	0	1 (16.7)	1	0	0	0	0	0	0	0	0
Nervous System Disorders	All	0	0	3 (8.3)	3	0	0	0	0	0	0	1 (16.7)	1	1 (16.7)	1	1 (16.7)	1
	Headache	0	0	3 (8.3)	3	0	0	0	0	0	0	1 (16.7)	1	1 (16.7)	1	1 (16.7)	1
General Disorders and Administration Site Conditions	All	1 (8.3)	1	1 (2.8)	1	0	0	1 (16.7)	1	0	0	0	0	0	0	0	0
	Vessel Puncture Site Haematoma	0	0	1 (2.8)	1	0	0	1 (16.7)	1	0	0	0	0	0	0	0	0
	Fatigue	1 (8.3)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Musculoskeletal and Connective Tissue Disorders	All	1 (8.3)	1	1 (2.8)	1	0	0	0	0	0	0	1 (16.7)	1	0	0	0	0
	Back Pain	1 (8.3)	1	1 (2.8)	1	0	0	0	0	0	0	1 (16.7)	1	0	0	0	0
Infections and Infestations	All	1 (8.3)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Nasopharyngitis	1 (8.3)	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0

ALL PLACEBO is all placebo subjects and ALL ACTIVE is all active subjects pooled over Cohorts 1 to 6.

Table 7 Incidence of Adverse Events: Safety Population (All females fasted)

System Organ Class	Preferred Term	Placebo (N = 2)		1200 mg DNDi-0690 (N = 6)	
		n (%)	Event n	n (%)	Event n
Subjects reporting TEAEs (all SOCs/PTs)		**1 (50.0)**	**1**	**4 (66.7)**	**5**
Gastrointestinal Disorder	All	0	0	2 (33.3)	2
	Flatulence	0	0	2 (33.3)	2
Infections and Infestations	All	0	0	2 (33.3)	2
	Gastroenteritis Viral	0	0	1 (16.7)	1
	Nasopharyngitis	0	0	1 (16.7)	1
Musculoskeletal and Connective Tissue Disorders	All	0	0	1 (16.7)	1
	Back Pain	0	0	1 (16.7)	1
Nervous System Disorders	All	1 (50.0)	1	0	0
	Headache	1 (50.0)	1	0	0

No AEs were recorded for male subjects receiving DNDI-0690 (or placebo) in the fed state.