

INTRODUCTION

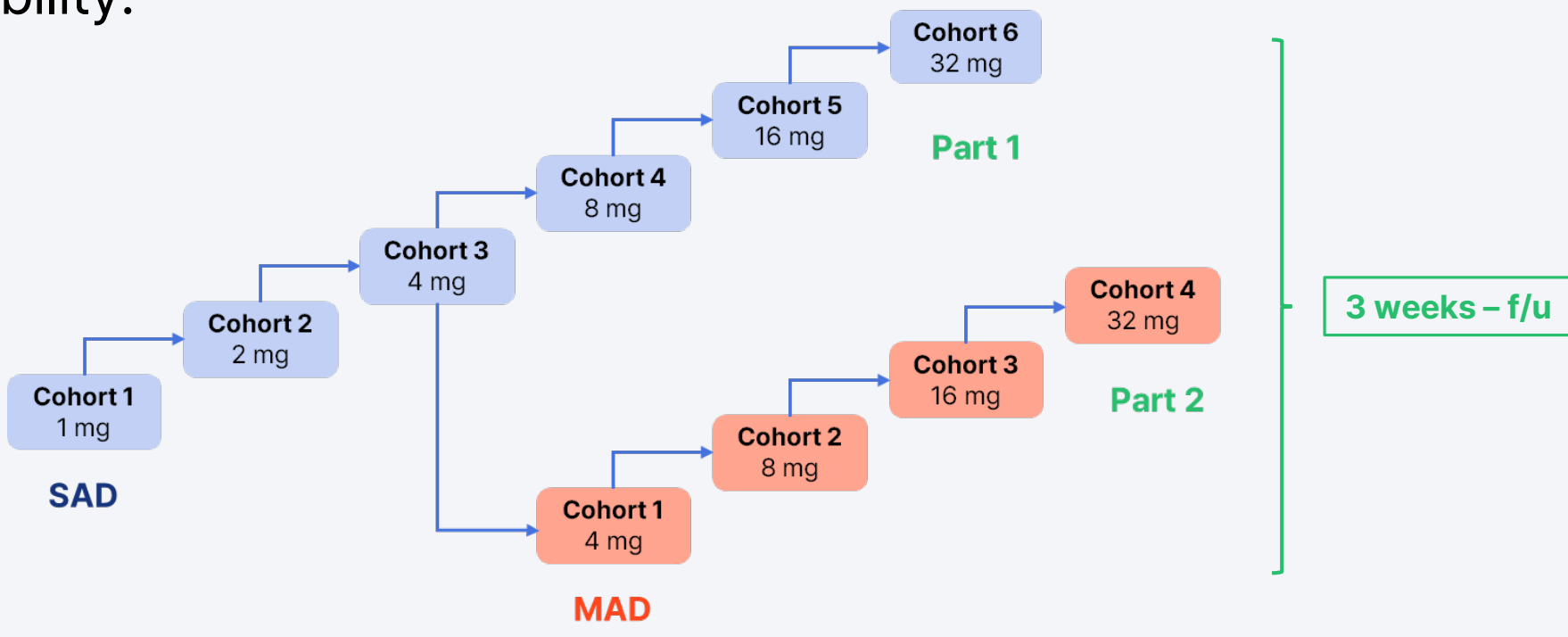
- DA-1726 is a novel oxyntomodulin analogue in Phase 1 clinical development, acting as a dual agonist of the GLP-1 and glucagon receptors (NCT06252220).
- DA-1726 promotes weight loss by reducing caloric intake and increasing energy expenditure.
- DA-1726 has demonstrated superior metabolic benefits over lead compounds in preclinical studies.

OBJECTIVE

This first-in-human phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK), and preliminary pharmacodynamics of DA-1726 in obese, otherwise healthy adults.

METHODS

A total of 90+ subjects were randomized to receive single ascending doses or multiple ascending doses of subcutaneous DA-1726 or placebo in a 2:1 ratio. In the MAD cohorts, dosing was once weekly for 28 days without titration. The primary objectives were to assess safety and tolerability.



- 9 subjects per cohort – DA-1726 : PBO = 6 : 3
 - MAD – Once a week, 28-day; No dose escalation
- Endpoint
 - Primary: Safety and tolerability of DA-1726
 - Secondary: Pharmacokinetic profiles of DA-1726
 - Exploratory: Pharmacodynamic outcomes of DA-1726

RESULTS

Demographics and Baseline Characteristics

Mean (SD)	SAD							MAD				
	1 mg	2 mg	4 mg	8 mg	16 mg	32 mg	Pooled PBO	4 mg	8 mg	16 mg	32 mg	Pooled PBO
N	6	6	6	6	6	6	18	6	6	6	6	12
Age, years	51.7 (9.1)	44.3 (15.0)	41.8 (10.2)	39.7 (15.8)	53.2 (11.3)	50.5 (13.5)	42.5 (11.4)	46.8 (11.8)	45.0 (8.7)	45.8 (13.4)	46.7 (5.9)	38.1 (10.9)
Gender M/F, N	3 / 3	3 / 3	5 / 1	4 / 2	2 / 4	2 / 4	14 / 4	2 / 4	4 / 2	4 / 2	2 / 4	8 / 4
Weight (kg)	89.8 (3.3)	95.0 (20.5)	96.4 (9.3)	91.6 (9.9)	87.2 (8.1)	96.5 (13.3)	92.7 (8.5)	84.4 (11.0)	89.3 (11.8)	96.0 (9.1)	90.4 (14.4)	96.7 (13.3)
BMI (kg/m ²)	33.5 (2.4)	34.2 (4.0)	31.9 (1.9)	32.2 (0.6)	33.0 (3.3)	36.1 (4.9)	33.1 (2.9)	32.6 (2.4)	31.2 (1.1)	35.3 (3.9)	34.0 (2.6)	34.8 (4.2)
FPG (mg/dL)	92.2 (2.6)	99.0 (6.4)	96.2 (2.7)	91.7 (6.9)	97.8 (4.8)	98.5 (8.3)	96.5 (8.7)	104.7 (10.1)	98.7 (12.6)	100.2 (8.4)	97.8 (11.7)	93.4 (5.3)

Favorable Tolerability of DA-1726

- Reported gastrointestinal adverse events were mostly mild in severity.
- No serious adverse events or treatment discontinuations were observed.

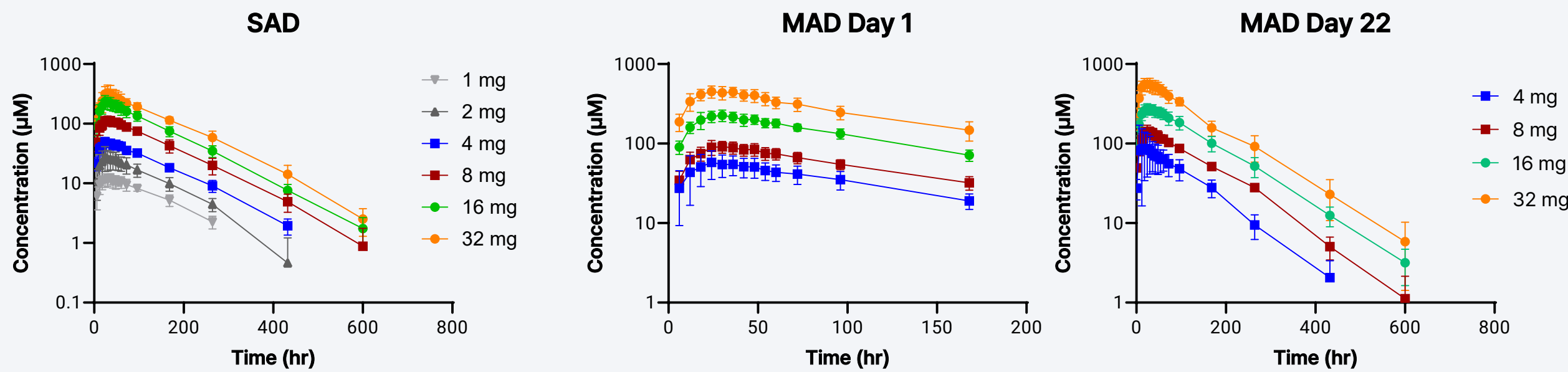
N (%)	SAD					MAD				
	4 mg	8 mg	16 mg	32 mg	Pooled PBO	4 mg	8 mg	16 mg	32 mg	Pooled PBO
Any TEAE	1 (16.7)	0	1 (16.7)	2 (33.3)	4 (22.2)	1 (16.7)	3 (50.0)	2 (33.3)	6 (100)	3 (25.0)
GI disorders	0	0	1 (16.7)	2 (33.3)	2 (11.1)	1 (16.7)	0	1 (16.7)	4 (66.7)	1 (8.3)
Vomiting	0	0	0	2 (33.3)	0	0	0	1 (16.7)	3 (50.0)	1 (8.3)
Nausea	0	0	0	1 (16.7)	1 (5.6)	0	0	1 (16.7)	2 (33.3)	1 (8.3)
Constipation	0	0	1 (16.7)	0	0	1 (16.7)	0	0	2 (33.3)	0
Abdominal Distension	0	0	0	0	0	0	0	0	1 (16.7)	0

SAD cohorts below 4mg are not presented in this table
Data presented here is subject to change as Phase I study is still ongoing

CONCLUSIONS

- Favorable safety and tolerability observed, even in the absence of dose titration
- The gastrointestinal adverse events reported were mostly mild and transient

Summary of Pharmacokinetics Profiles of DA-1726

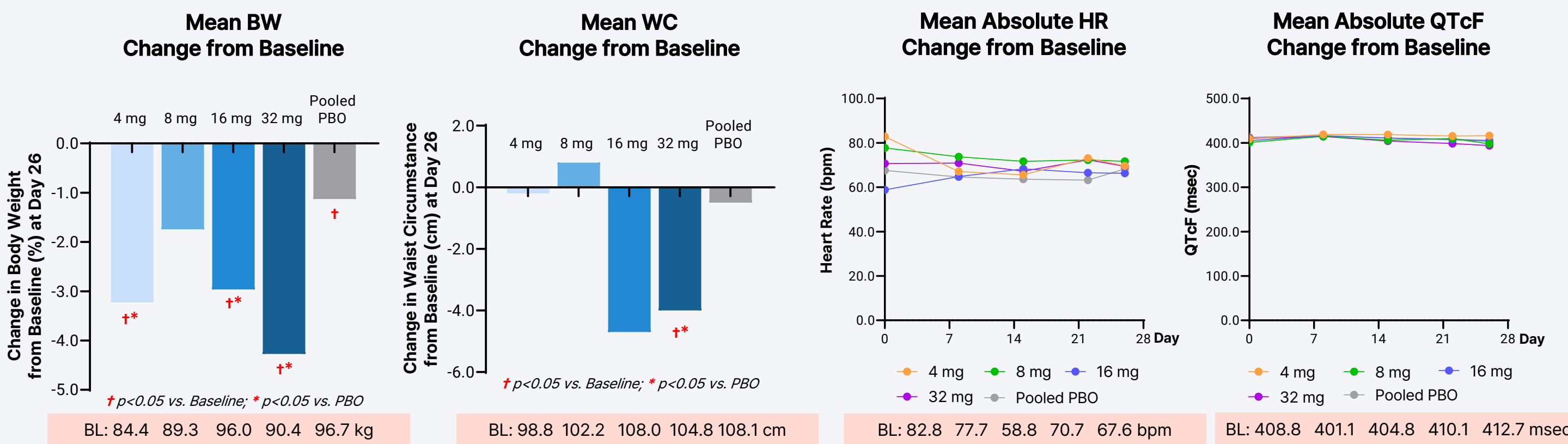


Mean (SD) Median (Range)	4 mg		8 mg		16 mg		32 mg	
	Day 1	Day 22	Day 1	Day 22	Day 1	Day 22	Day 1	Day 22
C _{max} (nM)	60.4 (21.5)	102.1 (79.3)	94.7 (16.9)	145.6 (24.6)	231.5 (33.6)	279.0 (39.3)	461.0 (72.0)	571.3 (101.6)
T _{max} (hr)	24.2 (24-36)	24 (6-30)	30 (24-36)	30 (24-36)	30 (24-30)	24 (23.98-36)	24 (24-36)	24 (18-42)
t _{1/2} (hr)	-	77.7 (7.6)	-	79.1 (9.1)	-	81.9 (6.6)	-	80.3 (13.5)
AUC _{0-tau} (h*nM)	6,070 (1726)	9,094 (3,666)	9,688 (1373)	15,578 (1,017)	23,347 (2978)	31,593 (5,149)	46,102 (8,417)	61,637 (9,422)
AUC _{0-inf} (h*nM)	-	12,239 (4,413)	-	21,417 (494)	-	43,077 (7,941)	-	85,582 (16,386)

T_{max} values are presented as median (min–max)

Metabolic Benefits and Safety of DA-1726

- DA-1726 32 mg achieved up to 6.3% maximum and 4.3% mean reductions at Day 26
- Waist circumference decreased by up to 3.9 in, with effects persisting 2 weeks post-treatment.
- No significant cardiovascular findings, including in heart rate or QTcF, were observed



- PK results indicate linear and dose proportionality, supporting the feasibility of weekly dosing
- Meaningful weight reduction observed at the 32 mg dose supports further clinical evaluation
- Additional cohort(s) are planned to continue to identify the maximum tolerated dose