obesityweek NOV 14-17, 2026 WASHINGTON, DC

Poster-229

DA-1726 Demonstrates Comparable Weight Loss and Distinct Metabolic Profile Compared with Retatrutide

Il-Hoon Jeong[1], Sujin Lee[1], Tae Hyoung Kim[1], Hyung Heon Kim[2], Mi-Kyung Kim[1], Yuna Chae[1]

[1] Dong-A ST Co., Ltd. South Korea [2] MetaVia Inc, United States * Contact.: Yuna Chae, ynchae@donga.co.kr; Mi-Kyung Kim, kmk@donga.co.kr, Hyung Heon Kim, HHKim@metaviatx.com

DONG-A ST MetaVia

BACKGROUND

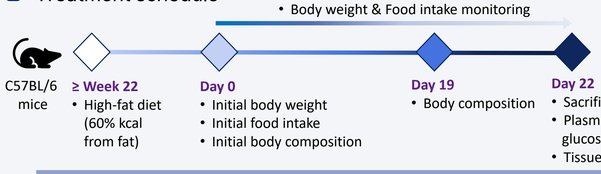
- DA-1726 is a novel oxyntomodulin analogue acting as a dual GLP-1R/GCGR agonist, currently in Phase 1 clinical development for obesity (NCT06252220)
- Although incretin-based therapies achieve substantial weight loss primarily through appetite suppression, concerns regarding inadequate nutritional intake and lean body mass loss highlight the need for complementary weight-loss mechanisms beyond reduced food intake[1,2)]
- Previous preclinical studies demonstrated that DA-1726 achieved greater weight loss and higher energy expenditure than tirzepatide, a GLP-1R/GIPR agonist, despite comparable food intake (ObesityWeek 2025, P-154).

OBJECTIVE

- To evaluate the potential advantages of DA-1726 in weight reduction and metabolic regulation compared with retatrutide, a GLP-1R/GIPR/GCGR triple agonist, in diet-induced obese mice, focusing on food intake, body composition, plasma metabolic parameters, and thermogenesis-related gene expression.

METHODS

- Treatment schedule



Group	Treatment	Dosing regimen
Normal Control	Vehicle	s.c., BIW
HF Control (DIO con)	Vehicle	s.c., BIW
DA-1726 (1726 LD)	DA-1726	300 nmol/kg, s.c., BIW
DA-1726 (1726 HD)	DA-1726	500 nmol/kg, s.c., BIW
Retatrutide (Reta LD)	Retatrutide	100 nmol/kg, s.c., BIW
Retatrutide (Reta HD)	Retatrutide	200 nmol/kg, s.c., BIW

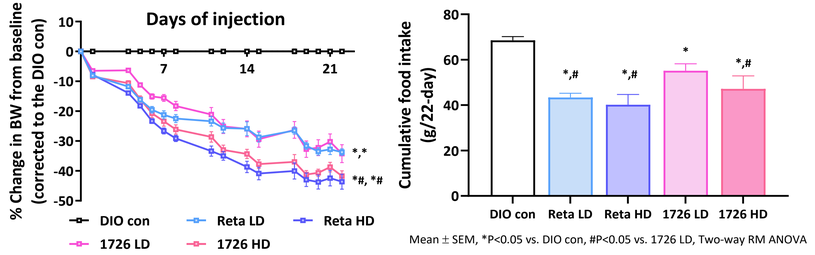
* Subcutaneous (s.c.) * BIW (twice weekly)

*** Dose Selection Rationale (PK Exposure-Based)**

- DA-1726 (500 nmol/kg): Estimated to approximate clinical exposure at 48 mg.
- Retatrutide (200 nmol/kg): Estimated to approximate clinical exposure at 12 mg.

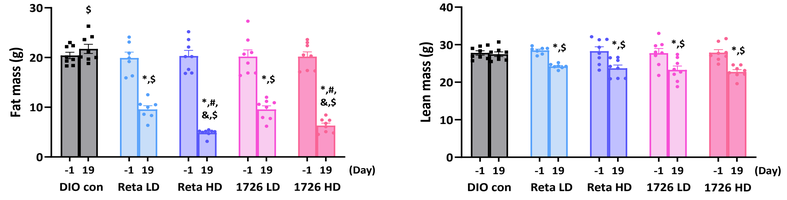
RESULTS

I. Comparable Weight Loss Despite Less Suppression of Food Intake



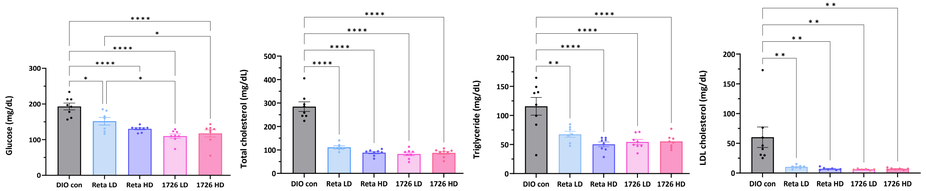
Mean ± SEM, *P<0.05 vs. DIO con, #P<0.05 vs. 1726 LD, Two-way RM ANOVA

II. Comparable Effects on Body Composition



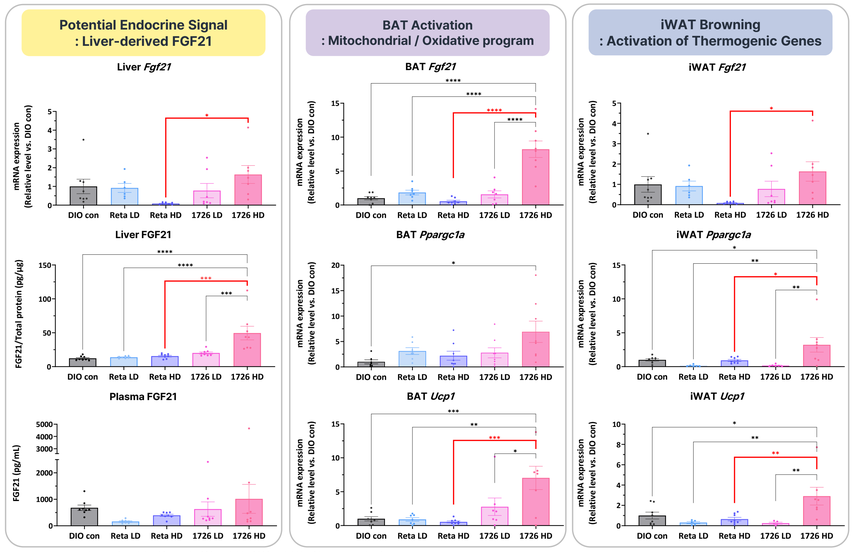
Mean±SEM, *P<0.05 vs. DIO con, #P<0.05 vs. Reta LD, &P<0.05 vs. 1726 LD, $P<0.05 vs. Day -1 (within group), Two-way RM ANOVA

III. Greater Glucose Lowering with Comparable Plasma Lipid Improvements



Mean ± SEM *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001 (One-way ANOVA)

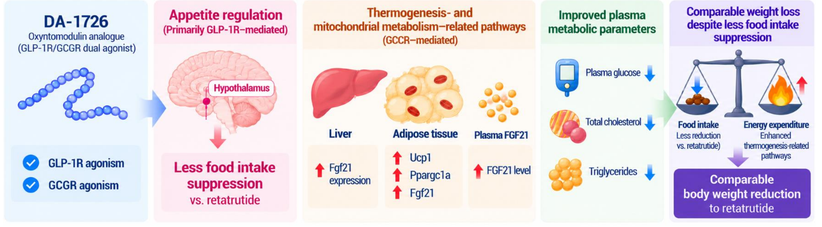
IV. FGF21 Induction and Enhanced Thermogenic Gene Expression in Adipose Tissue



Mean ± SEM *, p<0.05; **, p<0.01;***, p<0.001;****,p<0.0001 (One-way ANOVA)

* Brown Adipose Tissue (BAT) * Inguinal White Adipose Tissue (iWAT)

V. Proposed Mechanism Underlying the Distinct Metabolic Effects of DA-1726



CONCLUSION

- DA-1726 achieved comparable weight loss to Retatrutide with less food intake suppression.
- DA-1726 induced greater BAT thermogenic and iWAT browning-related gene expression, along with increased FGF21 expression and protein levels, while improving plasma glucose and lipid parameters.
- These findings highlight DA-1726's distinct metabolic profile and suggest a greater contribution of GCGR-associated energy expenditure to weight loss than with retatrutide.

1) Obesity. 2025;33(8):1493–1518.
2) Diabetes Obes Metab. 2025;27(5):2720–2729.