DA-1726, a GLP1R/GCGR Dual Agonist, A Promising Approach in Body Composition and Lipid Management

Tae-Hyoung Kim[1†], Il-Hun Jung[1], Su Jin Lee[1], Mi-Kyung Kim[1], Hyung Heon Kim[2], **Yuna Chae**[1*]

[1] Dong-A ST Co., Ltd., Seoul, Republic of Korea

[2] NeuroBo Pharmaceutical, Inc., Boston, MA, USA

[†]Presenter, *e-mail: ynchae@donga.co.kr

BACKGROUND

[1] Kenneth R et. al., 2023. Obesity and Dyslipidemia. Endotext [Internet]
[2] Nutrients. 2018;10(12):1876.

New Flow, New Shift

Disease

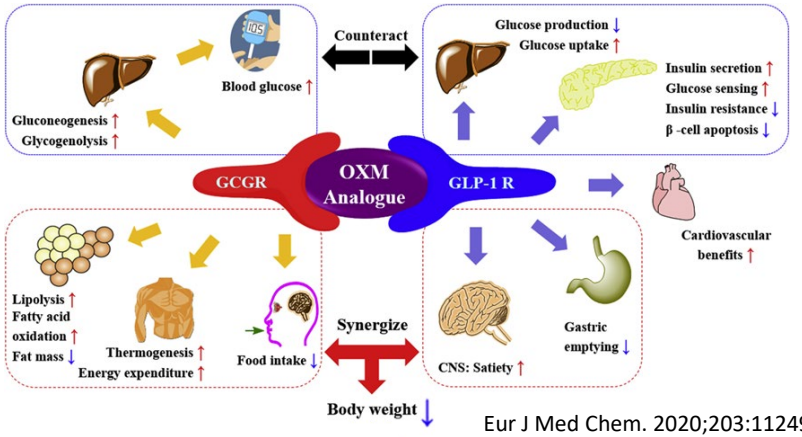
- Obesity is a chronic and complex disease characterized caused by excessive fat accumulation, leading to lipid metabolism abnormalities in many patients, with 60-70% experiencing dyslipidemia[1].
- When treating obesity, weight loss is often accompanied by a reduction in lean body mass. However, from a health perspective, preserving lean body mass is important because its decrease can lead to several negative effects[2].
- Effective treatment should combine weight loss with lipid control and the preservation of lean body mass.
- If a drug could provide beneficial lipid control while minimizing lean body mass loss during weight reduction, it would be an efficient treatment option.

OBJECTIVE

[1] 1403-P (ADA 2022) and 1676-P (ADA 2023) poster presentations
[2] 1668-P (ADA 2023) poster presentations

Oxyntomodulin

- Oxyntomodulin is a gut hormone released from intestinal L-cells after meal ingestion.
- Oxyntomodulin increases appetite suppression and energy expenditure through GLP-1 receptor and glucagon receptor activation, ultimately inducing weight loss.



Eur J Med Chem. 2020;203:112496

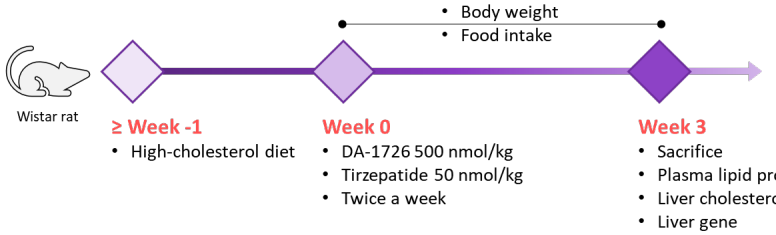
DA-1726

- **DA-1726 is a novel oxyntomodulin analogue** undergoing a Phase 1 clinical trial for obesity. Previous studies demonstrated **superior weight loss effects compared to Semaglutide**[1] and **similar effects to Tirzepatide**[2].
- This study focuses on **the pharmacological effects of improving body composition and lipid profiles** in rodent models.

METHODS AND MATERIALS

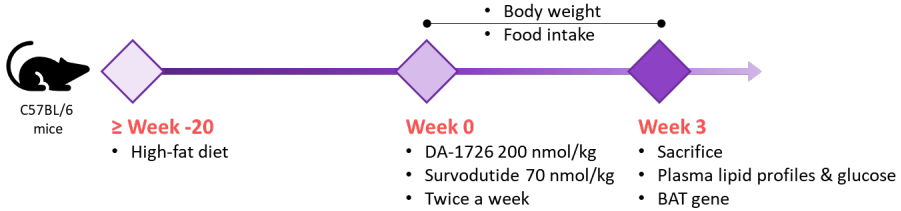
Comparison with Survodutide on Body Weight Loss

- DIO mice were subcutaneously injected with a vehicle or drugs twice a week for three weeks. Major plasma parameters and thermogenesis-related genes in brown adipose tissue were analyzed.



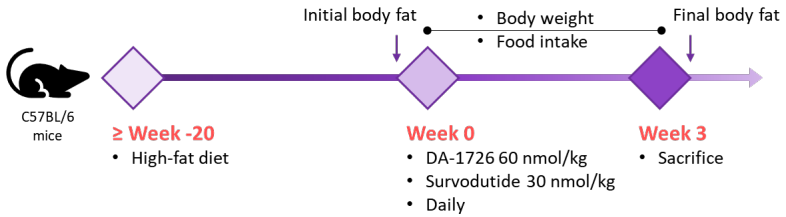
Comparison with Survodutide on Fat Mass Loss

- DIO mice were subcutaneously injected with a vehicle or drugs daily for three weeks. The initial and final values of body fat mass and lean body mass were measured to calculate the mass changes induced by the drugs. The browning of white adipose tissue was analyzed using epididymal fat.



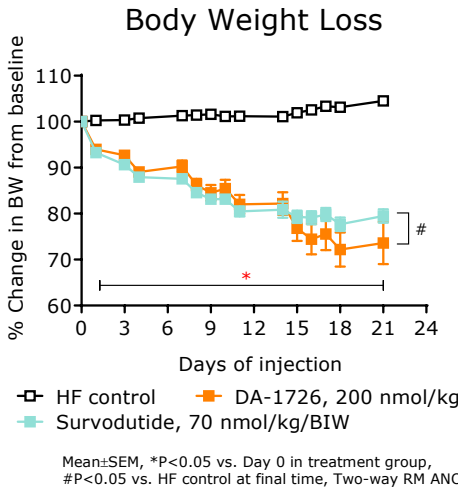
Comparison with Tirzepatide on Lipid-Lowering

- Hyperlipidemic rats were subcutaneously injected with a vehicle or drugs twice a week for three weeks. Major plasma parameters were analyzed through blood chemistry analysis.

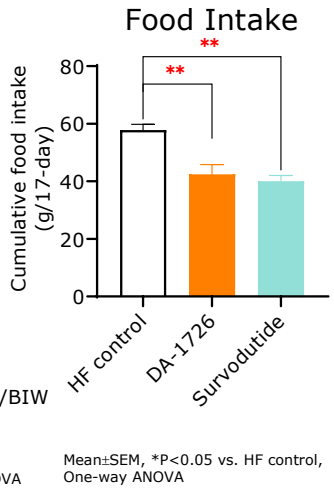


RESULTS – 1.
Comparative Study with Survodutide on Weight Loss & Lipid-Lowering

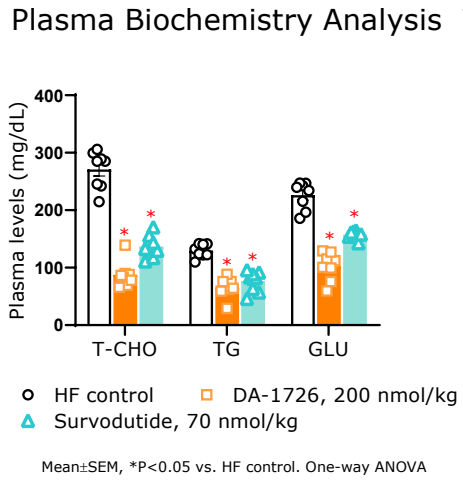
- ☑ **DA-1726 demonstrated superior weight loss efficacy compared to Survodutide despite more food consumption**
- ☑ **DA-1726 effectively lowered T-CHO, TG, and glucose levels while significantly increasing the expression of EE-related genes in brown adipose tissue**



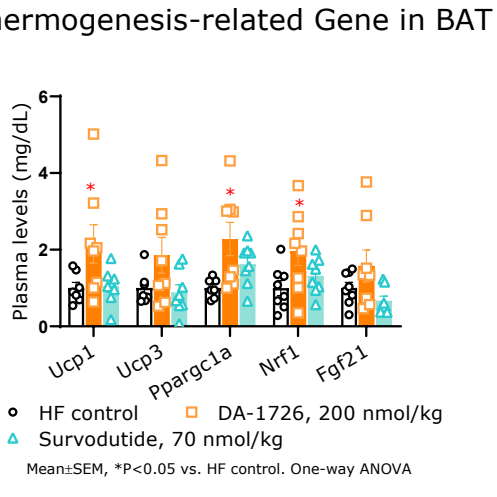
Mean±SEM, *P<0.05 vs. Day 0 in treatment group, #P<0.05 vs. HF control at final time, Two-way RM ANOVA



Mean±SEM, *P<0.05 vs. HF control, One-way ANOVA



Mean±SEM, *P<0.05 vs. HF control. One-way ANOVA

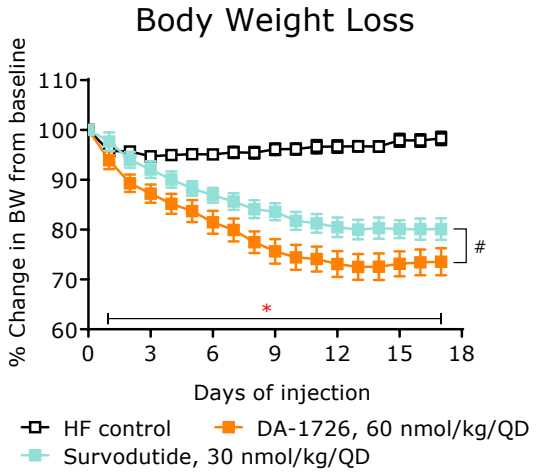


Mean±SEM, *P<0.05 vs. HF control. One-way ANOVA

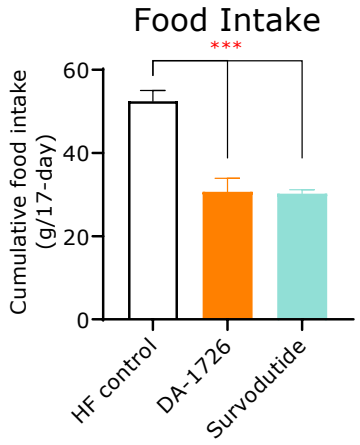
Abbreviation: EE, energy expenditure; BAT, brown adipose tissue

RESULTS – 2.
Comparative Study with Survodutide on Fat Mass Loss

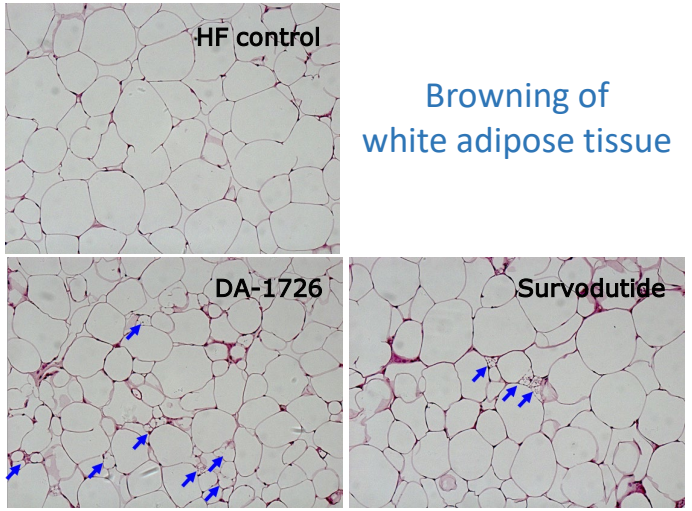
- ☑ **DA-1726 demonstrated superior weight loss efficacy compared to Survodutide in DIO mice under similar dietary intake conditions**
- ☑ **The increase in beige or brown adipose-like cells in white adipose tissue induced by DA-1726 supports the mechanism of enhanced energy expenditure**



Mean±SEM, *P<0.05 vs. Day 0 in treatment group, #P<0.05 vs. HF control at final time, Two-way RM ANOVA



Mean±SEM, *P<0.05 vs. HF control, One-way ANOVA

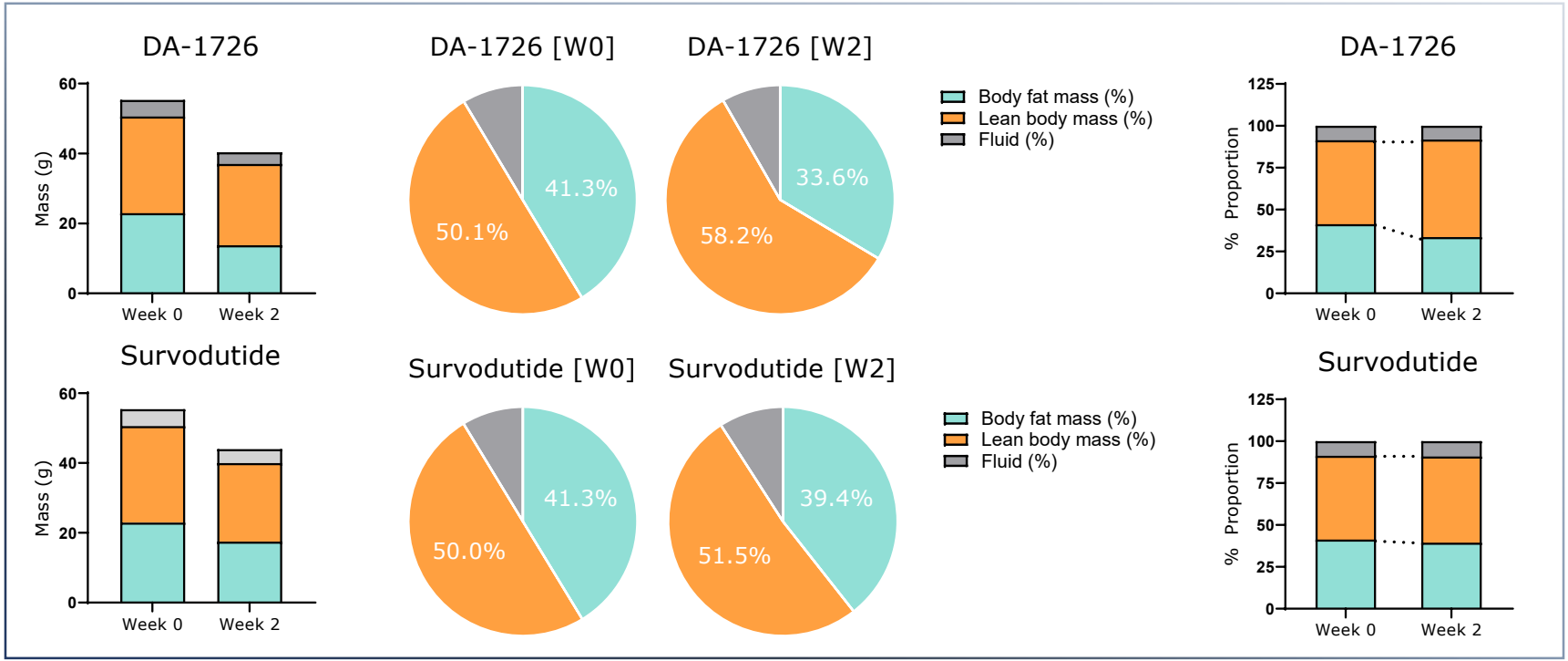


Browning of white adipose tissue

Blue arrows: browning-like adipocytes
Magnification: x200

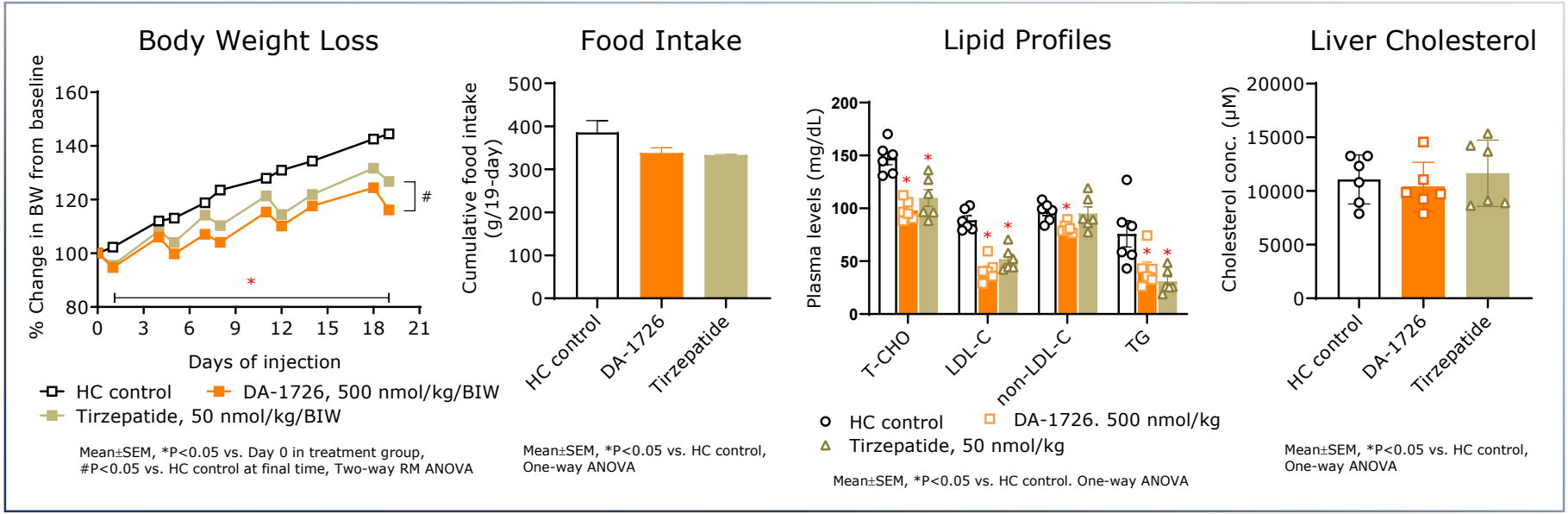
RESULTS – 3.
Comparative Study with Survodutide on Fat Mass Loss cont.

☑ **DA-1726 demonstrated superior body fat mass reduction and lean body mass relative preservation compared to Survodutide**



RESULTS – 3.
Comparative Study with Tirzepatide on Lipid-Lowering

☑ **DA-1726 was more effective in regulating lipid metabolism and suppressing weight gain, even though the rats had a similar food intake to those taking Tirzepatide.**



Conclusion and Summary

- DA-1726 is a novel oxyntomodulin analogue currently in Phase 1 clinical trials for obesity.
- Compared to Survodutide, DA-1726 led to greater weight loss, superior reduction in body fat mass, and better preservation of lean body mass in DIO mice.
- In a hypercholesterolemic rat model, DA-1726 was more effective in regulating lipid metabolism despite having a similar food intake to those taking Tirzepatide..
- These findings suggest that DA-1726 is a highly effective obesity treatment, offering more benefits in weight loss, overall body composition improvement, and lipid reduction compared to competitors.