769-P

ADA 2025

Bofanglutide (GZR18), a Novel GLP-1 RA, improved glycemic control and cardiometabolic risk factors in Chinese patients with T2D

Wenda Li[1], Ming Liu[2], Ruihua Dong[3], Xuhong Wang[4], Jing Zhao[5], Liyuan Zhao[5], Anshun He[5], Tian Xie[5], Yue Li[5], Haiya Wu[1], Spencer Carter[1], Zhong-Ru Gan[5], Wei Chen[5]

[1]Gan & Lee Pharmaceuticals, Bridgewater, NJ, USA; [2]Tianjin Medical University General Hospital, Tianjin, China; [3]Beijing Friendship Hospital, Capital Medical University, Beijing, China; [4]Beijing Luhe Hospital, Capital Medical University, Beijing, China; [5]Gan & Lee Pharmaceuticals, Beijing, China.

Introduction/Objective

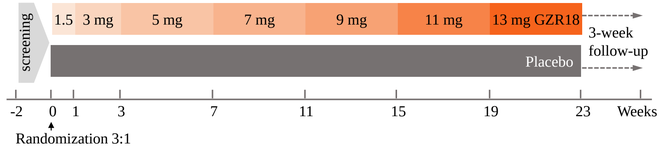
- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) targeting type 2 diabetes (T2D) and obesity are advancing to optimize efficacy and provide comprehensive metabolic improvements [1,2].
- Bofanglutide (also known as GZR18), is a novel long-acting GLP-1 RA being developed for treatment of T2D and obesity [3,4].
- In the first-in-human phase 1 study, GZR18 demonstrated a favorable safety and tolerability profile in healthy participants from both American and Chinese populations [4].
- This phase 2a study was designed to evaluate the safety and efficacy of GZR18 in Chinese adults with T2D.

Methods

Study design

In this randomized, double-blind, placebo-controlled phase 2a trial, eligible participants were adults aged 18 to 65 years with a confirmed diagnosis of T2D inadequately controlled by lifestyle interventions and/or with irregular use of OADs, HbA1c level of 7.0% to 10 %, and FPG <13.9 mmol/L.

Following a 2-week screening period, eligible participants were randomized 3:1 to receive GZR18 or placebo for 23 weeks, followed by 3-week follow-up.



Endpoints

Primary: The incidence of adverse events.

Secondary: Changes in HbA1c, FPG and GA from baseline to week 23; Proportion of participants achieving HbA1c targets of less than 7.0% and 6.5% or less at week 23; Changes in body weight and waist circumference from baseline to week 23; Changes in blood lipids and blood pressure from baseline to week 23.

HbA1c= Glycated hemoglobin A1c; FPG= Fasting plasma glucose; T2D= Type 2 diabetes; OADs= Oral anti-diabetic drugs; GA= Glycated albumin.

Results

Subject disposition

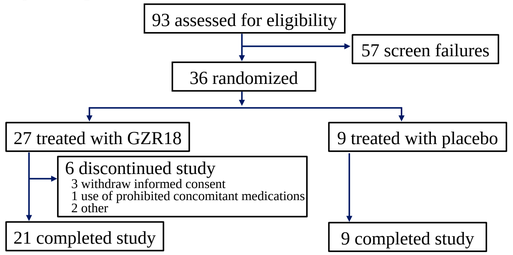


Table 1. Demographics and baseline characteristics

Characteristics	GZR18, N=26	Placebo, N=9
Age (years)	54.8 (10.1)	49.7 (11.6)
Sex (Male), n (%)	18 (69.2)	5 (55.6)
Race (Han), n (%)	24 (92.3)	9 (100)
HbA1c (%)	8.3 (0.7)	8.2 (0.6)
GA (%)	21.7 (3.7)	21.4 (2.7)
FPG (mmol/L)	9.8 (1.7)	9.9 (1.3)
Duration of diabetes (years)	4.1 (4.5)	4.6 (3.7)
Body Weight (kg)	76.1 (13.0)	72.2 (13.1)
BMI (kg/m^2)	27.1 (3.8)	25.8 (2.8)
Waist circumference (cm)	94.9 (9.5)	91.2 (6.5)

Data were Mean (SD) or n (%). BMI= Body mass index.

GZR18 induced a placebo-adjusted 1.93% HbA1c reduction

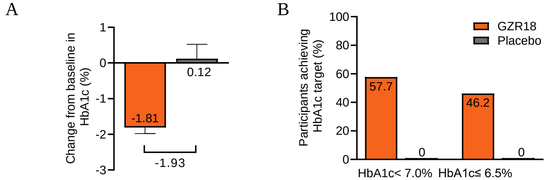


Figure 1. HbA1c change from baseline to week 23 (A); Proportion of participants with HbA1c targets of <7.0% and ≤ 6.5% at week 23 (B).

GZR18 achieved greater reductions in FPG and GA

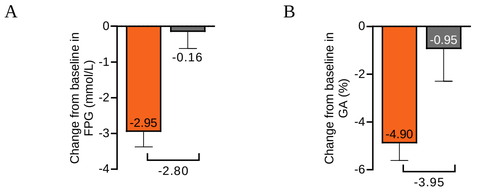


Figure 2. Changes in FPG (A) and GA (B) from baseline to week 23.

GZR18 induced robust weight reduction (-9.25 %)

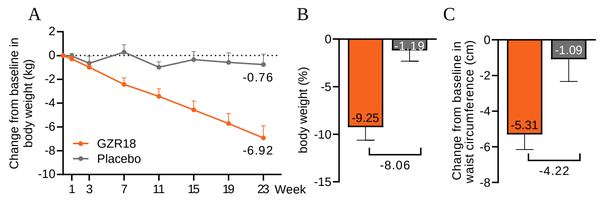


Figure 3. Body weight change from baseline over time (A) and percentage change from baseline to week 23 (B); Change in waist circumference from baseline to week 23 (C).

GZR18 improved blood lipids and blood pressure

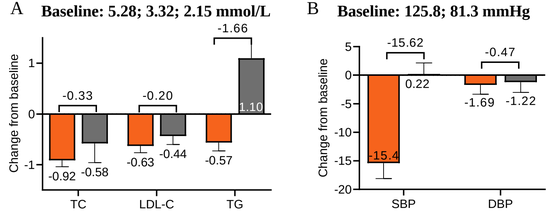


Figure 4. Changes in blood lipids (A) and blood pressure (B) from baseline to week 23. TC= Total cholesterol; LDL-C= Low-density lipoprotein cholesterol; TG= Triglycerides; SBP= Systolic blood pressure; DBP= Diastolic blood pressure.

Table 2. Summary of adverse events (AEs)

GZR18 was well tolerated, with most TEAEs being mild to moderate in severity. Two SAEs were reported, one case of sudden death and one case of enteritis, neither were considered IP-related by investigator.

The most frequently reported adverse events were gastrointestinal TEAEs, including nausea, diarrhea and vomiting.

AEs, n(%)	GZR18, N=27	Placebo, N=9
TEAE	25 (92.6)	8 (88.9)
Grade 3 or higher TEAE	3 (11.1)	1 (11.1)
IP-related TEAE	23 (85.2)	3 (33.3)
TEAE leading to discontinuation from the study	3 (11.1)	0 (0)
SAE	2 (7.4)	0 (0)
IP-related SAE	0 (0)	0 (0)
Death	1 (3.7)	0 (0)
Injection site reaction	3 (11.1)	1 (11.1)
Hypoglycemia	0 (0)	0 (0)
Gastrointestinal TEAE	15 (55.6)	2 (22.2)
Nausea	10 (37.0)	0 (0)
Diarrhea	8 (29.6)	2 (22.2)
Vomiting	3 (11.1)	1 (11.1)

IP= Investigational product; TEAE= Treatment-emergent adverse event; SAE= Serious adverse event.

Conclusion

- GZR18 was well tolerated in Chinese adults with T2D, demonstrating significant HbA1c reductions along with comprehensive improvements on body weight, blood pressure and lipid profile.
- These findings support further investigation of GZR18 for the treatment of T2D in future clinical trials.

References

1. Marso, S.P., et al. N Engl J Med. 2016 Jul 28;375(4):311-22.
2. Marso, S.P., et al. N Engl J Med. 2016 Nov 10;375(19):1834-1844.
3. Zhang, M., et al. Eur J Pharmacol. 2022 Aug 5;928:175107.
4. Liu, Y., et al. Diabetes Obes Metab. 2025 May;27(5):2777-2789.

Note: Data of all figure were plotted as least squares mean and standard error. Treatment difference were presented as mean.

This work was supported by Gan & Lee Pharmaceuticals and was registered with clinicaltrials.gov (NCT06256523).