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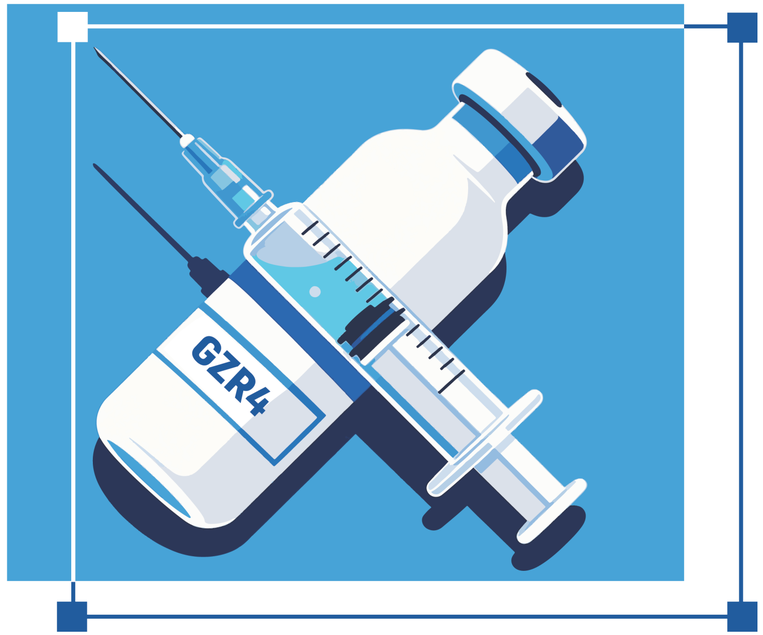


Overview of the SUPER phase 3 clinical development program for investigational once-weekly insulin Insulin GZR4 injection

The SUPER clinical development program in China comprises four phase 3 clinical trials evaluating the efficacy and safety of once-weekly insulin GZR4 injection in adults with type 2 diabetes, with an estimated total enrollment of more than 2,000 participants.

Gantt chart

SUPER-1

Insulin-naïve adults with T2D

580 participants
52 weeks (primary outcome week 26) vs. insulin glargine U100
Non-inferiority/Superiority* tests

SUPER-2

Basal insulin treated adults with T2D

620 participants
26 weeks vs. insulin degludec
Non-inferiority/Superiority* tests

SUPER-3

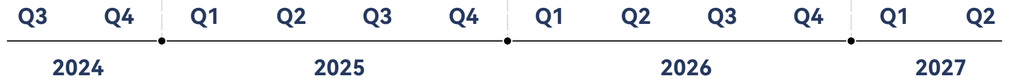
Basal-bolus insulin, premixed insulin or dual insulin analogue treated adults with T2D

580 participants
26 weeks vs. insulin glargine U100 + insulin aspart
Non-inferiority/Superiority* tests

SUPER-8

Basal insulin treated adults with T2D

300 participants
26 weeks vs. insulin icodec
Non-inferiority/Superiority * tests



Global development program

Phase 3 program in China:

- Aim to confirm efficacy and safety across four large-scale phase 3 trials
- Expected completion in 2026

Global program:

- **Completed:** Phase 1 steady-state glucose clamp studies comparing GZR4 with insulin degludec and insulin icodec are completed in Europe

*Superiority tests were conducted for each study if GZR4 injection was declared non-inferior to the daily or weekly basal comparator for the primary endpoint analysis.
Note: Study start dates are based on Gan & Lee's official press releases, while projected completion dates are based on estimated timelines registered on ClinicalTrials.gov.

SUPER 1

Once-weekly insulin GZR4 injection vs. once-daily insulin glargine U100 in Chinese adults with type 2 diabetes who have not previously been treated with insulin

Trial design

- Open-label, randomized
- Treat-to-target

Endpoints

Primary:

- The change in HbA_{1c} from baseline to week 26

Secondary:

- The change in HbA_{1c} from baseline to week 52
- The change in fasting plasma glucose (FPG) from baseline to week 26 and week 52
- The time in target blood glucose range (3.9–10.0 mmol/L) from weeks 25–26 and weeks 51–52
- Number of level 2 or level 3 hypoglycemia episodes

Inclusion criteria:

Female or male, age ≥ 18

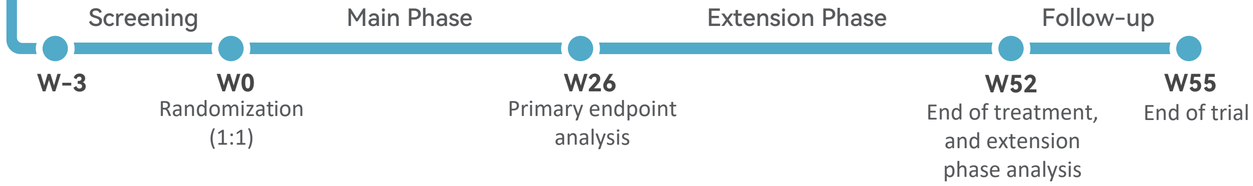
HbA_{1c}: 7.0–11.0%

Insulin-naïve T2D* treated with OADs** ± GLP-1 RA s.c.

Once-weekly insulin GZR4 injection + non-insulin glucose-lowering agents

Once-daily insulin glargine U100 + non-insulin glucose-lowering agents

Duration (weeks)



*Short-term insulin treatment for a maximum of 14 days prior to the day of screening was allowed, as was prior insulin treatment for gestational diabetes.

**Sulfonylureas or glinides were administered at a reduced (50%) dose at the discretion of the investigator, and maintained at the reduced dose throughout the treatment period.

SUPER 2

Once-weekly insulin GZR4 injection vs. once-daily insulin degludec in Chinese adults with type 2 diabetes who have previously been treated with basal insulin

Trial design

- Open-label, randomized
- Treat-to-target

Endpoints

Primary:

- The change in HbA_{1c} from baseline to week 26

Secondary:

- The change in fasting plasma glucose (FPG) from baseline to week 26
- The time in target blood glucose range (3.9–10.0 mmol/L) from weeks 25–26
- Number of level 2 or level 3 hypoglycemia episodes

Inclusion criteria:

Female or male, age ≥ 18

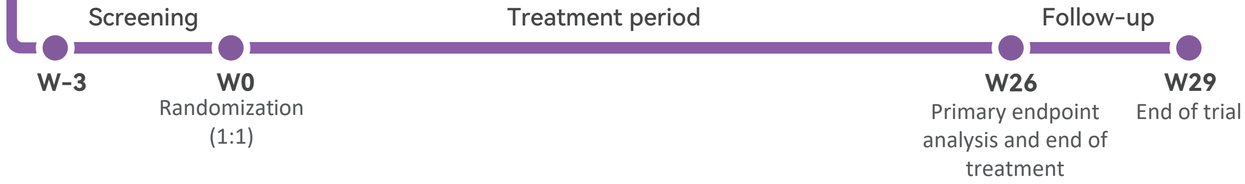
HbA_{1c}: 7.0–10.0%

T2D treated with OD/BID basal insulin ± OADs* ± GLP-1 RA s.c.

Once-weekly insulin GZR4 injection ± non-insulin glucose-lowering agents

Once-daily insulin degludec ± non-insulin glucose-lowering agents

Duration (weeks)



*Sulfonylureas and glinides were discontinued at randomization.

SUPER 3

Once-weekly insulin GZR4 injection vs. once-daily insulin glargine U100 in Chinese adults with type 2 diabetes previously treated with basal-bolus insulin therapy

Trial design

- Open-label, randomized
- Treat-to-target

Endpoints

Primary:

- The change in HbA_{1c} from baseline to week 26

Secondary:

- The change in fasting plasma glucose (FPG) from baseline to week 26
- The time in target blood glucose range (3.9–10.0 mmol/L) from weeks 25–26
- Number of level 2 or level 3 hypoglycemia episodes

Inclusion criteria:

Female or male, age ≥ 18

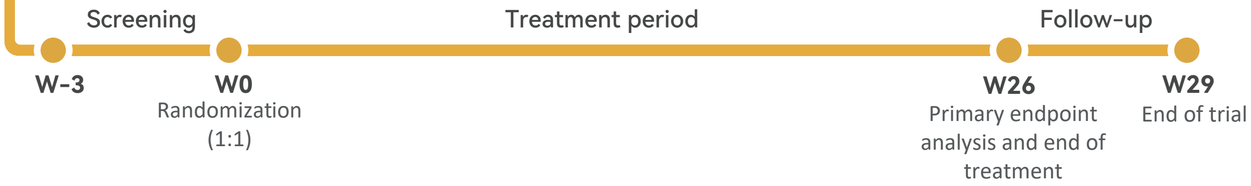
HbA_{1c}: 7.0–10.0%

T2D treated with basal-bolus insulin, premixed insulin or dual insulin ± OADs* ± GLP-1 RA s.c.

Once-weekly insulin GZR4 injection + insulin aspart ± non-insulin glucose-lowering agents

Once-daily insulin glargine U100 + insulin aspart ± non-insulin glucose-lowering agents

Duration (weeks)



*Sulfonylureas and glinides were discontinued at randomization.

SUPER 8

Once-weekly insulin GZR4 injection vs. once-weekly icodec in Chinese adults with type 2 diabetes who have previously been treated with basal insulin

Trial design

- Open-label, randomized
- Treat-to-target

Endpoints

Primary:

- The change in HbA_{1c} from baseline to week 26

Secondary:

- The change in fasting plasma glucose (FPG) from baseline to week 26
- The time in target blood glucose range (3.9-10.0 mmol/L) from weeks 25-26
- Number of level 2 or level 3 hypoglycemia episodes

Inclusion criteria:

Female or male, age ≥ 18

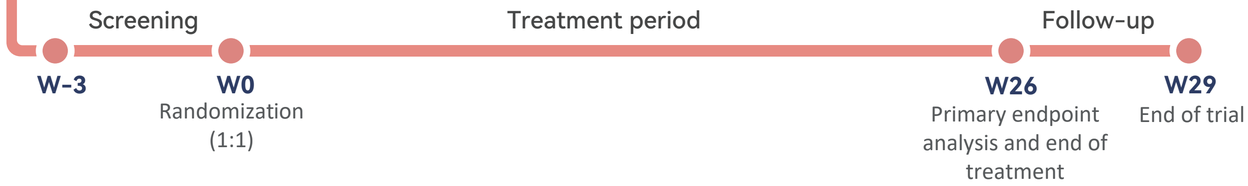
HbA_{1c}: 7.0-10.5%

T2D treated with OD/BID basal insulin or once-weekly insulin icodec ± OADs* ± GLP-1 RA s.c.

Once-weekly insulin GZR4 injection ± non-insulin glucose-lowering agents

Once-weekly insulin icodec ± non-insulin glucose-lowering agents

Duration (weeks)



*Sulfonylureas and glinides were discontinued at randomization.

Abbreviations

BID, twice a day; CGM, continuous glucose monitoring; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1C , glycated hemoglobin; OAD, oral antidiabetic medicine; OD, once daily; s.c., subcutaneous; T2D, type 2 diabetes; U100, 100 units per milliliter

Glossary

Level 2 hypoglycemia: Defined as a glucose < 3.0 mmol/L (< 54 mg/dL)

Level 3 hypoglycemia: A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia, irrespective of glucose level.

Insulin-naïve: People with type 2 diabetes who have not previously been treated with insulin.

References

SUPER 1: NCT06767735. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06767735
SUPER 2: NCT06767748. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06767748
SUPER 3: NCT06767761. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT06767761
SUPER 8: NCT07165223. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT07165223

Note: Study start dates are based on Gan & Lee's official press releases, while projected completion dates are based on estimated timelines registered on ClinicalTrials.gov.

Gan & Lee