*These results are supplied for informational purposes only.*
*Prescribing decisions should be made based on the approved package insert in the country of prescription.*

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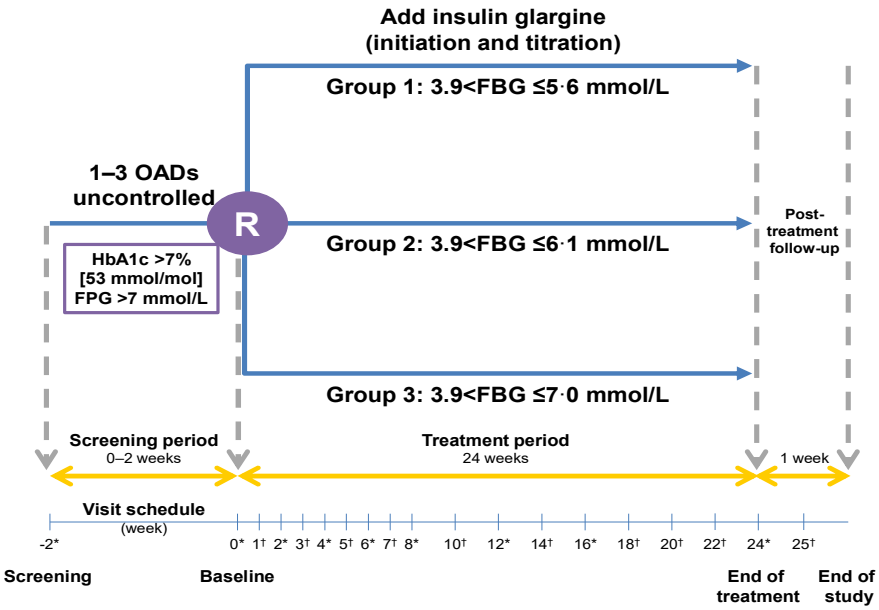
|---|---|
| **Sponsor:** Sanofi<br>**Drug substance(s):** INSULIN GLARGINE | **Study Identifiers:** U1111-1172-1058, NCT02545842<br>**Study code:** LANTUL07190 |
| **Title of the study:** Titration target for Chinese type 2 diabetes mellitus patients using insulin glargine 100 U/mL to achieve glycaemic goals: an assessment of three different fasting plasma glucose targets- BEYOND III/FPG GOAL study | |
| **2015Study center(s):** 44 centers in China | |
| **Study period:**<br>Date first subject enrolled: 07/Sep/2015<br>Date last subject completed: 20/Apr/2018 | |
| **Phase of development:** IV | |
| **Objectives:**<br>The primary objective of the study was to identify the optimal fasting glucose target for Chinese patients with type 2 diabetes that maximized the proportion of patients achieving an HbA1c <7.0% | |
| **Methodology:**<br>This is a 24-week, multicenter, open-label, randomized controlled trial.<br>After a 0-2 weeks screening period, the patients were stratified by the use of SU (with or without) and randomized with a centralized randomization service (IVRS/IWRS) using a 1:3:3 ratio to one of the three groups: Group 1 (3.9<FBG≤ 5.6 mmol/l), Group 2 (3.9<FBG≤ 6.1 mmol/l) or Group 3(3.9<FBG≤ 7.0 mmol/l). The efficacy parameters were evaluated after the 24-weeks treatment period. The safety parameters were evaluated at the end of the study.<br>  <br><br>FBG, self-monitored fasting blood glucose; FPG, laboratory-measured fasting plasma glucose; OADs, oral anti-hyperglycaemic drugs. *On-site visit; †Phone call. | |

| | |
|---|---|
| **Number of subjects:** | Planned: 934 subjects |
| | Randomized: 947 subjects |
| | Treated: 947 subjects |
| **Evaluated:** | |
| | Efficacy: 914 subjects |
| | Safety: 936 subjects |

**Diagnosis and criteria for inclusion:**

- 18 - 65 years old
- Type 2 diabetes patients insufficient controlled by 1-3 OADs with stable dose at least 3 months:
    - if on 1 OAD, provided with the following doses (including but not limited to):
        a. α-glucosidase inhibitor: 100 mg, tid;
        b. metformin: 1.5-2.0 g/day;
        c. sulphonylurea (SU): sub-maximum (half dose above) to maximum tolerated dose (details see the package inserts) ;
        d. thiazolidinediones: e.g. pioglitazone, 30-40 mg/day

    Besides the medications listed above, if on 1 OAD, others should be maximum tolerated dose allowed in package insert.

    - if on 2-3 OADs, any range of dose is acceptable
- HbA1c >7.0%, and ≤ 10.5%
- FPG > 7 mmol/L (biochemistry result)
- Body mass index (BMI) ≥ 20 kg/m2, and ≤ 40 kg/m2
- Diabetes duration ≥ 1year
- Physician decides to and the patient is willing to start basal insulin (BI) treatment
- Willing to join the study and sign the informed consent

**Study treatments**

All patients in the three groups initiated insulin glargine 100 U/mL (Gla-100) at a recommended initial dose of 0.2 U/kg, and 4U adjustment was allowed at the discretion of investigators based on patient's medical condition. The current type(s) and dose(s) of OAD(s) remained unchanged. Patient continued to receive their baseline OADs for the duration of the study, with the only changes at the discretion of investigators based on safety reasons.

During the study, patients measured their FBG daily using a blood glucose meter and the study physicians reviewed the self-monitored FBG values and titrated the basal insulin dose at each study visit. The FBG targets for the three groups were lower than 5.6 mmol/L, 6.1 mmol/L, and 7.0 mmol/L, respectively.

The lowest value of the last three consecutive self-monitored FBG values was used for decisions about insulin titration at each visit. The titration regimen was as follows:

| ***FBG (mmol/L)*** | ***Insulin Dose*** |
|---|---|
| All Groups < 3.9 mmol/L or nocturnal hypoglycemia | - 2 U |
| Group 2: 3.9 < FBG ≤ 5.6 mmol/L<br>Group 3: 3.9 < FBG ≤ 6.1 mmol/L | Decrease1~2 U or no change at investigator's discretion |
| Group 1: 3.9 < FBG ≤ 5.6 mmol/L<br>Group 2: 5.6 < FBG ≤ 6.1 mmol/L<br>Group 3: 6.1 < FBG ≤ 7.0 mmol/L | No change |
| Group 1: 5.6 < FBG < 10.0 mmol/L<br>Group 2: 6.1 < FBG < 10.0 mmol/L<br>Group 3: 7.0 < FBG < 10.0 mmol/L | + 2 U |
| All groups: FBG ≥ 10.0 mmol/L | Increase 2~4 U at investigator's discretion |

The reasons for "no titration" were collected during the entire study period. Meanwhile, a titration committee composed of the Principal Investigator (PI) and medical manger from Sanofi was established to periodically monitor titration at all involved sites.

**Duration of treatment:** 24 weeks

**Duration of observation:** 27 weeks

**Criteria for evaluation:**

- **Primary endpoint:**
  - ✓ The percentage of patients achieving HbA1c < 7.0% at week 24
- **Secondary endpoints:**
  - ✓ The percentage of patients achieving HbA1c < 7.0% without confirmed hypoglycemia (self-monitored blood glucose [SMBG]≤ 3.9 or 3.0 mmol/L) at week 24
  - ✓ The reduction of HbA1c from baseline to week 24
  - ✓ The reduction of FPG/FBG and PPG from baseline to week 24
  - ✓ The distribution of patients with an FPG or FBG of ≤ 5.6 mmol/L, 5.6–6.1 mmol/L, 6.1–7.0 mmol/L and >7.0 mmol/L at week 24
  - ✓ Insulin dose at week 24
  - ✓ Change in body weight from baseline to week 24

- ✓ Rate of hypoglycemia, including symptomatic hypoglycemia, confirmed hypoglycemia (SMBG ≤3.9 or 3.0 mmol/L), severe hypoglycemia, and nocturnal hypoglycemia at week 24

- **Other exploratory endpoints:**
  - ✓ The proportion of patients with an HbA1c <7.0% according to groups re-divided by actual 24-week FPG levels
  - ✓ The relationship between mean FBG over 1–12 weeks and HbA1c at 12 weeks and between mean FBG over 13–24 weeks and HbA1c at 24 weeks.
- **Safety endpoints:**
  - ✓ Frequency and severity of Adverse Events (AEs) at the end of the study

**Statistical methods:**

**Sample size determination:**

The primary efficacy endpoint was the percentage of patients achieving HbA1c <7.0% at week 24. Two hierarchical null hypotheses (H1 and H2) were defined to address the primary objective of the trial. The hypotheses were tested in sequence. H2 was tested only if H1 is rejected.

The null hypotheses were:

- H1: No difference between Group 1 (target: FBG ≤ 5.6 mmol/L) and Group 3 (target: FBG ≤ 7.0 mmol/L) on the primary efficacy endpoint
- H2: No difference between Group 2 (target: FBG ≤ 6.1 mmol/L) and Group 3 (target: FBG ≤ 7.0 mmol/L) on the primary efficacy endpoint

Subjects were randomized according to 1:3:3 ratios. 120 subjects in Group 1 and 360 subjects in Group 3 achieved 85% power to detect the between-group differences of 15% (45%* vs. 30%) at a 2-sided significant level of 0.05. 360 subjects in Group 2 and 360 subjects in Group 3 also achieved 80% power to detect the between-group differences of 10% (40%* vs. 30%). Assuming a dropout rate of approximately 10%, the total number of randomized subjects was 934 (134 in Group 1, 400 in Group 2 and 400 in Group 3).

* Mainly referring to the ATLAS study, a treat-to-target study, using 6.1mmol/L as the FPG target and achieving a control rate of 43.8% at week 24.

**Analysis set:**

Full analysis set (FAS): defined as all patients in the randomized population that have been dispensed at least one dose of study medication and contributed at least one treatment efficacy value. The primary analysis was based on FAS.

Safety set (SS): defined as randomized population who did actually receive at least 1 dose or part of a dose of IMP analyzed according to the treatment actually received.

**Primary analysis:**

For the primary endpoint of patients achieving an HbA1c <7.0%, the crude proportions of patients achieving the goal at 24 weeks were calculated with associated 95% confidence intervals estimated using the normal approximation to the binomial. For the analyses, missing data were imputed using the last observation carried forward (LOCF) method.

Pre-planned hierarchical testing was used for the primary endpoint: only if the difference between Group 1 and Group 3 was significant (nominal p-value <0.05), would testing proceed to compare the difference between Group 2 and Group 3. To compare between-group treatment effect differences, especially Group 3 as a control group, we further pre-specified exploratory multiple comparisons of interest using the Bonferroni correction method (adjusting p-value to 0.025).

**Analysis of secondary endpoints:**

The secondary endpoints of patients achieving an HbA1c <7.0% without hypoglycemia was similar to the primary analysis. Other secondary endpoints including changes from baseline in HbA1c, FBG, 2-hr PPG, insulin dose and body weight were modelled using ANCOVA with terms for treatment group and baseline value as covariate (Dunnett's test was applied for multiple

comparisons between Groups 1 and 3 and between Groups 2 and 3). Missing data were not imputed for the remaining secondary endpoints.

**Summary:**

Of 947 patients randomized (Group 1, 3.9<FBG≤ 5.6 mmol/L, n=136; Group 2, 3.9<FBG≤ 6.1 mmol/L, n=405; Group 3, 3.9<FBG ≤ 7.0 mmol/L, n=406), 914 were analyzed (mean age 53.9±7.4 years; mean HbA1c 8.59%), and 885 (93.4%) completed the study.

At 24 weeks, 44.4%, 46.1%, and 37.7% of patients achieved an HbA1c <7.0% in Group 1, 2, and 3, respectively (p=0.017; Group 2 vs Group 3). Significantly more patients in Group 2 than in Group 3 (45.0% vs 36.5%; p=0.014) achieved an HbA1c <7.0% without confirmed hypoglycemia (SMBG ≤ 3.0 mmol/L). Confirmed hypoglycemia (SMBG ≤ 3.9 mmol/L) was significantly more frequent in Group 1 vs Group 3 (38.9 vs 23.3%, p<0.001) but not in Group 2 vs Group 3 (27.5% vs 23.3%; p=0.177). Confirmed hypoglycemia (SMBG ≤ 3.0 mmol/L) was reported in 4.8%, 2.0% and 3.8% of patients in Groups 1, 2 and 3, respectively.

Based on the lowest of three consecutive FBG values, the proportions of patients achieving an FBG within their target range at 24 weeks were 70.1%, 67.6% and 79.0% in Groups 1, 2 and 3, respectively. However, based on laboratory fasting plasma glucose (FPG) measurements, these proportions were 31.9%, 39.5% and 47.7%, respectively.

Re-divided by the actual FPG level at 24 weeks, significantly more patients with an FPG ≤ 5.6 mmol/L (68.7%, p<0.001) and 5.6<FBG≤ 6.1 mmol/L (58.2%, p=0.013) achieved an HbA1c <7.0% than those with 6.1<FBG≤ 7.0 mmol/L (43.6%).

Linear regression analysis demonstrated a significant association between lower self-monitored FBG and lower HbA1c levels. These associations remained significant after adjustment for baseline covariates

**Population characteristics:**

947 patients from 44 sites in China were randomly assigned to a target 3.9<FBG≤ 5.6 mmol/L (n=136), 3.9<FBG≤ 6.1 mmol/L (n=405), or 3.9<FBG≤ 7.0 mmol/L (n=406). Of all enrolled patients, 885 (93.5%) of them completed the study and 62 (6.5%) patients discontinued. The reasons for discontinuation mainly including adverse events (0.8%), non-compliance with study drug (1.5%), major protocol violation (0.6%), study terminated by subject (2.3%), lost to follow-up (0.4%) and other reason (0.8%).

914 patients were included in FAS and analyzed. The mean age of patients in FAS was 53.9±7.4 years, 514 patients (56.2%) were male. The median time of T2DM duration was 7.0 (range from 0 to 39) years. The mean HbA1c at baseline was 8.59±0.92%, mean serum FPG 10.54±2.25mmol/L, mean FBG 9.50±1.96mmol/L, mean PPG 13.76±3.72 mmol/L. Mean initial Gla-100 dose was 12.6±2.7U/day, and 62.3% of the patients previously received treatment with a sulfonylurea. Furthermore, 64.5% of patients were previously treated with 2 types of OADs. Treatment groups were well balanced with respect to baseline variables. Only 73 patients decreased or discontinued their OADs (mostly due to hypoglycaemia) during the treatment period, which was equally distributed among the three groups (12, 31 and 30 patients respectively). No OADs were added during the study.

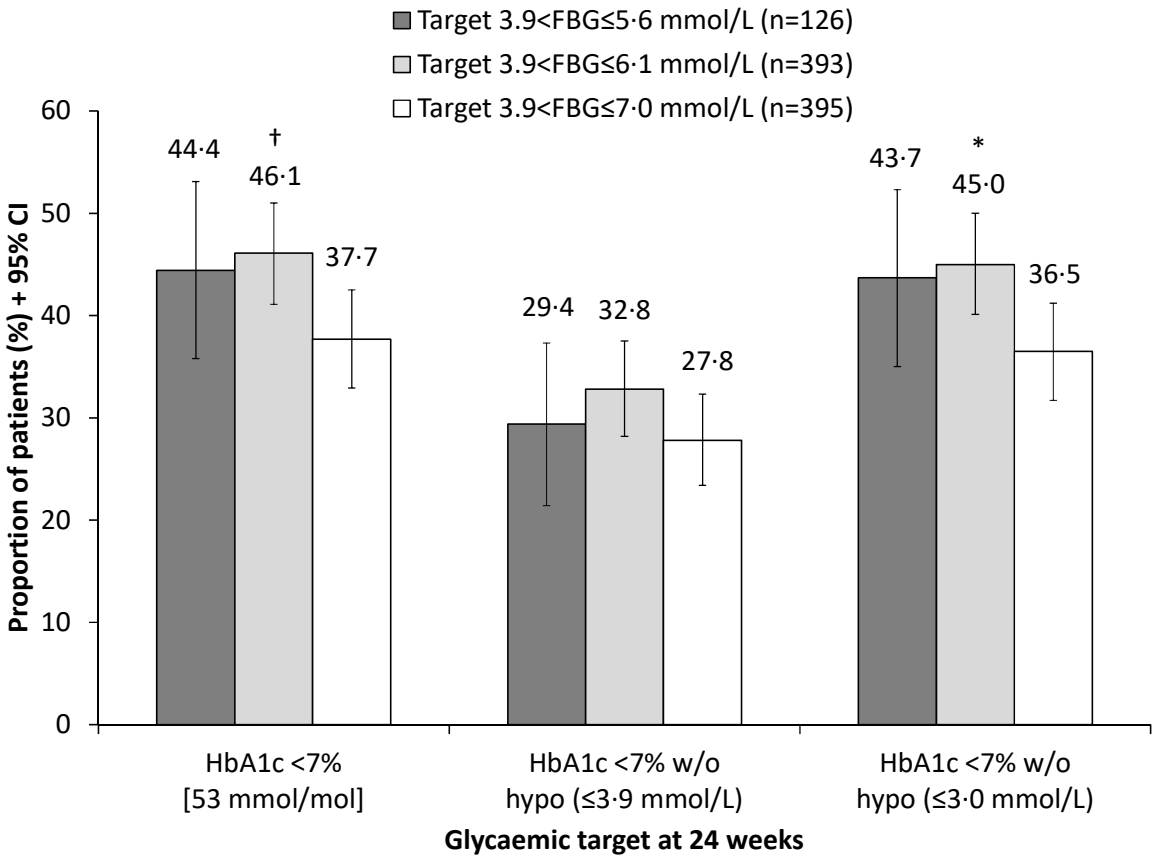
**Efficacy results:**

**Primary endpoint:**

At 24 weeks, 44.4%, 46.1% and 37.7% of patients achieved an HbA1c <7.0% in Groups 1, 2 and 3, respectively. The proportion of patients achieving an HbA1c <7.0% was numerically, but not significantly, higher among those randomized to Group 1 versus Group 3 (p=0.183), so the second fixed-sequence hypothesis test was not performed which meant the primary endpoint was failed to meet. The exploratory Bonferroni-adjusted (α<0.025) analysis showed a significant difference in the proportion of patients achieving an HbA1c <7.0% in Group 2 versus Group 3 (p=0.017).

**Secondary endpoints:**

When hypoglycaemia was considered, there was no difference between the three groups with regard to the proportion of patients who achieved an HbA1c <7.0% without experiencing confirmed hypoglycaemia (SMBG ≤ 3.9 mmol/L). In contrast, a significantly greater proportion of patients in Group 2 achieved an HbA1c <7.0% without experiencing confirmed hypoglycaemia (SMBG ≤ 3.0 mmol/L) than those in Group 3 (45.0% vs 36.5% of patients; p=0.014).




All patients showed mean reductions from baseline in glycaemic parameters. However, patients in Group 1 and Group 2 had significantly greater reductions from baseline in HbA1c, FBG, and FPG at 12 and 24 weeks compared with patients in Group 3. No significant differences in the changes from baseline in 2-hour PPG at 12 and 24 weeks were observed between the three groups.

The Gla-100 doses administered at 24 weeks to patients in Groups 1 and 2 were significantly higher (all p<0.001) than the dose administered to patients in Group 3.

Although body weight increased by 0.5–0.7 kg in all target FBG groups, no significant between-group differences in the change from baseline in body weight were observed.

Confirmed hypoglycemia (SMBG ≤ 3.9 mmol/L) incidence was significantly more frequent in Group 1 vs Group 3 (38.9 vs 23.3%, p<0.001) but not in Group 2 vs Group 3 (27.5% vs 23.3%; p=0.177). Similar findings were seen with any hypoglycemia, symptomatic hypoglycemia, and nocturnal hypoglycemia. However, there were no significant differences in confirmed hypoglycemia (SMBG≤ 3.0 mmol/L) between the three groups (4.8%, 2.0% and 3.8% respectively; all P≥ 0.05). Severe hypoglycemia only occurred in one patient each in Groups 2 and 3. The incidence rate of hypoglycemia showed similar findings to the frequency of hypoglycemia, except for the 'any hypoglycemia' category.

| | FBG Target, >3.9 mmol/L to | | |
|---|---|---|---|
| **Glycemic outcomes** | **≤ 5.6 mmol/L (n=126)** | **≤ 6.1 mmol/L (n=393)** | **≤ 7.0 mmol/L (n=395)** |
| **HbA1c, %** | | | |
| n | 119 | 367 | 377 |
| Mean ± SD | 7.06 ± 0.75 | 7.14 ± 0.92 | 7.30 ± 0.92 |

| | | | |
|---|---|---|---|
| LSM change ± SE | −1.49 ± 0.08 | −1.45 ± 0.04 | −1.28 ± 0.04 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | 0.033 | 0.010 | |
| **HbA1c, mmol/mol** | | | |
| n | 119 | 367 | 377 |
| Mean ± SD | 54 ± 8.2 | 55 ± 10.1 | 56 ± 10.1 |
| LSM change ± SE | −16.3 ± 0.9 | −15.8 ± 0.4 | −14.0 ± 0.4 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | 0.033 | 0.010 | |
| **Self-monitored FBG,a mmol/L** | | | |
| n | 117 | 368 | 377 |
| Mean ± SD | 6.06 ± 1.07 | 6.42 ± 1.25 | 6.88 ± 1.37 |
| LSM change ± SE | −3.42 ± 0.12 | −3.11 ± 0.07 | −2.62 ± 0.07 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | <0.001 | <0.001 | |
| **Fasting plasma glucose, mmol/L** | | | |
| n | 119 | 367 | 377 |
| Mean ± SD | 6.62 ± 1.65 | 6.81 ± 1.65 | 7.27 ± 1.70 |
| LSM change ± SE | −3.91 ± 0.15 | −3.75 ± 0.09 | −3.28 ± 0.09 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | <0.001 | <0.001 | |
| **2-hour PPG, mmol/L** | | | |
| n | 106 | 313 | 327 |
| Mean ± SD | 10.45 ± 3.05 | 10.29 ± 2.89 | 10.69 ± 2.96 |
| LSM change ± SE | −3.33 ± 0.29 | −3.52 ± 0.17 | −3.16 ± 0.16 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | 0.842 | 0.224 | |
| **Insulin dose, U** | | | |
| n | 122 | 374 | 382 |
| Mean ± SD | 20.0 ± 11.1 | 19.5 ± 9.3 | 16.5 ± 8.5 |
| LSM change ± SE | 8.1 ± 0.7 | 6.8 ± 0.4 | 3.9 ± 0.4 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | <0.001 | <0.001 | |
| **Insulin dose, U/ kg.db** | | | |
| n | 126 | 393 | 395 |
| Mean ± SD | 0.28 ± 0.13 | 0.27 ± 0.12 | 0.23 ± 0.11 |
| **Bodyweight, kg** | | | |
| n | 119 | 367 | 378 |
| Mean ± SD | 70.0 ± 11.5 | 71.2 ± 12.1 | 70.7 ± 11.4 |
| LSM change ± SE | 0.5 ± 0.3 | 0.7 ± 0.1 | 0.7 ± 0.1 |
| P-value vs 3.9<FBG≤ 7.0 mmol/L | 0.745 | 0.988 | |
| **Hypoglycemia** | | | |
| Any | 72 (57.1)*** | 169 (43.0) | 145 (36.7) |
| Symptomatic | 53 (42.1)*** | 113 (28.8) | 100 (25.3) |
| Confirmed hypoglycemia (SMBG≤ 3.9 mmol/L) | 49 (38.9)*** | 108 (27.5) | 92 (23.3) |

| | | | |
|---|---|---|---|
| Confirmed hypoglycemia (SMBG≤ 3.0 mmol/L) | 6 (4.8) | 8 (2.0) | 15 (3.8) |
| Severe | 0 | 1 (0.3) | 1 (0.3) |
| Nocturnal | 25 (19.8)*** | 42 (10.7) | 34 (8.6) |
| **Hypoglycemia incidence, person-years (95% CI)c** | | | |
| Any | 3.6 (3.1–4.1)*** | 2.0 (1.8–2.2)** | 1.6 (1.5–1.8) |
| Symptomatic | 1.9 (1.6–2.3)*** | 1.2 (1.1–1.4) | 1.0 (0.9–1.2) |
| Confirmed hypoglycemia (SMBG≤ 3.9 mmol/L) | 2.0 (1.7–2.4)*** | 1.1 (0.9–1.2) | 0.9 (0.8–1.1) |
| Confirmed hypoglycemia (SMBG≤ 3.0 mmol/L) | 0.1 (0.1–0.2) | 0.1 (0.0–0.1) | 0.1 (0.1–0.1) |
| Severe | – | 0 (0–0) | 0 (0–0) |
| Nocturnal | 0.8 (0.6–1.1)*** | 0.3 (0.3–0.4) | 0.3 (0.2–0.4) |

a Defined as the mean value of the last three consecutive self-monitored FBG values.
b Global P-value assessing difference between the three FBG target groups <0.001 (ANOVA).
*p<0.05, **p<0.01, ***p<0.001 vs FBG ≤ 7.0 mmol/L group (nominal p-values).
CI, confidence interval; FBG, fasting blood glucose; SMBG, self-monitored blood glucose; LSM, least squares mean; PPG, postprandial glucose; SD, standard deviation; SE, standard error;

The lowest value of the last three consecutive FBG values was used for decisions about insulin titration, rather than the mean value. After 24 weeks, 70.1%, 67.6% and 79.0% of patients in Groups 1, 2 and 3, respectively, had the lowest of three consecutive FBG values within their pre-defined target range. However, when measured by 3-day mean FBG values or FPG, these proportions dropped to 40.2%, 45.4% and 62.6% or 31.9%, 39.5% and 47.7% in Groups 1, 2 and 3, respectively.

| | **FBG Target, >3.9 mmol/L to** | | |
|---|---|---|---|
| | **≤ 5.6 mmol/L (n=126)** | **≤ 6.1 mmol/L (n=393)** | **≤ 7.0 mmol/L (n=395)** |
| **Serum FPG (mmol/L)** | | | |
| n | 119 | 367 | 377 |
| Distribution, n (%) | | | |
| ≤ 5.6 | 38 (31.9) | 86 (23.4) | 55 (14.6) |
| 5.6–6.1 | 18 (15.1) | 59 (16.1) | 45 (11.9) |
| 6.1–7.0 | 20 (16.8) | 79 (21.5) | 80 (21.2) |
| >7.0 | 43 (36.1) | 143 (39.0) | 197 (52.3) |
| P value vs. 3.9<FBG≤ 7.0a | <0.001 | <0.001 | |
| **Mean SM-FBG (mmol/L)** | | | |
| n | 117 | 368 | 377 |
| Distribution, n (%) | | | |
| ≤ 5.6 | 47 (40.2) | 93 (25.3) | 50 (13.3) |
| 5.6–6.1 | 30 (25.6) | 74 (20.1) | 54 (14.3) |
| 6.1–7.0 | 22 (18.8) | 113 (30.7) | 132 (35.0) |
| >7.0 | 18 (15.4) | 88 (23.9) | 141 (37.4) |
| P value vs. 3.9<FBG≤ 7.0a | <0.001 | <0.001 | |
| **Minimum SM-FBG (mmol/L)** | | | |
| n | 117 | 368 | 377 |

| | | | |
|---|---|---|---|
| Distribution, n (%) | | | |
| ≤ 5.6 | 82 (70.1) | 176 (47.8) | 126 (33.4) |
| 5.6–6.1 | 17 (14.5) | 73 (19.8) | 68 (18.0) |
| 6.1–7.0 | 10 (8.5) | 81 (22.0) | 104 (27.6) |
| >7.0 | 8 (6.8) | 38 (10.3) | 79 (21.0) |
| P value vs. 3.9<FBG≤ 7.0a | <0.001 | <0.001 | |

**Exploratory endpoints**

When re-divided by actual 24-week FPG levels, the proportions of patients achieving an HbA1c<7% among those with a 24-week FPG ≤ 5.6mmol/L (68.7%, p<0.001) or with a 24-week FPG >5.6 and ≤ 6.1 mmol/L (58.2%, p=0.013) were significantly greater than among those with a 24-week FPG >6.1 and ≤ 7.0mmol/L (43.6%).

Linear regression analysis demonstrated a significant association between lower self-monitored FBG and lower HbA1c levels, which was consistently observed during both early (1–12 weeks) treatment (β coefficient = 0.371, p<0.001, R2 = 0.21, equation: HbA1c, % = 4.734 + FBG × 0.371) and later (13–24 weeks) treatment (β coefficient = 0.480, p<0.001, R2 = 0.23, equation: HbA1c, % = 4.055 + FBG × 0.480). These associations remained after adjustment for baseline covariates including age, sex, BMI, diabetes duration, FPG, HbA1c, and PPG excursion (β coefficients = 0.348 and 0.498, respectively, both p<0.001).

**Safety results:**

Overall, 65% of patients experienced at least one adverse event over the 24 weeks treatment period, with the majority of these being mild in severity. The most common adverse events were hypoglycemia, upper respiratory tract infections, nasopharyngitis and toothache. Less than 2% of the study population discontinued the study due to an adverse event and no deaths occurred during the treatment period.

| | **FBG Target, >3.9 mmol/L to** | | |
|---|---|---|---|
| **Safety outcomes n (%)** | **≤ 5.6 mmol/L (n=133)** | **≤ 6.1 mmol/L (n=400)** | **≤ 7.0 mmol/L (n=403)** |
| Any AE | 91 (68.4) | 278 (69.5)a | 243 (60.3) |
| Mild | 78 (58.6) | 219 (54.8) | 197 (48.9) |
| Moderate | 13 (9.8) | 44 (11.0) | 40 (9.9) |
| Severe | 0 | 14 (3.5) | 6 (1.5) |
| Any AE except hypoglycemiab | 51 (38.3) | 188 (47.0) | 168 (41.7) |
| Serious AEs | 4 (3.0) | 25 (6.3) | 10 (2.5) |
| AEs leading to discontinuation | 0 | 7 (1.8) | 1 (0.2) |
| AEs except hypoglycemia occurring in ≥ 3% of patientse | | | |
| Hyperlipidemia | 1 (0.8) | 13 (3.3) | 11 (2.7) |
| Nasopharyngitis | 7 (5.3) | 17 (4.3) | 18 (4.5) |
| Toothache | 4 (3.0) | 3 (0.8) | 4 (1.0) |
| URTI | 11 (8.3) | 44 (11.0) | 37 (9.2) |

a One patient had an AE whose severity categorization (mild/moderate/severe) was missing.
b AEs including hypoglycemia defined by MedDRA.
*p<0.05, **p<0.01, ***p<0.001 vs FBG ≤ 7.0 mmol/L group (nominal p-values).
AEs, adverse events; URTI, upper respiratory tract infection

**Issue date**: 14/May/2019