Supplementary Appendix

SUSTAIN China (trial 4114)
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**Figure S1**  
**Trial design**

886 patients with T2D  
- Age ≥18 years  
- HbA1c 7.0–10.5%  
- Stable treatment with metformin 60 days prior to screening

- **Randomisation (2:2:1:1)**

- **Semaglutide 1.0 mg + sitagliptin 100 mg placebo**
- **Semaglutide 0.5 mg + sitagliptin 100 mg placebo**
- **Sitagliptin 100 mg + semaglutide 1.0 mg placebo**
- **Sitagliptin 100 mg + semaglutide 0.5 mg placebo**

- **Dose escalation** 4–8 weeks
- **Treatment maintenance** 22–26 weeks
- **Follow-up** 5 weeks

**Treatment duration: 30 weeks**

**Notes:** *Dose escalation from starting dose of 0.25 mg, dose doubled every 4 weeks until maintenance dose achieved.

**Figure S2**  
**Hierarchical testing of semaglutide versus sitagliptin**

- **Hypothesis testing stopped**
  - **Non-inferiority of semaglutide 1.0 mg vs sitagliptin 100 mg for HbA1c**  
    - YES, upper limit of the 95% CI <0.3%

- **Hypothesis testing stopped**
  - **Non-inferiority for semaglutide 0.5 mg vs sitagliptin 100 mg for HbA1c**  
    - YES, upper limit of the 95% CI <0.3%

- **Hypothesis testing stopped**
  - **Superiority of semaglutide 1.0 mg vs sitagliptin 100 mg for HbA1c**  
    - YES, upper limit of the 95% CI <0%

- **Hypothesis testing stopped**
  - **Superiority of semaglutide 1.0 mg vs sitagliptin 100 mg for body weight**  
    - YES, upper limit of the 95% CI <0 kg

- **Hypothesis testing stopped**
  - **Superiority of semaglutide 0.5 mg vs sitagliptin 100 mg for body weight**  
    - YES, upper limit of the 95% CI <0 kg

- **Hypothesis testing stopped**
  - **Superiority of semaglutide 0.5 mg vs sitagliptin 100 mg for HbA1c**  
    - YES, upper limit of the 95% CI <0 kg

**Notes:** The hierarchical testing begins with the non-inferiority of semaglutide 1.0 mg versus sitagliptin and semaglutide 0.5 mg versus sitagliptin in change in HbA1c, continues with the superiority in change in HbA1c and superiority in change in body weight of semaglutide 1.0 mg versus sitagliptin, and ends with superiority in change in body weight and superiority in change in HbA1c of semaglutide 0.5 mg versus sitagliptin. The null hypothesis for non-inferiority for the primary endpoint (i.e. change in HbA1c from baseline at week 30) was that semaglutide was inferior to sitagliptin with a margin of at least 0.3%. The null hypotheses for superiority for the primary endpoint and the secondary confirmatory endpoint were that semaglutide was no different from sitagliptin. If a null hypothesis was not rejected at any stage, testing was stopped and no further confirmatory conclusions could be drawn.

CI: confidence interval.
Table S1  Inclusion criteria

| Inclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|
| According to the trial protocol, an eligible patient was to meet all of the following inclusion criteria: |
| 1. Informed consent obtained before any trial-related activities. Trial-related activities are any procedures that are carried out as part of the trial, including activities to determine suitability for the trial |
| 2. Male or female, age ≥ 18 years at the time of signing informed consent          |
| 3. (For Korea: Male or female, age above or equal to 19 years at the time of signing informed consent.) |
| 4. Patients diagnosed with type 2 diabetes and on stable treatment in a period of 60 days prior to screening with metformin ≥ 1500 mg (or maximum tolerated dose ≥ 1000 mg). Stable is defined as unchanged medication and unchanged daily dose |
| 5. HbA1c 7.0 – 10.5 % (53-91 mmol/mol) (both inclusive)                             |

Table S2  Exclusion criteria

| Exclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|
| According to the trial protocol, an eligible patient was to meet none of the following exclusion criteria: |
| 1. Known or suspected hypersensitivity to trial product(s) or related products     |
| 2. Previous participation in this trial. Participation is defined as informed consent |
| 3. Female who is pregnant, breast-feeding or intends to become pregnant or is of childbearing potential not using an adequate contraceptive method throughout the trial including the 5-week follow-up period (adequate contraceptive measure as required by local regulation or practice) (China: Sterilisation, intrauterine device (IUD), oral contraceptives or barrier methods). (Brazil: For women who expressly declare free of the risk of pregnancy, either by not engaging in sexual activity or by having sexual activity with no birth potential risk, use of contraceptive method will not be mandatory). |
| 4. Receipt of any investigational medicinal product within 90 days before screening (Brazil: Participation in other trials within one year prior to screening visit (V1) unless there is a direct benefit to the research patient at the Investigator’s discretion) |
| 5. Any disorder which, in the opinion of the investigator, might jeopardise patient’s safety or compliance with the protocol |
| 6. Treatment with glucose lowering agent(s) other than stated in the inclusion criteria in a period of 60 days before screening. An exception is short-term treatment (≤7 days in total) with insulin in connection with inter-current illness |
| 7. Use of non-herbal Chinese medicine or other non-herbal local medicine with unknown/unspecified content. Herbal traditional Chinese medicine or other local herbal medicines may, at the Investigator’s discretion, be continued throughout the trial |
| 8. History of pancreatitis (acute or chronic)                                      |
| 9. Screening calcitonin value ≥ 50 ng/L (pg/mL)                                     |
| 10. Personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome type 2 (MEN 2) |
| 11. Impaired renal function defined as eGFR < 60 ml/min/1.73 m² per Modification of Diet in Renal Disease (MDRD) formula (4 variable version) |
Exclusion criteria

12. Acute coronary or cerebrovascular event within 90 days before randomisation
13. Heart failure, New York Heart Association (NYHA) class IV
14. Proliferative retinopathy or maculopathy requiring acute treatment. Verified by fundus photography or dilated fundoscopy performed within the past 90 days prior to randomisation in accordance with the instructions in trial protocol
15. Diagnosis of malignant neoplasm in the previous 5 years (except basal cell skin cancer or squamous cell skin cancer)
16. Mental inability, unwillingness or language barrier precluding adequate understanding of or compliance with study procedures

Table S3  FPG-based predefined rescue criteria

| Rescue criteria |
|-----------------|
| If any of the fasting plasma glucose (FPG) values exceed the limits outlined below and no intercurrent cause of the hyperglycaemia can be identified the patient should be called for an unscheduled visit as soon as possible: |
| • 15.0 mmol/L (270 mg/dl) from week 0 to end of week 5 |
| • 13.3 mmol/L (240 mg/dl) from week 6 to end of Week 11 |
| • 11.1 mmol/L (200 mg/dl) from week 12 to end of trial |

A confirmatory FPG should be obtained. If the confirmatory FPG exceeds the values described above the patient should be offered treatment intensification (rescue medication) at the discretion of the investigator and in accordance with the position statement by the American Diabetes Association/European Association for the Study of Diabetes1,2 (excluding glucagon-like peptide-1 receptor agonists [GLP-1RAs], dipeptidyl peptidase-4 [DPP-4] inhibitors and amylin analogues). Rescue medication (intensification of existing background medication and/or initiation of new medication) and any changes hereto should be captured on the concomitant medication form in the electronic case report form (eCRF). Rescue medication should be prescribed as add-on to randomised treatment unless contraindicated according to the local sitagliptin label. In this case trial medication should be discontinued before initiation of rescue therapy. Patients should continue to follow the protocol-specified visit schedule even if rescue treatment has been initiated.
**Figure S3**  
**HbA₁c – cumulative distribution function at week 30 (Total population)**

| Change from baseline in HbA₁c (%-point) |
|----------------------------------------|
| 0                                       |
| 10                                      |
| 20                                      |
| 30                                      |
| 40                                      |
| 50                                      |
| 60                                      |
| 70                                      |
| 80                                      |
| 90                                      |
| 100                                     |

Notes: On-treatment without rescue medication data. Missing data were imputed from an MMRM analysis with treatment and region (China/Other) as fixed factors and baseline value as covariate, all nested within visit. All site visits, except screening visit, were completed in fasting state.

MMRM: mixed model for repeated measurements.

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**Figure S4**  
**Body weight – cumulative distribution function at week 30 (Total population)**

| Change from baseline in body weight (kg) |
|-----------------------------------------|
| 0                                       |
| 10                                      |
| 20                                      |
| 30                                      |
| 40                                      |
| 50                                      |
| 60                                      |
| 70                                      |
| 80                                      |
| 90                                      |
| 100                                     |

Notes: On-treatment without rescue medication data. Missing data were imputed from an MMRM analysis with treatment and region (China/Other) as fixed factors and baseline value as covariate, all nested within visit. All site visits, except screening visit, were completed in fasting state.

MMRM: mixed model for repeated measurements.
Figure S5  Statistical sensitivity analyses (superiority) for change in HbA1c (Total population)

| Analysis Type                        | Treatment | Regression Estimate | 95% CI       | p-value |
|--------------------------------------|-----------|---------------------|--------------|---------|
| Primary analysis (MMRM)              | Sema 0.5 mg - Sitagliptin | -0.51 [-0.66: -0.36] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.65 [-1.00: -0.70] | <.0001       |
| Complete case analysis (MMRM)        | Sema 0.5 mg - Sitagliptin | -0.51 [-0.65: -0.36] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.79 [-0.93: -0.64] | <.0001       |
| In-trial analysis (MMRM)             | Sema 0.5 mg - Sitagliptin | -0.51 [-0.66: -0.37] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.76 [-0.90: -0.61] | <.0001       |
| ANCOVA (LOCF)                        | Sema 0.5 mg - Sitagliptin | -0.46 [-0.61: -0.32] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.77 [-0.92: -0.62] | <.0001       |
| Pattern mixture model (PMM)          | Sema 0.5 mg - Sitagliptin | -0.47 [-0.62: -0.32] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.75 [-0.90: -0.60] | <.0001       |
| Retrieved dropout analysis           | Sema 0.5 mg - Sitagliptin | -0.49 [-0.66: -0.33] | <.0001       |
|                                      | Sema 1.0 mg - Sitagliptin | -0.66 [-0.82: -0.49] | <.0001       |

Notes: Results from primary and sensitivity analyses of HbA1c.

Primary analysis: Regression: MMRM; treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data; imputation: not applicable.

Complete case analysis: Regression: MMRM; treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data at end-of trial (having a valid measurement at week 30); imputation: not applicable.

In-trial analysis: Regression: MMRM; treatment, region and baseline measurement; data from FAS: in-trial data; imputation: not applicable.

ANCOVA (LOCF): Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data at end-of trial; imputation: LOCF.

Pattern mixture model: Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data; imputation: jump to reference; missing measurements for the semaglutide groups followed the distribution of the sitagliptin measurements after introduction of rescue medication.

Retrieved dropout analysis: Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: in-trial data; imputation: measurements on and off randomised treatment at end of trial were used for imputation. ANCOVA: analysis of covariance (baseline measurement and visit 30 were used in analysis; pattern mixture models used 500 datasets pooled into one estimate and associated standard deviation); CI: confidence interval; ETD: estimated treatment difference; FAS: full analysis set; LOCF: last observation carried forward; MMRM: mixed model with repeated measurement.
Figure S6  Statistical sensitivity analyses (superiority) for change in body weight (Total population)

| Analysis Type | Treatment Group | ETD [95% CI] | p-value |
|--------------|-----------------|---------------|---------|
| Primary analysis (MMRM) | Sema 0.5 mg - Sitagliptin | -2.48 [-3.06; -1.90] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.79 [-4.37; -3.21] | <.0001 |
| Complete case analysis (MMRM) | Sema 0.5 mg - Sitagliptin | -2.53 [-3.14; -1.93] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.71 [-4.31; -3.10] | <.0001 |
| In-trial analysis (MMRM) | Sema 0.5 mg - Sitagliptin | -2.41 [-2.97; -1.84] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.56 [-4.13; -3.00] | <.0001 |
| ANCOVA (LOCF) | Sema 0.5 mg - Sitagliptin | -2.30 [-2.94; -1.77] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.47 [-4.00; -2.94] | <.0001 |
| Pattern mixture model (PMMI) | Sema 0.5 mg - Sitagliptin | -2.31 [-2.87; -1.76] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.41 [-3.96; -2.85] | <.0001 |
| Retrieved dropout analysis | Sema 0.5 mg - Sitagliptin | -2.33 [-3.05; -1.61] | <.0001 |
| | Sema 1.0 mg - Sitagliptin | -3.24 [-3.94; -2.54] | <.0001 |

Notes: Results from primary and sensitivity analyses of body weight.

**Primary analysis:** Regression: MMRM; treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data; imputation: not applicable.

**Complete case analysis:** Regression: MMRM; treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data at end-of trial (having a valid measurement at week 30); imputation: not applicable.

**In-trial analysis:** Regression: MMRM; treatment, region and baseline measurement; data from FAS: in-trial data; imputation: not applicable.

**ANCOVA (LOCF):** Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data at end-of trial; imputation: LOCF.

**Pattern mixture model:** Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: on-treatment without rescue medication data; imputation: jump to reference; missing measurements for the semaglutide groups followed the distribution of sitagliptin measurements after introduction of rescue medication.

**Retrieved dropout analysis:** Regression: ANCOVA with treatment, region and baseline measurement; data from FAS: in-trial data; imputation: measurements on and off randomised treatment at end of trial were used for imputation.

ANCOVA: analysis of covariance (baseline measurement and visit 30 were used in analysis; pattern mixture models used 500 datasets pooled into one estimate and associated standard deviation); CI: confidence interval; ETD: estimated treatment difference; FAS: full analysis set; LOCF: last observation carried forward; MMRM: mixed model with repeated measurement.
**Figure S7**  \( \text{HbA}_{1c} \) treatment target \( \leq 6.5\% \) and body weight loss \( \geq 10\% \) (Total population)

A) Proportion of patients with \( \text{HbA}_{1c} \leq 6.5\% \) after 30 weeks

B) Proportion of patients with \( \geq 10\% \) weight loss after 30 weeks

**Notes:** Proportion of patients achieving the \( \text{HbA}_{1c} \) target of \( \leq 6.5\% \) (A), proportion of patients achieving \( \geq 10\% \) weight loss (B).
### Figure S8  Change in glucose metabolism and beta-cell function (Total population)

| Metabolism                        | ETR    | [95% CI]          | p-value |
|-----------------------------------|--------|-------------------|---------|
| Plasma glucagon                   | 0.95   | [0.90;1.00]       | 0.0399  |
| Serum C-peptide                   | 1.07   | [1.02;1.13]       | 0.0083  |
| Fasting serum insulin             | 1.06   | [1.01;1.12]       | 0.0289  |
| HOMA-B                            | 1.02   | [0.99;1.05]       | 0.1198  |
| HOMA-IR                           | 1.42   | [1.31;1.54]       | <0.0001 |
| Serum pro-insulin                 | 1.50   | [1.33;1.62]       | <0.0001 |
| FFA                               |        |                   |         |
| HDL                               |        |                   |         |
| LDL                               |        |                   |         |
| VLDL                              |        |                   |         |
| Triglycerides                     |        |                   |         |
| Pro-insulin/insulin               |        |                   |         |

**Notes:** Results are from statistical analyses of glucose metabolism using on-treatment without rescue medication data from the FAS. CI: confidence interval; ETR: estimated treatment ratio; FAS: full analysis set; HOMA-B: homeostatic model assessment of beta-cell function; HOMA-IR: homeostatic model assessment of insulin resistance.

### Figure S9  Change in lipids (Total population)

| Lipids                             | ETR    | [95% CI]          | p-value |
|------------------------------------|--------|-------------------|---------|
| Total cholesterol                  | 0.96   | [0.94;0.99]       | 0.0088  |
| LDL-cholesterol                    | 0.96   | [0.94;0.99]       | 0.0096  |
| VLDL-cholesterol                   | 0.98   | [0.93;1.02]       | 0.3015  |
| Triglycerides                      | 0.95   | [0.89;1.02]       | 0.1326  |
| FFA                                | 0.89   | [0.84;0.95]       | 0.0008  |
| HDL                               | 0.89   | [0.83;0.95]       | 0.0007  |
| FFA                                | 0.94   | [0.86;1.04]       | 0.2349  |
| FFA                                | 0.92   | [0.83;1.01]       | 0.0757  |
| HDL                               | 0.99   | [0.97;1.02]       | 0.5089  |
| HDL                               | 1.02   | [0.99;1.04]       | 0.1519  |

**Notes:** Results are from statistical analyses of lipids. On-treatment without rescue medication data. All site visits, except screening visits, were completed in fasting state. CI: confidence interval; ETR: estimated treatment ratio; FFA: free fatty acid; HDL: high-density lipoprotein; LDL: low-density lipoprotein; VLDL: very low-density lipoprotein.
Figure S10  Change in DTSQs (Total population)

| ETD [95% CI] | p-value |
|---------------|---------|
| Overall treatment satisfaction score | 1.43 [0.57:2.11] | 0.0006 |
| Satisfaction with current treatment | 1.03 [0.26:1.70] | 0.0088 |
| Convenience of current treatment | 0.27 [0.11:0.43] | 0.0012 |
| Flexibility of current treatment | 0.25 [0.09:0.41] | 0.0028 |
| Satisfaction with understanding of diabetes | 0.16 [-0.03:0.35] | 0.0925 |
| Recommending treatment to others | 0.11 [-0.08:0.30] | 0.2456 |
| Satisfaction to continue with present treatment | 0.23 [0.06:0.40] | 0.0079 |
| CI: confidence interval; DTSQs: Diabetes Treatment Satisfaction Questionnaire (status version); ETD: estimated treatment difference. |

Notes: On-treatment without rescue medication data. All site visits, except screening visits, were completed in fasting state.

Figure S11  Change in SF-36v2® (Total population)

| ETD [95% CI] | p-value |
|---------------|---------|
| Physical component summary | 0.97 [0.04:1.90] | 0.0414 |
| Physical functioning | 0.78 [0.04:1.90] | 0.0970 |
| Role-physical | 0.39 [-0.58:1.36] | 0.4245 |
| Bodily pain | 0.55 [-0.42:1.52] | 0.2628 |
| General health | 0.89 [-0.20:1.07] | 0.1084 |
| Vitality | 0.17 [-0.06:0.25] | 0.7501 |
| Mental component summary | 0.78 [-0.64:2.00] | 0.2842 |
| Mental health | 0.26 [-1.16:1.67] | 0.7106 |
| Social functioning | 1.10 [-0.32:2.52] | 0.1281 |
| Role-emotional | 0.67 [-0.75:2.06] | 0.3546 |
| Vitality | 0.07 [-0.10:0.24] | 0.5170 |
| Mental health | -0.03 [-1.18:1.23] | 0.9042 |
| Mental health | -0.95 [-2.15:0.25] | 0.1221 |

Notes: ‘On-treatment without rescue medication’ data. All site visits, except screening visits, were completed in fasting state.

CI: confidence interval; ETD: estimated treatment difference; SF-36v2®: Short Form-36 Health Survey version 2®.
Figure S12  Premature treatment discontinuation due to adverse events – time to onset of first event (Total population)

Notes: Events are shown up until the scheduled follow-up visit.

Figure S13  Nausea and diarrhoea over time (Total population)

Notes: AE: adverse event.
*aAll but one event of nausea in the semaglutide 0.5 mg and 1.0 mg groups were mild or moderate in severity. None were serious and one event was severe (semaglutide 1.0 mg), which led to premature treatment discontinuation. All events had outcomes of recovered by the end of the trial. †All diarrhoea AEs in the semaglutide 0.5 mg and 1.0 mg groups were mild or moderate in severity. None were serious or severe. Only one event had the outcome not recovered, while the remaining events had the outcome recovered at the end of the trial.
Figure S14  Estimated mean amylase by treatment week (Total population)

Notes: On-treatment data. Mean estimates (± error bars) are from an MMRM analysis with treatment and region China/Other as fixed factors and baseline as covariate, all nested within visits, and are adjusted according to observed baseline distribution. Error bars are ± 1 standard errors of the means calculated on log-scale and back-transformed to original scale. Dashed line is the total average value at baseline. MMRM: mixed model for repeated measurements.

| Amylase          | ETR  | 95% CI          |
|------------------|------|-----------------|
| Sema 0.5 mg – sitagliptin | 1.05*| [1.01 ; 1.09]   |
| Sema 1.0 mg – sitagliptin  | 1.07*| [1.02 ; 1.11]   |

Notes: The log-transformed post-baseline responses were analysed using an MMRM with treatment and region China/Other as fixed factors and baseline value as covariate, all nested within visit. Mean estimates were adjusted according to observed baseline distribution. Standard errors were calculated on log-scale and back transformed to original scale. CI: confidence interval; ETR: estimated treatment ratio at week 30; MMRM: mixed model for repeated measurements. *Statistically significant.
**Figure S15  Estimated mean lipase by treatment week (Total population)**

Notes: On-treatment data. Mean estimates (± error bars) are from an MMRM analysis with treatment and region China/Other as fixed factors and baseline as covariate, all nested within visits, and are adjusted according to observed baseline distribution. Error bars are ±1 standard errors of the means calculated on log-scale and back-transformed to original scale. Dotted line is the total average value at baseline.

MMRM: mixed model for repeated measurements.

|                    | ETR | 95% CI          |
|--------------------|-----|-----------------|
| Sema 0.5 mg – sitagliptin | 1.10* | [1.02 ; 1.18] |
| Sema 1.0 mg – sitagliptin  | 1.17* | [1.09 ; 1.26] |

Notes: The log-transformed post-baseline responses were analysed using an MMRM with treatment and region China/Other as fixed factors and baseline value as covariate, all nested within visit. Mean estimates were adjusted according to observed baseline distribution. Standard errors were calculated on log-scale and back-transformed to original scale.

CI: confidence interval; ETR: estimated treatment ratio at week 30; MMRM: mixed model for repeated measurements.

*Statistically significant.
**Figure S16  Estimated mean pulse rate by treatment week (Total population)**

Notes: On-treatment data. Mean estimates are from an MMRM analysis with treatment and region (China/Other) as fixed factors, and baseline value as covariate, all nested within visit, and are adjusted according to observed baseline distribution. Error bars are ±1 standard errors of the means calculated on a log-scale and back-transformed to original scale.

bpm: beats per minute; CI: confidence interval; ETD: estimated treatment difference; MMRM: mixed model for repeated measurements.
Table S4  All neoplasms by system organ class and preferred term – predefined MedDRA search – in-trial (Total population)

|                                | Semaglutide 0.5 mg (N=287) | Semaglutide 1.0 mg (N=290) | Sitagliptin 100 mg (N=290) |
|--------------------------------|----------------------------|----------------------------|---------------------------|
| **Observation time**           | 183.7                      | 187.3                      | 190.6                     |
| **Events**                     |                            |                            |                           |
| N (%)                          | E                          | N (%)                      | E                          | N (%)                      | E                          |
| **Neoplasms (benign, malignant and unspecified (incl cysts and polyps)** |                            |                            |                           |
| Skin papilloma                 | 0                          | 1                          | 0.3                       | 1                          | 0.3                       | 1                          |
| Benign gastric neoplasm        | 0                          | 1                          | 0.3                       | 1                          | 0                          |                           |
| Haemangioma                    | 1                          | 0.3                       | 1                          | 0                          |                           |                           |
| Haemangioma of liver           | 1                          | 0.3                       | 1                          | 0                          |                           |                           |
| Lipoma                         | 0                          | 1                          | 0.3                       | 1                          | 0                          |                           |
| Malignant melanoma             | 0                          |                            |                            | 1                          |                            | 0.3                       | 1                          |
| Meningioma                     | 1                          | 0.3                       | 1                          | 0                          |                           |                           |
| Rectal adenoma                 | 0                          | 1                          | 0.3                       | 1                          | 0                          |                           |
| Uterine leiomyoma              | 0                          | 1                          | 0.3                       | 1                          | 0                          |                           |
| **Gastrointestinal disorders** |                            |                            |                           |                            |                            |                           |
| Large intestine polyp          | 1                          | 0.3                       | 1                          | 2                          | 0.7                       | 3                          |
| Gastric polyps                 | 1                          | 0.3                       | 1                          | 2                          | 0.7                       | 2                          |
| Rectal polyp                   | 0                          | 1                          | 0.3                       | 1                          | 1                          | 0.3                       | 1                          |
| Renal and urinary disorders    | 5                          | 1.7                       | 5                          | 2                          | 0.7                       | 2                          | 1                          | 0.3                       | 1                          |
| Renal cyst                     | 5                          | 1.7                       | 5                          | 2                          | 0.7                       | 2                          | 1                          | 0.3                       | 1                          |
| Hepatobiliary disorders        | 2                          | 0.7                       | 2                          | 2                          | 0.7                       | 2                          |                            |                            |                            |
| Gallbladder polyp              | 1                          | 0.3                       | 1                          | 0                          | 2                          | 0.7                       | 2                          |                            |                            |
| Hepatic cyst                   | 1                          | 0.3                       | 1                          | 2                          | 0.7                       | 2                          |                            |                            |                            |
| Reproductive system and breast disorders | 1                  | 0.3                       | 1                          | 1                          | 0.3                       | 1                          | 2                          | 0.7                       | 2                          |
| Cervical cyst                  | 0                          |                            |                            | 1                          | 0.3                       | 1                          |                            |                            |                            |
| Cervical dysplasia             | 0                          |                            |                            | 0                          |                            |                            | 1                          | 0.3                       | 1                          |
| Cervical polyp                 | 0                          |                            |                            | 0                          |                            |                            | 1                          | 0.3                       | 1                          |
| Ovarian cyst                   | 1                          | 0.3                       | 1                          | 0                          |                            |                            |                            |                            |                            |

Continued
|                                | Semaglutide 0.5 mg (N=287) | Semaglutide 1.0 mg (N=290) | Sitagliptin 100 mg (N=290) |
|--------------------------------|---------------------------|---------------------------|---------------------------|
|                                | N (% | E  | N (% | E  | N (% | E  |
| Congenital, familial and genetic disorders | 0 | 1 | 0.3 | 1 | 0 |
| Adenomatous polyposis coli      | 0 | 1 | 0.3 | 1 | 0 |
| Investigations                  | 1 | 0.3 | 1 | 0 | 0 |
| Lymphocyte morphology abnormal  | 1 | 0.3 | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | 1 | 0.3 | 1 | 0 | 0 |
| Pharyngeal mass                 | 1 | 0.3 | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | 0 | 1 | 0.3 | 1 | 0 |
| Dermal cyst                     | 0 | 1 | 0.3 | 1 | 0 |

**Notes:** MedDRA version 21.1. The summary includes a subset of all PTs within each SOC; the listed PTs were selected by a predefined MedDRA search and contribute to the total for each SOC. Table is sorted in descending order by system organ class, PT based on the total percentage of patients experiencing at least one event. E: number of events; MedDRA: Medical Dictionary for Regulatory Activities; N: number of patients experiencing at least one event; R: event rate per 100 years of observation; SOC: system organ class; PT: preferred terms; %: percentage of patients experiencing at least one event.
Table S5  Eye examination

Eye examination

A fundus photography or a dilated fundoscopy was to be performed by the investigator or according to local practice at screening and at the end-of-treatment visit, and, for patients who prematurely discontinued trial product, both at the end-of-treatment premature discontinuation visit and again within 5 weeks prior to the planned end-of-treatment visit.

If fundus photography/dilated fundoscopy had been performed within 90 days before randomisation, the procedure did not need to be repeated, unless a worsening of visual function since the last examination was noted. The eye examination results were to be available before randomisation. If the examination was performed before the patient had signed the informed consent form, it was to be documented in the medical records that the reason for performing the procedure was not related to this trial.

Fundoscopy required pharmacological dilation of both pupils. The results of the examination were to be interpreted for each eye (left/right) and categorised as normal, abnormal, not clinically significant or abnormal, clinically significant.

Table S6  Event categories predefined for event adjudication committee review

| Event category                                           |
|----------------------------------------------------------|
| Death*                                                   |
| Acute coronary syndrome                                  |
| Cerebrovascular event                                    |
| Heart failure requiring hospitalisation                  |
| Acute pancreatitis                                       |
| Malignant neoplasm                                       |
| Malignant thyroid neoplasm or C-cell hyperplasia         |

*: Death was not considered a separate event, but an outcome.
Definitions of adverse events

Severity assessment

The following three definitions were used when assessing an adverse event:

- **Mild** - no or transient symptoms, no interference with the patient's daily activities.
- **Moderate** - marked symptoms, moderate interference with the patient's daily activities.
- **Severe** - considerable interference with the patient's daily activities; unacceptable.

Serious adverse event

A serious adverse event (SAE) is an experience that at any dose results in any of the following:

- Death.
- A life-threatening experience.
- In-patient hospitalisation or prolongation of existing hospitalisation.
- A persistent or significant disability or incapacity.
- A congenital anomaly or birth defect.
- Important medical events that may not result in death, be life threatening or require hospitalisation may be considered an SAE when - based on appropriate medical judgement - they may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definition of SAE.

1. The term "life threatening" in the definition of SAE refers to an event in which the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it was more severe.

2. The term "hospitalisation" is used when a patient:
   - Is admitted to a hospital or in-patient, irrespective of the duration of physical stay, or
   - Stays at the hospital for treatment or observation for more than 24 hours.

   Medical judgement must always be exercised, and when in doubt, the hospital contact should be regarded as a hospitalisation. Hospitalisations for administrative, trial-related and social purposes do not constitute AEs and should therefore not be reported as AEs or SAEs. Hospital admissions for surgical procedures, planned before trial inclusion, are not considered AEs or SAEs.

3. A substantial disruption of a patient's ability to conduct normal life functions (eg following the event or clinical investigation the patient has significant, persistent or permanent change, impairment, damage or disruption in his/her body function or structure, physical activity and/or quality of life).

4. For example, intensive treatment in an emergency room or at home of allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse.

The following adverse events must always be reported as an SAE using the important medical event criterion if no other seriousness criteria are applicable:

- Suspicion of transmission of infectious agents via the trial product.
- Risk of liver injury defined as ALT or AST >3 x Upper Normal Limit (UNL) and total bilirubin >2 x UNL, where no alternative aetiology exists (Hy's law).

Additional assessments should be made for events meeting the criterion of Hy’s law as stated above.

Non-serious adverse event

A non-serious AE is any AE which does not fulfil the definition of an SAE.
| Table S8  | Baseline characteristics at randomisation (Chinese population) |
| :------: | :----------------------------------------------------------: |
|         | Semaglutide 0.5 mg (N=201) | Semaglutide 1.0 mg (N=202) | Sitagliptin 100 mg (N=202) |
| Age (years) | 52.4 (10.9) | 52.6 (10.4) | 51.8 (10.3) |
| HbA₁c (%) | 8.0 (0.9) | 8.1 (0.9) | 8.0 (0.9) |
| FPG concentration (mmol/L) | 9.28 (2.61) | 9.35 (2.28) | 8.96 (2.03) |
| Diabetes duration (years) | 6.1 (5.5) | 6.6 (4.9) | 5.5 (4.5) |
| Body weight (kg) | 75.0 (13.7) | 74.5 (15.1) | 73.7 (13.3) |
| BMI (kg/m²) | 27.1 (3.7) | 27.1 (4.4) | 26.6 (4.0) |
| eGFR (MDRD: mL/min/1.73m²) | 112.0 (59; 196) | 112.0 (61; 274) | 111.0 (60; 222) |
| Sex | | | |
| Female | 81 (40.3%) | 87 (43.1%) | 71 (35.1%) |
| Male | 120 (59.7%) | 115 (56.9%) | 131 (64.9%) |
| Ethnicity | | | |
| Hispanic or Latino | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) |
| Not Hispanic or Latino | 200 (99.5%) | 200 (99.0%) | 200 (99.0%) |
| Race | | | |
| Asian | 201 ( 100%) | 202 ( 100%) | 202 ( 100%) |
| White | - | - | - |
| Black or African American | - | - | - |
| Concomitant illness reported at screening | | | |
| Hypertension | 101 (50.2%) | 98 (48.5%) | 97 (48.0%) |
| Hyperlipidaemia | 80 (39.8%) | 78 (38.6%) | 74 (36.6%) |
| Dyslipidaemia | 12 (6.0%) | 22 (10.9%) | 19 (9.4%) |
| Diabetic retinopathy | 35 (17.4%) | 36 (17.8%) | 38 (18.8%) |
| Diabetes medications at randomisation | | | |
| Biguanides | 200 (99.5%)* | 202 (100%) | 202 (100%) |
| Other concomitant medications at randomisation (≥5% in any group) | | | |
| Statins | 47 (23.4%) | 52 (25.7%) | 48 (23.8%) |
| Calcium channel blockers | 43 (21.4%) | 39 (19.3%) | 44 (21.8%) |
| ARBs | 38 (18.9%) | 29 (14.4%) | 31 (15.3%) |
| Antiplatelet drugs excl. heparin | 34 (16.9%) | 30 (14.9%) | 33 (16.3%) |
| Herbal and traditional medicine | 18 ( 9.0%) | 22 (10.9%) | 17 ( 8.4%) |
| β-blockers | 15 ( 7.5%) | 21 (10.4%) | 13 ( 6.4%) |
| ACE inhibitors | 6 ( 3.0%) | 14 ( 6.9%) | 10 ( 5.0%) |

**Notes:** Data are mean (SD), median (range), or N (%).
ACE: angiotensin-converting enzyme; ARBs: angiotensin II receptor blockers; BMI: body mass index; eGFR: estimated glomerular filtration; FPG: fasting plasma glucose; MDRD: Modification of Diet in Renal Disease.
*All except one patient met the inclusion criteria related to the background metformin treatment (a stable dose of metformin [≥ 1500 mg or maximum tolerated dose ≥ 1000 mg] for a period of 60 days prior to screening.*
| Study outcomes by treatment group at week 30 (Chinese population) |
|---------------------------------------------------------------|
|                                                           |
| **Glycaemic outcomes**                                         |
| Mean HbA1c (%)                                               |
| 8.0 (0.9)                                                    |
| -1.5 -0.53 (-0.70; -0.36)*                                   |
| -1.8 -0.87 (-1.04; -0.70)*                                   |
| -0.9                                                         |
| Mean fasting plasma glucose (mmol/L)                         |
| 9.20 (2.32)                                                  |
| -2.05 -0.98 (-1.33; -0.66)*                                  |
| -2.60 -1.54 (-1.88; -1.20)*                                  |
| -1.06                                                        |
| Seven-point self-measured plasma glucose (mmol/L)            |
| Mean Increment†                                              |
| 10.7                                                        |
| -2.4 -0.60 (-0.93; -0.26)*                                   |
| -3.0 -1.17 (-1.51; -0.84)*                                   |
| -1.8                                                         |
| Mean (SD)                                                    |
| 3.2                                                         |
| -1.1 -0.29 (-0.59; -0.02)                                    |
| -1.2 -0.36 (-0.67; -0.06)*                                   |
| -0.8                                                         |
| **Body weight-related outcomes**                             |
| Mean body weight (kg)                                        |
| 74.4 (14.1)                                                  |
| -3.1 -2.52 (-3.20; -1.85)*                                   |
| -4.0 -3.38 (-4.05; -2.70)*                                   |
| -0.6                                                         |
| Mean body weight (%)                                         |
| 74.4 (14.1)                                                  |
| -4.2 -3.48 (-4.38; -2.58)*                                   |
| -5.5 -4.78 (-5.67; -3.89)*                                   |
| -0.7                                                         |
| Mean BMI (kg/m²)                                             |
| 26.9 (4.1)                                                   |
| -1.1 -0.92 (-1.17; -0.67)*                                   |
| -1.5 -1.24 (-1.49; -0.99)*                                   |
| -0.2                                                         |
| Mean waist circumference (cm)                                |
| 94.2 (10.4)                                                  |
| -2.9 -1.91 (-2.82; -1.01)*                                   |
| -4.2 -3.15 (-4.05; -2.25)*                                   |
| -1.0                                                         |
| **Blood pressure and pulse rate**                            |
| Mean systolic blood pressure (mmHg)                         |
| 128.2 (14.4)                                                 |
| -3.5 -1.9 (-4.5; -0.6)                                      |
| -7.1 -5.5 (-8.0; -2.9)*                                      |
| -1.6                                                         |
| Mean diastolic blood pressure (mmHg)                         |
| 80.4 (9.7)                                                   |
| -0.5 0.3 (-1.3; 1.8)                                         |
| -1.5 -0.7 (-2.3; 0.9)                                        |
| -0.8                                                         |
| Mean pulse rate (beats per minute)                           |
| 78.5                                                        |
| 3.9 3.4 (1.8; 5.1)*                                          |
| 4.6 4.1 (2.5; 5.8)*                                          |
| 0.5                                                          |

**Notes:** Data are mean (SD) or treatment difference (95% CI). The post-baseline responses were analysed using an MMRM with treatment and region China/other as fixed factors and baseline value as covariate, all nested within visit. CI: confidence interval; ETD: estimated treatment difference; MMRM: mixed model for repeated measurements; N: number of patients contributing to analysis; SD: standard deviation.

*Statistically significant. †Mean postprandial glucose increment (over all meals).
Figure S17  Primary and secondary efficacy endpoints (HbA1c and body weight) from baseline to week 30 (Chinese population, N=605)

A) Estimated change in mean HbA1c by week  
B) Estimated change in mean HbA1c after 30 weeks

C) Estimated change in mean body weight by week  
D) Estimated change in mean body weight after 30 weeks

Notes: Change in mean HbA1c by week (A), change in mean HbA1c after 30 weeks (B), estimated change in mean body weight by week (C) and estimated change in mean body weight after 30 weeks (D).
CI: confidence interval; ETD: estimated treatment difference.
Figure S18  HbA1c treatment targets and composite endpoint (Chinese population, N=605)

A) Observed proportion of patients with HbA1c <7% after 30 weeks

B) Observed proportion of patients with HbA1c ≤6.5% after 30 weeks

C) Observed proportion of patients with HbA1c <7% without severe or blood glucose-confirmed symptomatic hypoglycaemia and no weight gain after 30 weeks

Notes: Proportion of patients achieving the HbA1c target of < 7.0% (A), proportion of patients achieving the HbA1c target of ≤ 6.5% (B) and proportion of patients achieving HbA1c less than 7.0% without severe or blood glucose-confirmed symptomatic hypoglycaemia and no weight gain (C).

CI: confidence interval; OR: odds ratio.
Figure S19  Body weight loss responders (Chinese population, N=605)

A) Observed proportion of patients with ≥5% weight loss after 30 weeks
B) Observed proportion of patients with ≥10% weight loss after 30 weeks

Notes: Proportion of patients achieving ≥5% weight loss (A) and proportion of patients achieving ≥10% weight loss (B).
CI: confidence interval; OR: odds ratio.
## Table S10  Interaction between region and treatment for change in HbA1c (%), absolute body weight (kg), and relative body weight (%) at week 30

| Change in HbA1c (%) at week 30 | Region            | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------|-------------------|-------------------|---------|---------------------|
| semaglutide 0.5 mg - sitagliptin | Region China     | -0.53 [-0.71; -0.35] | <0.0001 |                     |
|                                 | Other countries   | -0.47 [-0.74; -0.19] | <0.0001 |                     |
| semaglutide 1.0 mg - sitagliptin | Region China     | -0.88 [-1.05; -0.70] | 0.001   |                     |
|                                 | Other countries   | -0.79 [-1.06; -0.51] | <0.0001 |                     |

| Change in body weight (kg) at week 30 | Region            | Estimate [95% CI] | P-value | Interaction p-value |
|-------------------------------------|-------------------|-------------------|---------|---------------------|
| semaglutide 0.5 mg - sitagliptin     | Region China      | -2.5 [-3.2; -1.9]  | <0.0001 |                     |
|                                     | Other countries   | -2.3 [-3.4; -1.2]  | <0.0001 |                     |
| semaglutide 1.0 mg - sitagliptin     | Region China      | -3.4 [-4.1; -2.7]  | <0.0001 |                     |
|                                     | Other countries   | -4.8 [-5.9; -3.7]  | <0.0001 |                     |

| Change in body weight (%) at week 30 | Region            | Estimate [95% CI] | P-value | Interaction p-value |
|-------------------------------------|-------------------|-------------------|---------|---------------------|
| semaglutide 0.5 mg - sitagliptin     | Region China      | -3.5 [-4.41; -2.59] | <0.0001 |                     |
|                                     | Other countries   | -3.4 [-4.79; -1.97] | <0.0001 |                     |
| semaglutide 1.0 mg - sitagliptin     | Region China      | -4.8 [-5.69; -3.89] | <0.0001 |                     |
|                                     | Other countries   | -6.5 [-7.89; -5.06] | <0.0001 |                     |

**Notes:** Region China (mainland China, Taiwan and Hong Kong). Body weight at baseline in Region China: 74.4 kg; and in Other countries: 80.9 kg. 'On-treatment without rescue medication' data. The post-baseline responses were analysed using an MMRM with treatment and region China/Other as fixed factors and baseline value as covariate, all nested within visit. Additionally, an interaction term for treatment by region, nested within visit, is included in the model. All site visits, except screening visit, were to be completed in fasting state. CI: confidence interval; MMRM: mixed model for repeated measurements.
Table S11  Interaction between country and treatment for change in HbA1c (%) and absolute body weight (kg) at week 30

| Change in HbA1c (%) at week 30 | Country             | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------|---------------------|-------------------|---------|---------------------|
| Semaglutide 0.5 mg - sitagliptin | Region China        | -0.53 [-0.71; -0.36] | <0.0001 |                     |
|                                 | Brazil              | -0.57 [-1.06; -0.07] | 0.02    |                     |
|                                 | Republic of Korea   | -0.66 [-1.08; -0.24] | 0.002   |                     |
|                                 | South Africa        | -0.19 [-0.84; -0.47] | 0.57    |                     |
|                                 | Ukraine             | -0.04 [-0.77; 0.84]  | 0.93    |                     |
|                                 | Region China        | -0.87 [-1.05; -0.70] | 0.001   | 0.70               |
|                                 | Brazil              | -1.03 [-1.54; -0.52] | <0.0001 |                     |
| Semaglutide 1.0 mg - sitagliptin | Republic of Korea   | -0.90 [-1.33; -0.48] | <0.0001 |                     |
|                                 | South Africa        | -0.34 [-0.97; 0.29]  | 0.29    |                     |
|                                 | Ukraine             | -0.42 [-1.27; 0.42]  | 0.33    |                     |

| Change in body weight (kg) at week 30 | Country             | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------------|---------------------|-------------------|---------|---------------------|
| Semaglutide 0.5 mg - sitagliptin      | Region China        | -2.5 [-3.2; -1.9]  | <0.0001 |                     |
|                                     | Brazil              | -2.8 [-4.8; -0.8]  | 0.005   |                     |
|                                     | Republic of Korea   | -2.8 [-4.4; -1.1]  | 0.001   |                     |
|                                     | South Africa        | -2.0 [-4.6; 0.5]   | 0.12    |                     |
|                                     | Ukraine             | -0.2 [-3.0; 3.3]   | 0.92    | 0.17               |
|                                     | Region China        | -3.4 [-4.1; -2.7]  | <0.0001 |                     |
|                                     | Brazil              | -6.0 [-8.0; -4.0]  | <0.0001 |                     |
| Semaglutide 1.0 mg - sitagliptin      | Republic of Korea   | -4.7 [-6.4; -3.1]  | <0.0001 |                     |
|                                     | South Africa        | -3.9 [-6.4; -1.5]  | 0.002   |                     |
|                                     | Ukraine             | -2.6 [-5.9; 0.7]   | 0.12    |                     |

Notes: Region China (mainland China, Taiwan and Hong Kong). 'On-treatment without rescue medication' data. The post-baseline responses were analysed using an MMRM with treatment and region as fixed factors and baseline value as covariate, all nested within visit. Additionally, an interaction term for treatment by region, nested within visit, was included in the model. All site visits, except screening visit, were to be completed in fasting state.
CI: confidence interval; MMRM: mixed model for repeated measurements.
Figure S20  Primary and secondary efficacy endpoints (HbA\textsubscript{1c} and body weight) from baseline to week 30 (Korean population, N=110)

A) Estimated change in mean HbA\textsubscript{1c} by week

B) Estimated change in mean HbA\textsubscript{1c} after 30 weeks

C) Estimated change in mean body weight by week

D) Estimated change in mean body weight after 30 weeks

Notes: Estimated change in mean HbA\textsubscript{1c} by week (A), estimated change in mean HbA\textsubscript{1c} after 30 weeks (B), estimated change in mean body weight by week (C) and estimated change in mean body weight after 30 weeks (D). CI: confidence interval; ETD: estimated treatment difference.
Table S12  Interaction between sex and treatment for change in HbA₁c (%) and absolute body weight (kg) at week 30 (Total population)

| Change in HbA₁c (%) at week 30 | Sex    | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------|--------|-------------------|---------|--------------------|
| semaglutide 0.5 mg - sitagliptin | Male   | -0.55 [-0.74; -0.35] | <0.0001 | 0.68               |
|                                | Female | -0.50 [-0.74; -0.27] | <0.0001 |                    |
| semaglutide 1.0 mg - sitagliptin | Male   | -0.83 [-1.03; -0.63] | <0.0001 |                    |
|                                | Female | -0.92 [-1.16; -0.68] | <0.0001 |                    |

| Change in body weight (kg) at week 30 | Sex    | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------------|--------|-------------------|---------|--------------------|
| semaglutide 0.5 mg - sitagliptin      | Male   | -2.1 [-2.87; -1.38] | <0.0001 |                    |
|                                      | Female | -2.8 [-3.73; -1.92] | <0.0001 | 0.14               |
| semaglutide 1.0 mg - sitagliptin      | Male   | -3.2 [-3.94; -2.44] | <0.0001 |                    |
|                                      | Female | -4.4 [-5.26; -3.47] | <0.0001 |                    |

Notes: On-treatment without rescue medication data. The post-baseline responses were analysed using an MMRM with treatment and sex as fixed factors and baseline value as covariate, all nested within visit. Additionally, an interaction term for treatment by sex, nested within visit, was included in the model. All site visits, except screening visit, were to be completed in fasting state.

CI: confidence interval; MMRM: mixed model for repeated measurements.

Table S13  Interaction between sex and treatment for change in HbA₁c (%) and absolute body weight (kg) at week 30 (Chinese population)

| Change in HbA₁c (%) at week 30 | Sex    | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------|--------|-------------------|---------|--------------------|
| semaglutide 0.5 mg - sitagliptin | Male   | -0.51 [-0.73; -0.30] | <0.0001 | 0.46               |
|                                | Female | -0.59 [-0.86; -0.31] | <0.0001 |                    |
| semaglutide 1.0 mg - sitagliptin | Male   | -0.80 [-1.01; -0.58] | <0.0001 |                    |
|                                | Female | -1.01 [-1.28; -0.74] | <0.0001 |                    |

| Change in body weight (kg) at week 30 | Sex    | Estimate [95% CI] | P-value | Interaction p-value |
|--------------------------------------|--------|-------------------|---------|--------------------|
| semaglutide 0.5 mg - sitagliptin      | Male   | -2.1 [-3.01; -1.32] | <0.0001 | 0.28               |
|                                      | Female | -3.0 [-4.08; -1.88] | <0.0001 |                    |
| semaglutide 1.0 mg - sitagliptin      | Male   | -2.9 [-3.72; -2.01] | <0.0001 |                    |
|                                      | Female | -3.9 [-5.00; -2.86] | <0.0001 |                    |

Notes: On-treatment without rescue medication data. The post-baseline responses were analysed using an MMRM with treatment and sex as fixed factors and baseline value as covariate, all nested within visit. Additionally, an interaction term for treatment by sex, nested within visit, was included in the model. All site visits, except screening visit, were to be completed in fasting state.

CI: confidence interval; MMRM: mixed model for repeated measurements.
References

1. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*. 2012;35(6):1364-1379.

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