Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to:

**Variables associated with HbA1c and weight reductions when adding liraglutide to multiple daily insulin injections in persons with type 2 diabetes (MDI Liraglutide trial 3)**

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# Tables

## Table S1. Predictors of effect on HbA1c reduction (mmol/mol)

| **Baseline predictor** | **Regression coefficient (95% CI)** |
| --- | --- |
| **Liraglutide** | **Placebo** | **Liraglutide-Placebo** |
| Abdominal sagittal diameter (cm) | 0.17 (-0.55; 0.90)p=0.64 | 0.28 (-0.49; 1.05) | -0.11 (-1.17; 0.95) |
| Adiponectin (mg/l) | 0.18 (-0.99; 1.35)p=0.76 | 0.89 (-0.30; 2.09) | -0.71 (-2.38; 0.96) |
| Age (years) | -0.10 (-0.40; 0.21)p=0.54 | -0.01 (-0.35; 0.33) | -0.09 (-0.54; 0.38) |
| BMI (kg/m2) | 0.19 (-0.41; 0.78)p=0.54 | 0.17 (-0.48; 0.83) | 0.01 (-0.87; 0.90) |
| CGM Mean (mmol/l) | -1.39 (-2.46; -0.32)p=0.012 | -0.69 (-1.85; 0.48) | -0.70 (-2.28; 0.88)p=0.38 |
| CGM SD (mmol/l) | -0.03 (-3.65; 3.59)p=0.99 | -1.54 (-4.94; 1.85) | 1.51 (-3.45; 6.48) |
| Diabetes duration (years) | -0.10 (-0.43; 0.23)p=0.56 | -0.28 (-0.59; 0.04) | 0.18 (-0.28; 0.63) |
| Metformin usage | 2.85 (-2.52; 8.22)p=0.30 | 3.72 (-2.10; 9.53) | -0.87 (-8.78; 7.05) |
| Fasting C-peptide (nmol/l) | -3.97 (-9.27; 1.32)p=0.14 | 0.89 (-4.40; 6.17) | -4.86 (-12.34; 2.62) |
| Fasting proinsulin (pmol/l) | -0.11 (-0.22; -0.00)p=0.047 | 0.07 (-0.05; 0.19) | -0.18 (-0.34; -0.02)p=0.026 |
| Female sex | -2.82 (-8.04; 2.40)p=0.29 | 1.58 (-3.91; 7.06) | -4.44 (-11.97; 3.18) |
| HbA1c (IFCC) (mmol/mol) | -0.28 (-0.50; -0.05)p=0.018 | -0.20 (-0.41; 0.01) | -0.07 (-0.38; 0.24)p=0.64 |
| Percent meal insulin of total insulin | -4.63 (-25.69; 16.42)p=0.66 | -4.11 (-23.54; 15.32) | -0.52 (-29.17; 28.12) |
| Total daily insulin dose (units) | 0.01 (-0.05; 0.07)p=0.77 | -0.02 (-0.08; 0.05) | 0.03 (-0.06; 0.11) |
| Waist circumference (cm) | 0.08 (-0.16; 0.32)p=0.50 | -0.07 (-0.30; 0.17) | 0.15 (-0.19; 0.49) |
| Waist-hip-ratio | 21.63 (-14.01; 57.27)p=0.23 | 5.85 (-32.44; 44.14) | 15.78 (-36.53; 68.09) |
| Weight (kg) | 0.07 (-0.11; 0.25)p=0.43 | -0.03 (-0.21; 0.14) | 0.10 (-0.15; 0.36) |
| Statistical tests were performed in the liraglutide group only, and tests for treatment with predictor interactions were performed only for predictors that were significant in the liraglutide group at the 5% level. |

## Table S2. Predictors of effect on weight reduction (kg)

| **Baseline predictor** | **Regression coefficient (95% CI)** |
| --- | --- |
| **Liraglutide** | **Placebo** | **Liraglutide-Placebo** |
| Abdominal sagittal diameter (cm) | 0.25 (0.05; 0.46)p=0.016 | -0.19 (-0.41; 0.02) | 0.45 (0.15; 0.74)p=0.004 |
| Adiponectin (mg/l) | -0.22 (-0.56; 0.12)p=0.21 | -0.08 (-0.43; 0.27) | -0.14 (-0.62; 0.35) |
| Age (years) | -0.01 (-0.10; 0.08)p=0.75 | -0.02 (-0.12; 0.08) | 0.00 (-0.13; 0.14) |
| BMI (kg/m2) | 0.10 (-0.08; 0.27)p=0.27 | -0.09 (-0.28; 0.10) | 0.19 (-0.07; 0.44) |
| CGM Mean (mmol/l) | 0.48 (0.17; 0.79)p=0.003 | 0.07 (-0.27; 0.41) | 0.41 (-0.05; 0.87)p=0.08 |
| CGM SD (mmol/l) | 0.75 (-0.30; 1.80)p=0.16 | 0.37 (-0.61; 1.35) | 0.38 (-1.06; 1.82) |
| Diabetes duration (years) | 0.01 (-0.08; 0.11)p=0.78 | 0.03 (-0.07; 0.12) | -0.01 (-0.15; 0.12) |
| Metformin usage | -1.39 (-2.95; 0.17)p=0.08 | 0.29 (-1.41; 1.98) | -1.67 (-3.98; 0.63) |
| Fasting C-peptide (nmol/l) | 0.46 (-1.08; 2.01)p=0.55 | -1.14 (-2.68; 0.40) | 1.60 (-0.58; 3.78) |
| Fasting proinsulin (pmol/l) | 0.02 (-0.01; 0.05)p=0.21 | -0.06 (-0.09; -0.02) | 0.08 (0.03; 0.12) |
| Female sex | -0.78 (-2.30; 0.75)p=0.32 | -0.52 (-2.12; 1.08) | -0.26 (-2.47; 1.95) |
| HbA1c (IFCC) (mmol/mol) | 0.10 (0.04; 0.17)p=0.002 | -0.00 (-0.06; 0.06) | 0.12 (0.02; 0.20)p=0.020 |
| Percent meal insulin of total insulin | -4.12 (-10.21; 1.98)p=0.18 | 1.81 (-3.81; 7.43) | -5.93 (-14.22; 2.37) |
| Total daily insulin dose (units) | 0.01 (-0.01; 0.03)p=0.20 | -0.01 (-0.03; 0.01) | 0.02 (-0.00; 0.05) |
| Waist circumference (cm) | 0.06 (-0.01; 0.13)p=0.10 | -0.04 (-0.12; 0.03) | 0.10 (0.00; 0.21) |
| Waist-hip-ratio | 3.14 (-8.08; 14.37)p=0.58 | -2.28 (-14.34; 9.78) | 5.42 (-11.05; 21.90) |
| Weight (kg) | 0.05 (-0.00; 0.10)p=0.06 | -0.02 (-0.07; 0.03) | 0.07 (-0.01; 0.14) |
| Statistical tests were performed in the liraglutide group only, and tests for treatment with predictor interactions were performed only for predictors that were significant in the liraglutide group at the 5% level. |

## Table S3. Predictors of effect on reduction in total daily insulin dose (units)

| **Baseline predictor** | **Regression coefficient (95% CI)** |
| --- | --- |
| **Liraglutide** | **Placebo** | **Liraglutide-Placebo** |
| Abdominal sagittal diameter (cm) | 1.52 (0.02; 3.03)p=0.048 | 0.15 (-1.46; 1.76) | 1.38 (-0.83; 3.58)p=0.22 |
| Adiponectin (mg/l) | 1.50 (-1.01; 4.00)p=0.24 | 0.11 (-2.45; 2.66) | 1.39 (-2.19; 4.98) |
| Age (years) | 0.15 (-0.51; 0.81)p=0.65 | 0.24 (-0.49; 0.97) | -0.09 (-1.07; 0.89) |
| BMI (kg/m2) | -0.34 (-1.61; 0.93)p=0.60 | -0.12 (-1.52; 1.28) | -0.22 (-2.11; 1.68) |
| CGM Mean (mmol/l) | 1.84 (-0.50; 4.17)p=0.12 | 1.28 (-1.26; 3.82) | 0.56 (-2.90; 4.01) |
| CGM SD (mmol/l) | -1.86 (-9.64; 5.91)p=0.64 | 0.64 (-6.66; 7.94) | -2.50 (-13.17; 8.16) |
| Diabetes duration (years) | -0.23 (-0.94; 0.48)p=0.52 | 0.10 (-0.59; 0.79) | -0.33 (-1.32; 0.66) |
| Metformin usage | -3.32 (-14.91; 8.28)p=0.57 | -3.04 (-15.58; 9.51) | -0.28 (-17.36; 16.81) |
| Fasting C-peptide (nmol/l) | -7.57 (-18.93; 3.78)p=0.19 | 1.07 (-10.26; 12.40) | -8.64 (-24.68; 7.40) |
| Fasting proinsulin (pmol/l) | -0.03 (-0.26; 0.20)p=0.80 | -0.03 (-0.29; 0.22) | 0.00 (-0.34; 0.35) |
| Female sex | -11.82 (-22.81; -0.82)p=0.035 | -4.78 (-16.34; 6.78) | -7.03 (-22.99; 8.92)p=0.38 |
| HbA1c (IFCC) (mmol/mol) | 0.35 (-0.15; 0.85)p=0.17 | -0.05 (-0.52; 0.41) | 0.40 (-0.28; 1.08) |
| Percent meal insulin of total insulin | -40.21 (-84.57; 4.14)p=0.08 | -18.68 (-59.62; 22.25) | -21.53 (-81.89; 38.83) |
| Total daily insulin dose (units) | -0.19 (-0.31; -0.08)p=0.001 | -0.13 (-0.26; -0.01) | -0.06 (-0.23; 0.11)p=0.50 |
| Waist circumference (cm) | 0.07 (-0.49; 0.62)p=0.81 | 0.04 (-0.51; 0.59) | 0.02 (-0.76; 0.80) |
| Waist-hip-ratio | 37.87 (-46.34; 122.08)p=0.37 | 7.75 (-82.71; 98.22) | 30.12 (-93.48; 153.71) |
| Weight (kg) | 0.30 (-0.08; 0.68)p=0.12 | 0.02 (-0.35; 0.40) | 0.28 (-0.26; 0.81) |
| Statistical tests were performed in the liraglutide group only, and tests for treatment with predictor interactions were performed only for predictors that were significant in the liraglutide group at the 5% level. |