Levemir® - from clinical trials to clinical experience

The PREDICTIVE™ Study
Predictable Results and Experience in Diabetes through Intensification and Control to Target: an International Variability Evaluation
Overview: Clinical Trial with Levemir

- **Efficacy:**
  - HbA$_{1c}$
  - Fasting glycaemia
  - Glycaemic variability (variability for self-made intra-individual fasting glycaemic measurements)

- **Safety and tolerability:**
  - Hypoglycaemic events
  - Weight gain
### Published - phase 3 clinical studies: type 1 diabetes

#### Clinical Trial

<table>
<thead>
<tr>
<th>Study</th>
<th>Vs.</th>
<th>Bolus</th>
<th>Basal frequency</th>
<th>Subjects</th>
<th>n</th>
<th>Design</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vague</td>
<td>NPH</td>
<td>IAsp</td>
<td>BD</td>
<td>Type 1</td>
<td>447</td>
<td>6-month, parallel RCT</td>
<td><em>Diabetes Care</em> 2003 26:590–6</td>
</tr>
<tr>
<td>Home</td>
<td>NPH</td>
<td>IAsp</td>
<td>BD (varied)</td>
<td>Type 1</td>
<td>408</td>
<td>4-month, 3-group RCT</td>
<td><em>Diabetes Care</em> 2004;27:1081–7</td>
</tr>
<tr>
<td>Russell-Jones</td>
<td>NPH</td>
<td>HSI</td>
<td>OD</td>
<td>Type 1</td>
<td>747</td>
<td>6-month, parallel RCT</td>
<td><em>Clin Ther</em> 2004;26:724–36</td>
</tr>
<tr>
<td>Standl</td>
<td>NPH</td>
<td>HSI</td>
<td>BD</td>
<td>Type 1</td>
<td>288</td>
<td>12-month, parallel RCT</td>
<td><em>Diabetes Technol Ther</em> 2004;6(5):579–88</td>
</tr>
<tr>
<td>De Leeuw</td>
<td>NPH</td>
<td>IAsp</td>
<td>BD</td>
<td>Type 1</td>
<td>315</td>
<td>12-month, parallel RCT</td>
<td><em>Diabetes Obes Metab</em> 2005;7:73–82</td>
</tr>
<tr>
<td>Pieber</td>
<td>NPH</td>
<td>IAsp</td>
<td>BD (varied)</td>
<td>Type 1</td>
<td>290</td>
<td>4-month, 3-group RCT</td>
<td><em>Diabet Med</em> 2005:22(7):850–7</td>
</tr>
<tr>
<td>Kølendorf</td>
<td>NPH</td>
<td>IAsp</td>
<td>BD</td>
<td>Type 1</td>
<td>131</td>
<td>2 x 4-month crossover</td>
<td><em>Diabet Med</em> 2006;23(7):729–35</td>
</tr>
<tr>
<td>Hermansen</td>
<td>IDet + IAsp vs. NPH + HSI</td>
<td>BD</td>
<td>Type 1</td>
<td>595</td>
<td>3-month, parallel RCT</td>
<td><em>Diabetologia</em> 2004;47:622–9</td>
<td></td>
</tr>
</tbody>
</table>

*The Levemir® Lectures – from clinical trials to clinical experience*
## Published - phase 3 clinical studies: type 2 diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>Vs.</th>
<th>Bolus</th>
<th>Basal frequency</th>
<th>Subjects</th>
<th>n</th>
<th>Design</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1373 Rosenstock</td>
<td>IGlarg</td>
<td>OAD</td>
<td>OD/BD vs. OD</td>
<td>Type 2</td>
<td>582</td>
<td>52-week, parallel RCT</td>
<td><em>Diabetologia</em> 2007; in press</td>
</tr>
<tr>
<td>1336 Haak</td>
<td>NPH</td>
<td>IAsp</td>
<td>OD/BD</td>
<td>Type 2</td>
<td>505</td>
<td>6-month, parallel RCT</td>
<td><em>Diabetes Obes Metab</em> 2005; 7:56–64</td>
</tr>
<tr>
<td>1530 Hermansen</td>
<td>NPH</td>
<td>OAD</td>
<td>BD</td>
<td>Type 2</td>
<td>476</td>
<td>24-week, parallel RCT</td>
<td><em>Diabetes Care</em> 2006; 29(6):1269–74</td>
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<tr>
<td>1632 Philis-Tsimikas</td>
<td>NPH</td>
<td>OAD</td>
<td>OD</td>
<td>Type 2</td>
<td>498</td>
<td>20-week, parallel RCT</td>
<td><em>Clin Ther</em> 2006; 28(10):1569–81</td>
</tr>
</tbody>
</table>

The Levemir® Lectures – from clinical trials to clinical experience

General features of the phase 3 and PREDICTIVE™ trials

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Clinical Experience</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCP</td>
<td>Observational</td>
</tr>
<tr>
<td>Few</td>
<td>Many</td>
</tr>
<tr>
<td>Strict</td>
<td>Few</td>
</tr>
<tr>
<td>Strict</td>
<td>Per clinical practice</td>
</tr>
</tbody>
</table>
Predictable Results and Experience in Diabetes through Intensification and Control to Target: An International Variability Evaluation

- The PREDICTIVE™ observational study
- Efficacy data from PREDICTIVE™
- Safety and tolerability data from PREDICTIVE™
PREDICTIVE™ global overview

- One of the largest observational studies in diabetes
- 35,000+ adults and children with type 1 and type 2 diabetes
- 25+ countries involved
- Started June 2004

As of February 2007.
The Levemir® Lectures – from clinical trials to clinical experience

PREDICTIVE™ study design: data collected during each visit

Clinical Trial

Clinical Experience

Week 0

~Week 12

~Week 26

~Week 52

BASELINE DATA
- Previous hypo events
- Pre-study and new treatment regimen
- Demographics
- HbA₁c
- Weight
- Last six FBG measurements
- Reason for changing therapy

3-MONTH DATA
- Hypo events
- Adverse events
- Current treatment regimen
- HbA₁c
- Weight
- Last six FBG measurements
- Continuing on Levemir®

6-MONTH DATA
- Hypo events
- Adverse events
- Current treatment regimen
- HbA₁c
- Weight
- Last six FBG measurements
- Continuing on Levemir®

12-MONTH DATA
- Hypo events
- Adverse events
- Current treatment regimen
- HbA₁c
- Weight
- Last six FBG measurements
- Continuing on Levemir®

HbA₁c = glycosylated haemoglobin
FBG = fasting blood glucose

35,000+ PATIENTS

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The Levemir® Lectures – from clinical trials to clinical experience

**PREDICTIVE™ Study**
3-month, 11-European country cohort

**Clinical Trial**

**Clinical Experience**

Full analysis set
20,531 patients

Efficacy analysis set
16,935 (82%)

Excluded
3,596 (18%)

- No efficacy measurements
  - 1,156
- Follow-up time <8 or >18 weeks
  - 2,429
- Both
  - 11

The efficacy analysis set (EAS):
All subjects who have a final visit at Week 12, and at least one measurement of FBG, HbA1c, weight or hypoglycaemic events at baseline and final visit, and follow-up interval between eight and 18 weeks.

Type 2:
10,978 (65%)

Type 1:
5,852 (15%)

Others:
105 (1%)
The Levemir® Lectures – from clinical trials to clinical experience

**PREDICTIVE™ Study**
6-month, 6-European country cohort

**Clinical Trial**
**Clinical Experience**

Full analysis set\(^1,2,3\)

5,590 patients

Efficacy analysis set

4,588 (82%)

Excluded

1,032 (18%)

No efficacy measurements

484 (47%)

Follow-up time <18 or >34 weeks

548 (53%)

The efficacy analysis set (EAS):

- All subjects that have at least one measurement of FBG, HbA\(_{1c}\), weight or hypoglycaemic events at baseline and one of the follow-up visits.

1. 825 patients were withdrawn during study (281 lost contact; 94 AE, and/or 369 other)
2. Mean follow-up time was 28.6 weeks – Q10 is 24 and Q90 35 weeks (n=4727)
3. No therapy with Levemir® (n=13) and Levemir® treatment history (n=2374)
• Dornhorst A et al. *Int J Clin Pract* 2007
  Safety and efficacy at 14-week follow-up in the PREDICTIVE™ European cohort.

• Meneghini LF et al. *Diabetes, Obes Metab* 2007
  Main results from the large German subgroup.

• Lüddeke HJ et al. *Diabetes, Obes Metab* 2007
  Baseline characteristics and predictors of hypoglycaemia from the European cohort.

• Hermansen K et al. *Rev Diabet Stud* 2007
  Main results from the Danish subgroup.

• Meneghini L et al. *Diabetes, Obes Metab* 2007
  Main results of the randomized, controlled US PREDICTIVE™ 303 study.

• More in submission and preparation
Type 1: European cohort_6 months Summary

**Glycaemic control**
- Reduction in
  - HbA1c by 0.4%
  - FPG by -23 mg/dL

**Body weight**
- A small change in body weight of -0.3kg was observed (74.2kg → 73.9kg)

**Safety: SADR**
- SADR including major hypoglycaemic events: 1.1%

**Hypoglycaemia**
- Number of episodes per patient-year: 51.4 → 30.4
- Number of major episodes per patient-year: 4.0 → 0.8
Type 2: European cohort_6 months Summary

**Glycaemic control**
- Reduction in
  - HbA1c by 0.7%
  - FPG by -36 mg/dL

**Body weight**
- A small change in body weight of -0.3kg was observed (90.0kg → 89.7kg)

**Safety: SADR**
- SADR including major hypoglycaemic events: 0.2%

**Hypoglycaemia**
- Number of episodes per patient-year: 12.7 → 6.6
- Number of major episodes per patient-year: 0.9 → 0.1
PREDICTIVE™ Study_Korea result

- Study design
- Safety
- Efficacy
- Summary & Conclusion
PREDICTIVE™ Study design

- PREDICTIVE™ was a multi-centre, open label, non-randomised, non-interventional, observational, safety study in subjects using insulin detemir for the treatment of insulin dependent type 1 or type 2 diabetes mellitus

* This study was conducted in Korean patients and it was part of the global PREDICTIVE™ study.
To evaluate the safety and efficacy of insulin detemir in diabetic population under normal clinical practice conditions.

**Primary Objective:**
- To evaluate the incidence of serious adverse drug reactions while using insulin detemir under normal clinical practice conditions

**Secondary Objectives:**
- To evaluate the efficacy of insulin detemir under normal clinical practice conditions
Study design

- Data were collected from sites at baseline, at the interim visit and at the final visit, which was approximately 12 and 26 weeks after starting insulin detemir, respectively.
- All patients were to be prescribed insulin detemir.
- There was no comparator group.

**BASELINE DATA**
- Previous hypoglycaemic events
- Pre-study & new regimen
- Demographics
- HbA1c
- Weight
- Last 6 FPG measurements
- PPBG measurements
- Reason for changing therapy

**3 MONTH DATA**
- Hypoglycaemic events
- Adverse events
- Current regimen
- HbA1c
- Weight
- Last 6 FPG measurements
- PPBG measurements

**6 MONTH DATA**
- Hypoglycaemic events
- Adverse events
- Current regimen
- HbA1c
- Weight
- Last 6 FPG measurements
Of the 9084 patients enrolled, 100.0% received insulin detemir and constituted the FAS and 90.1% the EAS.
**Flow chart**

<table>
<thead>
<tr>
<th>Informed Consent</th>
<th>Baseline</th>
<th>Interim Visit (12 weeks)</th>
<th>Final Visit (26 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Check inclusion/exclusion criteria according to pack insert</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demography data</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Diabetic history</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current insulin therapy</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Current oral antidiabetics</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Fasting blood glucose information (historical)</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Recent HbA1c data</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Record number of hypoglycaemic events in the past 4 weeks</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Record new insulin therapy/oral antidiabetics prescribed</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Prescribe Levemir</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Record all adverse events*</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

* Each adverse event will need to be recorded on a separate adverse event form. If the adverse event is of a serious nature then a serious adverse event form will also have to be completed and the sponsor or their designee notified within the period specified in the protocol.
The primary endpoint was the incidence of SADR including major hypoglycaemic episodes during 12 weeks of insulin detemir therapy and during 26 weeks of insulin detemir therapy.

- The secondary safety endpoints were: the number and incidence of hypoglycaemic episodes in the 4 weeks preceding the interim visit (12 weeks) or the final visit (26 weeks); number of serious adverse event (SAE) and number of adverse event (AE).
The efficacy endpoints were change from baseline in HbA1c, FPG and variability in FPG and body weight and analyzed using paired t-tests.
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>9084</td>
<td>224</td>
<td>8855</td>
</tr>
<tr>
<td>% of total</td>
<td>100%</td>
<td>2.5%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Mean age, years(SD)</td>
<td>56.4 (12.9)</td>
<td>36.0 (16.0)</td>
<td>56.9 (12.4)</td>
</tr>
<tr>
<td>Gender, M/F, %</td>
<td>50.8/49.2</td>
<td>47.8/52.2</td>
<td>50.9/49.1</td>
</tr>
<tr>
<td>Mean weight, kg(SD)</td>
<td>63.9 (11.1)</td>
<td>60.2 (11.5)</td>
<td>64.0 (11.0)</td>
</tr>
<tr>
<td>Mean BMI, kg/m²(SD)</td>
<td>24.1 (3.3)</td>
<td>22.3 (3.5)</td>
<td>24.1 (3.3)</td>
</tr>
<tr>
<td>Mean HbA1c, %(SD)</td>
<td>9.4 (1.9)</td>
<td>9.9 (2.4)</td>
<td>9.3 (1.9)</td>
</tr>
<tr>
<td>Mean diabetes duration, yrs(SD)</td>
<td>10.1 (6.8)</td>
<td>9.4 (7.7)</td>
<td>10.1 (6.8)</td>
</tr>
</tbody>
</table>

* SD: standard deviation
Data presented as Mean (SD)
## Reasons for starting a new therapy

<table>
<thead>
<tr>
<th>Reason(s) for starting a new therapy, n (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improve glycemic control</td>
<td>7510 (82.7%)</td>
</tr>
<tr>
<td>Reduce risk of hypoglycemia</td>
<td>1935 (21.3%)</td>
</tr>
<tr>
<td>Try new insulin</td>
<td>2314 (25.5%)</td>
</tr>
<tr>
<td>Improve weight control</td>
<td>908 (10.0%)</td>
</tr>
<tr>
<td>Reduce plasma glucose variability</td>
<td>1058 (11.6%)</td>
</tr>
<tr>
<td>Change due to insulin pen</td>
<td>333 ( 3.7%)</td>
</tr>
<tr>
<td>Patient dissatisfaction with current therapy</td>
<td>520 ( 5.7%)</td>
</tr>
<tr>
<td>Unstable diabetes</td>
<td>747 ( 8.2%)</td>
</tr>
<tr>
<td>Side effects from current therapy</td>
<td>57 ( 0.6%)</td>
</tr>
</tbody>
</table>

Percentages are based on the number of subjects with non-missing values
A subject may have findings in more than one category in Reason(s) for starting a new therapy
# Daily dose of insulin detemir (U)

<table>
<thead>
<tr>
<th>Time Point</th>
<th>N</th>
<th>Nmiss</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (new)</td>
<td>9079</td>
<td>5</td>
<td>20.7</td>
</tr>
<tr>
<td>Week 12</td>
<td>8133</td>
<td>951</td>
<td>24.2</td>
</tr>
<tr>
<td>Week 26</td>
<td>7442</td>
<td>1642</td>
<td>25.4</td>
</tr>
<tr>
<td>Change: Week 12 - new</td>
<td>8128</td>
<td>956</td>
<td>3.5</td>
</tr>
<tr>
<td>Change: Week 26 - new</td>
<td>7437</td>
<td>1647</td>
<td>4.7</td>
</tr>
<tr>
<td>Change: Week 26 - Week 12</td>
<td>7434</td>
<td>1650</td>
<td>1.3</td>
</tr>
</tbody>
</table>

_N = Number of responders
Nmiss = Number of patients with missing values

* Duration of treatment : 27.2 weeks
- Study design
- Safety
- Efficacy
- Summary & Conclusion
## Safety: Serious adverse drug reactions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of subjects (N = 9084)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major hypoglycaemic events overall, n (%)</td>
<td>7 (0.08%)</td>
</tr>
<tr>
<td>Hyperglycemia, n (%)</td>
<td>4 (0.04%)</td>
</tr>
<tr>
<td>Hypoglycemia, n (%)</td>
<td>2 (0.02%)</td>
</tr>
<tr>
<td>Total Serious adverse drug reactions</td>
<td>13 (0.14%)</td>
</tr>
</tbody>
</table>

*Major Hypoglycemia : 7 cases (2 in week 12, 5 in week 26)*
### Safety: All adverse events (AEs)

- **111 adverse events were reported in 92 patients in this study**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Number of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity</strong></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>55 (49.5%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>38 (34.2%)</td>
</tr>
<tr>
<td>Severe</td>
<td>17 (15.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
</tr>
<tr>
<td><strong>Relationship</strong></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>26 (23.4%)</td>
</tr>
<tr>
<td>Possible</td>
<td>30 (27.0%)</td>
</tr>
<tr>
<td>Unlikely</td>
<td>55 (49.5%)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
</tr>
<tr>
<td><strong>Changes to product</strong></td>
<td></td>
</tr>
<tr>
<td>Product withdrawn</td>
<td>60 (54.1%)</td>
</tr>
<tr>
<td>Dose reduced</td>
<td>7 (6.3%)</td>
</tr>
<tr>
<td>Dose increased</td>
<td>24 (21.6%)</td>
</tr>
<tr>
<td>Dose not changed</td>
<td>0</td>
</tr>
<tr>
<td>Unknown</td>
<td>13 (11.7%)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>0</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td></td>
</tr>
<tr>
<td>Not recovered</td>
<td>5 (4.5%)</td>
</tr>
<tr>
<td>Recovered</td>
<td>81 (73.0%)</td>
</tr>
<tr>
<td>Recovering</td>
<td>12 (10.8%)</td>
</tr>
<tr>
<td>Recovered with sequelae</td>
<td>0</td>
</tr>
<tr>
<td>Not recovered</td>
<td>0</td>
</tr>
<tr>
<td>Fatal</td>
<td>12 (10.8%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of subjects (N = 9084)
Safety: Hypoglycaemic episodes

Patients who reported hypoglycaemic episodes (%):

- Baseline: 9.6%
- Week 12: 6.8%
- Week 26: 5.0%
Safety: Major hypoglycaemic episodes

Patients who reported major hypoglycaemic episodes (%)

- Baseline: 1.8%
- Week 12: 0.0%
- Week 26: 0.1%
Safety: Daytime & nocturnal hypoglycaemia

Daytime hypoglycaemic episodes (%)
- Baseline: 8.6%
- Week 26: 4.4%

Nocturnal hypoglycaemic episodes (%)
- Baseline: 2.7%
- Week 26: 1.1%
Safety: Daytime & nocturnal major hypoglycaemia

Daytime major hypoglycaemic episodes (%)

Baseline: 1.5%
Week 26: 0.0%

Nocturnal major hypoglycaemic episodes (%)

Baseline: 0.4%
Week 26: 0.0%
Safety: Hypoglycaemic episodes per patient

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of hypoglycaemic episodes/patient</td>
<td>0.31</td>
<td>0.12</td>
</tr>
<tr>
<td>Number of major hypoglycaemic events/patient</td>
<td>0.03</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Safety: Daytime & nocturnal hypoglycaemic episodes per patients

- **Number of daytime hypoglycaemic episodes/patient**
  - Baseline: 0.25
  - Week 26: 0.10

- **Number of nocturnal hypoglycaemic episodes/patient**
  - Baseline: 0.06
  - Week 26: 0.02

*Levemir*® (insulin detemir)
Safety conclusions

- The incidence of serious adverse drug reactions including major hypoglycemia was 0.14% during the study. Apart from major hypoglycaemic episode, six SADRs were reported in six patients in this study.

- 111 adverse events were reported in 92 patients in this study.
  - 55 events were mild, 38 events were moderate and 17 events were severe.
  - 26 events were assessed as probable to be related to study product, 30 events were assessed as possibly related to study product and 55 events were assessed as unlikely related to study product.

- 48 SAEs were reported in 38 patients.
• Study design
• Safety
• Efficacy
• Summary & Conclusion
Efficacy: HbA$_1$c

- Baseline: 9.4
- Week 26: 8.1

*p < 0.0001

HbA$_1$c [%] at Baseline
- N: 6110
- Mean (SD): 9.4 (1.9)
- Median: 9.1

HbA [%] at Week 26
- N: 4752
- Mean (SD): 8.1 (1.5)
- Median: 7.9
- 95% CI: [8.1, 8.2]

HbA [%] Absolute Change from Baseline to week 26
- N: 4181
- Mean (SD): -1.1 (1.8)
- Median: -0.9
- 95% CI: [-1.2, -1.1]
- p-value (paired t-test): <0.0001
Efficacy: Patient with HbA1c < 7.0%

- Baseline: 7.3%
- Week 26: 21.8%

Bar chart showing the increase in the percentage of patients with HbA1c < 7.0% from baseline to Week 26.
Efficacy: FPG

Baseline: 10.66 (192mg/dl)
Week 26: 7.74 (139mg/dl)

*p <0.0001

Mean FPG [mmol/l] at Baseline
N: 4881
Mean (SD): 10.66 (4.09)
Median: 9.90
95% CI: [10.54, 10.77]

Mean FPG [mmol/l] at week 26
N: 4617
Mean (SD): 7.74 (2.65)
Median: 7.00
95% CI: [7.66, 7.82]

Mean FPG [mmol/l] Change from Baseline to week 26
N: 3558
Mean (SD): -2.64 (4.01)
Median: -2.20
95% CI: [-2.78, -2.51]
p-value (paired t-test): <0.00001
Efficacy: FPG Variability

Baseline Week 26

FPG Variability (mmol/L)

1.48 (27mg/dl)

0.94 (17mg/dl)

* p < 0.0001

FPG Variability [mmol/l] at Baseline
N: 1224
Mean (SD): 1.48 (1.50)
Median: 1.00
95% CI: [1.40, 1.57]

FPG Variability [mmol/l] at week 26
N: 1382
Mean (SD): 0.94 (1.17)
Median: 0.58
95% CI: [0.88, 1.00]

FPG Variability [mmol/l] Change from Baseline to week 26
N: 638
Mean (SD): -0.47 (1.35)
Median: -0.20
95% CI: [-0.57, -0.37]
p-value (paired t-test): <0.0001
Body weight

Baseline: 63.9 kg
Week 26: 64.0 kg

+0.1 kg

*p = 0.0044
Main effectiveness conclusions

- HbA$_1c$ was reduced by 1.1% (95% CI = [1.2, 1.1]) after 26 weeks treatment. The proportion of patients who achieved HbA$_1c$ glycaemic target <7% increased from 7.3% at baseline to 21.8% after 26 weeks.
- FPG was reduced by 2.64mmol/L (95% CI = [-2.78,-2.51]) after 26 weeks treatment.
- FPG variability was reduced by 0.47mmol/L (95% CI = [-0.57,-0.37]) after 26 weeks treatment.
- Body weight was increased by 0.1kg after 26 weeks of treatment (95% CI = [0.0, 0.1]).
- Study design
- Safety
- Efficacy
- Summary & Conclusion
Summary (Type 1 & 2)

**Glycaemic control**
- Reduction in
  - HbA1c by 1.1%
  - FPG by -2.64mmol/L
- Patients with HbA1c <7%
  - 7.3% → 21.8%

**Body weight**
- A small change in body weight of 0.1kg was observed

**Safety: SADR**
- SADR including major hypoglycaemic events: 0.1%

**Hypoglycaemia**
- Number of episodes per patient: 0.31 → 0.12
- Number of major episodes per patient: 0.03 → 0
Conclusions

*In routine clinical practice in Korea, treatment with insulin detemir:*

- was showed that hypoglycaemic episodes did not increase in frequency.
- was well-tolerated as the proportion of patients who reported a serious adverse drug reactions (SADRs) including a major hypoglycaemic episode during the study was 0.14%.
- was associated with improvements in glycaemic control.
- was associated with weight neutral.

*Subgroup analyses showed the following results:*

- Similar safety and efficacy profile of insulin detemir was observed in patients with type 1 and type 2 diabetes.
Thank you!