Long-Term, Injection-Free Treatment with ITCA 650, Continuous Subcutaneous Delivery of Exenatide via DUROS® Device, Leads to Sustained Improved Glycemic Control and Weight Loss for 48 Weeks in Metformin-Treated Type 2 Diabetes

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For the Intarcia Study Group
Disclosure

Julio Rosenstock, MD

- **Research Support:**
  Merck, Pfizer, Sanofi, Novo Nordisk, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Takeda, Novartis, AstraZeneca, Amylin, Lexicon, Johnson & Johnson, Daiichi Sankyo, MannKind and Intarcia

- **Advisory Boards, Consulting Honoraria:**
  Pfizer, Roche, Sanofi, Eli Lilly, MannKind, GlaxoSmithKline, Takeda, Daiichi Sankyo, Johnson & Johnson, Novartis, Amylin, Lexicon and Intarcia
Study Background

- **Exenatide Administered Twice Daily**
  - ✓ Modest A1C lowering (0.9% at Week 12)
  - ✓ Favorable Body Weight Profile
  - ✓ Limited by:
    - ❖ GI Side Effects and BID Injections
    - ❖ High Rate of Discontinuation and Low Adherence

- **ITCA 650 Placed Every 3 Months**
  - ✓ Continuous Subcutaneous Delivery of Exenatide via DUROS® Device
    - ❖ Significant A1C Lowering after 12 and 24 Weeks (1.0 – 1.6%)*
    - ❖ Favorable Body Weight Profile after 12 and 24 Weeks*
  - ✓ Potential for Greater Adherence by Use of 6 or 12 Month ITCA 650
  - ✓ Potential for Improved Outcomes and a Favorable Side Effect Profile

*Henry R et al. Presented at EASD, 2010*
Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM

**ITCA 650 – Exenatide Delivered via DUROS Device**

- **Osmotic Mini-Pump**

- **Small Device Inserted in a 10-15 min Office Procedure**

- **Continuous Delivery of Exenatide**

![Graph showing release rate over time](image)
Proof of Concept Dose Ranging Study Design

- Type 2 DM on MET
- HbA1c 7-10%
- 155 subjects, 50 sites
- Devices placed every 3 months

Weeks 1 - 12
- ITCA 650 20 mcg/day
- exenatide inj. BID
- ITCA 650 40 mcg/day

Weeks 13 - 24
- ITCA 650 60 mcg/day

Weeks 25 - 48
- ITCA 650 80 mcg/day

Henry R et al. Presented at EASD, 2010
HbA1c Changes at Week 24

Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM

Henry R et al. Presented at EASD, 2010

HbA1c (%)

ITCA 650 20 mcg/day (n=20)

ITCA 650 40 mcg/day (n=42)

ITCA 650 60 mcg/day (n=41)

ITCA 650 80 mcg/day (n=19)

Mean ± SE

* p< 0.001

Henry R et al. Presented at EASD, 2010
Body Weight Changes at Week 24

Mean ± SE

ITCA 650 20 mcg/day (n=20)
ITCA 650 40 mcg/day (n=42)
ITCA 650 60 mcg/day (n=41)
ITCA 650 80 mcg/day (n=19)

* p<0.05

Henry R et al. Presented at EASD, 2010
### Patient Disposition Over Study Periods

<table>
<thead>
<tr>
<th></th>
<th>ITCA 650</th>
<th>Exenatide Injections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Weeks 1-12</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion rate</td>
<td>93%</td>
<td>89%</td>
</tr>
<tr>
<td>Withdrawals due to nausea</td>
<td>3.9%</td>
<td>5.7%</td>
</tr>
<tr>
<td>Withdrawals prior to re-randomization</td>
<td></td>
<td>7.7%</td>
</tr>
<tr>
<td><strong>Weeks 13-24</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completion rate</td>
<td>95%</td>
<td>NA</td>
</tr>
<tr>
<td>Withdrawals due to nausea</td>
<td>&lt;1%</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM**

Henry R et al. Presented at EASD, 2010
GI Tolerability of ITCA 650 vs. Exenatide Injections

Weeks 1-12

- ITCA 650 20 mcg/d
- ITCA 650 40 mcg/d
- Exenatide injections

Weeks 13-24

- Transient nausea in some subjects with dose escalation
- Mainly in subjects that previously reported nausea
- Only one discontinuation secondary to nausea in a subject switched from exenatide injections to ITCA 650

Henry R et al. Presented at EASD, 2010
Optional Extension Weeks 25 - 48

- Subjects were given the opportunity to continue treatment for an additional 24 weeks

- ITCA 650 was maintained at same dose

- 85% of subjects at participating sites chose to continue treatment with ITCA 650
## Patient Disposition During Extension to 48 Weeks

<table>
<thead>
<tr>
<th>ITCA 650</th>
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</thead>
<tbody>
<tr>
<td>20 mcg/day</td>
</tr>
<tr>
<td>40 mcg/day</td>
</tr>
<tr>
<td>60 mcg/day</td>
</tr>
<tr>
<td>80 mcg/day</td>
</tr>
</tbody>
</table>

| Entered extension | 15 | 28 | 27 | 16 |
| Completed 48 weeks| 14 | 23 | 23 | 13 |

### Withdrawals

<table>
<thead>
<tr>
<th></th>
<th>ITCA 650 20 mcg/day</th>
<th>ITCA 650 40 mcg/day</th>
<th>ITCA 650 60 mcg/day</th>
<th>ITCA 650 80 mcg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Withdrew consent</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HbA$_1c$ elevation</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Adverse event</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM
FPG Changes Over Time

Mean ± SE

Weeks

FPG (mg/dL)

- ITCA650 20 mcg/day (n=13)
- ITCA650 40 mcg/day (n=22)
- ITCA650 60 mcg/day (n=22)
- ITCA650 80 mcg/day (n=13)
Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM

HbA$_{1c}$ Changes Over Time

Mean ±SE
At 48 weeks, p< 0.0001 for all dose groups
HbA₁c Changes at Week 24 and Week 48

At 48 weeks, p< 0.0001 for all dose groups
Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM

Body Weight Changes Over Time

![Graph showing body weight changes over time for different doses of ITCA 650.](image)

- **ITCA 650 20 mcg/day (n=13)**
- **ITCA 650 40 mcg/day (n=22)**
- **ITCA 650 60 mcg/day (n=22)**
- **ITCA 650 80 mcg/day (n=13)**

Change in Weight (kg) vs. Weeks

Mean ±SE
* p<0.05  ** p<0.001
Body Weight Changes at Week 24 and Week 48

Mean ± SE

Change in Weight (kg)

Week 24
Week 48

ITCA 650
20 mcg/day
(n=13)

-2.12

-2.74

ITCA 650
40 mcg/day
(n=22)

-3.93

-4.93

ITCA 650
60 mcg/day
(n=22)

-3.43

-3.49

ITCA 650
80 mcg/day
(n=13)

-3.34

-3.57

Sustained Exenatide Effects Via DUROS Subcutaneous Delivery in MET-Treated Type 2 DM
Adverse Events of Interest during Extension: Weeks 24 – 48

**Gastrointestinal**
- Nausea 10.5%
- Diarrhea 3.5%

**Skin Insertion Site**
- Irritation 7%
- Pain 7%
- Erythema 4.7%
- Pruritus 3.5%
- Hematoma 3.5%
ITCA 650 Dose Selected for Phase 3 Studies: 20 → 60 mcg/day

During 6 month extension:

- Sustained HbA1c and body weight reductions
- No patient withdrew for any reason
- One report of nausea and no reports of vomiting
- No hypoglycemia
ITCA 650 Phase 2 Study Conclusions

- Initial treatment with ITCA 650 at 20 mcg/day and dose escalation to 60 mcg/day was well tolerated and led to significant reductions in HbA$_{1c}$, FPG and weight.

- The extension phase revealed favorable patient acceptance and sustained reductions in HbA$_{1c}$, FPG and weight with continued treatment to 48 weeks.

- These results support further evaluation of ITCA 650 using longer duration devices (6 and 12 months) for injection-free therapy in type 2 diabetes.

- Ensured adherence with this DUROS subcutaneous device may improve long-term outcomes.
Big Thank You to the investigators and research subjects for their participation!