

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

**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**

Julio Rosenstock, Robert Henry, Thomas Alessi, Kenneth Luskey

for the Intarcia Study Group

Disclosure Information

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 Honorarium:**

Pfizer, Roche, Sanofi, Novo Nordisk, Eli Lilly, MannKind, GlaxoSmithKline, Takeda, Daiichi Sankyo, Johnson & Johnson, Novartis, Amylin, Lexicon and Intarcia

Study Background

■ Exenatide Administered Twice Daily

- ✓ Effective A1C Lowering
- ✓ Favorable Body Weight Profile
- ✓ Limited by:
 - GI Side Effects and BID Injections
 - High Rate of Discontinuation and Low Adherence

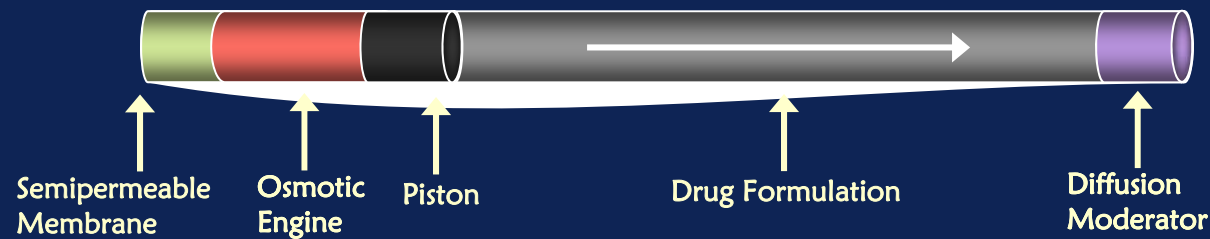
■ ITCA 650 Implanted Every 3 Months

- ✓ Continuous Subcutaneous Delivery of Exenatide via DUROS® Device
 - Effective A1C Lowering after 12 and 24 Weeks*
 - Favorable Body Weight Profile after 12 and 24 Weeks*
- ✓ Potential for Greater Adherence by Implanting Every 6 or 12 Months
- ✓ Potential for Enhanced Efficacy and Reduced Side Effect Profile

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

ITCA 650 – DUROS

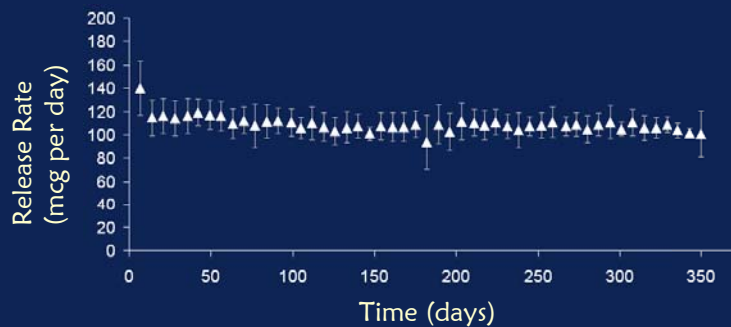
- Osmotic Mini-Pump



- Small Device Inserted in a 10-15' Simple Office Procedure

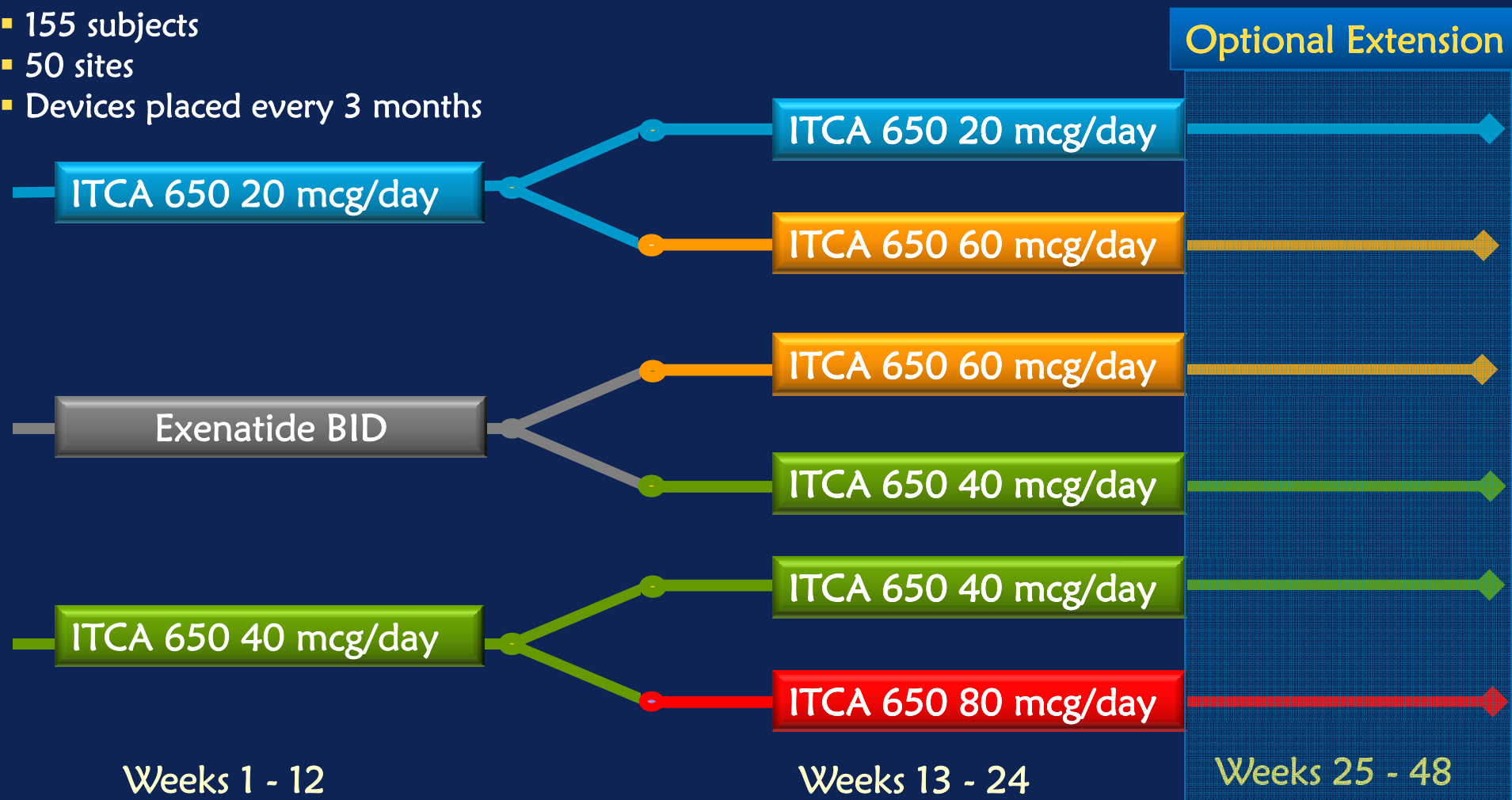


- Continuous Subcutaneous Delivery of Exenatide



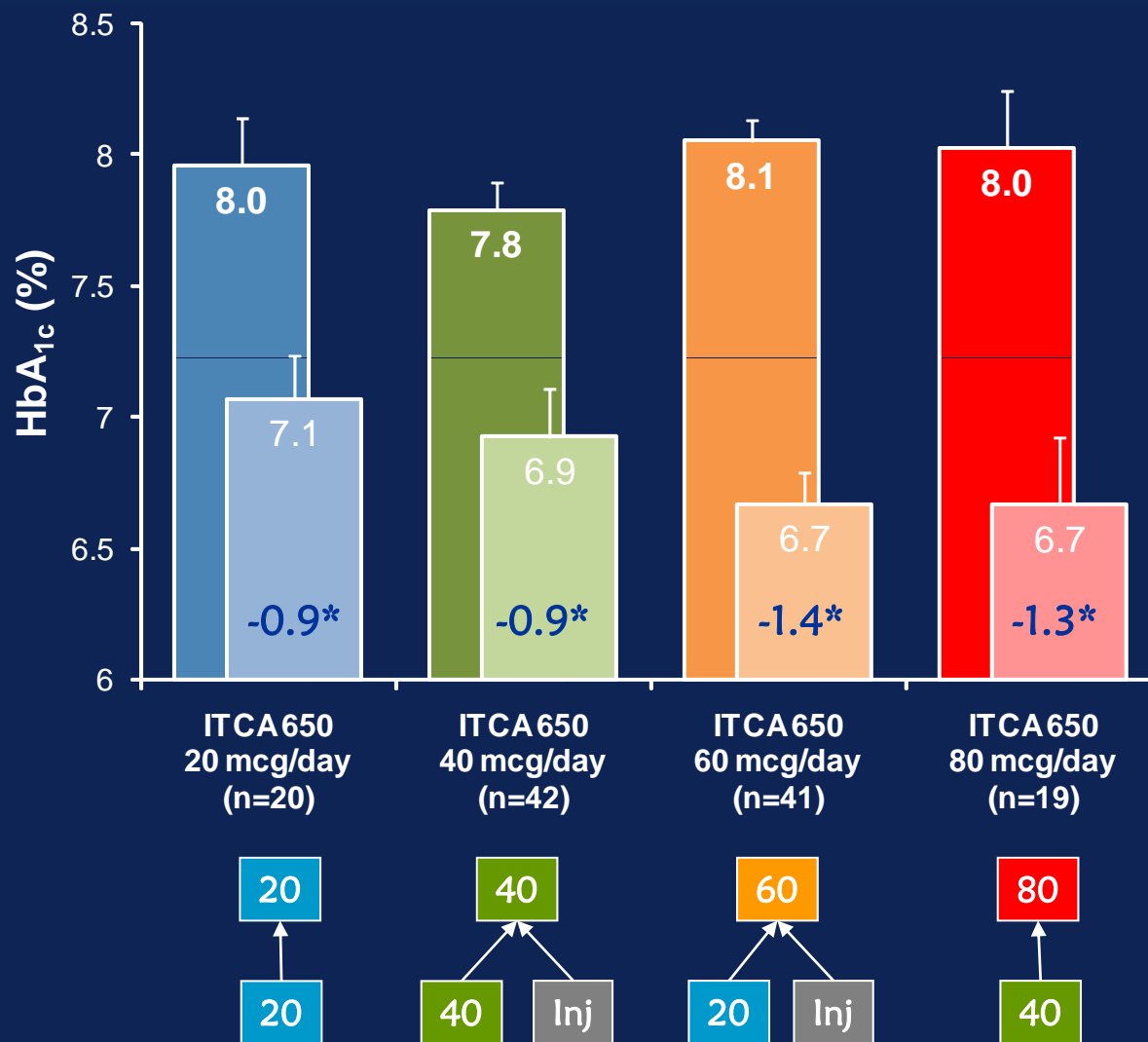
Proof of Concept Dose Ranging Study Design

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



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

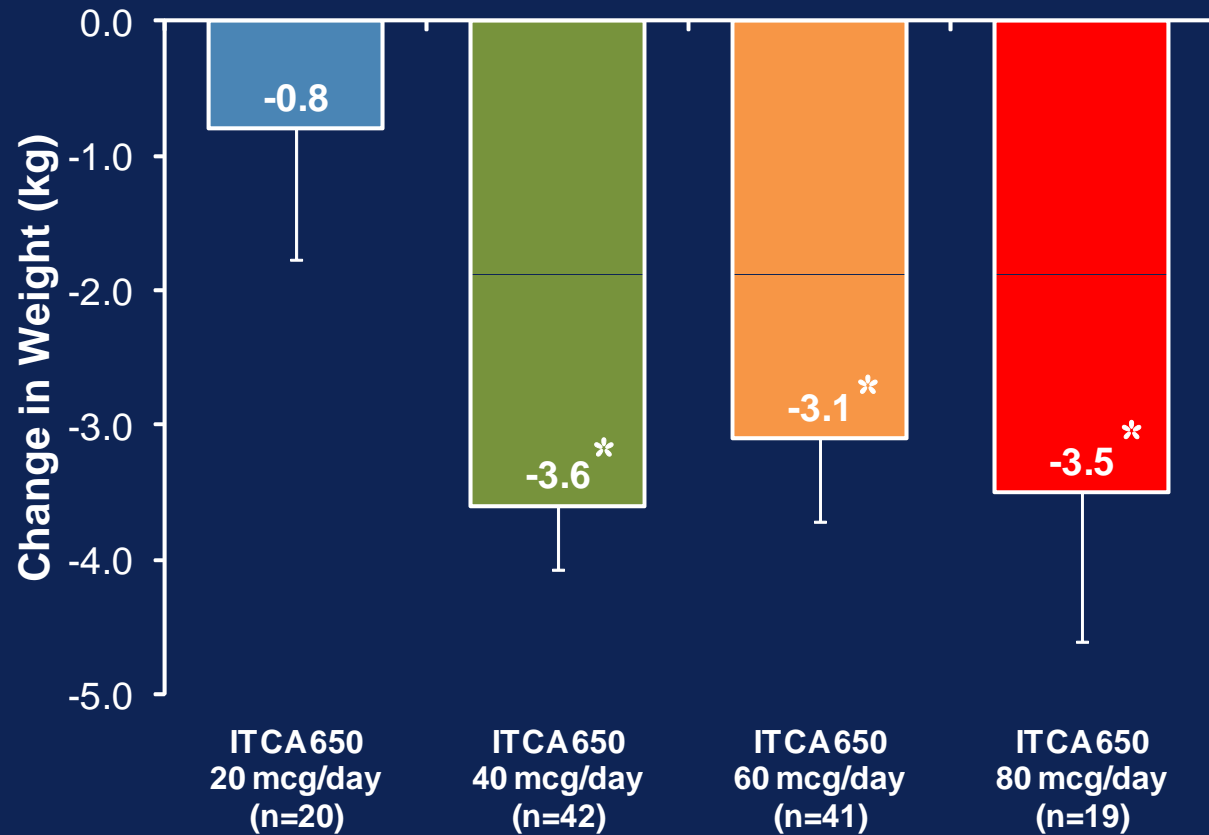
HbA_{1c} Changes at Week 24



* p < 0.001

Mean ±SE

Body Weight Changes at Week 24



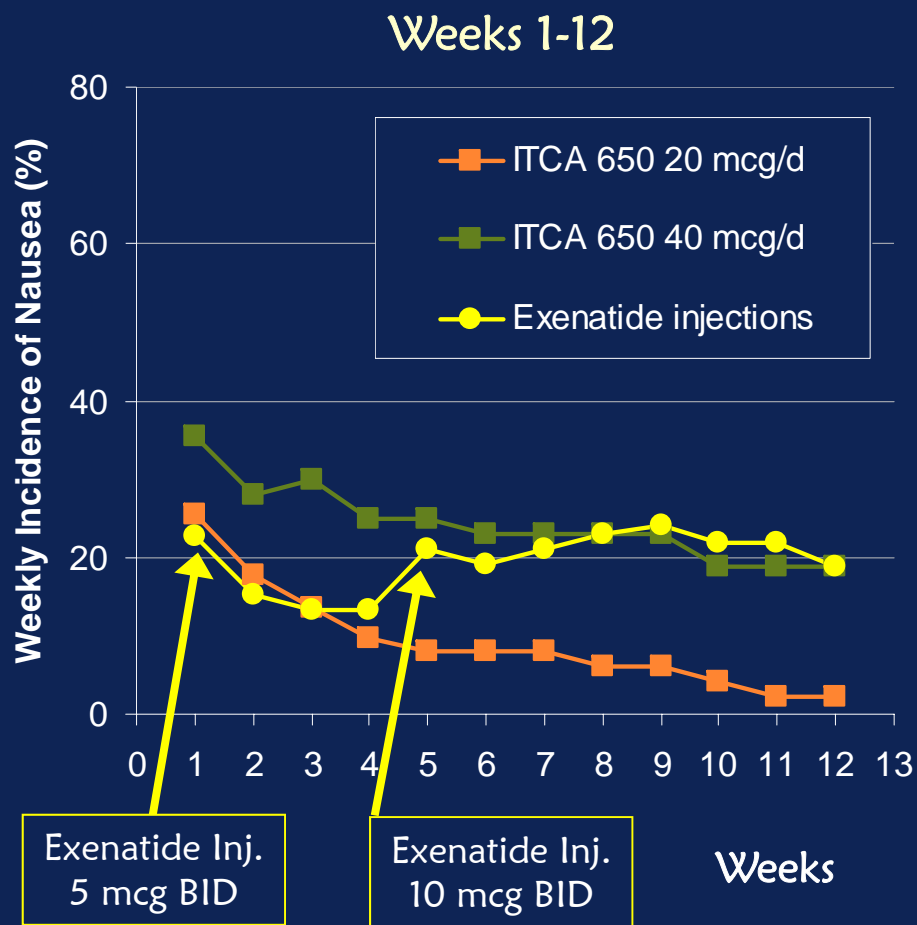
* p<0.05

Mean \pm SE

Patient Disposition Over Study Periods

	ITCA 650	Exenatide Injections
Weeks 1-12		
Completion rate	93%	89%
Withdrawals due to Nausea	3.9%	5.7%
Withdrawals prior to Re-randomization	7.7%	
Weeks 13-24		
Completion rate	95%	NA
Withdrawals due to Nausea	<1%	NA

GI Tolerability of ITCA 650 vs. Exenatide Injections



- 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

Optional Extension Weeks 25-48

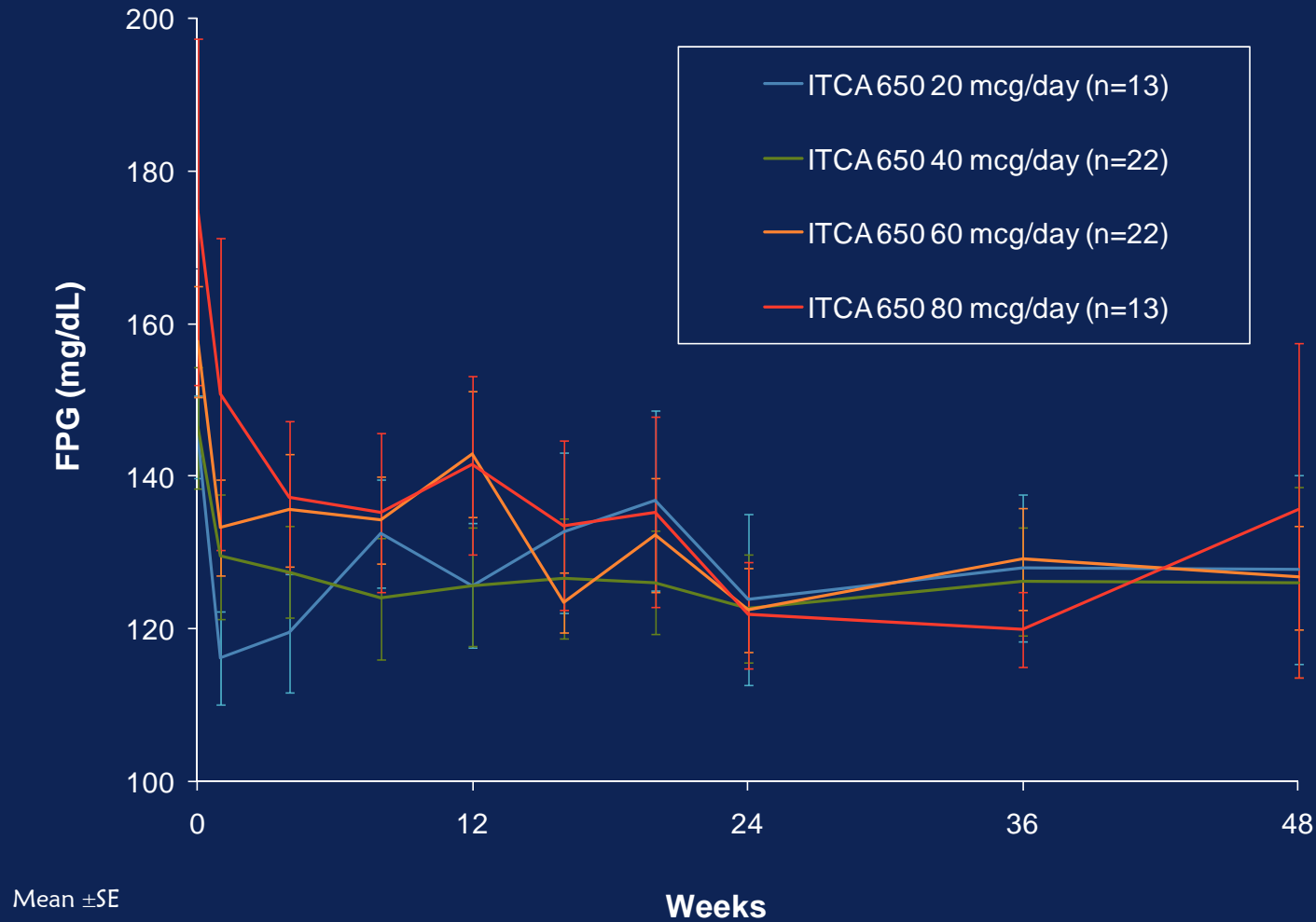
- Subjects were given the opportunity to continue treatment for an additional 24 weeks
- ITCA 650 was maintained at same dose
- 85% of subjects at participating sites chose to continue treatment with ITCA 650

Patient Disposition During Extension to 48 Weeks

	ITCA 650 20 mcg/day	ITCA 650 40 mcg/day	ITCA 650 60 mcg/day	ITCA 650 80 mcg/day
Entered Extension	15	28	27	16
Completed 48 weeks	14	23	23	13
Withdrawals				
Nausea	0	0	0	0
Withdrew consent	0	1	3	0
Hypoglycemia	0	0	0	1
HbA _{1c} elevation	0	1	0	0
Adverse event	0	2	1	2
Other	1	1	0	0

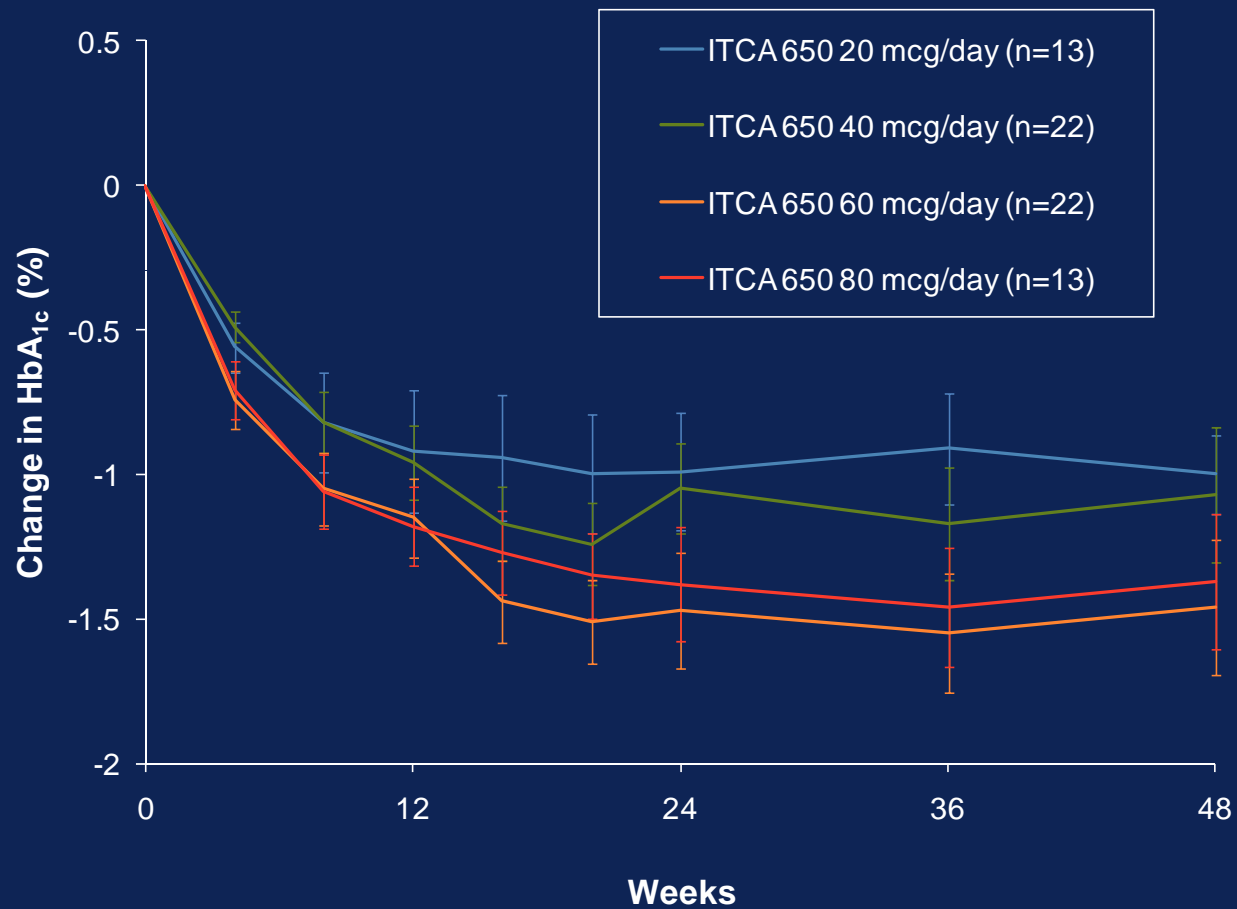
Sustained Exenatide Effects Via DUROS Subcutaneous Implants in MET-Treated Type 2 DM

FPG Changes at Over Time



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

HbA1c Changes Over Time

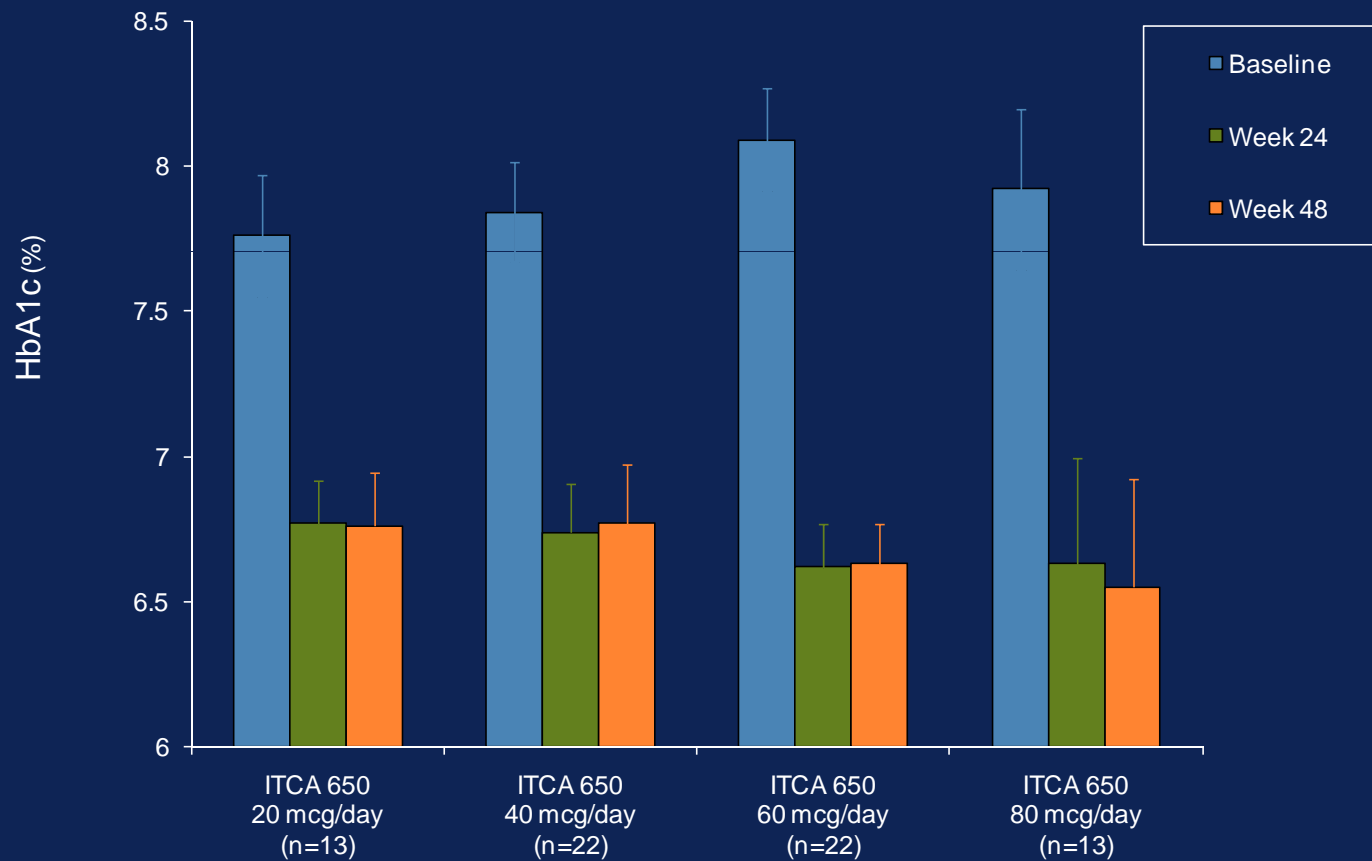


Mean \pm SE

At 48 weeks, $p < 0.0001$ for all dose groups

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

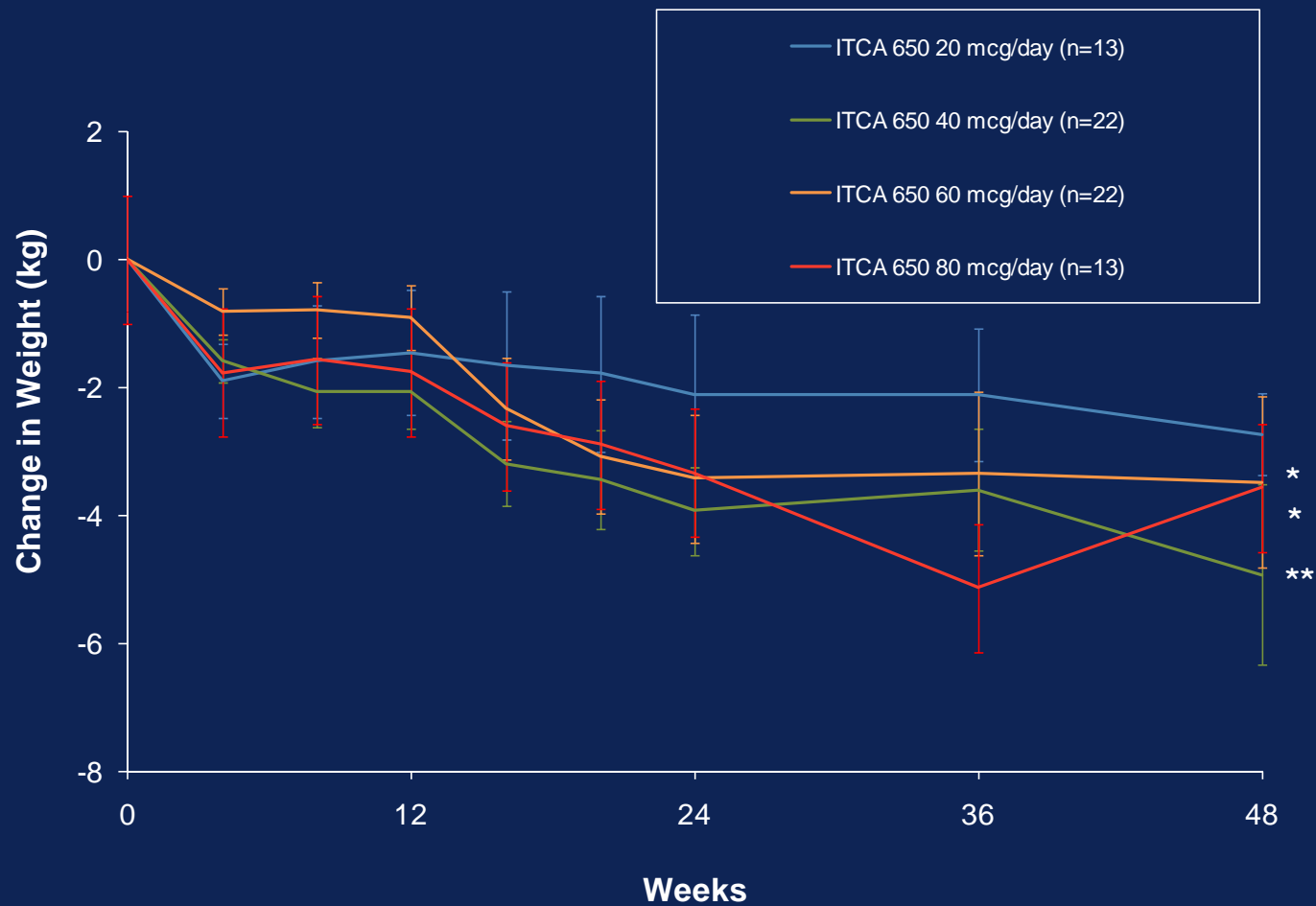
HbA1c Changes at Week 24 and Week 48



At 48 weeks, $p < 0.0001$ for all dose groups

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

Body Weight Changes Over Time

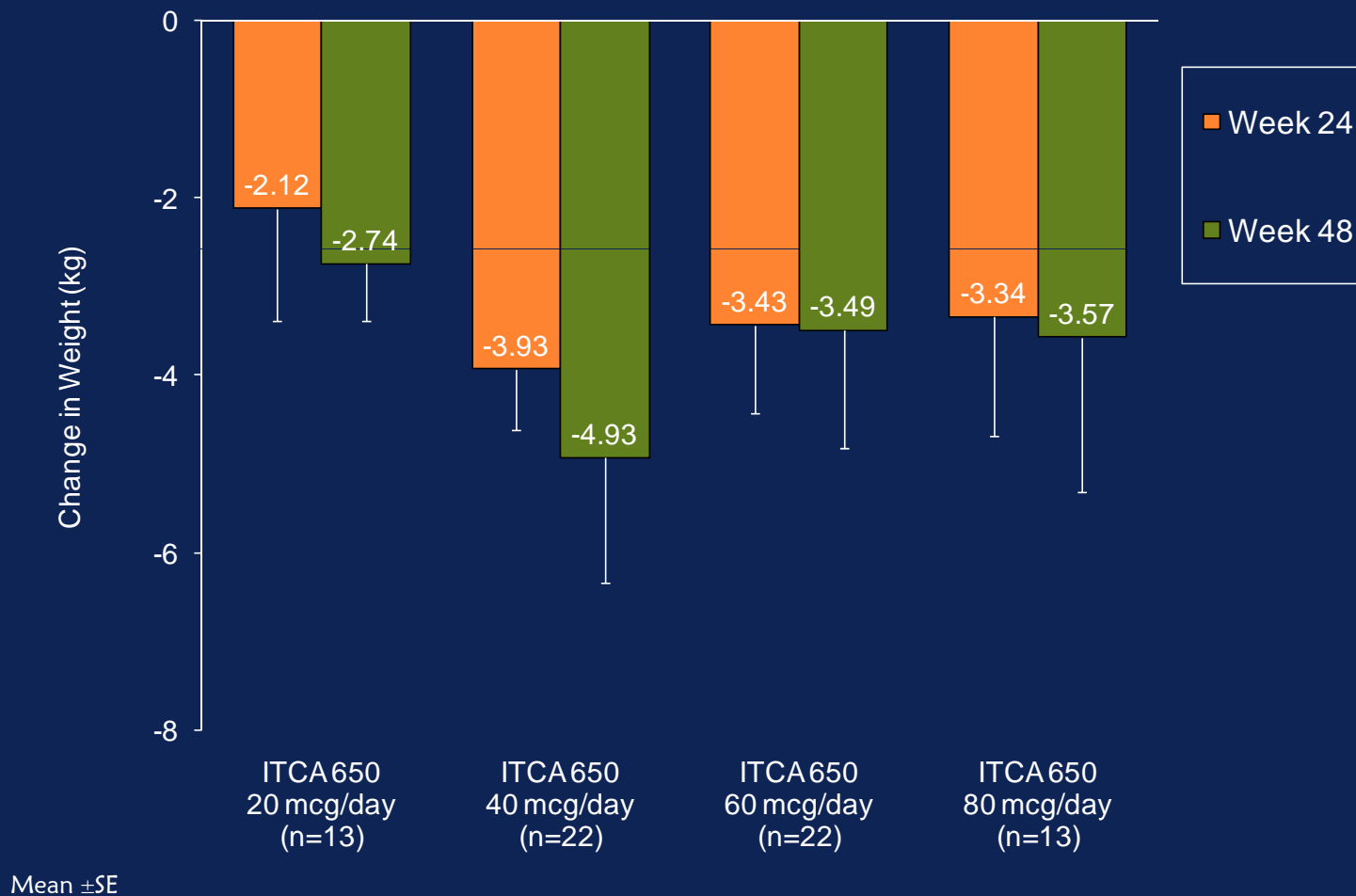


Mean \pm SE

* $p < 0.05$ ** $p < 0.001$

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

Body Weight Changes at Week 24 and Week 48



Adverse Events of Special Interest in Extension 48 Weeks

- **Gastrointestinal**

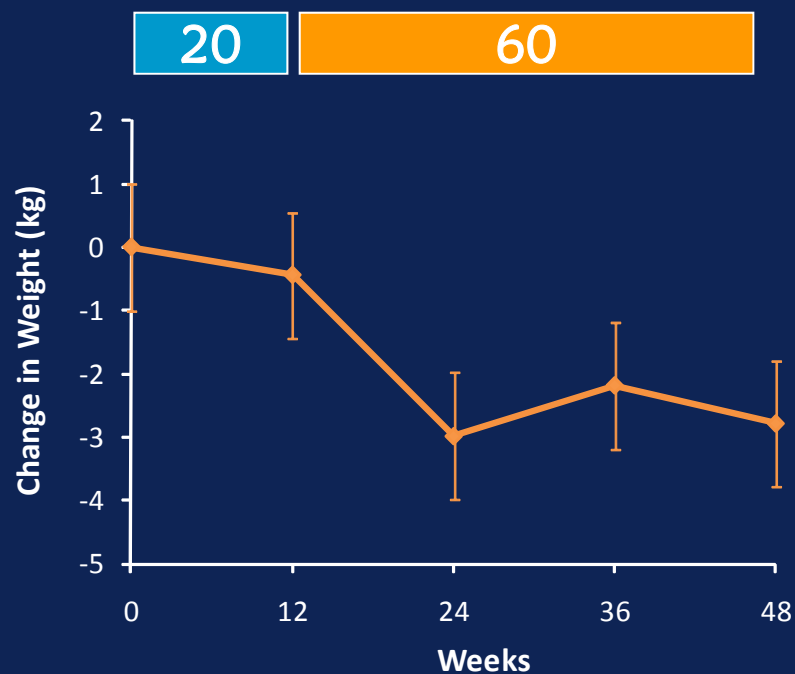
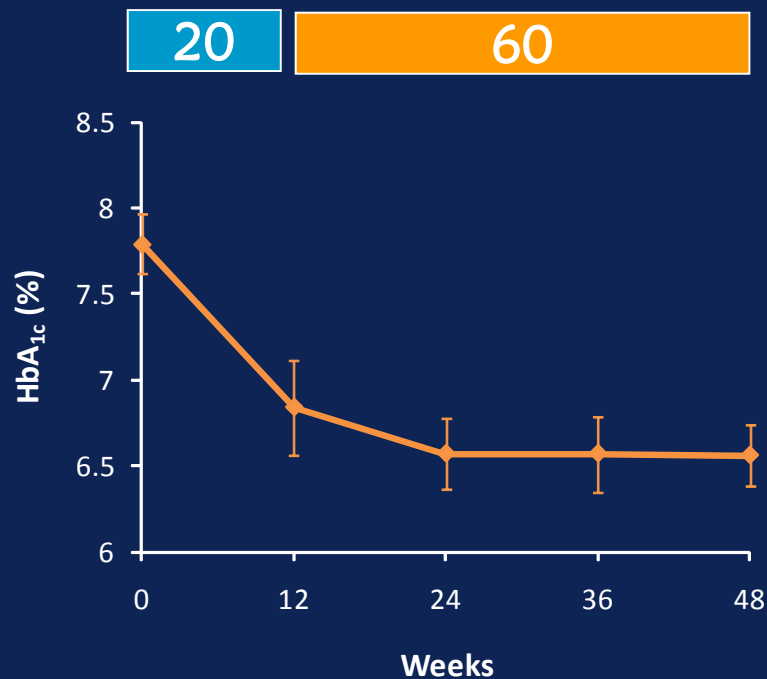
✓ Nausea	10.5%
✓ Diarrhea	3.5%

- **Skin Insertion Site**

✓ Irritation	7%
✓ Pain	7%
✓ Erythema	4.7%
✓ Pruritus	3.5%
✓ Hematoma	3.5%

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

ITCA 650 Dose Selected for Phase 3 Studies: 20→60 mcg/day



■ During 6 Month Extension

- ✓ Sustained HbA_{1c} and body weight reductions
- ✓ No subjects withdrew for any reason
- ✓ One report of nausea and no reports of vomiting
- ✓ No hypoglycemia

ITCA 650 Phase 2 Study Conclusions

- 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 body 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 subcutaneous devices (up to 6 and 12 months) for injection-free exenatide therapy in Type 2 Diabetes
- Ensured adherence with this DUROS implantable device may improve long-term outcomes

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

Investigators

Atoya B. Adams

Eddie Armas

Richard L. Beasley

Gary W. Bedel

Richard Bergenstal

Maria Bermudez

Patricia Buchanan

Rafael Canadas

James P. Capo, Jr.

David Carter

William Cefalu

Louis B. Chaykin

Lisa Connery

Ralph Cox

Douglas Denham

John K. Earl

Richard H. Egelhof

Rochelle Elijah

Eli Engel

Neil Fraser

Ernesto Fuentes

Kenneth S. Hershon

Frederick D. Jenkin

Dean Kereiakes

Judith Kirstein

Eric J. Klein

Lawrence R. Koehler

Douglas Logan

Barry Lubin

Sunder Mudaliar

Lyle Myers

Thomas C. Nussdorfer

E. David Pampe

Ashokkumar Patel

Andres Patron

Monica Perlman

David Podlecki

Geri Poss

Luis Carlos Quintero

George Raad

Julio Rosenstock

Michael Sanson

Gladstone Sellers

Ronald Stegemoller

Danny Sugimoto

Mark Turner

Jeffrey Unger

James Vanderlugt

Carol Wysham

Douglas Young

Big Thank You to the investigators and research subjects for their participation!