Intranasal Administration of Exenatide in Patients with Type 2 Diabetes: Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability

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Presenter Disclosure Information

Erich Blase

- Stockholder: Amylin Pharmaceuticals, Inc.
- Employee: Amylin Pharmaceuticals, Inc.

Introduction

- Exenatide, an incretin mimetic, has multiple mechanisms of action that improve glucose control in patients with type 2 diabetes:
  - Enhancement of glucose-dependent insulin secretion
  - Suppression of inappropriately elevated postprandial glucagon secretion
  - Slowing of gastric emptying
  - Reduction of food intake
- Exenatide is currently administered twice daily via subcutaneous injection prior to major meals
- Intranasal delivery of exenatide
  - Non-invasive mealtime dosing

Objective

- Examine the pharmacokinetics, pharmacodynamics, safety, and tolerability of intranasal administration of exenatide in patients with type 2 diabetes using at least one OAD

Study Design

- Single-blind, dose-escalation, placebo-controlled study of intranasal administration of exenatide in subjects with type 2 diabetes
  - Single dose delivered (one to three 100-μL nasal sprays)
  - Standardized breakfast given after medication
  - Blood samples prior to and during the 8 hours following medication

	Screening	Treatment (visits occurred 2-8 days apart; 28 day maximum duration)					
Visit	1	2	3	4	5	6	7
Low Dose (n=12)	Screening	Saline IN ⋮ 30 min ⋮ ▼ Exen SC 5 mcg	Placebo IN	Exen IN 60 mcg	Exen IN 200 mcg (alt form)	Exen IN 200 mcg	Exen IN 600 mcg

Abbreviations: IN = intranasal; SC = subcutaneous

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High Dose Group (n=8)				Exen IN 600 mcg	Exen IN 800 mcg	Exen IN 1200 mcg	Exen IN 1800 mcg

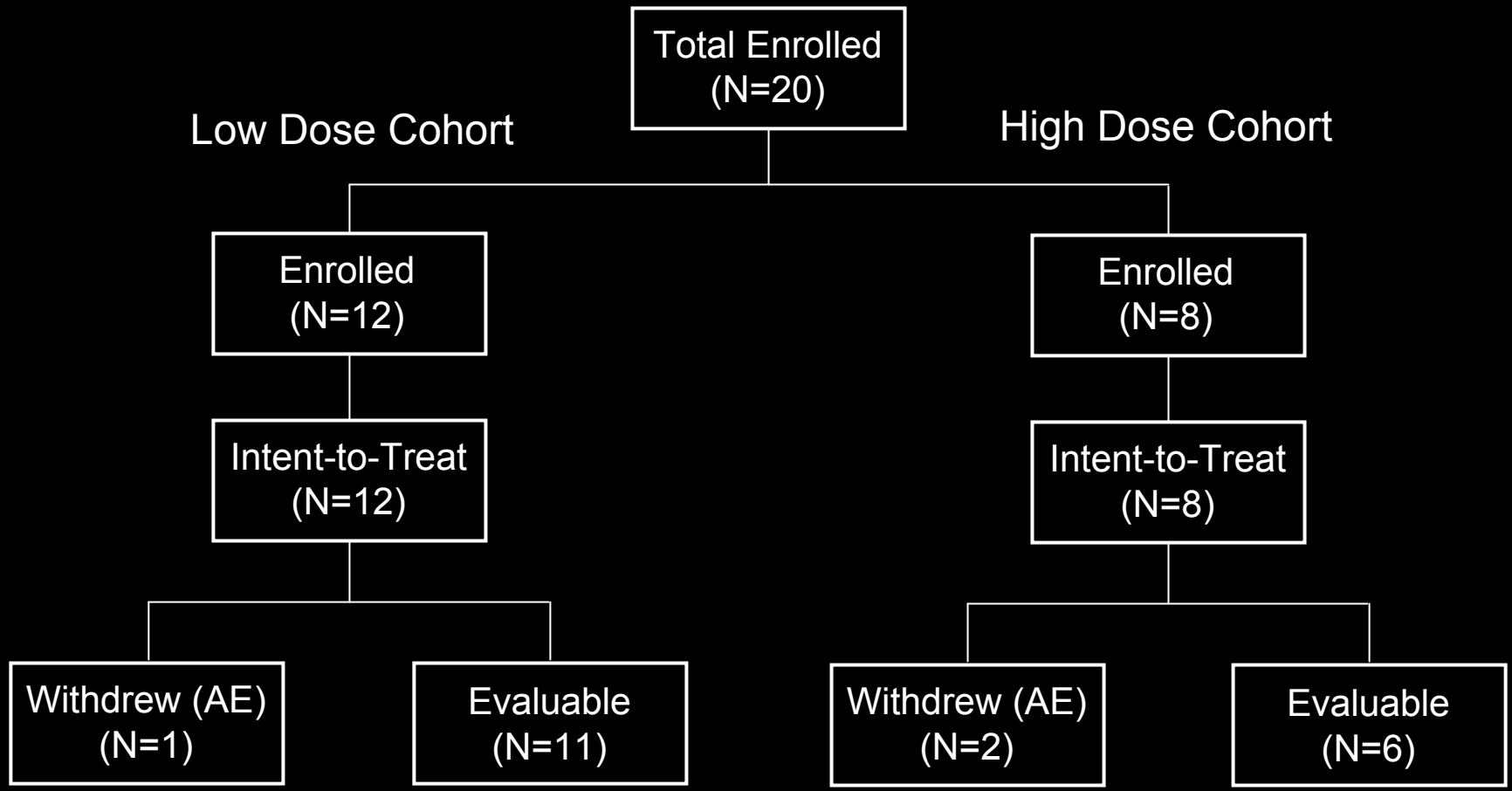
Abbreviations: IN = intranasal; SC = subcutaneous

Demographics and Baseline Characteristics

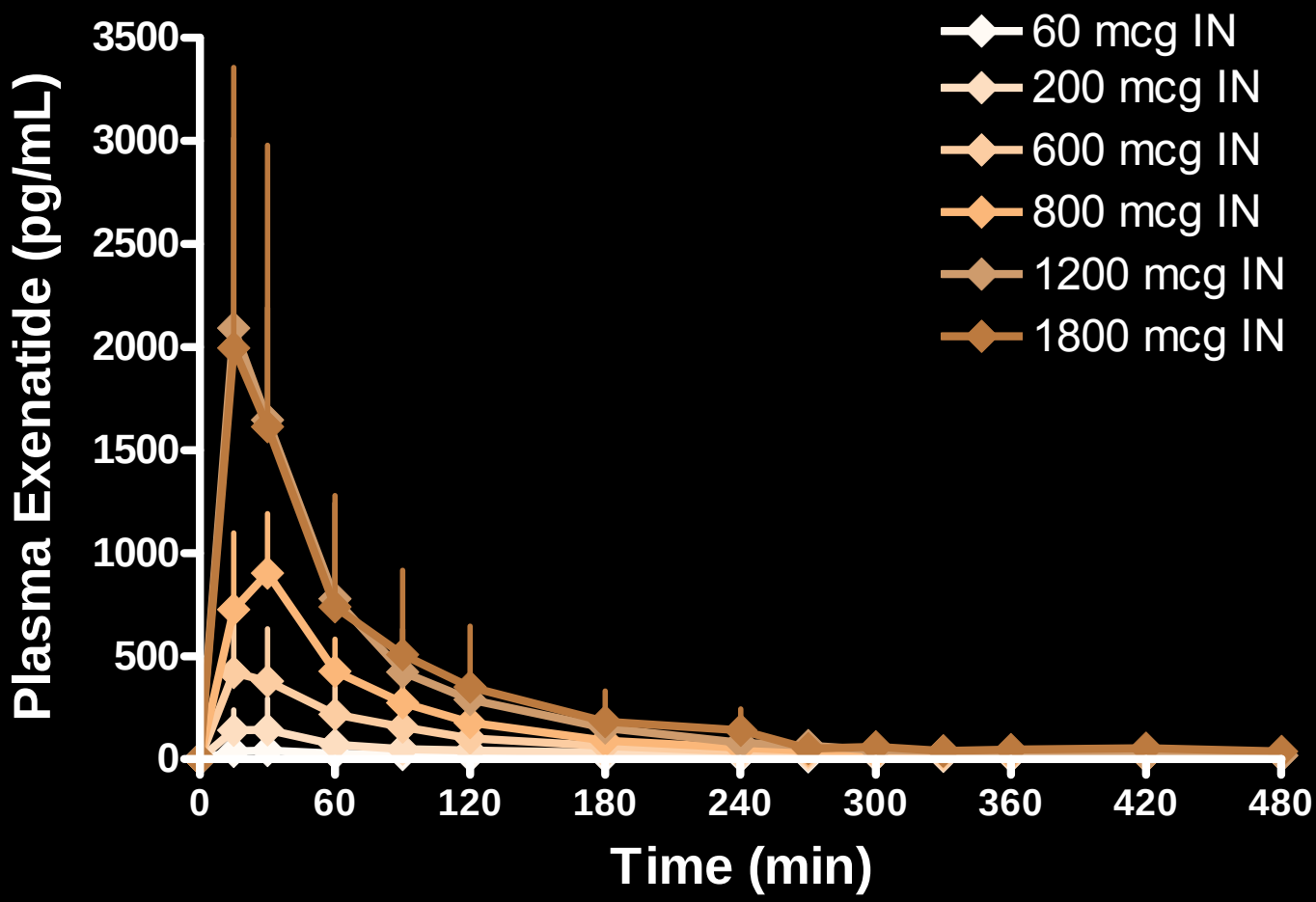
	All subjects (N=20)
Sex, male/female (%)	65/35
Age (y)	55 ± 9
Body weight (kg)	93 ± 12
BMI (kg/m^2)	31 ± 3
A1C (%)	8.1 ± 1.3
FPG (mg/dL)	156.4 ± 34.6
Duration of diabetes (y)	9 ± 8

ITT Population. Data are mean ± SD, except for sex.

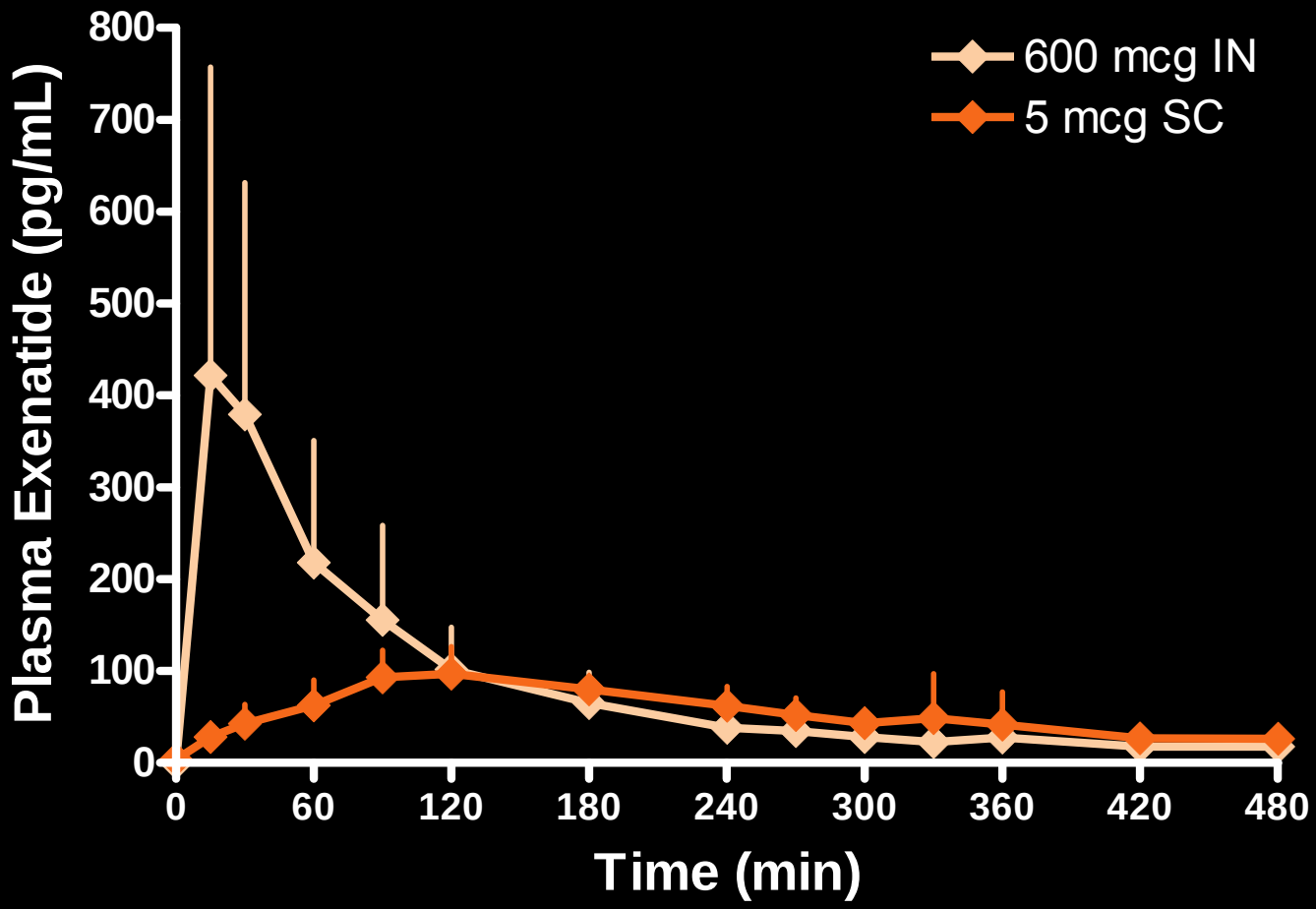
Disposition



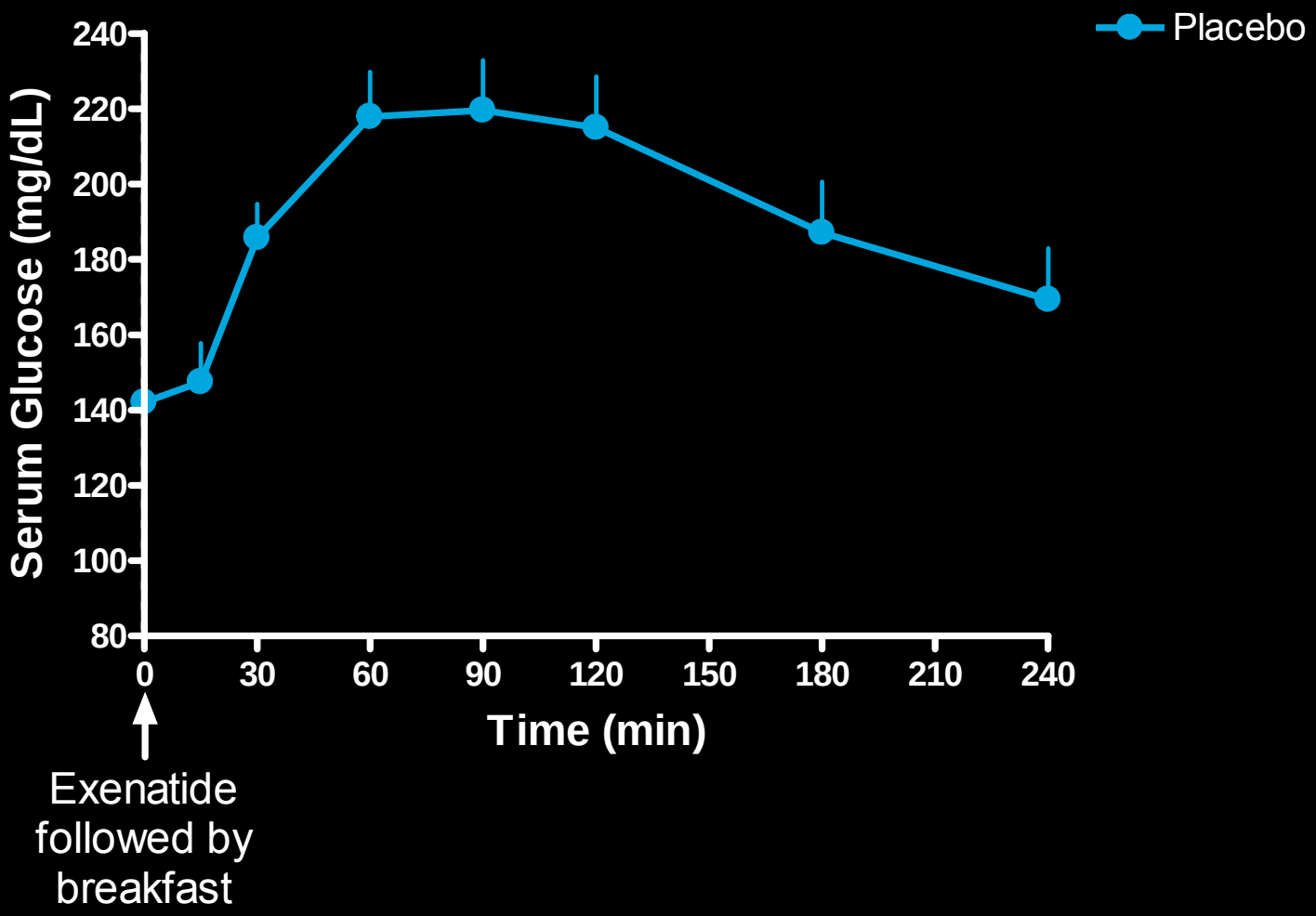
Pharmacokinetic Results



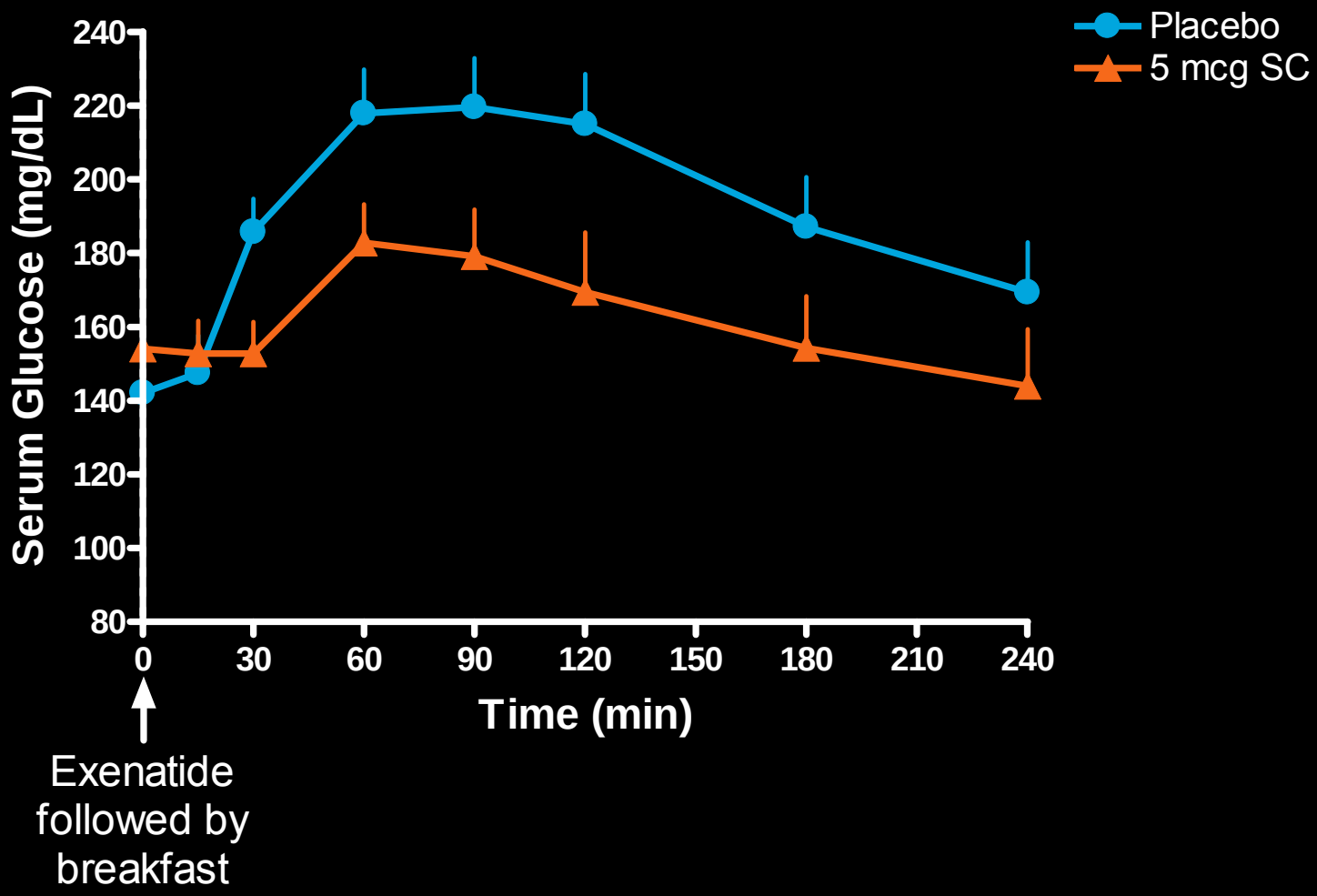
Pharmacokinetic Results



Serum Glucose



Serum Glucose



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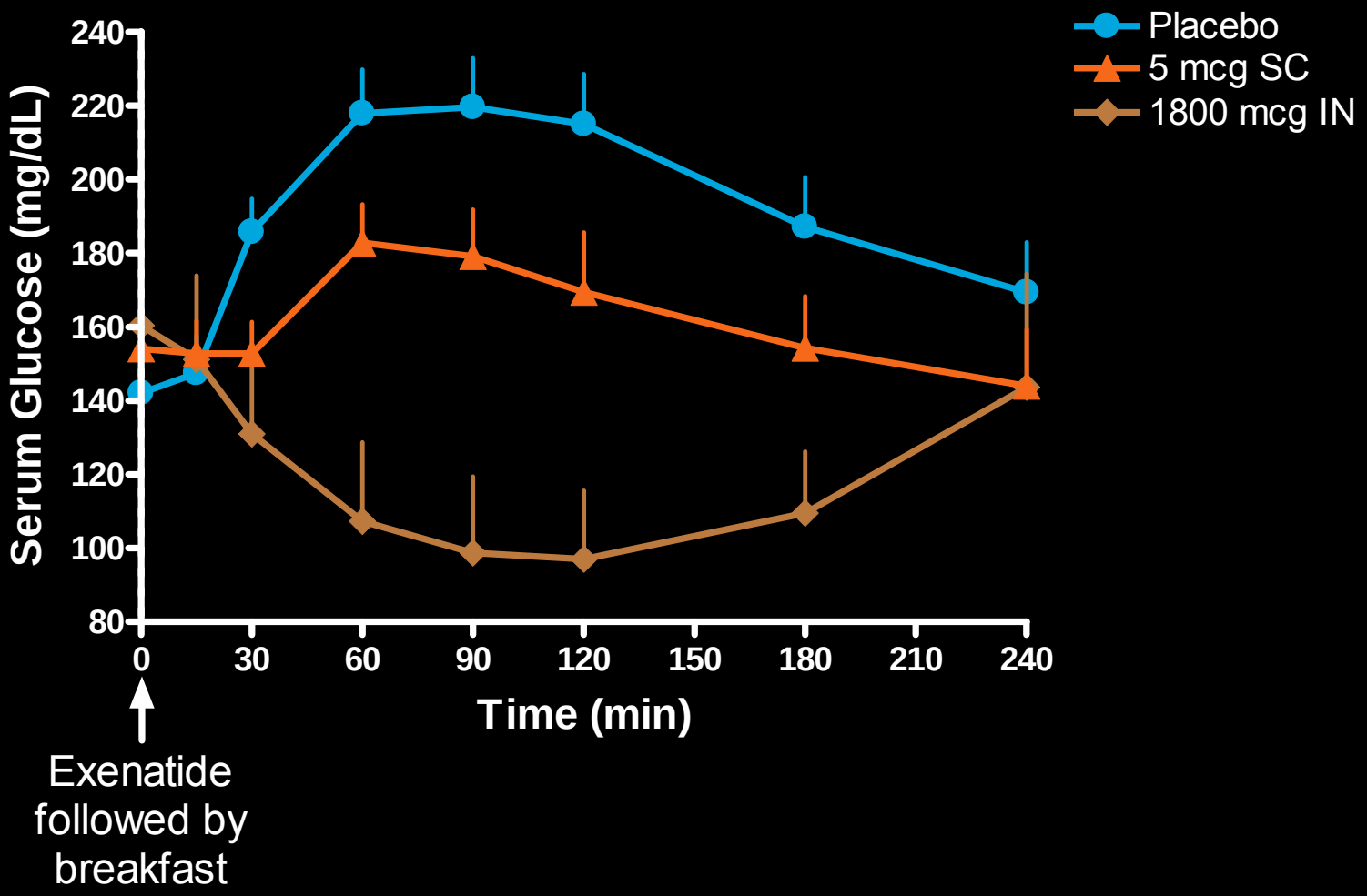
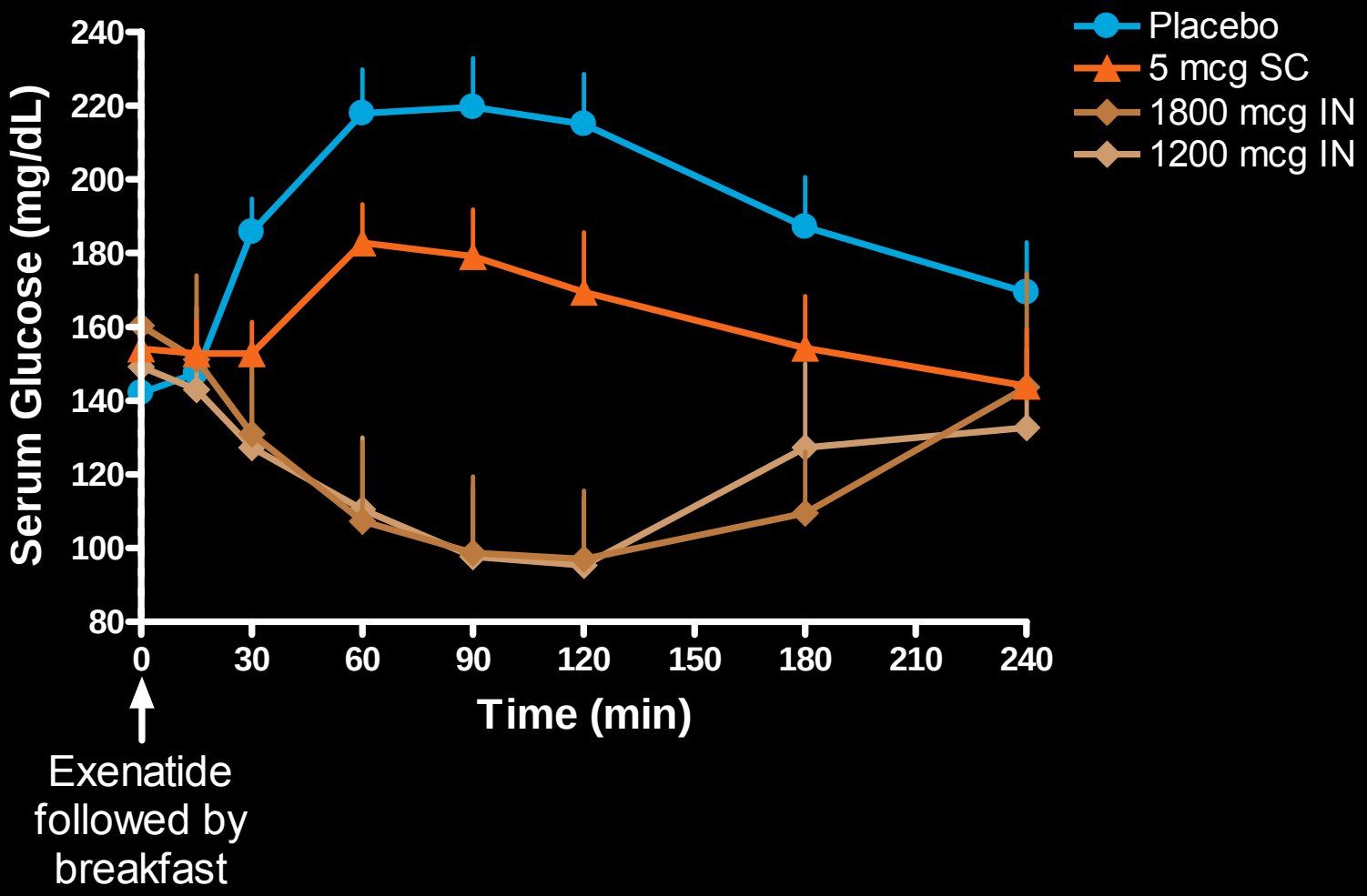


Serum Glucose



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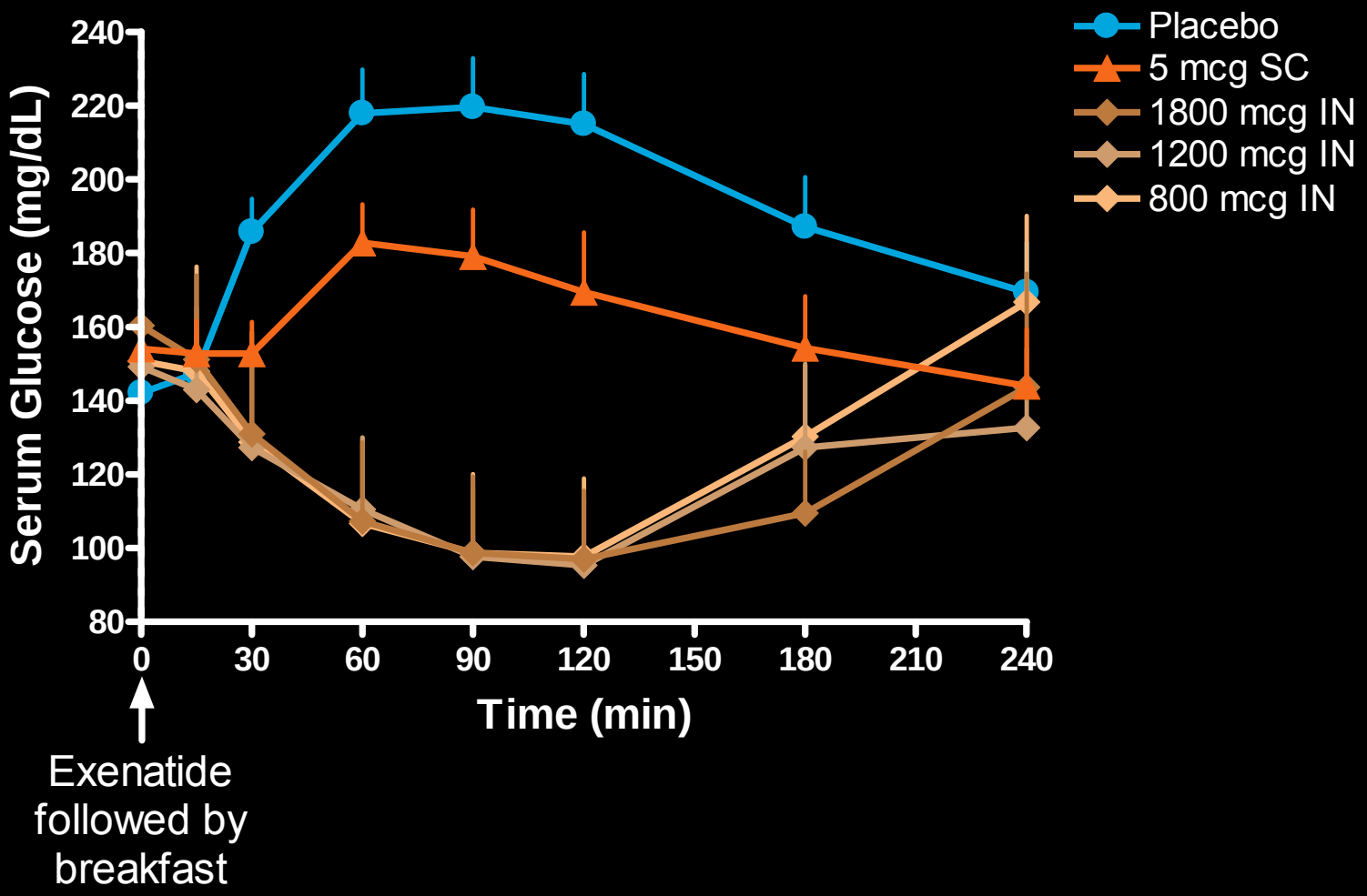
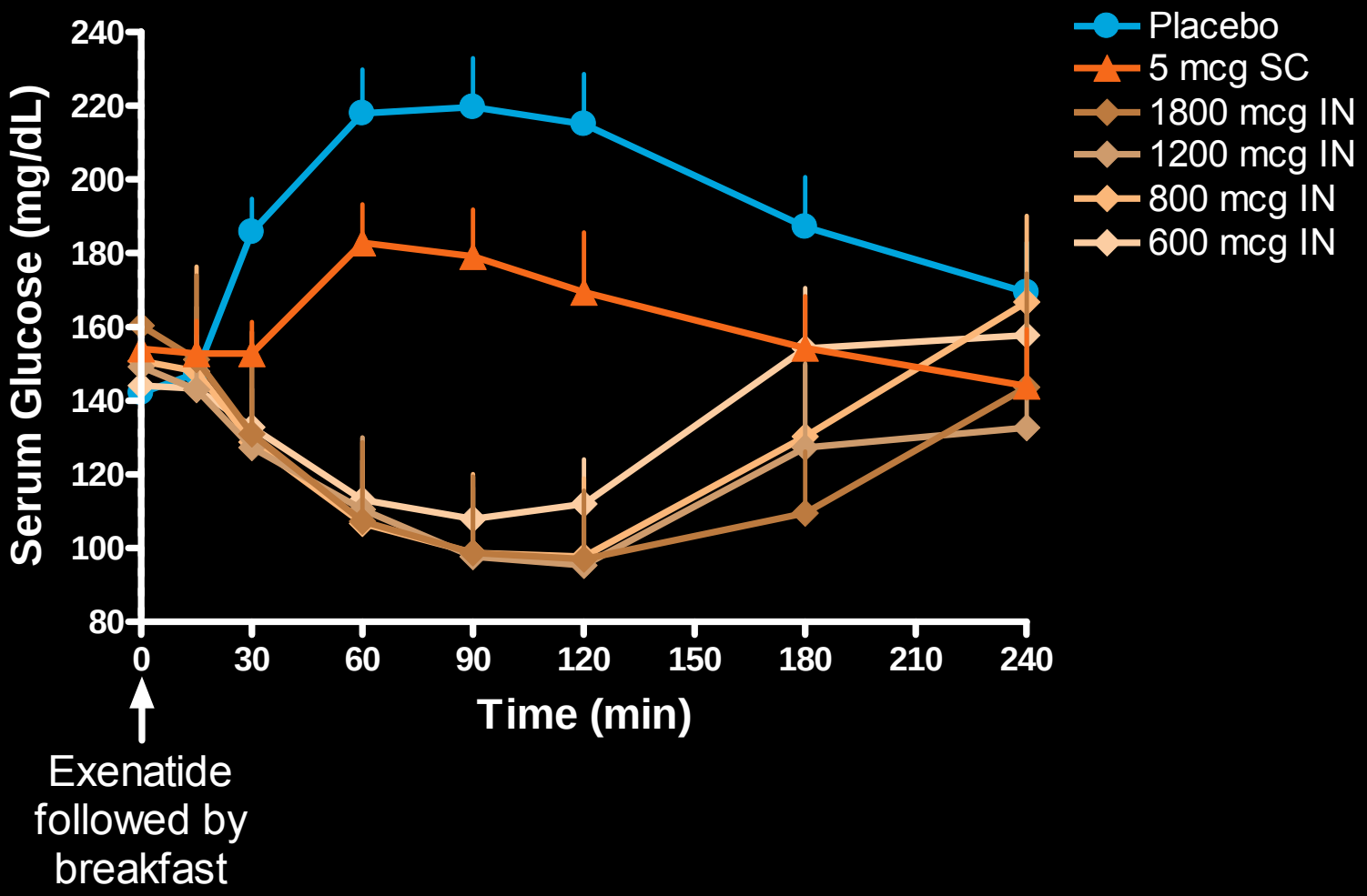


Serum Glucose



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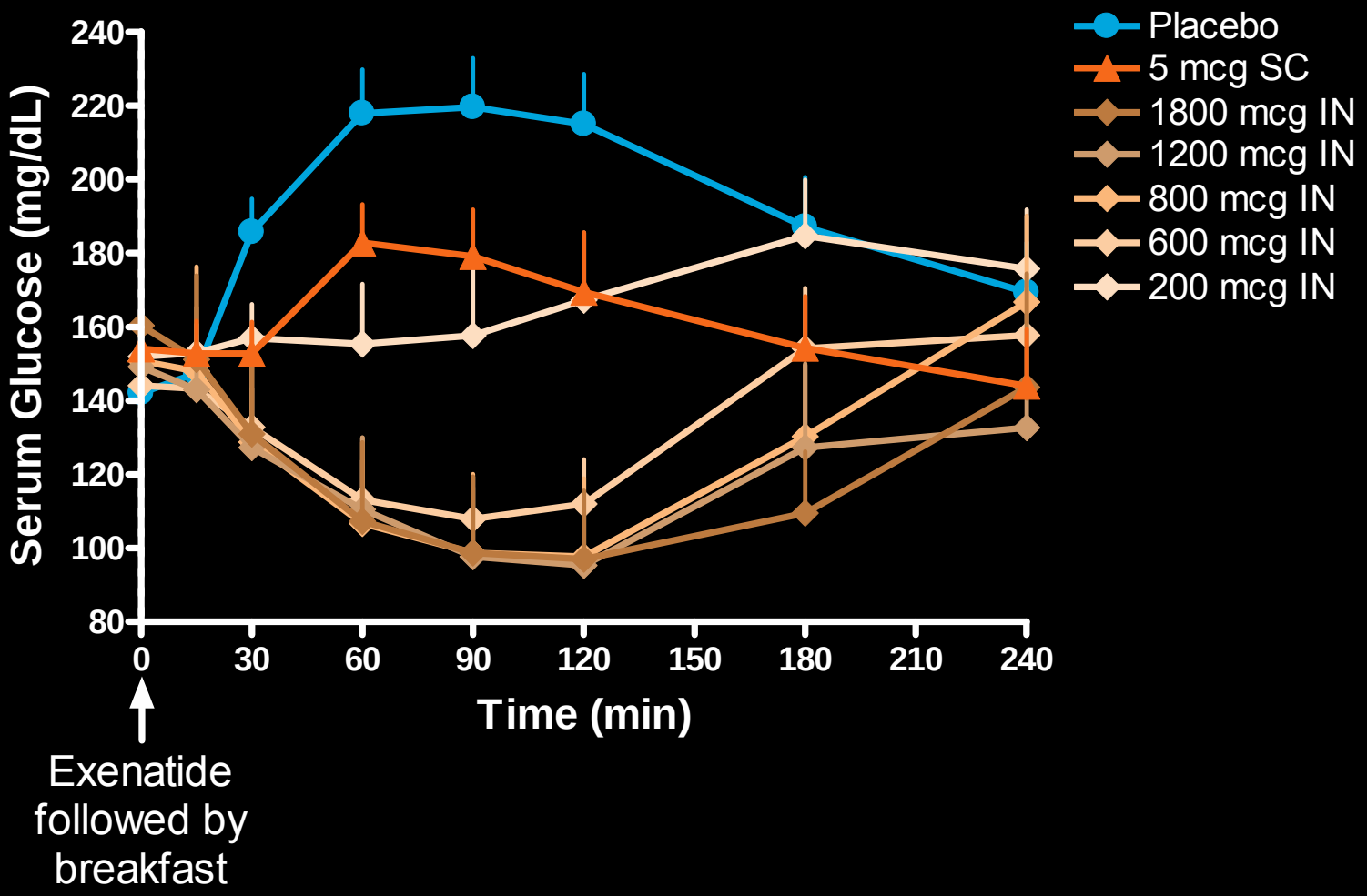
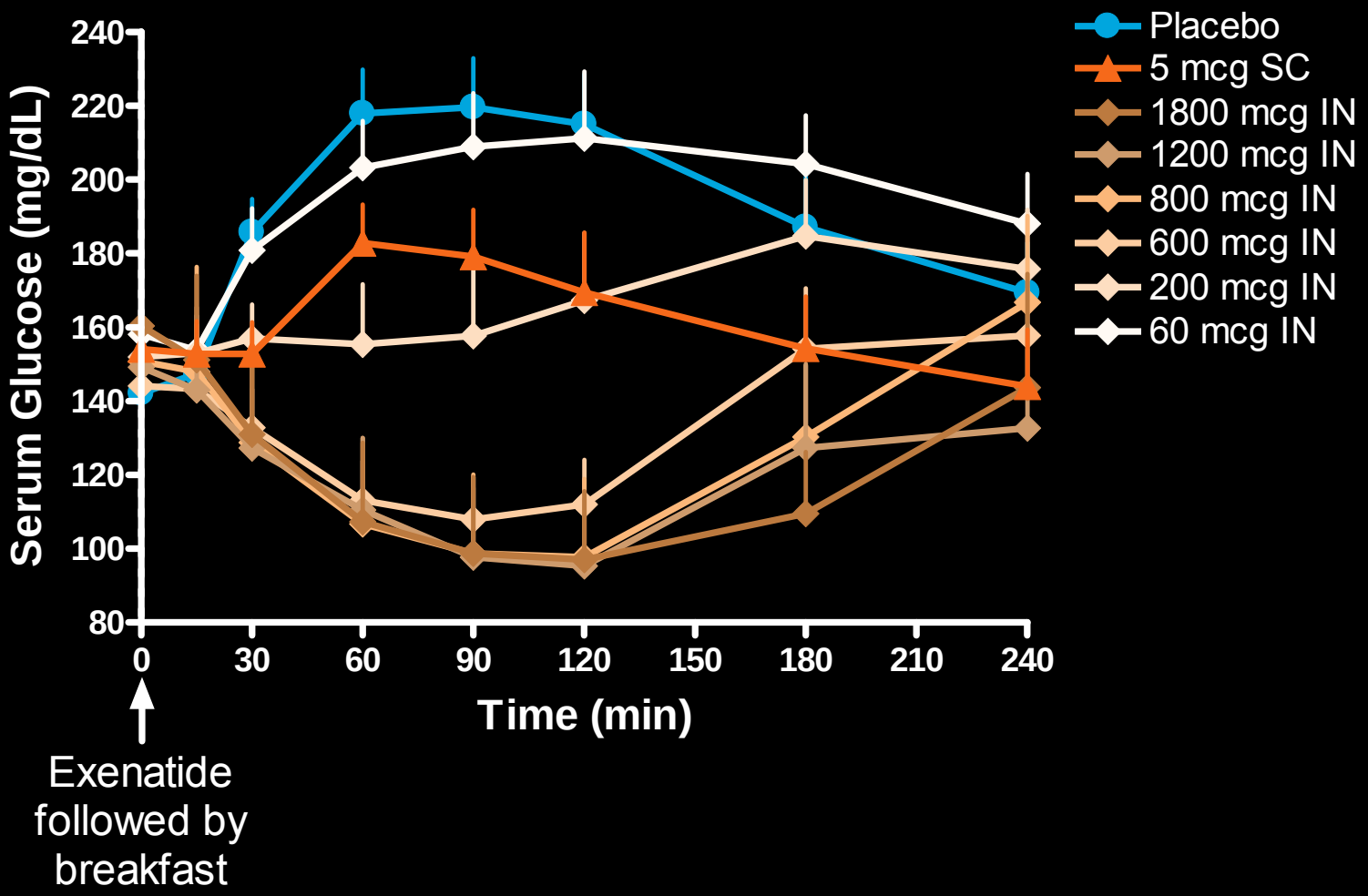
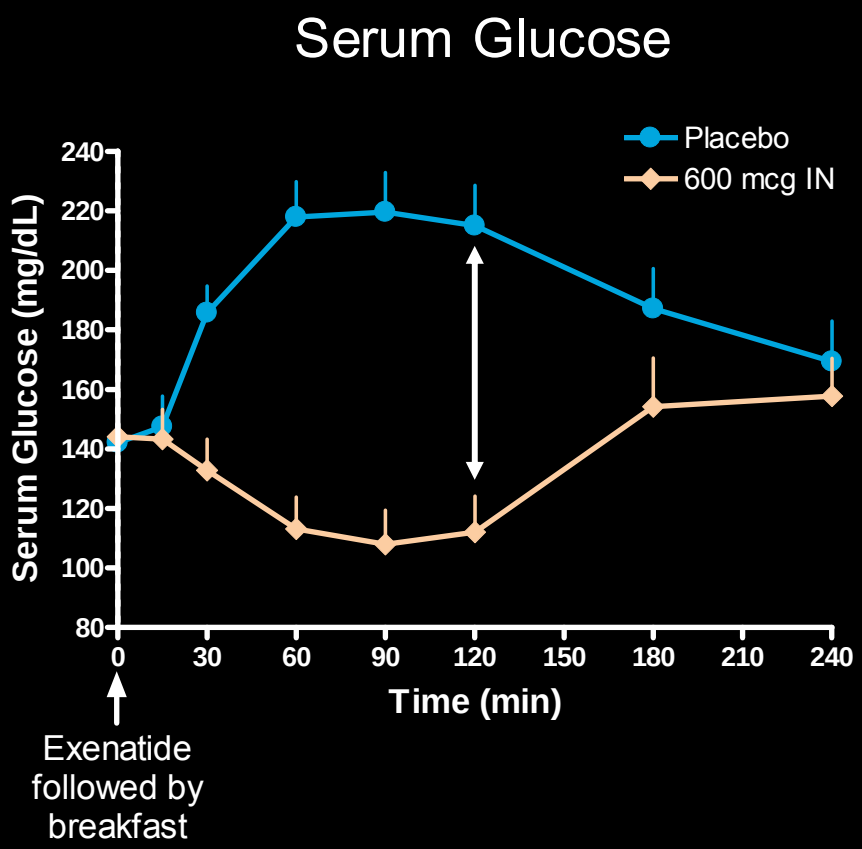
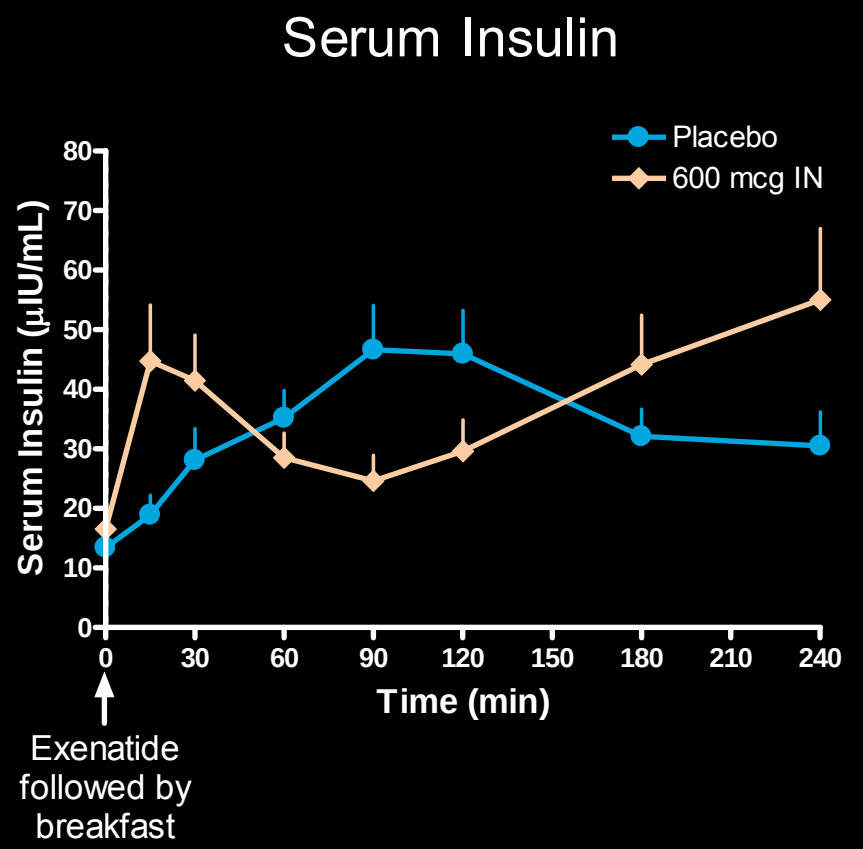


Serum Glucose



Serum Glucose and Insulin





Safety and Tolerability

- The most frequent adverse events with intranasal exenatide administration were nausea (6 patients) and vomiting (5 patients)
  - Nausea and vomiting occurred at doses ≥ 600 mcg
  - Nausea also occurred in 1 patient with placebo
- Sneezing occurred with intranasal administration of exenatide (2 patients) and placebo (1 patient)
- Intranasal administration of exenatide was generally well tolerated with no serious adverse events or hypoglycemic events

Conclusion

- Intranasal administration of exenatide in patients with type 2 diabetes was well tolerated and resulted in:
  - Therapeutic plasma exenatide concentrations
  - Enhanced glucose-dependent insulin secretion
  - Improved PPG control
- These data support the further development of intranasal exenatide delivery in the range of 600 mcg as a non-invasive treatment option for patients with type 2 diabetes

Additional Slides

Pharmacokinetic Results