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Avexitide for Post-Bariatric Hypoglycemia: Results from the Pivotal Phase 3 LUCIDITY Trial

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On Behalf of the LUCIDITY Investigators

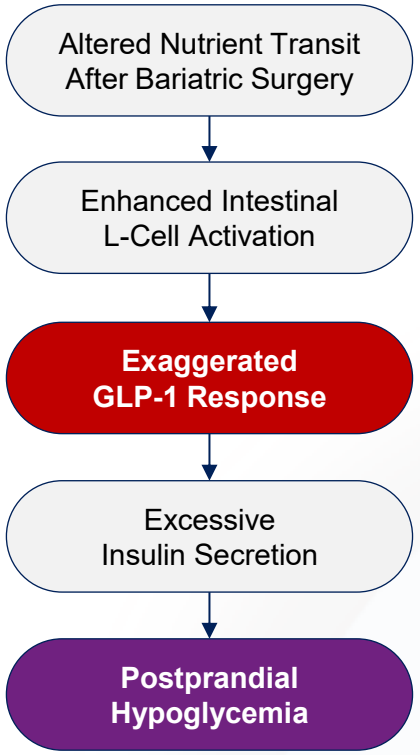
Avexitide is an investigational product and has not been approved by any regulatory agency

PBH is a Chronic Metabolic Condition Characterized by Exaggerated Postprandial GLP-1 Responses, Recurrent Hypoglycemia, and Substantial Clinical Burden

About Post-Bariatric Hypoglycemia[1-5]

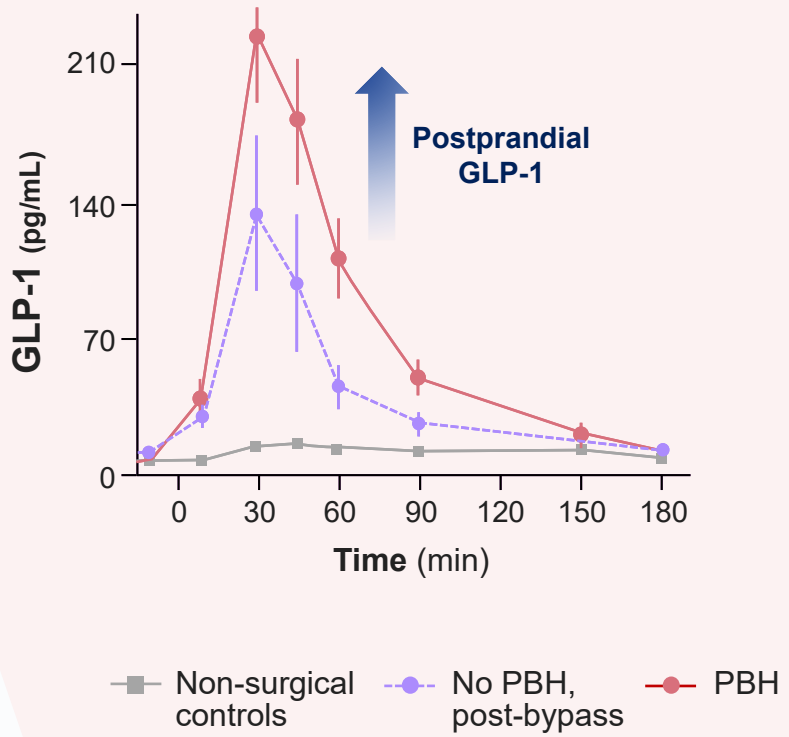
- Characterized by **recurrent postprandial hypoglycemia**, typically 1-3 hours after meals and developing months to years after surgery
- Requires medical management in **~12% of patients after Roux-en-Y gastric bypass (RYGB)** and **~5% after sleeve gastrectomy**
- Associated with **substantial clinical burden**, including effects on patient safety, daily functioning, and long-term health
  - In a recent survey, **>90% of respondents with PBH considered themselves functionally disabled** by their condition

The Role of GLP-1 in PBH[3,4]



Episodes may also be triggered by stress, physical activity, and other factors

GLP-1 Response to Meal Challenge[6]



GLP-1, glucagon-like peptide-1; PBH, post-bariatric hypoglycemia; RYGB, Roux-en-Y gastric bypass.

1. Craig CM, et al. *Surg Obes Rel Dis.* 2026;22(6):674-683. **2.** Patti ME, Goldfine AB. *Lancet Diabetes Endocrinol*. 2016;4(2):94-96. **3.** Salehi M, et al. *J Clin Endocrinol Metab.* 2018;103(8):2815-2826. **4.** Patti ME, Goldfine A. *Gastroenterology*. 2014;146(3):605-608. **5.** Craig CM, McLaughlin TL. *Surg Obes Relat Dis.* 2021;17(11):1865-1872. **6.** Salehi M, et al. *Gastroenterology*. 2014;146(3):669-680.e2. Graph adapted from Salehi M, et al. *Gastroenterology*. 2014;146(3):669-680.e2.

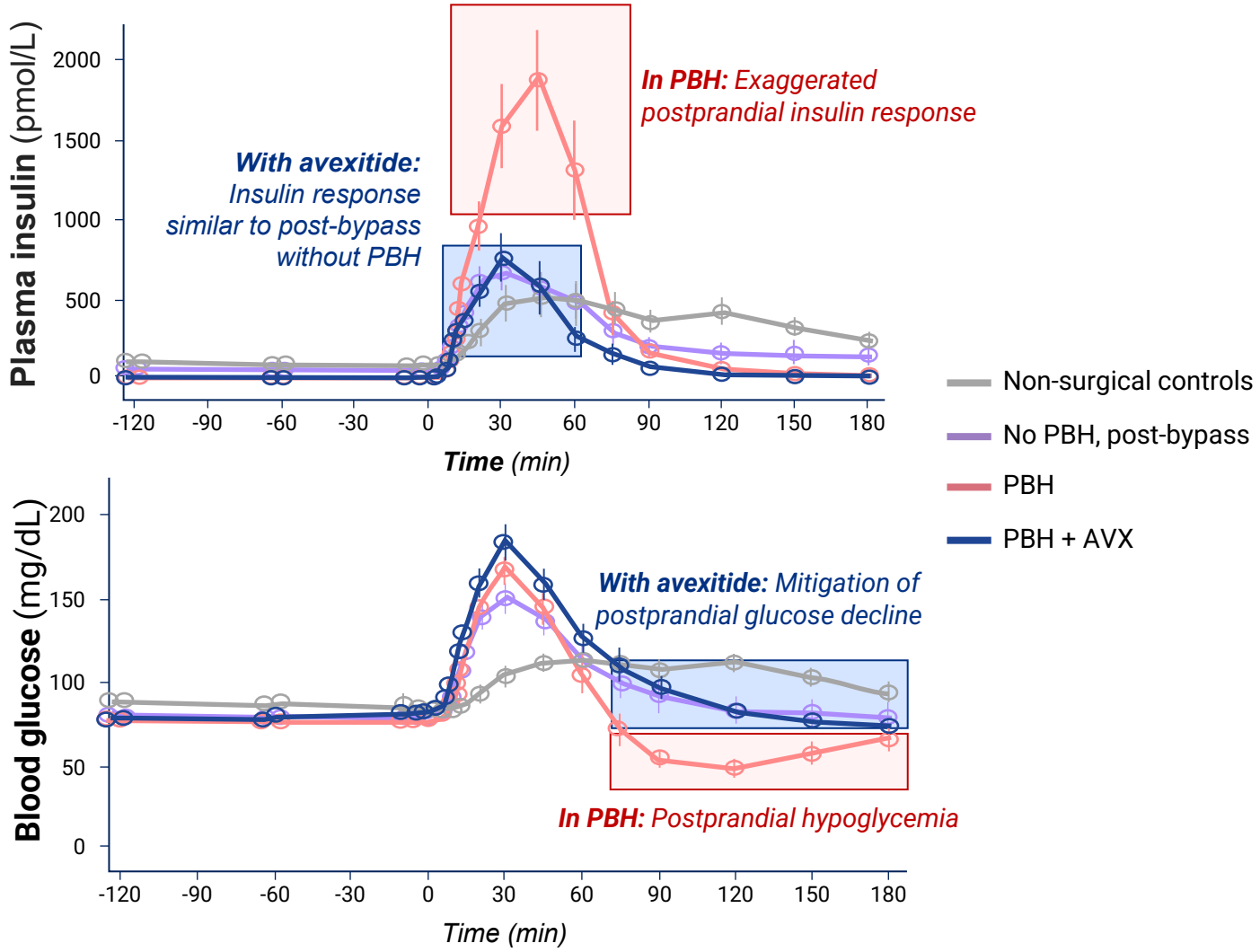
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Avexitide Consistently Reduced Hypoglycemia Across a Mechanistic Study and Five Positive Clinical Trials in PBH

Avexitide
Investigational GLP-1 Receptor Antagonist

- **In a mechanistic study, avexitide attenuated the exaggerated postprandial insulin response** and subsequent glucose decline, with responses resembling those of post-bariatric individuals without PBH[1]
- **In 5 prior clinical trials, avexitide reduced hypoglycemia across multiple measures** with acceptable safety and tolerability, supporting Phase 3 evaluation[2-6]

Representative Mechanistic Meal Challenge Study[1]

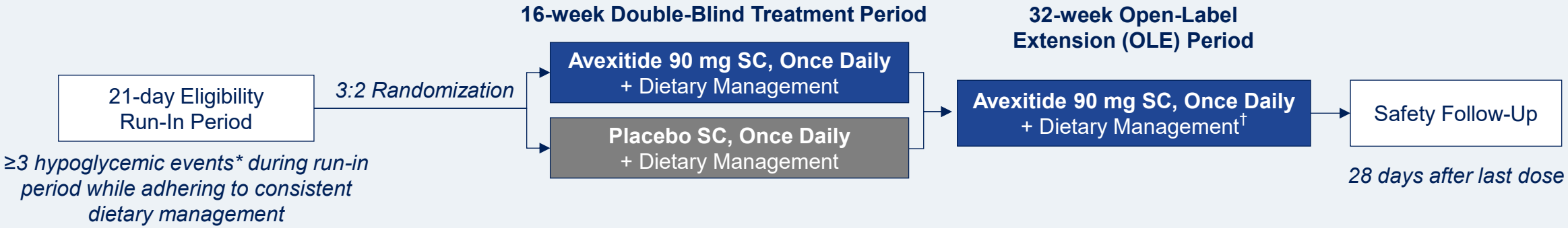


AVX, avexitide; PBH, post-bariatric hypoglycemia

1. Salehi M, et al. *Gastroenterology*. 2014;146(3):669-680.e2. **2.** Craig CM, et al. *Diabetologia*. 2017;60(3):531-540. **3.** Craig CM, et al. *Diabetes Obes Metab*. 2018;20(2):352-361. **4.** Tan M, et al. *Diabetes Obes Metab*. 2020;22(8):1406-1416. **5.** Craig CM, et al. *J Clin Endocrinol Metab*. 2021;106(8):e3235-e3248. **6.** Craig C, et al. *Metabolism*. 2026;184:156773. Graphs adapted from Salehi M, et al. *Gastroenterology*. 2014;146(3):669-680.e2.

Phase 3 LUCIDITY Trial Design

Multicenter, randomized, double-blind, placebo-controlled trial



KEY TRIAL ENTRY CRITERIA

- History of RYGB ≥12 months prior to screening
- Clinical diagnosis of PBH
- No current or recent use (within five drug-specific half-lives) of drugs that alter glucose metabolism or promote weight loss (eg, semaglutide, acarbose)

DIETARY MANAGEMENT

- Written dietary guidance and training provided at screening
- Guidance reviewed and reinforced by site personnel at each study visit
- Dietary recommendations included ≤30 g carbohydrate/meal and ≤15 g/snack, avoidance of simple/high-GI carbohydrates, and adequate protein intake

RYGB, Roux-en-Y gastric bypass; SC, subcutaneous; EAC, Event Adjudication Committee; SMBG, self-monitoring of blood glucose; OLE, open-label extension
*At least one event had to be adjudicated as level 3 by the independent Event Adjudication Committee (EAC), while the remaining two or more events could be documented as level 2 by SMBG or adjudicated as level 3
†For the first 8 weeks of the OLE, participants were instructed to follow the same dietary guidance as the run-in and double-blind periods

LUCIDITY Assessed Hypoglycemia Using Multiple Complementary Measures

Efficacy Endpoints

All assessed during the 16-week double blind period

Primary Efficacy Endpoint[1]

- Composite rate of SMBG-confirmed level 2 and blinded EAC-adjudicated level 3 hypoglycemic events

Secondary Efficacy Endpoints[1]

- Level 2 hypoglycemic events (SMBG)*
- Level 3 hypoglycemic events (EAC)*
- Level 2 hypoglycemic events (CGM)*
- % change from baseline in composite level 2/3 event rate

HYPOGLYCEMIC EVENT DEFINITIONS[1]

Level 2: Glucose <54 mg/dL†

Threshold at which neuroglycopenic symptoms begin to occur

Level 3: Hypoglycemic event characterized by altered mental and/or physical function requiring external assistance for recovery

Adjudication by a blinded, independent Event Adjudication Committee

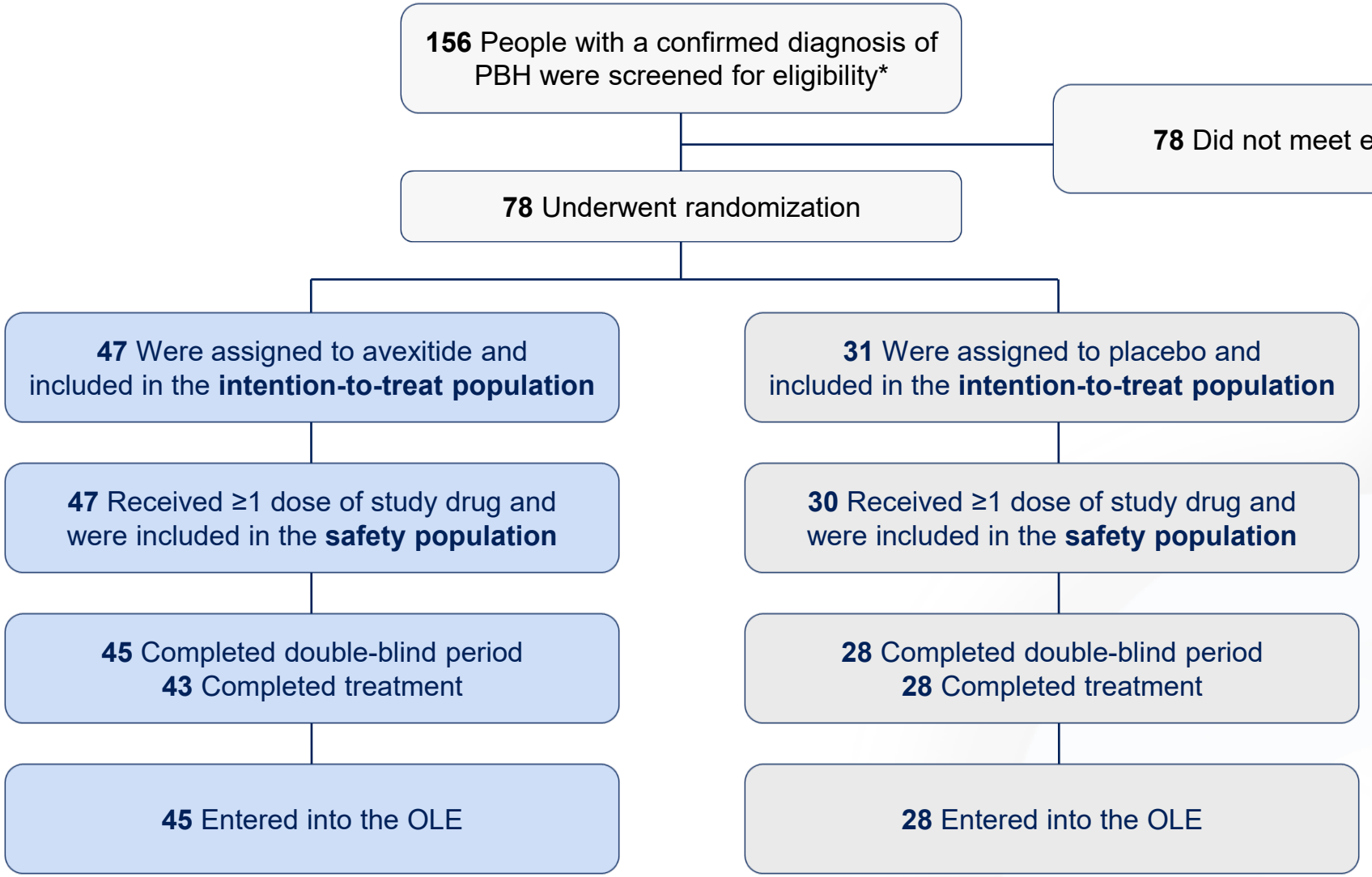
SMBG, self-monitoring of blood glucose; EAC, Event Adjudication Committee; CGM, continuous glucose monitoring

*Event-rate endpoints were multiplicity-controlled and tested hierarchically in the order listed

†SMBG: glucose <54 mg/dL; CGM: glucose <54 mg/dL for at least 15 minutes

1. ADA Professional Practice Committee. *Diabetes Care*. 2026;49(Suppl 1):S132-S149.

>90% of Participants Completed the Double-Blind Treatment Period; All Completers Continued into the OLE



The PBH Experience Prior to Study Entry

*"**I cannot do the same things I was doing**, like go out, like be with my friends, drink a coffee, [be] outside, go hiking, things like that. Yeah, **all my life changed.**"*

LUCIDITY Participant Asked About Life Prior to Study Entry

OLE, Open-label extension period
*Participants who failed initial screening could be re-screened once, for a maximum of two screening attempts.
Quote from qualitative interviews performed in subgroup of LUCIDITY participants at Week 16 when asked to describe the hypoglycemic events they experienced before entering LUCIDITY and the impact of PBH on their daily life.

Baseline Characteristics Were Generally Balanced Between Groups

	Avexitide (n=47)	Placebo (n=31)	Overall (N=78)
DEMOGRAPHICS			
Age (years)	50.5 ± 9.7	51.3 ± 10.0	50.8 ± 9.8
Female – no. (%)	45 (96)	30 (97)	75 (96)
BMI (kg/m^2)	29.0 ± 4.3	27.1 ± 3.6	28.3 ± 4.1
Weight loss since surgery (kg)*	45.2 ± 21.5	44.7 ± 19.2	45.0 ± 20.5
PBH HISTORY			
Months since RYGB	136.1 ± 92.1	111.1 ± 87.5	126.2 ± 90.6
Months since first experience of postprandial hypoglycemia†	101.4 ± 84.7	73.8 ± 71.2	90.5 ± 80.3
Months since PBH diagnosis	68.3 ± 76.5	49.3 ± 57.9	60.7 ± 69.9
History of treatment for PBH – no. (%)	39 (85)	29 (94)	68 (88)
DISEASE BURDEN			
Daily hypoglycemia symptoms‡ – no. (%)	27 (64)	21 (72)	48 (68)
History of loss of consciousness§ – no. (%)	20 (44)	15 (52)	35 (47)
Prior PBH-related hospitalization§ – no. (%)	12 (26)	9 (31)	21 (28)
MEAN WEEKLY HYPOGLYCEMIC EVENT RATES (RUN-IN PERIOD)			
Composite level 2 by SMBG / level 3 by EAC	2.15 ± 1.73	2.75 ± 1.56	2.39 ± 1.68
Level 2 by SMBG	1.27 ± 1.74	1.27 ± 0.90	1.27 ± 1.46
Level 3 by EAC	1.58 ± 1.06	2.46 ± 1.65	1.93 ± 1.38
Level 2 by CGM	3.83 ± 3.89	2.96 ± 2.07	3.48 ± 3.30

Plus/minus values are means ± SD

The PBH Experience Prior to Study Entry

"I think just the burden of my husband having to babysit me, take me to all my appointments, drive me everywhere. ***It feels like [being] an invalid sometimes to have somebody have to care for me all the time."***

LUCIDITY Participant Asked About Life Prior to Study Entry

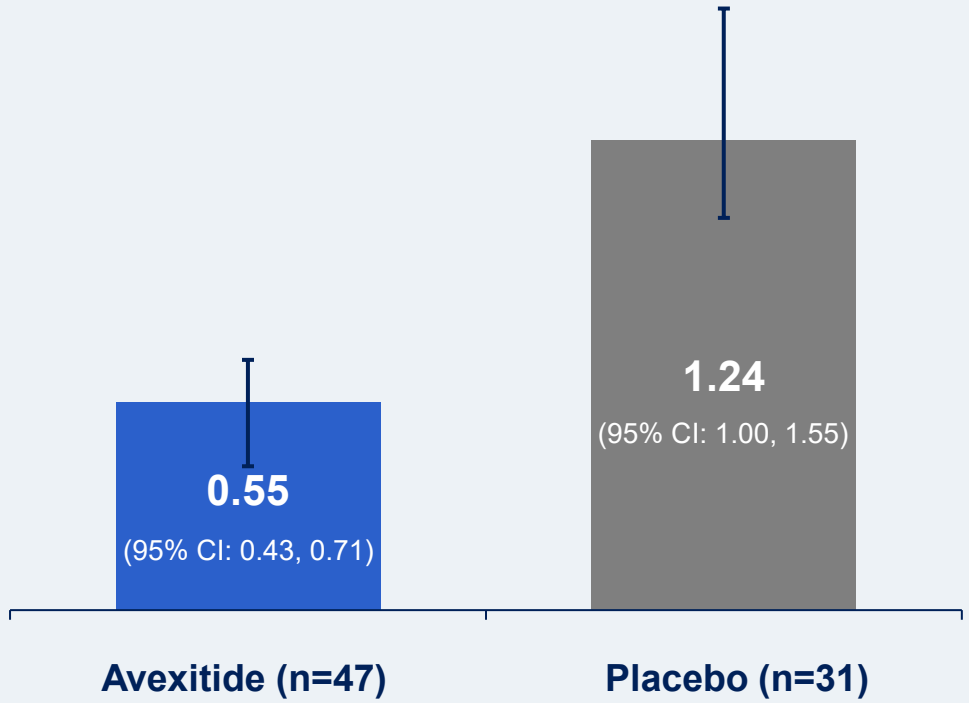
BMI, body mass index; SD, standard deviation
*Data available for 43 participants in the avexitide group and 28 participants in the placebo group
†Data available for 46 participants in the avexitide group and 30 participants in the placebo group
Quote from qualitative interviews performed in subgroup of LUCIDITY participants at Week 16 when asked to describe the hypoglycemic events they experienced before entering LUCIDITY and the impact of PBH on their daily life

‡Data available for 42 participants in the avexitide group and 29 participants in the placebo group
§ Data available for 46 participants in the avexitide group and 29 participants in the placebo group

Primary Endpoint Met: Avexitide Reduced the Composite Level 2/3 Hypoglycemic Event Rate by 55% vs Placebo

Mean Weekly Composite Level 2/3 Events (Model-Adjusted)

Double-blind treatment period (ITT, N=78)



Prespecified primary analysis: *Negative binomial regression adjusted for baseline composite event rate, with multiple imputation for missing follow-up time due to early study withdrawal. Bars show LS mean event rates (95% CI). Results use the treatment policy estimand.*

PRIMARY ENDPOINT

55% Reduction in composite level 2/3 hypoglycemic event rate vs placebo

Rate ratio: 0.45 (95% CI: 0.32-0.63)

***p* = 0.0000034**

Results consistent across prespecified sensitivity analyses and evaluated prespecified subgroups

Sensitivity Analyses:

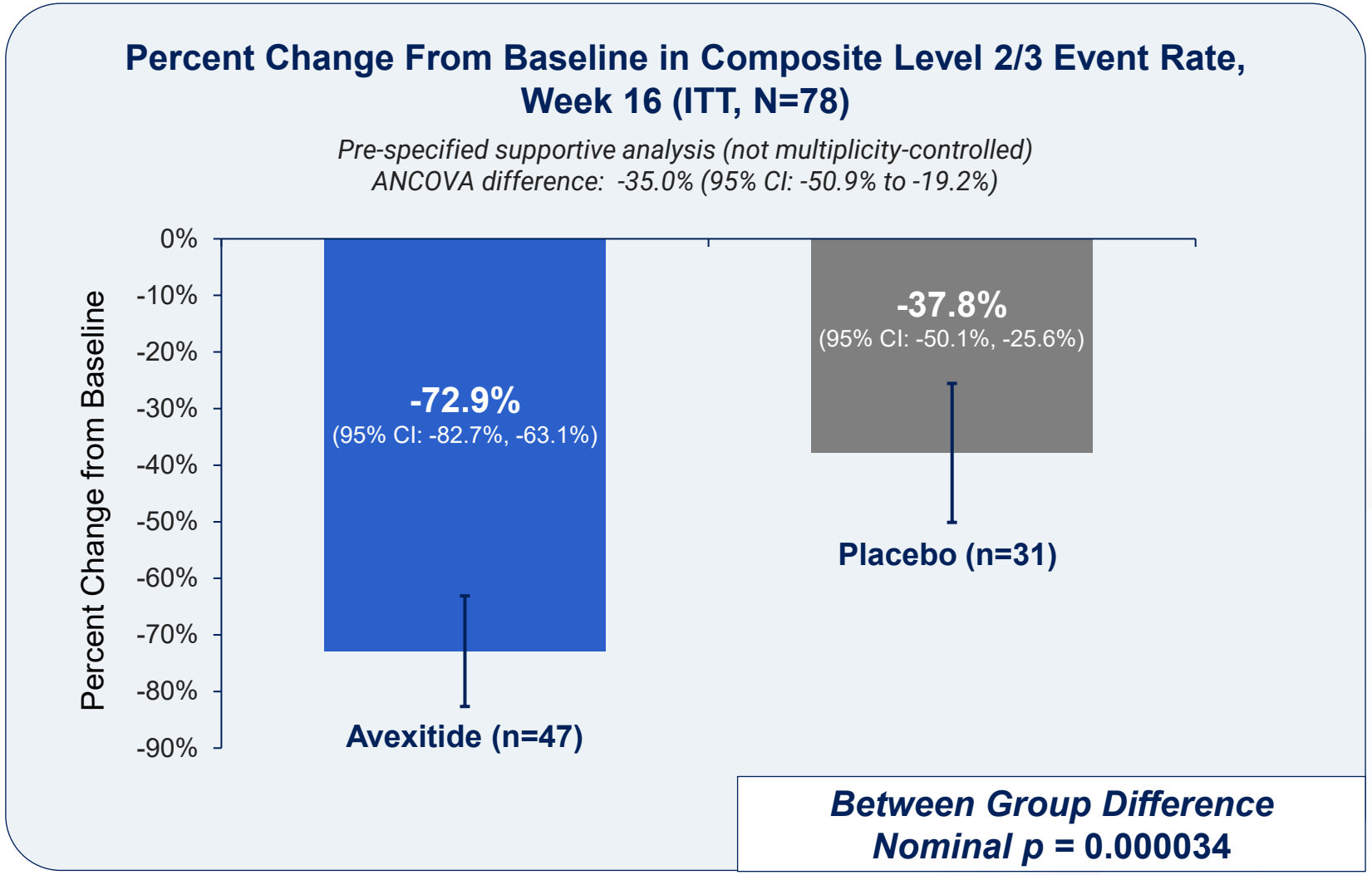
- Alternative missing-data handling
- Alternative estimation methods
- On-treatment estimand
- Alternative modeling of baseline event rate
- Alternative handling of adjudication-discordant level 3 events

Subgroup Analyses:

- Age
- Sex
- Race and ethnicity
- Body mass index

ITT, intent-to-treat; LS, least squares

Avexitide Demonstrated Greater Reductions From Baseline in Composite Level 2/3 Hypoglycemic Event Rate Than Placebo at Week 16



Study Factors That May Help to Explain Changes in the Placebo Group

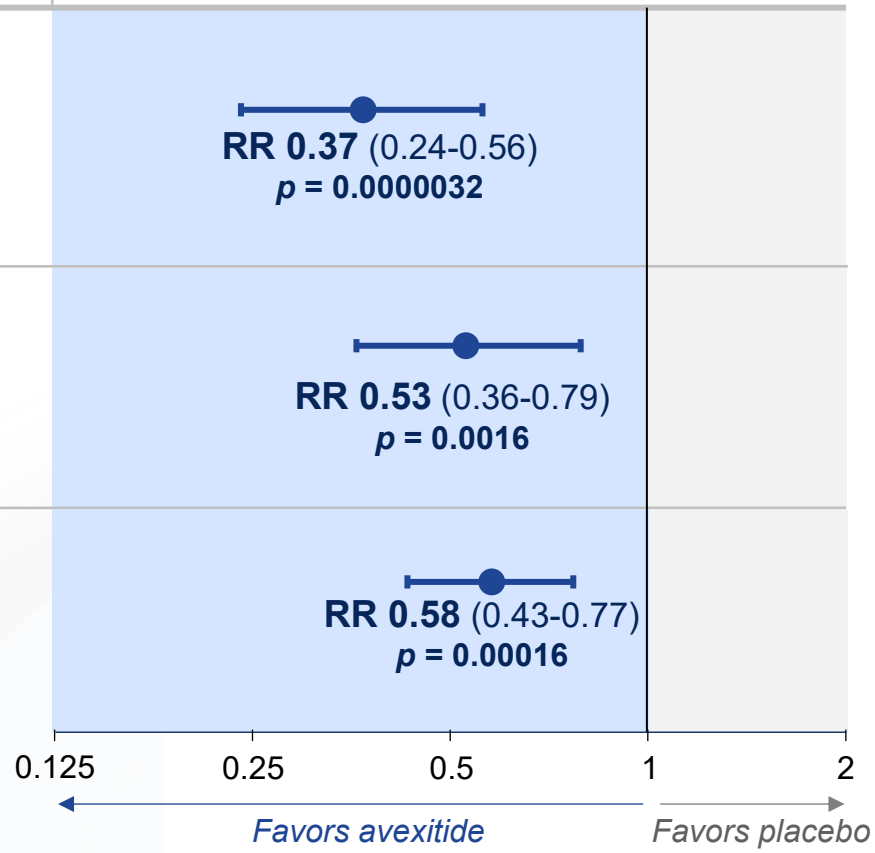
- Regression to the mean
- Structured dietary management with ongoing reinforcement
- Increased monitoring, including CGM, and access to a healthcare team

ANCOVA (analysis of covariance) of percent change from baseline, adjusted for baseline (run-in) event rate; estimate represents the LS mean difference; p-value is nominal.
LS, least squares

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All Prespecified, Multiplicity-Controlled Secondary Endpoints Met With Robust Statistical Significance

	PERCENT REDUCTION Mean weekly event rate over double-blind period (model-adjusted, ITT, N=78)	RATE RATIO (95% CI) Log scale
Level 2 (SMBG)	**63% Reduction vs Placebo** **Avexitide: 0.24** | Placebo: 0.66	**RR 0.37** (0.24-0.56) ***p* = 0.0000032**
Level 3 (EAC)	**47% Reduction vs Placebo** **Avexitide: 0.46** | Placebo: 0.87	**RR 0.53** (0.36-0.79) ***p* = 0.0016**
Level 2 (CGM)	**42% Reduction vs Placebo** **Avexitide: 1.72** | Placebo: 2.99	**RR 0.58** (0.43-0.77) ***p* = 0.00016**



Clinically meaningful and consistent reductions across all individual endpoint components and concordant SMBG- and CGM-based assessments supported the primary endpoint result

Rate ratios used a negative binomial model adjusted for baseline event rate and accounting for missing data due to loss to follow-up. Event rates shown are LS means (model-adjusted).
RR, rate ratio; LS, least squares

TEAEs Were Primarily Gastrointestinal and Injection-Site Related and Generally Mild to Moderate

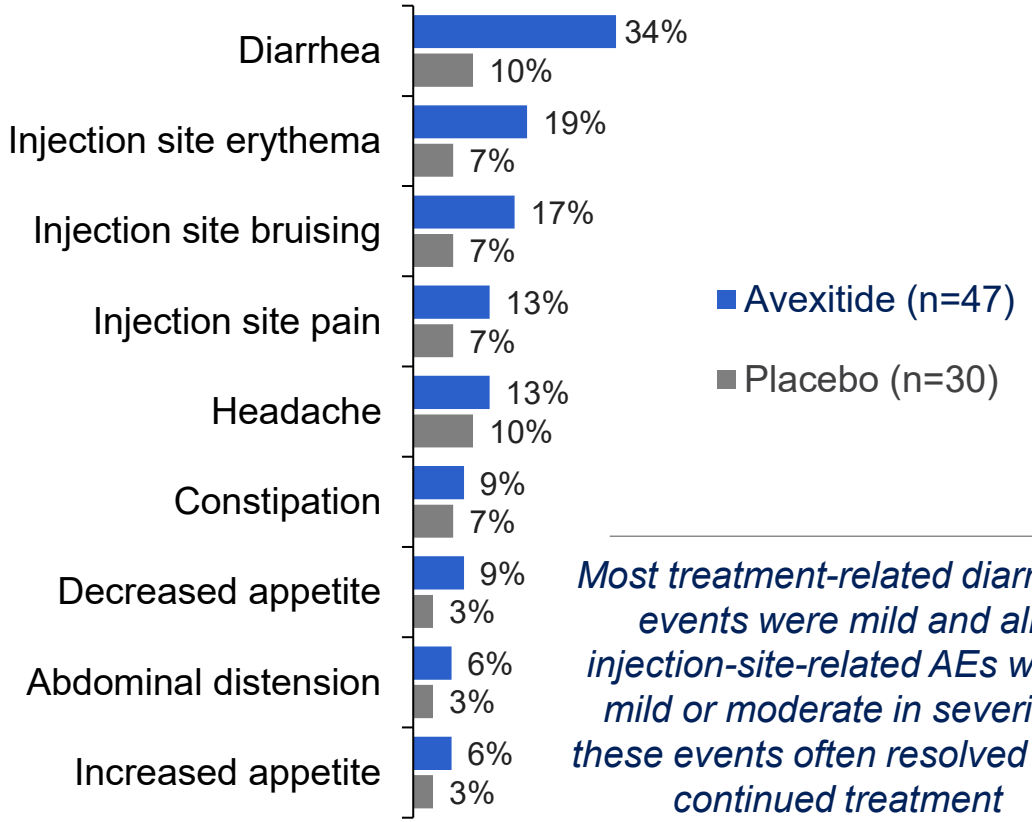
Summary of Treatment-Emergent Adverse Events (TEAEs)

(Participants with ≥1 event, n (%), double-blind period, safety population, N=77)

	Avexitide (n=47)	Placebo (n=30)
TEAE	39 (83)	19 (63)
Drug-related TEAE	27 (57)	14 (47)
Treatment-emergent SAE	1 (2)	1 (3)
Related to study drug	0	0
TEAE leading to discontinuation	2 (4)	1 (3)
Related to study drug	1 (2)	1 (3)
Deaths	0	0

Most Common TEAEs

≥5% overall and more frequent with avexitide



Most treatment-related diarrhea events were mild and all injection-site-related AEs were mild or moderate in severity; these events often resolved with continued treatment

AE, adverse event; SAE, serious adverse event

No Clinically Meaningful Changes in Body Weight or Fasting Plasma Glucose Through Week 16

Body Weight Summary

kg, mean ± SD

	Avexitide	Placebo
Baseline	79.4 ± 15.2	71.2 ± 9.4
Week 16	80.0 ± 16.1	72.6 ± 10.6
Change from Baseline at Week 16	**+0.8 ± 3.7**	**+1.5 ± 3.2**

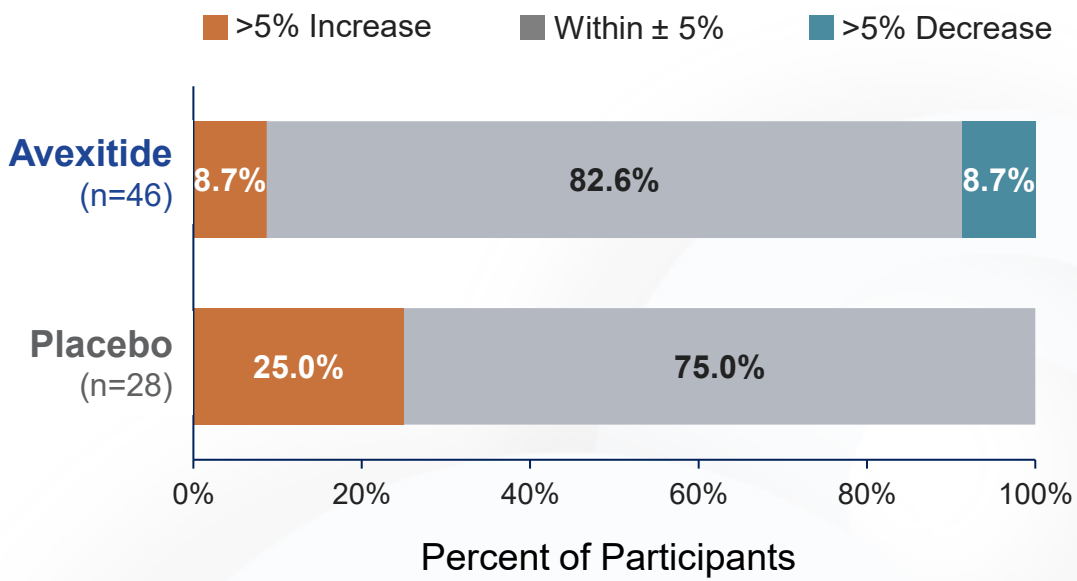
Fasting Plasma Glucose Summary

mg/dL, mean ± SD

	Avexitide	Placebo
Baseline	87.9 ± 11.4	85.3 ± 7.2
Week 16	91.1 ± 12.0	87.7 ± 8.8
Change from Baseline at Week 16	**+3.1 ± 12.7**	**+2.8 ± 9.2**

Distribution of Body Weight Change

From Baseline to Week 16



At Week 16, **91.3% (42/46) of avexitide-treated participants had body weight within 5% of baseline or lower** vs. 75% (21/28) of placebo-treated participants

SD, standard deviation

Sample sizes, n (baseline / Week 16 / change):

Weight: avexitide 47 / 46 / 46, placebo 30 / 28 / 28

Fasting plasma glucose: avexitide 47 / 45 / 45, placebo 29 / 26 / 25

n = participants with non-missing data. Change from baseline includes only participants with non-missing values at both baseline and Week 16

Key Conclusions

STUDY FINDINGS

1. **Avexitide, a GLP-1 receptor antagonist, reduced composite level 2/3 hypoglycemic event rates by 55% versus placebo (p = 0.0000034),** meeting the primary efficacy endpoint
2. **Consistent reductions across SMBG-confirmed level 2, adjudicated level 3, and CGM-detected level 2 events** supported the primary result
3. **TEAEs were primarily gastrointestinal and injection-site related, generally mild to moderate, and often resolved with continued treatment;** body weight and fasting plasma glucose remained stable

CLINICAL AND SCIENTIFIC IMPLICATIONS

1. **LUCIDITY represents a landmark study in PBH,** demonstrating clinically meaningful reductions in hypoglycemia with avexitide
2. The **findings are consistent with five prior avexitide studies,** supporting a reproducible efficacy and safety profile across the clinical program
3. **LUCIDITY establishes a rigorous framework for PBH clinical trials** using SMBG, CGM, and adjudicated level 3 hypoglycemia endpoints
4. The results **further support GLP-1 receptor signaling as a central driver of PBH pathophysiology**
5. Together, these findings **advance both the understanding of PBH and the development of targeted therapies**

Thank You and Q&A

We are grateful to the trial participants, people with PBH, caregivers, clinicians, site teams, and advisors whose partnership has made the LUCIDITY study possible

Impact of Hypoglycemic Events in Participants' Own Words



"I get very confused, very sleepy to the point that I can't almost hold my head up and I sweat profusely. […] And I usually sleep at least 2 hours after I get my blood sugar back up, my body doesn't recover. **It can ruin a day.**"

"Severely disoriented to the point where I actually felt drunk. Disoriented confusion […] And uncoordinated, completely uncoordinated. And like I said, disoriented. **I could not put a simple thought together.**"

"I actually had my own in-home daycare. I was taking care of several kids and when the episodes started getting bad enough and so unpredictable **I had to close my daycare** because I just felt like it was really unsafe for me to be caring for infants and other children when I'd have these episodes of being confused and just absolutely exhausted afterwards."

"They could happen in my car, and I would just pull over on the highway just because I'd kind of **forget where I was at.**"

"I do a lot of administration work, and there are times that I have to take a break because, like I said, when I'm having an episode, I seem to be confused. Like, I'm in a daze kind of, and rather than make a mistake, **I just [do] not work until it passes.**"

Quotes from qualitative interviews performed in subgroup of LUCIDITY participants at Week 16 when asked to describe the hypoglycemic events they experienced before entering LUCIDITY and the impact of PBH on their daily life.