How does Basaglar® (insulin glargine) compare with Lantus® (insulin glargine)?

SUMMARY

- Basaglar and Lantus, insulin glargine products with identical amino acid sequences, are indicated to improve glycemic control in adults and pediatric patients with T1DM and in adults with T2DM.[1,2]
- ELEMENT 1 and ELEMENT 2 were phase 3 studies that assessed the efficacy and safety of Basaglar compared with Lantus in the treatment of patients with T1DM or T2DM.[3,4]
- In the ELEMENT 1 and ELEMENT 2 studies, the primary objective of the LSM change in HbA1c levels from baseline to week 24 was similar between treatment groups, thus demonstrating noninferiority, at 0.4% and 0.3% margins, of Basaglar treatment compared with Lantus treatment.[3,4]
- In the ELEMENT 1 and ELEMENT 2 studies, both treatment groups demonstrated significant improvement in HbA1c levels from baseline to study endpoints ($p<.001$). The percentage of patients who achieved HbA1c target levels ≤6.5% and <7% was similar between treatment groups.[3,4]
- In the ELEMENT 1 and ELEMENT 2 studies, safety outcomes, such as the incidence and rate of hypoglycemia, change in body weight, and the overall incidence of AEs and insulin antibodies, were similar between treatment groups.[3,4]

DESCRIPTION

Basaglar® (insulin glargine) 100 units/mL and Lantus® (insulin glargine) 100 units/mL are insulin glargine products administered as subcutaneous injections.[1,2]

Basaglar and Lantus are long-acting human insulin analogs indicated to improve glycemic control in

- adults and pediatric patients with type 1 diabetes (T1DM), and
- adults with type 2 diabetes (T2DM).[1,2]

STRUCTURE

Basaglar and Lantus have an identical amino acid sequence.[3,5]

Insulin glargine has a different amino acid sequence to that of human insulin (Table 1).[1]

Table 1. Structure of Insulin Glargine Compared With Human Insulin[1]

Position	Insulin Glargine	Human Insulin
A21	Glycine	Asparagine

Position	Insulin Glargine	Human Insulin
C-terminus of the beta chain	Addition of 2 arginines	NA

Abbreviation: NA = not applicable.

ELEMENT 1 AND ELEMENT 2 STUDIES

In 2 phase 3 studies, ELEMENT 1 and ELEMENT 2, the efficacy and safety of Basaglar was compared with Lantus in the treatment of patients with T1DM or T2DM (Table 2).[3,4]

The primary objective of both studies was to determine that once-daily Basaglar was noninferior to once-daily Lantus as assessed by change in glycated hemoglobin (HbA1c) from baseline to 24 weeks.[3,4]

The secondary objectives of the study were to compare Basaglar treatment with Lantus treatment regarding

- noninferiority of Lantus treatment with Basaglar treatment as measured by change in HbA1c from baseline to 24 weeks
- HbA1c levels at predetermined time points
- percentage of patients with HbA1c levels ≤6.5% and <7% at study endpoints
- insulin doses at study endpoints
- 7-point self-monitored blood glucose (SMBG) profiles at study endpoints
- incidence and rate of hypoglycemia at study endpoints
- change in body weight at study endpoints
- incidence of adverse events (AE) during the studies, and
- incidence of anti-insulin antibodies at study endpoints./../../../#reference-6e3ecfda-7281-45e1-9707-335ecc968482 ,[4]

A subsequent evaluation was performed to assess for potential effects of insulin antibodies on select clinical outcomes.[6]

Table 2. Characteristics of the ELEMENT 1 and ELEMENT 2 Studies[3,4]

Characteristic	ELEMENT 1	ELEMENT 2
Design	Phase 3, multinational, multicenter, randomized, open-label, parallel, 2-treatment group	Phase 3, multinational, multicenter, randomized, double-blind, parallel, 2-treatment group
Patient population	Adults with T1DM	Adults with T2DM
Prestudy treatment	Basal-bolus insulin	≥2 OAMs ± Lantus
Comparator	Lantus	Lantus

Characteristic	ELEMENT 1	ELEMENT 2
Concomitant treatment	Prandial insulin lispro	OAMs
Duration	24-week treatment and 28-week extension	24-week treatment

Abbreviations: Lantus = Lantus® (insulin glargine) 100 units/mL; OAM = oral antihyperglycemic medication; T1DM = type 1 diabetes mellitus; T2DM = type 2 diabetes mellitus.

HbA1c, Fasting Plasma Glucose, and Insulin Dose

In the ELEMENT 1 study, the least squares mean (LSM) change in HbA1c from baseline to week 24, as assessed by last observation carried forward (LOCF), was similar between treatment groups, thus demonstrating noninferiority, at 0.4% and 0.3% margins, of Basaglar treatment compared with Lantus treatment and of Lantus treatment compared with Basaglar treatment. Both treatment groups demonstrated significant improvement in HbA1c from baseline to week 52 (p<.001) (Table 3).[3]

In the ELEMENT 2 study, the LSM change in HbA1c from baseline to week 24 as assessed by LOCF was similar between treatment groups, thus demonstrating noninferiority, at 0.4% and 0.3% margins, of Basaglar treatment compared with Lantus treatment and of Lantus treatment compared with Basaglar treatment. Both treatment groups demonstrated significant improvement in HbA1c from baseline to week 24 (p<.001) (Table 3).[4]

Table 3. Summary of Change in HbA1c in the ELEMENT 1 and ELEMENT 2 Studies[3,4]

HbA1c, %[a]	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
Baseline, mean (SD)	7.75 (1.13)	7.79 (1.03)	8.34 (1.09)	8.31 (1.06)
Endpoint, 24 weeks	7.42 (0.05)	7.31 (0.05)	7.04 (0.06)	6.99 (0.06)
Change from baseline, 24 weeks	-0.35 (0.05)	-0.46 (0.05)	-1.29 (0.06)	-1.34 (0.06)
LSM difference (95% CI)	0.108 (-0.002 to 0.219)		0.052 (-0.070 to 0.175)	
Endpoint, 52 weeks	7.52 (0.06)	7.50 (0.06)	NA	NA
Change from baseline, 52 weeks	-0.26 (0.06)	-0.28 (0.06)	NA	NA
LSM difference (95% CI)	0.020 (-0.099 to 0.140)		NA	

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; HbA1c = glycated hemoglobin; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; NA = not applicable.

[a] Data from LOCF and presented as LSM (SE) unless otherwise indicated.

In the ELEMENT 1 study, the LSM HbA1c levels were similar between treatment groups at 6, 24, 36, and 52 weeks; however, at 12 weeks, patients treated with Basaglar were noted with a significantly higher LSM HbA1c level compared with those treated with Lantus (7.42% vs 7.31%; p=.03).[3]

In the ELEMENT 2 study, the LSM HbA1c levels were similar between treatment groups at all assessed time points that included 4, 8, 12, 16, 20, and 24 weeks.[4]

In the ELEMENT 1 study, there was no significant difference between treatment groups at 24 and 52 weeks (LOCF) in the

- percentage of patients who achieved HbA1c target levels ≤6.5% and <7%, and
- LSM daily basal and prandial insulin doses (Table 4).[3]

In the ELEMENT 2 study, there was no significant difference between treatment groups at 24 weeks (LOCF) in the

- percentage of patients who achieved HbA1c target levels ≤6.5% and <7%, and
- LSM daily insulin dose (Table 4).[4]

Table 4. Summary of Secondary Outcomes in the ELEMENT 1 and ELEMENT 2 Studies[3,4,7]

Assessment[a]	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
HbA1c ≤6.5%, n (%)				
24 weeks	54 (20)	49 (18)	99 (27)	114 (30)
52 weeks	42 (16)	36 (14)	NA	NA
HbA1c <7.0%, n (%)				
24 weeks	92 (35)	86 (32)	180 (49)	197 (53)
52 weeks	81 (30)	67 (25)	NA	NA
FPG by SMBG, mg/dL				
Baseline, mean (SD)	151 (54)	147 (54)	159 (45)	160 (44)
24 weeks	144 (4)	141 (4)	-48 (3)[b]	-46 (3)[b]
52 weeks	145 (4)	149 (4)	NA	NA
Basal insulin dose, units/kg/d				
Baseline, mean (SD)	0.33 (0.14)	0.31 (0.13)	0.16 (0.01)[c]	0.14 (0.01)[c]
24 weeks	0.37 (0.01)	0.36 (0.01)	0.50 (0.03)	0.48 (0.03)
52 weeks	0.38 (0.01)	0.36 (0.01)	NA	NA
Prandial insulin dose, units/kg/d				
Baseline, mean (SD)	0.40 (0.19)	0.40 (0.22)	NA	NA
24 weeks	0.35 (0.02)	0.35 (0.02)	NA	NA

Assessment[a]	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
52 weeks	0.37 (0.02)	0.37 (0.02)	NA	NA

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; FPG = fasting plasma glucose; HbA1c = glycated hemoglobin; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; NA= not applicable; SMBG = self-monitored blood glucose.

[a] Data presented as LSM (SE) and represent LOCF unless otherwise indicated.

[b] Data reported as change from baseline.

[c] Data reported as LSM (SE).

Self-Monitored Blood Glucose

In the ELEMENT 1 study, the LSM 7-point self-monitored blood glucose (SMBG) concentrations were similar between treatment groups at 24 and 52 weeks (LOCF) except for significantly lower LSM SMBG concentrations at bedtime at 24 and 52 weeks and at 3 AM at 24 weeks for patients treated with Basaglar compared with those treated with Lantus (p<.05) (Figure 1) (Figure 2).[3,7]

Figure 1. Summary of the 7-Point SMBG Concentrations by Treatment Group at 24 Weeks (LOCF) in the ELEMENT 1 Study[7]

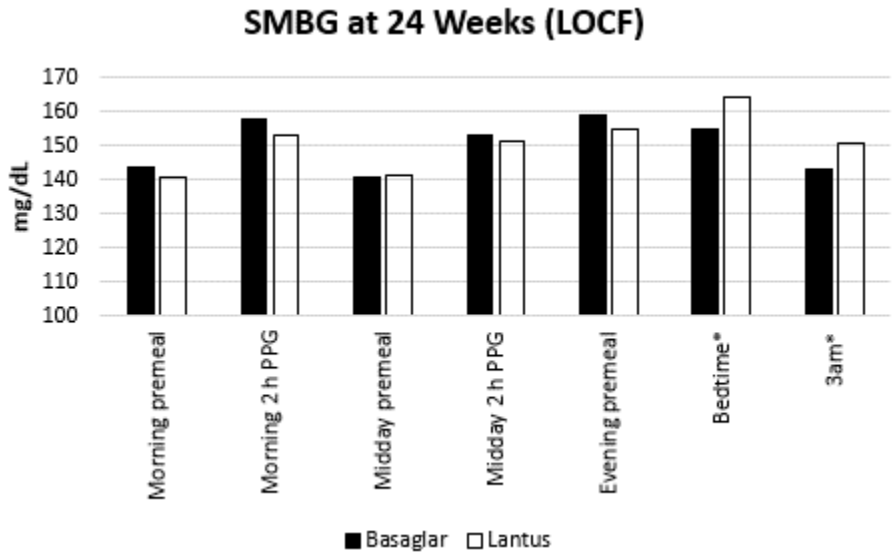

Figure 1 description: The graphical summary illustrates seven-point mean self-monitored blood glucose (SMBG) values at 24 weeks assessed by last observation carried forward in the ELEMENT 1 study. There were no statistically significant treatment differences observed for any SMBG time point, except for the small differences at bedtime and 03:00 AM time points, where blood glucose values were statistically significantly lower in the Basaglar than in the Lantus group.

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; PPG = postprandial glucose; SMBG = self-monitored blood glucose.

Data presented as LSM.

*p<.05 for treatment difference.

Figure 2. Summary of the 7-Point SMBG Concentrations by Treatment Group at 52 Weeks (LOCF) in the ELEMENT 1 Study[7]

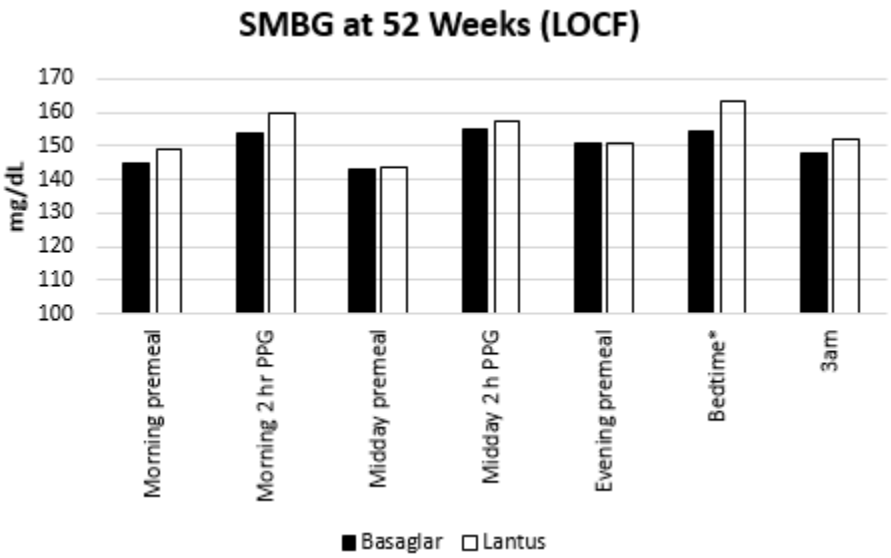

Figure 2 description: The graphical summary illustrates seven-point mean self-monitored blood glucose (SMBG) values at 52 weeks assessed by last observation carried forward in the ELEMENT 1 study. There were no statistically significant treatment differences were observed for any SMBG time point, except for the bedtime time point, where blood glucose values were statistically significantly lower in the Basaglar than in the Lantus group.
Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; PPG = postprandial glucose; SMBG = self-monitored blood glucose.
Data presented as LSM.
*p<.05 for treatment difference.

In the ELEMENT 2 study, the LSM 7-point SMBG concentrations were similar between treatment groups at 24 weeks (LOCF) except for a significantly lower LSM SMBG concentration at the midday premeal time point for patients treated with Basaglar compared with those treated with Lantus (p=.04) (Figure 3).[4,7]

Figure 3. Summary of the 7-Point SMBG Concentrations by Treatment Group at 24 Weeks (LOCF) in the ELEMENT 2 Study[7]

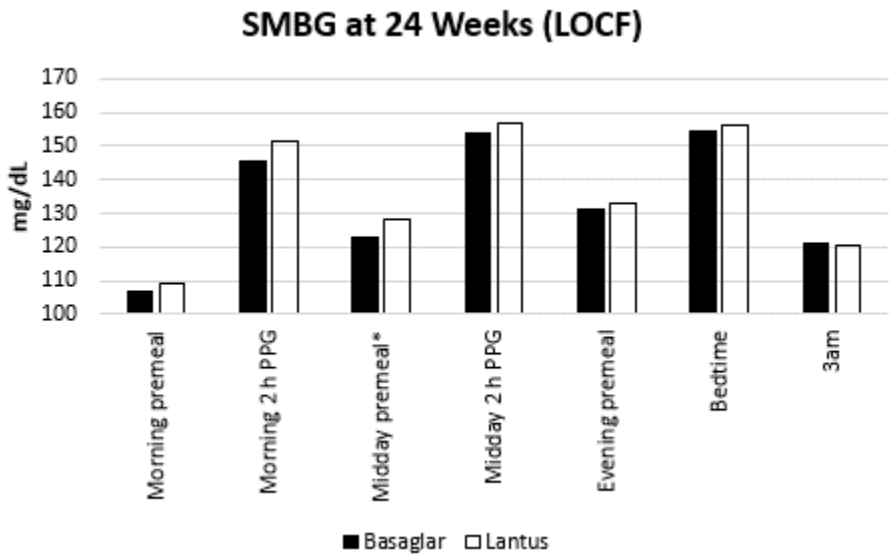

Figure 3 description: The graphical summary illustrates seven-point mean self-monitored blood glucose (SMBG) values at 24 weeks assessed by last observation carried forward in the ELEMENT 2 study. The LS mean blood glucose value was significantly lower at the mid-day pre-meal time point in the Basaglar group compared with the Lantus group at the morning 2-h postprandial time point. No statistically significant treatment differences were observed for any other time point at any visit or endpoint.
Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; PPG = postprandial glucose; SMBG = self-monitored blood glucose.
Data presented as LSM.
*p=.04 for treatment difference.

Hypoglycemia

In the ELEMENT 1 and ELEMENT 2 studies, the incidence and rate of hypoglycemia, including total, nocturnal, and severe, were similar between treatment groups (Table 5).[3,4]

Table 5. Incidence and Rate of Hypoglycemia in the ELEMENT 1 and ELEMENT 2 Studies[3,4]

Hypoglycemia	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
Incidence, %				
Total at 24 weeks	94	95	79	78
Nocturnal at 24 weeks	82	80	57	54
Severe at 24 weeks	2	3	<1	<1
Total at 52 weeks	96	97	NA	NA
Nocturnal at 52 weeks	86	88	NA	NA

Hypoglycemia	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
Severe at 52 weeks	4	4	NA	NA
Rate, mean (SD)[a]				
Total at 24 weeks	86.5 (77.3)	89.2 (80.1)	21.3 (24.4)	22.3 (28.2)
Nocturnal at 24 weeks	18.3 (23.6)	18.4 (21.5)	7.6 (11.8)	8.1 (14.6)
Severe at 24 weeks	0.06 (0.52)	0.09 (0.50)	0.04 (0.66)	0.01 (0.16)
Total at 52 weeks	77.0 (68.7)	79.8 (74.5)	NA	NA
Nocturnal at 52 weeks	16.1 (20.2)	17.3 (19.5)	NA	NA
Severe at 52 weeks	0.07 (0.46)	0.08 (0.46)	NA	NA

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; NA = not applicable.

[a] Events/patient/year; represents all events reported during the 24-week treatment and 52-week (treatment and extension) periods.

Body Weight

In the ELEMENT 1 and ELEMENT 2 studies, there was no significant difference between treatment groups in change in body weight (Table 6).[3,4]

Table 6. Change in Body Weight in the ELEMENT 1 and ELEMENT 2 Studies

Body weight, kg[a]	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1[3,7]		ELEMENT 2[4,7]	
Baseline, mean (SD)	76 (17)	75 (15)	90 (20)	90 (19)
Week 24	74 (1)	73 (1)	86 (1)	85 (1)
Change at week 24	+0.36 (0.2)	+0.12 (0.2)	+1.8 (0.3)	+2.0 (0.3)
Week 52	74 (1)	73 (1)	NA	NA
Change at week 52	+0.71 (0.3)	+0.36 (0.3)	NA	NA

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; NA = not applicable.

[a] Data presented as LSM (SE) and represent LOCF unless otherwise indicated.

Adverse Events

In the ELEMENT-1 and ELEMENT-2 studies, there was no significant difference between treatment groups in the incidence of

- Adverse events (AE), defined as events that first occurred or worsened in severity after randomization
- Serious adverse events, that included episodes of severe hypoglycemia, and

- discontinuations due to AEs (Table 7).[3,4]

In the ELEMENT 1 and ELEMENT 2 studies, the incidence of allergic events and injection site reactions was similar between treatment groups (Table 7). Allergic events

- were predominantly mild or moderate in severity, and
- did not result in discontinuation.[3,4]

Pain was the most commonly reported injection site reaction and was primarily reported as mild to moderate in severity (Table 7).[3,4]

Table 7. Adverse Events During the ELEMENT 1 and ELEMENT 2 Studies[3,4]

Assessment, n (%)[a]	**Basaglar (n=268)**	**Lantus (n=267)**	**Basaglar (n=376)**	**Lantus (n=380)**
	ELEMENT 1[b]		**ELEMENT 2[c]**	
AE	167 (62)	166 (62)	196 (52)	184 (48)
AE possibly related to study drug	17 (6)	14 (5)	26 (7)	23 (6)
AE possibly related to study procedure	2 (1)	2 (1)	6 (2)	8 (2)
AE possibly related to study disease state of DM	21 (8)	16 (6)	19 (5)	18 (5)
Special topic assessment of allergic reactions	20 (8)	11 (4)	21 (6)	27 (7)
Dermatitis, pruritus, rash, other[d]	7 (3)	4 (2)	8 (2)	12 (3)
Arthralgia, arthritis, periarthritis	4 (2)	5 (2)	7 (2)	9 (2)
Injection site[e]	6 (2)	2 (1)	5 (1)	4 (1)
Hypersensitivity	1 (<1)	1 (<1)	NR	NR
Allergic respiratory symptom, asthma, nasal edema	2 (1)	0 (0)	3 (1)	5 (1)
Injection site reaction[f]	7 (3)	3 (1)	13 (4)	11 (3)
Pain	6 (2)	2 (1)	10 (3)	5 (1)
Pruritus	2 (1)	1 (<1)	4 (1)	4 (1)
Rash	2 (1)	1 (<1)	3 (1)	3 (1)
SAE	20 (8)	24 (9)	15 (4)	18 (5)
Discontinuation due to an AE	2 (1)	6 (2)	6 (2)	11 (3)

Assessment, n (%)[a]	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1[b]		ELEMENT 2[c]	
Death	0 (0)	1 (<1)	1 (<1)	1 (<1)

Abbreviations: AE = adverse event; Basaglar = Basaglar® (insulin glargine) 100 units/mL; DM = diabetes mellitus; Lantus = Lantus® (insulin glargine) 100 units/mL; NR = not reported; SAE = serious adverse event.

[a] Patients may be counted in >1 category.

[b] Treatment comparisons were not performed if there were <4 patients with events.

[c] Treatment comparisons were not performed for injection site reactions.

[d] Angioedema, macular rash, papular rash, photosensitivity reaction, pruritic rash, urticaria, vesicular rash.

[e] Induration, nodule, pruritus, reaction, swelling.

[f] Patient questionnaires.

Antibodies

In the ELEMENT 1 and ELEMENT 2 studies, the number of patients with detectable antibodies and the median insulin antibody binding were similar between treatment groups (Table 8).[3,4]

Table 8. Incidence of Detectable Antibodies and Percent Insulin Antibody Binding in the ELEMENT 1 and ELEMENT 2 Studies[3,4]

Assessment	Basaglar (n=268)	Lantus (n=267)	Basaglar (n=376)	Lantus (n=380)
	ELEMENT 1		ELEMENT 2	
Incidence of detectable antibodies, n (%)[a]				
24 weeks	80 (30)	90 (34)	56 (15)	40 (11)
52 weeks	107 (40)	105 (39)	NA	NA
Percent insulin antibody binding, median[b]				
24 weeks	1.17	1.10	1.07	0.65
52 weeks	0.92	0.89	NA	NA

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; NA = not applicable.

[a] Data represent overall 24- and 52-week study periods and not LOCF.

[b] Data represent LOCF.

A treatment-emergent antibody response (TEAR) was noted when patients

- who were insulin antibody-negative at baseline developed insulin antibody binding values ≥1.26% postbaseline, or
- with detectable insulin antibody levels at baseline presented with a ≥1% increase in insulin antibody binding and a ≥30% relative increase in insulin antibody binding from baseline.[6]

In the ELEMENT 1 and ELEMENT 2 studies, the incidence of TEAR during the treatment periods and at the study endpoints last observation carried forward (LOCF) was similar between treatment groups (Table 9).[6]

Table 9. Incidence of TEAR Among Patients in the ELEMENT 1 and ELEMENT 2 Studies[6]

Assessment, n (%)	Basaglar (n=265)	Lantus (n=267)	Basaglar (n=365)	Lantus (n=365)
	ELEMENT 1		ELEMENT 2	
Endpoint, LOCF[a]	18 (6.8)	12 (4.5)	12 (3.3)	7 (1.9)
Week 24, overall	25 (9.4)	17 (6.4)	14 (3.8)	14 (3.8)
Week 52, overall	29 (10.9)	25 (9.4)	NA	NA

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; NA = not applicable; TEAR = treatment-emergent antibody response.

[a] Represents week 52 in ELEMENT 1 and week 24 in ELEMENT 2.

There were no significant treatment-by-TEAR interactions for change in glycated hemoglobin (HbA1c), basal insulin dose, and total hypoglycemia rate from baseline to the 52-week endpoint (LOCF) in the ELEMENT 1 study (Figure 4) and from baseline to the 24-week endpoint (LOCF) in the ELEMENT 2 study (Figure 5), indicating no significant differential treatment effect on these clinical outcomes for patients with or without TEAR.[6,7]

Figure 4. Effect of TEAR on Clinical Outcomes – ELEMENT 1[7]

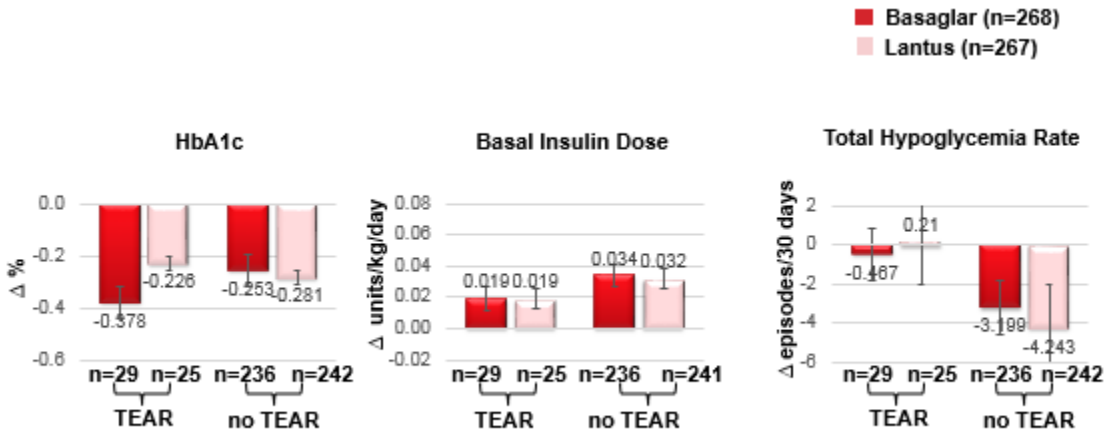

Figure 4 description: In the ELEMENT 1 study, there were no significant treatment-by-treatment emergent antibody response interactions for change in glycated hemoglobin, basal insulin dose, and total hypoglycemia rate from baseline to the 52-week endpoint (last observation carried forward).

Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; HbA1c = glycated hemoglobin; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; TEAR = treatment-emergent antibody response.

Data presented as LSM (SE) change from baseline to LOCF endpoint.

Figure 5. Effect of TEAR on Clinical Outcomes – ELEMENT 2[7]

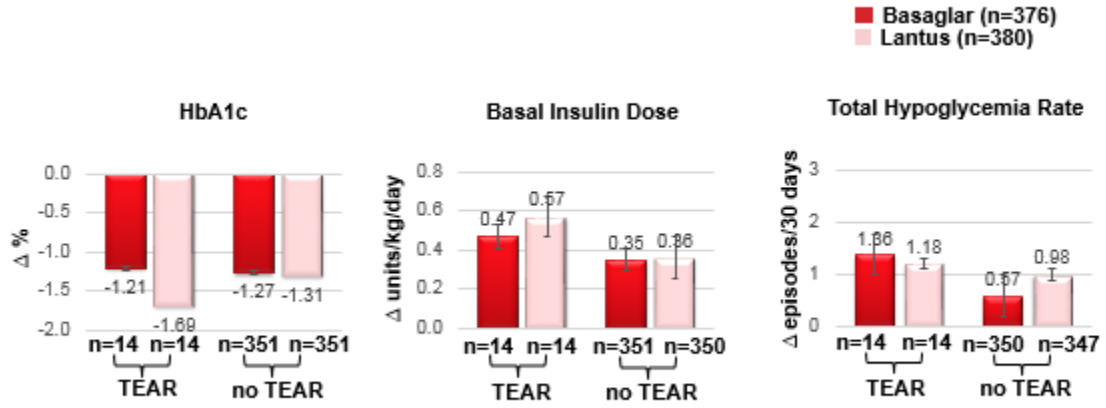

Figure 5 description: In the ELEMENT 2 study, there were no significant treatment-by-treatment emergent antibody response interactions for change in glycated hemoglobin, basal insulin dose, and total hypoglycemia rate from the baseline to the 24-week endpoint (last observation carried forward).
Abbreviations: Basaglar = Basaglar® (insulin glargine) 100 units/mL; HbA1c = glycated hemoglobin; Lantus = Lantus® (insulin glargine) 100 units/mL; LOCF = last observation carried forward; LSM = least squares mean; TEAR = treatment-emergent antibody response.
Data presented as LSM (SE) change from baseline to LOCF endpoint.

Last Reviewed: 05-December-2023

ENCLOSED PRESCRIBING INFORMATION

BASAGLAR® (insulin glargine) injection, for subcutaneous use, Lilly

HUMALOG® (insulin lispro injection), for subcutaneous or intravenous use, Lilly

REFERENCES

The published references below are available by contacting 1-800-LillyRx (1-800-545-5979).

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7. Data on file, Eli Lilly and Company and/or one of its subsidiaries.