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A1C Goal Attainment Without Hypoglycemia Using Gla-300 vs Other BIs in Older Adults With T2D: ACHIEVE Control Pragmatic Study

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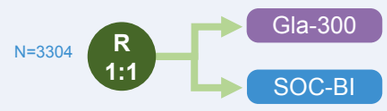
EXECUTIVE SUMMARY

- Older patients with type 2 diabetes (T2D) are vulnerable to hypoglycemia and its adverse consequences, which is a particular concern in patients receiving insulin therapy.
- The risk of hypoglycemia is reduced with second-generation basal insulins (BIs) such as insulin glargine 300 U/mL (Gla-300) compared with standard of care basal insulins (SOC-BIs).
- The ACHIEVE Control pragmatic randomized trial compared the effectiveness and safety of Gla-300 versus other SOC-BIs.
- The primary composite endpoint was attainment of individualized A1C target at 6 months without documented symptomatic or severe hypoglycemia at any time of day (24 h) from baseline to 6 months.

ACHIEVE Control

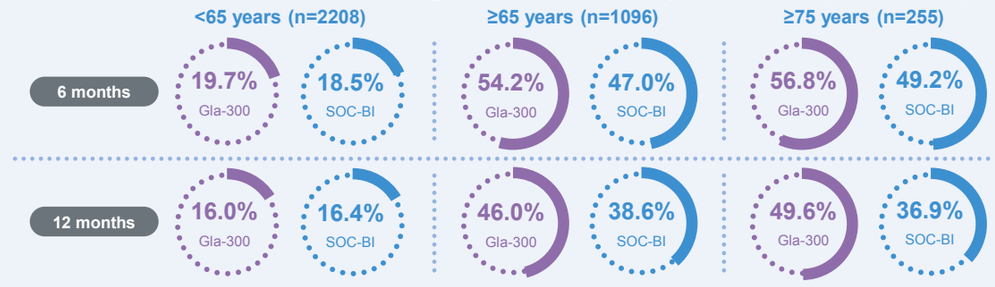
- Insulin-naive patients with T2D
- ≥18 years
- A1C 8%–11%



A1C, glycated hemoglobin; R, randomization

- This poster presents findings of a post hoc subgroup analysis of the ACHIEVE Control data.
- Outcomes for Gla-300 versus SOC-BI were compared in individuals aged <65 years, ≥65 years, and ≥75 years.

Patients with individualized A1C target attainment per HEDIS criteria[a] at 6 and 12 months without documented symptomatic (BG ≤70 mg/dL) or severe hypoglycemia at any time of day (24 h)



[a]<8% for patients aged ≥65 years or with defined comorbidities; <7% for all others
BG, blood glucose; HEDIS, Healthcare Effectiveness Data and Information Set

- Patients aged ≥65 years who received Gla-300 achieved their individualized HEDIS A1C target without documented symptomatic hypoglycemia (BG ≤70 mg/dL) and/or severe hypoglycemia at any time of day (24 h) more often than those who received SOC-BI at both 6 and 12 months.

INTRODUCTION

- Many patients with type 2 diabetes (T2D) will eventually require insulin as pancreatic β-cell function declines.[1] Use of insulin must balance effective control of blood glucose (BG) while mitigating the risk for hypoglycemia.
- Older patients are typically more vulnerable to hypoglycemia and its adverse consequences than their younger counterparts.[2]
- Compared with older formulations, second-generation basal insulins (BIs; insulin glargine 300 U/mL [Gla-300] and insulin degludec) have flatter pharmacokinetic and pharmacodynamic profiles, longer duration of action, and reduced risk of hypoglycemia.[3,4]
- ACHIEVE Control was a large (N=3304) randomized, prospective, open-label, pragmatic real-life study comparing the efficacy and safety of Gla-300 versus other standard-of-care basal insulins (SOC-BI; insulin glargine 100 U/mL and detemir) in insulin-naive patients with T2D (glycated hemoglobin [A1C] 8%–11%) aged ≥18 years.[5]
- Prospective, pragmatic real-life studies complement randomized controlled trials by using more inclusive patient selection criteria and providing real-life treatment settings to evaluate medication effectiveness,[6] while maintaining the internal validity of randomization.[7]
- The trial demonstrated superiority of Gla-300 versus SOC-BI from baseline to 6 months in the primary composite endpoint of individualized A1C target attainment (<8% for patients aged ≥65 years or with defined comorbidities; <7% for all other patients) without documented symptomatic (BG ≤70 mg/dL) or severe hypoglycemia at any time of day (24 h).
  - Gla-300: 31.3% versus SOC-BI: 27.9%; odds ratio (OR): (95.4% CI): 1.19 (1.01–1.39); *P*=0.03.[5]

OBJECTIVE

- This post hoc subanalysis of the ACHIEVE Control trial assessed the likelihood of attaining individualized A1C targets without documented symptomatic and/or severe hypoglycemia at any time of day (24 h) from baseline to 6 and 12 months, according to age for patients who received Gla-300 versus SOC-BI.

METHODS

- The methodology of this study has been previously reported.[5]
- Outcomes (A1C target attainment without documented symptomatic and/or severe hypoglycemia at any time of day [24 h], A1C target attainment regardless of hypoglycemia, and hypoglycemia avoidance) were compared for Gla-300 versus SOC-BI from baseline to 6 and 12 months according to different age categories.

Statistical analysis

- ORs were determined by logistic regression using treatment arm as a fixed effect and adjusting for: randomization strata of A1C target, sulfonylurea use, glucagon-like peptide-1 receptor agonist (GLP-1 RA) use, baseline A1C (as continuous), and adding age group and age group-by-treatment arm interaction.
- Patients with missing information were treated as not having reached the composite endpoint.

RESULTS

- Age, sex, body weight, body mass index, and A1C were well balanced between treatment arms for all age categories (**Table 1**).
- It should be noted that the number of patients in the ≥75-years subgroup was small.

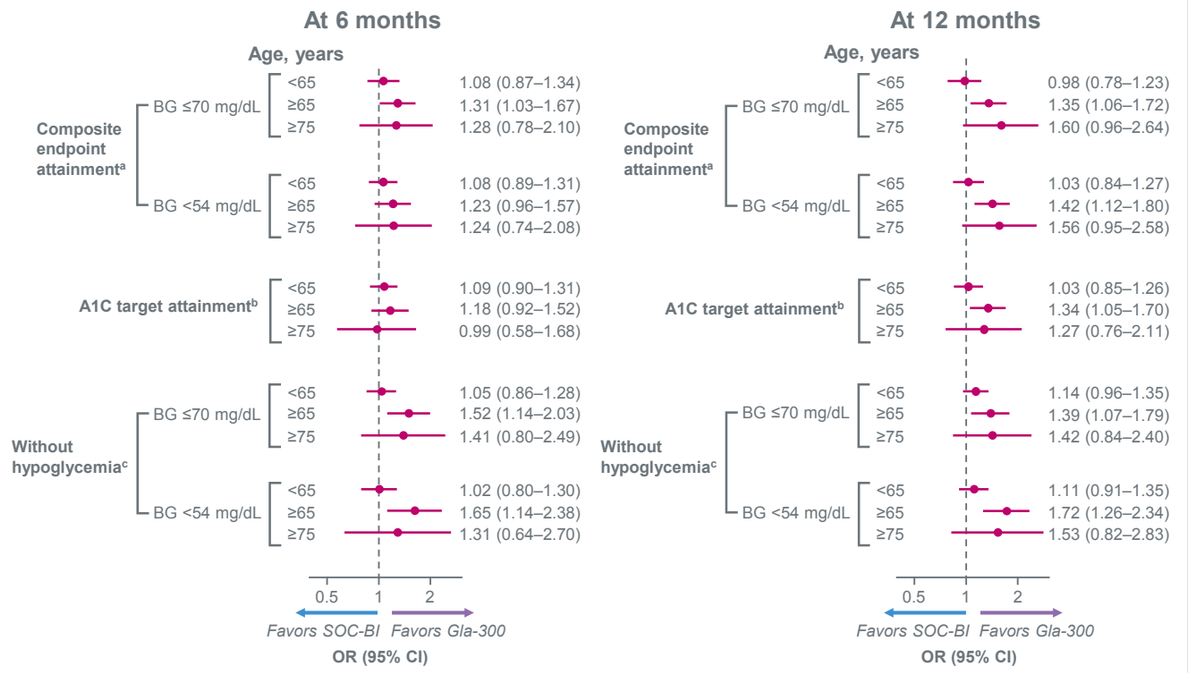
Table 1: Baseline demographics and patient characteristics according to age group

	<65 years		≥65 years[a]		≥75 years	
	Gla-300 (n=1097)	SOC-BI (n=1111)	Gla-300 (n=554)	SOC-BI (n=542)	Gla-300 (n=125)	SOC-BI (n=130)
Age, years	53.6 (7.8)	53.2 (7.8)	71.0 (5.0)	71.2 (5.2)	78.5 (3.1)	78.9 (3.5)
Male	597 (54.4)	621 (55.9)	307 (55.4)	301 (55.5)	73 (58.4)	69 (53.1)
BMI, kg/m²	34.7 (7.6)	34.6 (7.7)	32.1 (5.9)	31.9 (6.1)	30.8 (5.4)	30.5 (5.4)
A1C, %	9.2 (0.8)	9.2 (0.8)	9.0 (0.7)	9.1 (0.8)	8.9 (0.7)	9.0 (0.8)
Duration of T2D, years	9.8 (6.1)	9.8 (6.2)	14.7 (8.6)	14.0 (8.5)	17.1 (10.1)	15.4 (8.9)
Previous noninsulin antihyperglycemic treatments of interest	n=1097	n=1110	n=553	n=542	n=124	n=130
Sulfonylurea	825 (75.2)	817 (73.6)	439 (79.4)	439 (81.0)	95 (76.6)	115 (88.5)
DDP-4 inhibitors	442 (40.3)	467 (42.1)	260 (47.0)	273 (50.4)	59 (47.6)	71 (54.6)
SGLT-2 inhibitors	321 (29.3)	317 (28.6)	124 (22.4)	118 (21.8)	14 (11.3)	23 (17.7)
GLP-1 RA	200 (18.2)	188 (16.9)	85 (15.4)	71 (13.1)	19 (15.3)	10 (7.7)

Values are mean (SD), except for male and previous noninsulin antihyperglycemic treatment, which are n (%)
[a] This subgroup includes patients in the ≥75-years subgroup
BMI, body mass index; DDP-4, dipeptidyl peptidase-4; SD, standard deviation; SGLT-2, sodium-glucose cotransporter-2

- At 6 and 12 months, a higher percentage of patients aged ≥65 and ≥75 years who received Gla-300 achieved their individualized A1C target without severe and/or documented symptomatic hypoglycemia at both BG ≤70 mg/dL and <54 mg/dL versus those who received SOC-BI (**Figure 1** and **Table 2**).
- Numerically higher percentages of patients aged ≥65 and ≥75 years who received Gla-300 achieved their A1C target regardless of hypoglycemia compared with SOC-BI at 12 months (**Figure 1** and **Table 2**).
- More patients aged ≥65 and ≥75 years who received Gla-300 completed 6 and 12 months of treatment without hypoglycemia (at both BG ≤70 mg/dL and <54 mg/dL cutoffs) compared with those who received SOC-BI (**Figure 1** and **Table 2**).

Figure 1: ORs (95% CI) for attainment of composite endpoints and their components according to age (<65 years, n=2208; ≥65 years n=1096; ≥75 years, n=255) at 6 and 12 months



[a]Individualized A1C target attainment (<8% for patients aged ≥65 years or with defined comorbidities; <7% for all other patients) without documented symptomatic (BG ≤70 mg/dL or <54 mg/dL) or severe hypoglycemia at any time of day (24 h); [b]Individualized A1C target attainment (<8% for patients aged ≥65 years or with defined comorbidities; <7% for all other patients); [c]Documented symptomatic (BG ≤70 mg/dL or BG <54 mg/dL) or severe hypoglycemia at any time of day (24 h)
CI, confidence interval

Table 2: Proportions of patients aged <65 years (n=2208), ≥65 years (n=1096), or ≥75 years (n=255) who attained composite endpoints and their components at 6 and 12 months

	<65 years		≥65 years		≥75 years	
	Gla-300	SOC-BI	Gla-300	SOC-BI	Gla-300	SOC-BI
At 6 months						
Composite endpoint attainment[a]						
≤70 mg/dL	19.7	18.5	54.2	47.0	56.8	49.2
<54 mg/dL	25.2	23.8	61.2	55.9	66.4	60.0
A1C target attainment regardless of hypoglycemia[b]	27.3	25.7	65.0	60.7	68.0	66.9
Patients without hypoglycemia[c]						
≤70 mg/dL	76.8	76.0	81.4	74.2	77.6	70.8
<54 mg/dL	86.8	86.6	90.4	85.2	88.0	84.6
At 12 months						
Composite endpoint attainment[a]						
≤70 mg/dL	16.0	16.4	46.0	38.6	49.6	36.9
<54 mg/dL	21.5	21.0	55.8	46.9	60.0	47.7
A1C target attainment regardless of hypoglycemia[b]	24.5	23.9	60.8	53.5	64.0	56.9
Patients without hypoglycemia[c]						
≤70 mg/dL	64.4	61.6	71.8	64.8	70.4	62.3
<54 mg/dL	77.5	75.7	85.2	77.1	83.2	76.2

[a] Individualized A1C target attainment (<8% for patients aged ≥65 years or with defined comorbidities; <7% for all other patients) without documented symptomatic (BG ≤70 mg/dL or <54 mg/dL) or severe hypoglycemia at any time of day (24 h)); [b]Individualized A1C target attainment (<8% for patients aged ≥65 years or with defined comorbidities; <7% for all other patients); [c]Documented symptomatic (BG ≤70 mg/dL or BG <54 mg/dL) or severe hypoglycemia at any time of day (24 h)

CONCLUSIONS

- In the ACHIEVE Control trial, Gla-300 demonstrated superiority compared with first-generation SOC-BI in the primary composite endpoint of reaching individualized HEDIS A1C targets without symptomatic and/or severe hypoglycemia at 6 months.
- The results of this exploratory analysis suggest that the efficacy benefit and lower hypoglycemia rate demonstrated by Gla-300 over SOC-BIs in the overall ACHIEVE Control study population is maintained in patients aged ≥65 years and in those aged ≥75 years.
- The benefit favoring Gla-300 over SOC-BI at 6 months showed a trend of being further improved after 12 months of continued treatment and may be of particular importance in patients aged ≥75 years.

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DISCLOSURES

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