ORIGINAL ARTICLE

Self-management with biphasic insulin aspart 70/30 overcomes poor glycemic control irrespective of patient race or ethnicity (INITIATE*plus* trial)[*]

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Running title: INITIATE*plus* demographic analysis

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ABSTRACT

Objective: To determine if self-titration using biphasic insulin aspart 70/30 (BIAsp 30) had a different impact on efficacy and safety across different racial/ethnic subgroups.

Research design/methods: This was an exploratory, post hoc analysis by race (White vs. Black/African-American) and ethnicity (Hispanic/Latino vs. non-Hispanic/Latino) of data from the INITIATEplus trial (Oyer 2009 Am J Med). Participants were treated twice daily with BIAsp 30 over 24 weeks.

Trial registration: NCT00101751.

Main outcome measures: Efficacy endpoints included reductions in mean A1C and fasting plasma glucose (FPG). Safety endpoints included hypoglycemia rates (events/patient-year) and adverse events. Body weight changes were also measured.

Results: Final mean A1C decreases for White vs Black/African-American subjects were 2.41% and 2.54%, respectively, and those for Hispanic/Latino vs. non-Hispanic/Latino subjects were 2.61% and 2.42%, respectively. Final FPG values were similar among all groups (141-146 mg/dL [7.83-8.10 mmol/L]). Hypoglycemia was low for White, Black/African-American, Hispanic/Latino, and non-Hispanic/Latino subjects (0.08, 0.04, 0.03, and 0.07 major events/patient-year, with 0.3, 0.6, 0.37, and 0.52 minor events/patient-year, respectively). Body weight increases were 3.16 and 3.08 kg (White vs. African-American, respectively) and 3.03 and 3.15 kg (Hispanic/Latino vs non-Hispanic/Latino). Final weight-adjusted total daily insulin doses were 0.60 U/kg for Black/African-American subjects, 0.78 U/kg for White, and 0.70 U/kg for Hispanic/Latino and non-Hispanic/Latino subjects.

Conclusions: Diabetes self-management with BIAsp 30 using an easily-followed self-titration algorithm produced low hypoglycemia rates. All subgroups achieved similar large A1C and FPG

declines, demonstrating that self-titration of BIAsp 30 can successfully be pursued in a primary care setting by patients from racial and ethnic minorities who had previously failed oral antidiabetes therapy, irrespective of race or ethnicity. Because this trial was not powered for comparisons across race/ethnicity, the subgroups showed numerical and baseline A1C disparities. The very poor baseline glycemic control among these patients may not be representative of larger untreated populations.

Keywords: type 2 diabetes, **b**iphasic insulin aspart 70/30, BIAsp 30, NovoLog Mix 70/30, self-titration, glucose control, race, ethnicity

INTRODUCTION

Insulin treatment of type 2 diabetes is often delayed for years, with some patients continuing only on oral agents long after these agents cease to provide optimal levels of glucose control. Landmark studies in the 1990s highlighted the importance of early and aggressive insulin treatment for glycemic control and for diminishing the risk of microvascular complications associated with diabetes[1–3]. Since that time, the American Diabetes Association (ADA)[4] established guidelines for glucose control, namely an A1C value of <7%, while the American Association of Clinical Endocrinologists (AACE) has recommended a more stringent A1C target of ≤6.5%[5]. Despite these clear treatment goals, to this day too many patients with diabetes fail to achieve population-based glycemic targets. In spite of being placed on insulin therapy, glycemic control may still not be attained due to the reluctance by either the patient to optimize their dosing regimen, or by the health care professional's perception of the challenges.

In the INITIATE*plus* trial, insulin therapy with BIAsp 30 (biphasic insulin aspart 70/30 = 70% insulin aspart protamine suspension and 30% insulin aspart injection [rDNA origin])[6] was initiated twice daily for 24 weeks in insulin-naïve patients with type 2 diabetes who had failed therapy with oral antidiabetes drugs (OAD)[7]. Patients were instructed to self-titrate their insulin dose based on daily self-measured plasma glucose determinations (SMPG) over the course of the study. The primary purpose of the study was to compare differences in efficacy and safety resulting from 3 different levels of intensity of dietary counseling to which these patients were randomized. Results reported by Oyer et al[7]. revealed high efficacy and similar A1C decreases for all counseling treatments (2.4% to 2.5%) from a mean overall baseline of 9.9%. The high baseline A1C underscores some of the challenges of initiating insulin therapy at an appropriate

point in disease progression since this level is far above any recommended target for glycemic control and far above recommended action points to achieve improved glycemic control.

Many challenges exist in caring for patients with diabetes, including the transition to therapy with insulin, an approach traditionally felt to be more aggressive by patient and health care professional alike. Cultural, racial, and ethnic factors can play a role in choice of therapy or aggressiveness of approach. In this report, we analyzed efficacy and safety data for patients from INITIATE*plus* according to racial and ethnic subgroups, irrespective of dietary counseling.

PAIENTS AND METHODS

Overall study design

This 24-week, multicenter, open-label, study in insulin-naive type 2 diabetes subjects assessed the impact of initiating twice-daily BIAsp 30 (biphasic insulin aspart 70/30 = 70% insulin aspart protamine suspension and 30% insulin aspart injection [rDNA]; Novo Nordisk, Bagsvaerd, Denmark). The study randomized 4,875 adult subjects ≥18 years of age at 934 predominantly primary care centers in the United States. Ethical approval was provided by the ethics committee of participating centers and all subjects provided written informed consent prior to trial-related activities. The study was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonisation Guideline for Good Clinical Practice. Subjects were randomized to receive a different number of individualized dietary counseling sessions, with all receiving BIAsp 30 twice daily and the same self-titration algorithm. For this post hoc analysis, subjects were grouped only by race or ethnicity, irrespective of original dietary counseling cohort. Subjects who self-reported race as Black/African-American and ethnicity as Hispanic-

Latino were the largest minority groups represented in this trial, and were compared against White or non-Hispanic/Latino subjects, respectively.

Treatments

Subjects initiated insulin therapy with subcutaneous injection of 6 units BIAsp 30 15 min before breakfast and supper. Prior to initiation of BIAsp 30 treatment, subjects discontinued use of pre-study secretagogue oral hypoglycemic agents, but continued other oral agents. The initial dose was self-adjusted every 3 to 5 days using a titration algorithm based on the average self-measured plasma glucose (SMPG) value of the 3 days preceding the titration. The breakfast dose was titrated to the pre-supper SMPG value, and the evening dose was titrated to pre-breakfast SMPG value. Subjects were encouraged to titrate one of the doses every 3 to 5 days unless an episode of hypoglycemia had occurred. Subjects with plasma glucose (PG) <80 mg/dL (<4.44 mmol/L) reduced their insulin dose by 3 units, those between 80-110 mg/dL (4.44-6.11 mmol/L) left their dose unchanged, and those between 111-140 mg/dL (6.16-7.77 mmol/L), 141-180 mg/dL (7.83-10.0 mmol/L) or >180 mg/dL (>10.0 mmol/L) increased their dose by 3, 6 or 9 units, respectively. If hypoglycemia occurred within 24 hours prior to a scheduled titration, the subject deferred any dose increase and re-evaluated their insulin dose on the following day. Plasma glucose was measured with a OneTouch UltraSmart blood glucose monitor (LifeScan, Inc., Milpitas, CA), which is calibrated to read plasma glucose.

Efficacy assessments

A1C was measured at baseline and at the end of the study in the office using the A1CNow test (Metrika, Inc., Sunnyvale, CA). Efficacy endpoints also included the glucose values from 8-point

SMPG profiles. The first SMPG measurements were taken starting with visit 1, before BIAsp 30 initiation. Plasma glucose measurements were recorded 30 minutes before and 2 hours after breakfast, lunch and dinner, at bedtime, and at 3:00 a.m.

Safety assessments

Safety was assessed by physical examination findings, reporting of episodes of hypoglycemia and adverse events. Minor hypoglycemia was defined as plasma glucose values <56 mg/dL (<3.11 mmol/L) with or without symptoms that the subject was able to self-treat. Major hypoglycemia was defined as an episode with severe central nervous system symptoms consistent with hypoglycemia and requiring assistance of another individual, with a plasma glucose value <56 mg/dL (<3.11 mmol/L), or reversal of symptoms after either food intake or glucagon/IV glucose administration.

Statistical analysis

Efficacy data were originally analyzed for the intent-to-treat (ITT) population, defined as all randomized subjects who received at least one dose of trial medication and had at least one post-baseline efficacy assessment. Missing data were imputed by carrying the last observation forward (LOCF). Baseline A1C and fasting plasma glucose (FPG), final A1C and FPG, A1C and FPG changes from baseline, and SMPG values were reported as observed means. Body weight and weight-adjusted insulin dose were reported as observed means from the safety population, defined as all randomized subjects who received at least one dose of study medication. Hypoglycemia data were also obtained from the safety population and reported as the percentage of subjects having at least one episode of hypoglycemia and as an incidence rate. Because

hypoglycemia rates were low (i.e., ≤0.6 events ppy) no statistics were applied to rate ratios of subgroups.

Results showing statistical significance should not be over-interpreted because our analysis was performed post hoc on nonrandomized groups, and therefore suffers from limitations such as reduced statistical power and increased variability.

Trial registration

This trial is registered at http://clinicaltrials.gov/ct2/show/NCT00101751 as "INITIATE Plus (INITiation of Insulin to Reach A1C TargEt) Study (INITIATE *plus*)," ClinicalTrials.gov registry ID NCT00101751.

RESULTS

Baseline and disposition data

The intent-to-treat study population comprised subjects who were categorized according to race (White, Black/African-American) and ethnicity (Hispanic/Latino and non-Hispanic/Latino). The original randomization into 3 dietary counseling groups occurred such that the racial and ethnic distribution was the same in each dietary counseling group.

Baseline (Table 1) A1C values were highly dissimilar for these groups, especially for Black/African-American subjects, whose mean A1C values were 0.7% higher than those of White subjects. The Black/African-American group had a comparatively lower male:female ratio. For the total population, 50.4% of all subjects were male and 49.6% were female; average

age (SD) was 54 (12) years; mean (SD) baseline A1C was 9.91% (1.65%); and mean BMI was 34.1 (7.3) kg/m^2.

Compared to the total population and to White and non-Hispanic/Latino subjects, a higher percentage of noncompleters occurred within the Black/African-American and Hispanic/Latino cohorts, with voluntary withdrawals amounting to 7.9% and 9.8% for these 2 groups, respectively. Withdrawals due to nonadherence were 6.4% for African-American subjects and 5.2% for Hispanic subjects. The overall withdrawal rate due to adverse events was 1.4%, considerably lower than that reported as voluntary or due to nonadherence.

Efficacy

Glucose control

For all subjects, mean A1C declined by 2.4% from a mean baseline of 9.9%[7]. Final A1C values for White and African-American subgroups were 7.31% and 7.90%, reduced from baselines of 9.72% and 10.44%, respectively, with A1C decreases from baseline of 2.41% and 2.54% ($p < 0.0001$) (Table 1). A1C decreases for Hispanic/Latino vs. non-Hispanic/Latino subjects were 2.61% and 2.42% respectively ($p > 0.05$). Reductions in A1C from baseline levels of 10.16% and 9.88%, resulted in final A1C values of 7.55% and 7.46% ($p > 0.05$).

Eight-point SMPG profiles shown in Figure 1 reveal that subjects achieved similar final plasma glucose profiles and similar final FPG values, regardless of race (Table 1). Fasting plasma glucose declined from baseline by 85.9, 90.0, 81.1 and 86.8 mg/dL (4.77, 5.0, 4.50, and 4.82 mmol/L) for White, Black/African-American, Hispanic and non-Hispanic/Latino subjects,

respectively ($p > 0.5$ between each pair of race or ethnic groups). Final SMPG profiles were higher for Hispanic/Latino compared to non-Hispanic/Latino subjects at all time points, and were significantly different at all time points except for FPG (pre-breakfast).

Safety

Hypoglycemia

Low rates of major and minor hypoglycemia prevailed among subjects in all groups, none of which exceeded 0.6 events per patient-year (ppy). Fewer than 11% of subjects experienced minor hypoglycemia and less than 2% of subjects experienced major hypoglycemic episodes (Table 2). Major hypoglycemia was reported in 1.9% of White and 1.7% of Black/African-American subjects, with rates of 0.08 and 0.04 events ppy, respectively. Major hypoglycemia occurred in 1.9% of non-Hispanic/Latino subjects and 0.8% of Hispanic/Latino subjects, at rates of 0.07 and 0.03 events ppy, respectively.

White subjects incurred a higher minor hypoglycemia frequency (10.8%) at a rate of 0.6 events ppy, compared to Black/African-American (frequency = 6.1%, rate = 0.3 events ppy) subjects. Minor hypoglycemia rates were 9.6% for non-Hispanic/Latino and 7.3% for Hispanic/Latino subjects with rates of 0.52 and 0.37 events ppy, respectively.

Body weight increases and final insulin dose

Baseline and final body weights were similar for White and Black/African-American subjects and were lower for Hispanic/Latino than those for non-Hispanic/Latino subjects. However, there

were no significant differences in net changes in body weight. Changes in body weight as a percent of baseline were significant between races and ethnic groups (Table 3).

Weight-adjusted final daily insulin dose (Table 3) was lower for Black/African-American subjects compared to White subjects (0.60 U/kg vs. 0.78 U/kg, $p < 0.0001$). Weight-adjusted insulin doses for Hispanic/Latino and non-Hispanic/Latino subjects were the same (0.70 U/kg).

DISCUSSION

Effective insulin self-titration in patients with diabetes can yield successful attainment of glycemic goals and has the potential to positively impact the outcome of this chronic disease for which treatment continues over a lifetime. Self-titration is an empowering process. However, the degree of success for self-titration depends on a number of variables that could include the insulin formulation and dosing algorithm, possible cultural and physiological variables that differ by race or ethnicity, and the extent of health care professional involvement. Data from this trial show that disparities in baseline glycemic control between patients of different racial and ethnic backgrounds can be overcome in a primary care setting using a self-titration dosing algorithm. This study examined data from the INITIATE*plus* trial[7] in which insulin-naïve patients with type 2 diabetes began twice-daily BIAsp 30 using a self-adjusting dose paradigm that was maintained for 24 weeks. This post hoc exploratory analysis examined the question of whether there were differences in treatment success and safety based on race or ethnicity.

There was low hypoglycemia and high efficacy across all demographics. Minor hypoglycemia rates were no higher than 0.6 events ppy, and were lower in this trial than reported (3 to 22

events ppy) for other BIAsp 30 trials[8–10]. Patient apprehension over hypoglycemia is a steep barrier to insulin initiation for many patients to overcome. It is therefore noteworthy that a high degree of efficacy accompanied the low hypoglycemia in this population of insulin-naïve patients who had failed OAD therapy, who had high mean baseline A1C (overall mean [SD] A1C = 9.9% [1.8%]), and had been living with type 2 diabetes for multiple years. The fact that these were insulin-naïve patients whose baseline glycemia greatly exceeded recommended ADA guidelines implies that too long a time elapsed before insulin therapy was initiated. The improvements in glycemic control with BIAsp 30 indicate, though, that despite high baseline A1C and FPG, insulin resistance was not a factor for their poor baseline glycemic values.

There were no overall differences in final 8-point SMPG values between the racial subgroups. Hispanic/Latino and non-Hispanic/Latino patients showed similar levels of reductions in A1C, but the final SMPG values were statistically significantly lower for non-Hispanic/Latino patients than for Hispanic/Latino patients at all time points except before breakfast.

It is noteworthy that in this trial, conducted in a primary care setting with insulin-naïve patients, all demographic groups achieved impressive A1C declines that fell within a relatively narrow range (2.41% to 2.54% for White vs. Black/African-Americans, 2.61% vs. 2.42% for Hispanic/Latino vs non-Hispanic/Latino patients, respectively), despite the clearly high A1C baseline values and their relatively large differences between the subgroups being compared. A1C declined by 24.5% to nearly 26% of baseline values between these subgroups.

Net weight gains and weight gains as a percent of baseline weight by all groups were similar, although Black/African-American patients, who had baseline weights similar to those of White patients, had a lower weight-adjusted final insulin dose. Lower insulin dosing among Black/African-Americans has been reported previously[11]. Other studies suggest physiological reasons[12–16] for Black/African-Americans having different final insulin doses than White patients. These studies suggest a physiological basis, like insulin utilization, as partly responsible for some racial disparities in glucose control as measured by A1C. Larger studies are needed to confirm these findings.

There is a large body of literature that points towards physiological, societal, cultural, and economic differences to account for racial disparities in glycemic control and insulin usage[15–20] that may partly explain why A1C values for Black/African-Americans and for Hispanic/Latino patients were higher than those for White or non-Hispanic/Latino patients, respectively. Genetic or physiological differences in addition to cultural preferences may, therefore, require more careful attention by health care providers. Nonetheless, final SMPG profiles between White and Black/African-American patients in this trial were similar, and final FPG, and A1C and FPG changes from baseline in this trial were nearly the same among the various groups.

A limitation of this post-hoc, exploratory analysis is that the INITIATE*plus* trial was not powered for comparisons across race or ethnicity. There were disproportionately more White vs. Black/African-Americans, and more non-Hispanic/Latino than Hispanic/Latino patients. There were also wide disparities in baseline A1C between the pairs of groups being compared here. Consequently, it is difficult to accurately correct for covariates, allowing only an analysis using

descriptive statistics as the most appropriate option. Many of the population chosen for the trial had not only failed oral antidiabetes therapy but had what can be considered extremely poor glycemic control. It may not be representative of the entire population of untreated patients with diabetes, only those whose diabetes has been inadequately controlled to a greater extent than most. Data for duration of disease were not collected. Nevertheless, this study was conducted in a real-world PCP setting among 934 sites, and may be a more accurate reflection of potential outcomes for patients given the opportunity and tools for self-titration.

The changes reported for INITIATE*plus* compare well to outcomes from other trials with BIAsp 30 with insulin-naïve patients, as shown in the 1-2-3 Study[9] (ΔA1C = –1.9%), IMPROVE Study[21] (ΔA1C = –2.1%), and INITIATE Study[10] (ΔA1C = –2.8%). In the 4T trial[22], a large UK study, patients who initiated insulin with twice daily BIAsp 30 reported at the 3-year endpoint low hypoglycemia incidence, FPG declines of 50 mg/dL (2.78 mmol/L), mean final A1C of 7.1%, and an absolute A1C decline from baseline of 1.3%, with 49% achieving A1C ≤7%. These trials had considerably fewer patients than INITIATE*plus*, which included over 4,000 patients, among whom over 1,000 were Black/African-American, as well as a relatively large number of Hispanic/Latino patients. The results reported here compare favorably to those of the 4T trial[22] and demonstrate that that insulin-naïve patients in primary care settings with inadequate glucose control (in the US or UK) can safely be titrated with biphasic insulin aspart 70/30 (BiAsp30) to achieve glycemic control while avoiding the complications of hypoglycemia. A recently published pooled analysis of 3 small studies with premixed insulin lispro (75/25) showed equivalent findings in terms of demonstrating A1C declines that did not vary between different racial and ethnic groups[23].

CONCLUSIONS

It is important to note that the data in this exploratory, post hoc analysis come from a single, real-world trial conducted predominantly in a primary care setting, with large numbers of patients from different racial and ethnic backgrounds, most of whom had poor baseline glycemic control. All demographic groups achieved high efficacy, with A1C reductions that fell within a relatively narrow range (2.41% to 2.54% for White vs. Black/African-Americans, 2.61% vs. 2.42% for Hispanic/Latino vs non-Hispanic/Latino patients, respectively). FPG reductions from baseline ranged from 81.1-90.0 mg/dL (4.5-5.0 mmol/L) and were not significantly different between groups. Hypoglycemia rates were low throughout. The very similar glycemic changes among all groups in response to BIAsp 30 treatment in this trial imply that empowering patients to self-adjust their insulin regimen might have a powerful influence on successful glycemic control, and may be an important component in treatment paradigms for eliminating racial/ethnic disparities otherwise seen in diabetes control survey data. The result also demonstrates the ability of an analog premix, BIAsp 30, when used twice daily with a clear, easily followed dosing protocol, to rectify existing poor glycemic control that could not be controlled by oral antidiabetes therapy. Health care practitioners may still need to provide more individualized treatment approaches that take cultural influences on medical outcomes into consideration and may need to take a more proactive stance regarding patient education and disease self-management, but this increased attention would benefit all patients.

TRANSPARENCY

Declaration of funding

Funding to support this study and the preparation of this manuscript was provided by Novo Nordisk Inc. Novo Nordisk provided clinical trial supplies, monitored the trial, performed the statistical analyses, and prepared the clinical trial report. The authors had full access to the data and take responsibility for the accuracy of the data and its analysis.

Author contributions: BST, MDS, FCC, and AB conducted the research, contributed to discussions, and helped write, review, and revise the manuscript. JB and DSO conducted the research, analyzed data, contributed to discussions, and helped write, review, and revise the manuscript. P-LC performed the statistical analyses, and helped review and revise the manuscript. The paper was prepared according to the ICMJE's Uniform Requirements for Manuscripts Submitted to Biomedical Journals and the International Society for Medical Publication Professionals' "Good Publication Practice for Communicating Company-Sponsored Medical Research: The GPP2 Guidelines."

Declaration of financial/other relationships

BST has been a Novo Nordisk speakers bureau member and has received grant support from Novo Nordisk for clinical research. MDS is affiliated with Novo Nordisk as a consultant, national speaker, researcher, recipient of grant support, and owns Novo Nordisk stock. FCC has been a Novo Nordisk speaker bureau member and is a Novo Nordisk advisory board member. AB is a Novo Nordisk speakers bureau member and has received grant support from Novo Nordisk for clinical research. DSO is a Novo Nordisk speakers bureau and advisory board member. JB and P-LC are employees of Novo Nordisk and own Novo Nordisk stock.

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Table 1. Baseline characteristics, efficacy data and subject disposition.

	White	**Black/ African-American**	**Hispanic/Latino**	**Non-Hispanic/Latino**
Baseline data				
n	2,887	1,025	489	3,720
A1C	9.72 (1.56)	10.44 (1.79)	10.16 (1.68)	9.88 (1.64)
Weight (kg)	99.3 (23.2)	98.4 (23.2)	90.3 (22.4)	99.01 (22.4)
BMI	34.35 (7.25)	34.27 (7.30)	33.08 (7.19)	34.19 (7.30)
Age	54.8 (11.95)	52.06 (2.04)	50.64 (11.96)	54.39 (11.95)
Gender (M/F)	1519/1367	430/595	252/237	1871/1849
A1C data				
Final A1C	7.31 (1.44)	7.90 (1.64)	7.55 (1.44)	7.46 (1.49)
ΔA1C	–2.41 (1.85)	–2.54 (2.04)	–2.61 (1.97)	–2.42 (1.89)
	$p < 0.0001$*		$p = 0.677$**	
Δ as % of baseline	24.8	24.3	25.7	24.5
FPG data				
Baseline	228.8 (75.5)	231.4 (85.6)	227.3 (73.2)	228.5 (78.2)
Final	143 (48.6)	141.6 (52.1)	146.3 (52.4)	141.8 (48.8)
ΔFPG	–85.9 (80.7)	–90.0 (91.4)	–81.1 (80.0)	–86.8 (83.5)
	($p < 0.272$*)		($p = 0.53$**)	
Withdrawals, n/N (%)				
Voluntary	194/3236 (6.0)	97/1222 (7.9)	58/591 (9.8)	279/4225 (6.6)
Noncompliant	121/3236 (3.8)	78/1222 (6.4)	31/591 (5.2)	178/4225 (4.2)
All noncompleters	552/3236 (17.1)	281/1222 (23)	151/591 (25.5)	771/4225 (18.2)

Baseline data are for the intent-to-treat population, and are shown as observed means (SD).

*White patients compared to Black/African-American patients.

** Hispanic/Latino patients compared to Non-Hispanic/Latino patients.

A1C data are from the LOCF intent-to-treat population, and are shown as observed means (SD).

FPG data are from the LOCF intent-to-treat population, reporting the starting (baseline) and end-of-trial

SMPG pre-breakfast measurements, which are shown as observed means (SD)..

Withdrawal data are from the safety population. Numbers in parentheses are within-group percentages.

All other data shown as means (SD), unless indicated otherwise.

Table 2. Hypoglycemia episodes by race and ethnicity.

	N	n	%	E	R	Rate ratio*
Major hypoglycemia						
White	3,236	63	1.9	103	0.08	
Black/African-American	1,222	21	1.7	21	0.04	1.74
Non-Hispanic/Latino	4,225	82	1.9	120	0.07	
Hispanic/Latino	591	5	0.8	7	0.03	2.28
Minor hypoglycemia						
White	3,236	351	10.8	811	0.60	
Black/African-American	1,222	74	6.1	142	0.30	2.03
Non-Hispanic/Latino	4,225	407	9.6	909	0.52	
Hispanic/Latino	591	43	7.3	86	0.37	1.40

Data are from the safety population and are observed values.

N = total number of patients; n = number of patients reporting at least one hypoglycemic event; % = number of patients reporting hypoglycemic episode/N x 100; E = number of events; R = rate (number of hypoglycemic events/patient-year).

*White vs Black/African-American, and Non-Hispanic/Latino vs Hispanic/Latino.

Table 3. Body weight increases and final insulin doses by race and ethnicity.

Race/Ethnicity	**Baseline body wt (kg)**	**Final body wt (kg)**	**ΔBody wt (kg)**	**ΔBody wt as % of baseline**	**Final weight-adjusted insulin dose (U/kg)**
White	99.3 (23.2)	102.6 (23.5)	3.16 (6.1)	3.51 (6.5) ($p < 0.0001$*)	0.78 (0.5) ($p < 0.0001$*)
Black/African-American	98.4 (23.2)	101.6 (23.4)	3.08 (5.5)	3.48 (6.0)	0.60 (0.4)
Hispanic/Latino	90.3 (22.4) ($p < 0.001$**)	93.6 (22.2) ($p < 0.0001$**)	3.03 (5.4)	3.79 (6.6) ($p < 0.0001$**)	0.70 (0.45)
Non-Hispanic/Latino	99.0 (23.3)	102.3 (23.7)	3.15 (6.0)	3.51 (6.4)	0.70 (0.50)

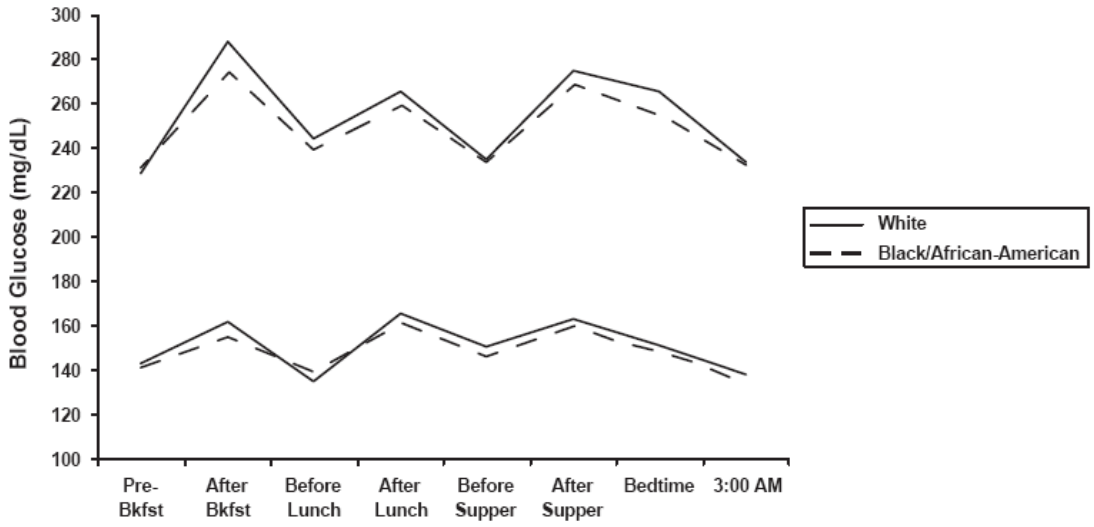
All values are observed means (SD).

*White patients compared to Black/African-American patients.

**Hispanic/Latino patients compared to Non-Hispanic/Latino patients.

Figure 1. Eight-point SMPG changes by race (A) and by ethnicity (B). Eight-point self-measured blood glucose readings taken 30 minutes before breakfast, lunch, and dinner; 2 hours after breakfast, lunch, and dinner; and at bedtime and 3:00 a.m. The upper tracings in each panel are baseline readings and the lower tracings were taken at end of trial. All SMPG values at end of trial for Hispanic/Latino patients were statistically significant compared to those for non-Hispanic/Latino patients, except for pre-breakfast values.

A



B