

# DURAbility of Basal Versus Lispro Mix 75/25 Insulin Efficacy (DURABLE) Trial 24-Week Results

Safety and efficacy of insulin lispro mix 75/25 versus insulin glargine added to oral antihyperglycemic drugs in patients with type 2 diabetes

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**OBJECTIVE** — To compare the ability of two starter insulin regimens to achieve glycemic control in a large, ethnically diverse population with type 2 diabetes.

**RESEARCH DESIGN AND METHODS** — During the initiation phase of the DURABLE trial, patients were randomized to a twice-daily lispro mix 75/25 (LM75/25; 75% lispro protamine suspension, 25% lispro) ( $n = 1,045$ ) or daily glargine (GL) ( $n = 1,046$ ) with continuation of prestudy oral antihyperglycemic drugs.

**RESULTS** — Baseline A1C was similar (LM75/25:  $9.1 \pm 1.3\%$ ; GL:  $9.0 \pm 1.2\%$ ;  $P = 0.414$ ). At 24 weeks, LM75/25 patients had lower A1C than GL patients ( $7.2 \pm 1.1$  vs.  $7.3 \pm 1.1\%$ ,  $P = 0.005$ ), greater A1C reduction ( $-1.8 \pm 1.3$  vs.  $-1.7 \pm 1.3\%$ ,  $P = 0.005$ ), and higher percentage reaching A1C target  $<7.0\%$  ( $47.5$  vs.  $40.3\%$ ,  $P < 0.001$ ). LM75/25 was associated with higher insulin dose ( $0.47 \pm 0.23$  vs.  $0.40 \pm 0.23$  units  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>,  $P < 0.001$ ) and more weight gain ( $3.6 \pm 4.0$  vs.  $2.5 \pm 4.0$  kg,  $P < 0.0001$ ). LM75/25 patients had a higher overall hypoglycemia rate than GL patients ( $28.0 \pm 41.6$  vs.  $23.1 \pm 40.7$  episodes  $\cdot$  pt<sup>-1</sup>  $\cdot$  year<sup>-1</sup>,  $P = 0.007$ ) but lower nocturnal hypoglycemia rate ( $8.9 \pm 19.3$  vs.  $11.4 \pm 25.3$  episodes  $\cdot$  pt<sup>-1</sup>  $\cdot$  year<sup>-1</sup>,  $P = 0.009$ ). Severe hypoglycemia rates were low in both groups (LM75/25:  $0.10 \pm 1.6$  vs. GL:  $0.03 \pm 0.3$  episodes  $\cdot$  pt<sup>-1</sup>  $\cdot$  year<sup>-1</sup>,  $P = 0.167$ ).

**CONCLUSIONS** — Compared with GL, LM75/25 resulted in slightly lower A1C at 24 weeks and a moderately higher percentage reaching A1C target  $<7.0\%$ . Patients receiving LM75/25 experienced more weight gain and higher rates of overall hypoglycemia but lower rates of nocturnal hypoglycemia. Durability of regimens will be evaluated in the following 2-year maintenance phase.

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In patients with type 2 diabetes inadequately controlled on oral antihyperglycemic drugs (OADs), therapeutic options include the addition of once-daily basal or twice-daily premixed insulin (1–8). Previous studies comparing these two

insulin initiation strategies (6–8) have noted greater A1C reduction with analog mixture therapy; however, these studies did not use the same oral agents in both arms and therefore compared treatment strategies rather than specific insulin regimens.

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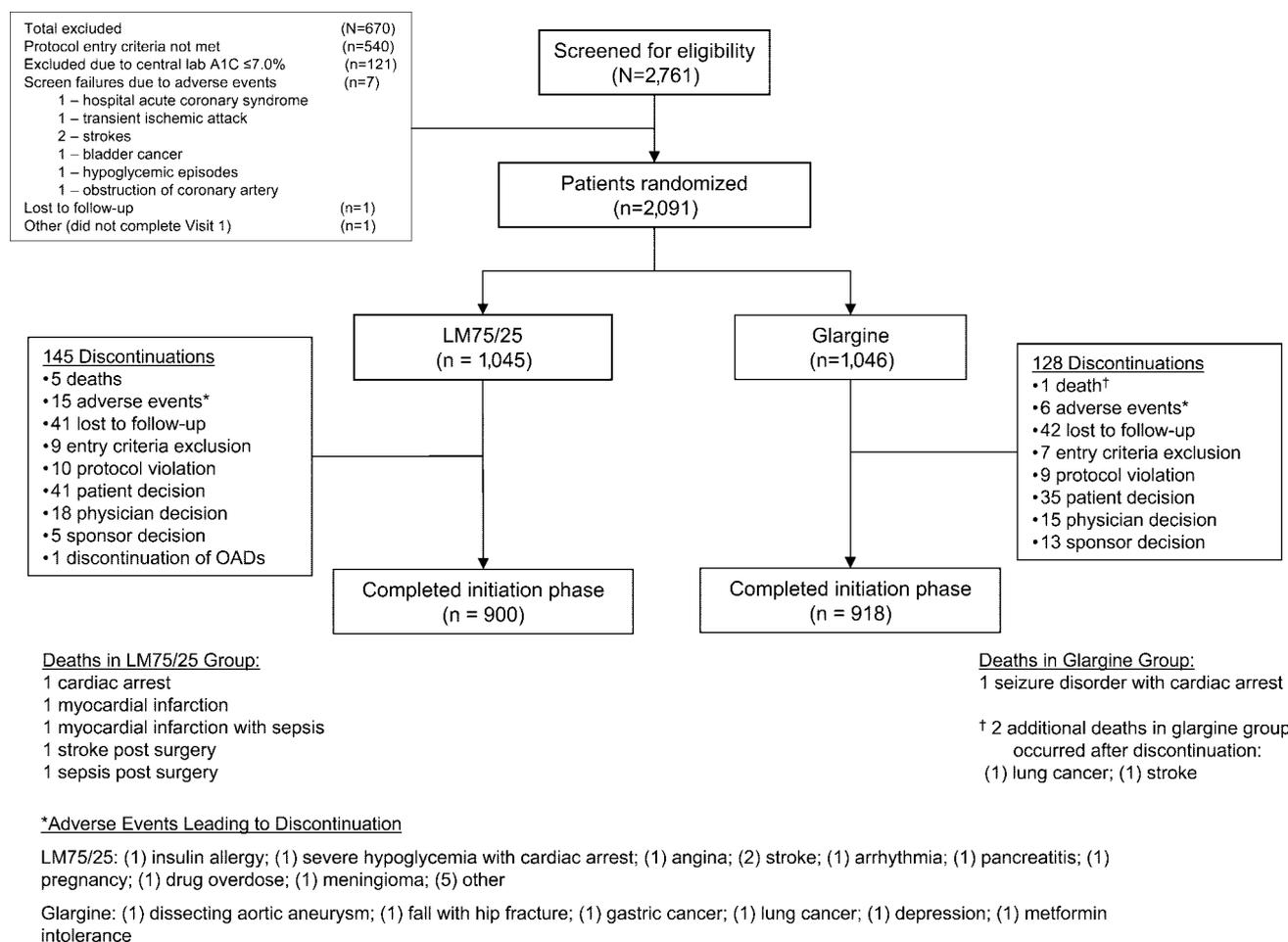
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Few large studies have compared starter insulin regimens in combination with OADs. One such study, Treating To Target in Type 2 Diabetes (4-T), is an ongoing 3-year trial evaluating the safety, efficacy, and need to intensify therapy among analog insulin regimens (basal, rapid acting, or premixed) used in combination with dual OAD therapy in over 700 insulin-naïve patients with type 2 diabetes from the U.K. and Ireland (9). The present study, DURABLE (assessing DURAbility of Basal versus Lispro mix 75/25 insulin Efficacy), was designed to study the efficacy, safety, and durability of two common insulin initiation regimens: twice-daily insulin lispro mixture 75/25 (LM75/25; Humalog Mix 75/25: 75% insulin lispro protamine suspension, 25% lispro) versus once-daily insulin glargine (GL; Lantus insulin glargine [rDNA origin] injection) within the context of continued OADs. The results of the 24-week initiation phase, presented here, will provide the first comparison of safety and efficacy for these two regimens in a large, ethnically diverse population. The ongoing, 2-year maintenance phase will evaluate the length of time each starter insulin regimen is able to maintain A1C goals (i.e., regimen durability).

## RESEARCH DESIGN AND METHODS

A detailed description of the DURABLE study design has previously been published (10). The 24-week initiation phase was a randomized, open-label, parallel trial conducted at 242 centers in 11 countries (Argentina, Australia, Brazil, Canada, Greece, Hungary, India, the Netherlands, Romania, Spain, and the U.S.) between December 2005 and July 2007. The trial was conducted in accordance with the International Conference on Harmonization Guidelines for Good Clinical Practice and the Declaration of Helsinki (11); all patients provided written informed consent.

The trial enrolled 2,091 insulin-naïve patients with type 2 diabetes, aged 30–80



**Figure 1**—Flow of patients through the initiation phase (first 24 weeks) of the DURABLE trial.

years, with A1C  $>7.0\%$  on at least two OADs for 90 days (minimum doses: 1,500 mg/day metformin, one-half maximum daily dose sulfonylurea [SFU], 30 mg/day pioglitazone, or 4 mg/day rosiglitazone). Patients were excluded if they had a history of scheduled long-term insulin use; recent use of other antihyperglycemic agents; BMI  $>45$  kg/m<sup>2</sup>; recent history of severe hypoglycemia; significant concomitant hematologic, oncological, renal, cardiac, hepatic, or gastrointestinal disease; recent systemic steroid use; or were pregnant or breastfeeding. A1C was measured centrally by Covance Laboratories. In the 2 weeks preceding the 24-week visit, patients recorded three seven-point self-monitored plasma glucose (SMPG) profiles consisting of three premeal measurements (first measurement fasting), three 2-h postprandial measurements, and a 3:00 A.M. measurement (Roche Active or Roche Aviva meters).

**Study medications and treatments**

Eligible patients were randomly assigned to one of two treatment arms by stratified

randomization through an interactive voice-response system. Patients were randomized by country and stratified within country based on SFU and thiazolidinedione (TZD) use. Patients received LM75/25 twice daily before morning and evening meals or GL once daily before morning or evening meal or at bedtime. Both insulin therapies were added to patients' prestudy OADs. Following randomization, patients were required to maintain prestudy OADs at current dosages.

The minimum starting dose was 10 units twice daily for LM75/25 and 10 units once daily for GL. Insulin dose adjustments were made to achieve a target A1C goal of  $\leq 6.5\%$ , utilizing regimen-specific, insulin dose titration algorithms (12,13) (online appendix Table A1 [available at <http://care.diabetesjournals.org/cgi/content/full/dc08-2117/DC1>]). Patients monitored plasma glucose at least twice daily (before morning and evening meals). Each patient's dose was assessed and adjusted frequently (at a minimum, once weekly for the first 6 weeks, once every 2 weeks for the next 6 weeks, and then once

every 6 weeks to the 24-week end point). An electronic case report form–based system encouraged titration per protocol, and a data monitoring committee monitored insulin dose adjustments to ensure patient safety and provide investigators feedback regarding appropriate adherence to dosing algorithms.

Safety was monitored throughout the study, and the occurrence and nature of serious adverse events (SAEs) were recorded. Hypoglycemia was predefined as a plasma glucose value  $\leq 70$  mg/dl (3.9 mmol/l) or symptoms that the patient typically associated with hypoglycemia. Episodes of hypoglycemia that occurred after bedtime and before the morning meal/insulin dose were considered nocturnal. Severe hypoglycemia was defined as an episode requiring assistance from another person for treatment with oral carbohydrate, intravenous glucose, or glucagon (14). SAEs were defined as events resulting in death, life-threatening experience, hospitalization, or persistent or significant disability.

Table 1—Baseline demographics and characteristics of randomized patients

	LM75/25 group	GL group	P
n	1,045	1,046	
Age (years)	57 ± 10	57 ± 10	0.264
Male (%)	552 (52.8)	552 (52.8)	0.979
Race/ethnicity			
Caucasian	651 (62.3)	668 (63.9)	0.469
East/Southeast Asian	18 (1.7)	27 (2.6)	0.228
Western Asian	139 (13.3)	136 (13.0)	0.846
Hispanic	136 (13.0)	116 (11.1)	0.180
Black/African descent	62 (5.9)	70 (6.7)	0.529
Other	39 (3.7)	29 (2.8)	0.221
Weight (kg)	89 ± 21	88 ± 21	0.497
BMI (kg/m <sup>2</sup> )	32 ± 6	32 ± 6	0.917
Diabetes duration (years)	9.7 ± 6.3	9.3 ± 5.9	0.109
A1C (%)	9.1 ± 1.3	9.0 ± 1.2	0.414
Fasting plasma glucose (mg/dl)	193 ± 53.2	196 ± 55.1	0.179
Fasting plasma glucose (mmol/l)	10.7 ± 3.0	10.9 ± 3.1	0.179
Concomitant OADs at study entry			
MET/SFU/TZD	233 (22.3)	225 (21.5)	0.689
MET/SFU	674 (64.5)	665 (63.6)	0.724
MET/TZD	81 (7.8)	78 (7.5)	0.814
SFU/TZD	51 (4.9)	69 (6.6)	0.088

Data are means ± SD or n (%).

### Outcome measures

The primary efficacy measure was A1C at end point (last observation carried forward [LOCF] to 24 weeks). Secondary outcome measures included change in A1C from baseline to end point, A1C at each visit, percentage of patients with end point A1C <7.0% and ≤6.5%, seven-point SMPG profiles, weight change from baseline, total daily insulin (TDI) dose at end point, and incidence and rate of hypoglycemic episodes.

### Statistical methods

We calculated that 1,000 subjects per group would provide ~97% power to detect a difference of 0.2% in 24-week end point A1C between treatment groups (two-sided  $\alpha = 0.05$  assuming a 1.1% SD and a drop-out rate of 10%). The sample size calculation was primarily based on the maintenance-phase primary objective. The analyses of initiation-phase data were prespecified and performed with LOCF method on the intent-to-treat population who had at least one postbaseline assessment. The primary outcome (end point A1C) was analyzed by ANCOVA with treatment, baseline A1C, country, and SFU and TZD use as covariates. Secondary outcomes (SMPG, TDI, weight change, hypoglycemia rate, and severe hypoglycemia rate) were analyzed using ANCOVA with treatment, country, and

SFU and TZD use as covariates. Percentage of patients achieving A1C goals was analyzed using Cochran-Mantel-Haenszel statistic controlling for country, TZD use, and SFU use. Categorical safety variables were compared between groups with a Fisher's exact test.

## RESULTS

### Patient disposition and baseline characteristics

Of 2,091 patients randomized, 1,045 were assigned to LM75/25 and 1,046 to GL. Approximately 86% ( $n = 900$ ) of patients in the LM75/25 group and 88% ( $n = 918$ ) in the GL group completed the trial; reasons for discontinuation are summarized in Fig. 1. There was no significant difference between overall discontinuations or any individual reported reason for discontinuation between groups ( $P > 0.05$  for all comparisons).

At baseline, treatment groups were similar with regard to demographic, anthropometric, and disease characteristics (Table 1). The patient population was 63% non-Hispanic Caucasian, 2% East/Southeast Asian, 13% Western Asian, 12% Hispanic, 6% African descent, and 3% other racial/ethnic origin. Overall, the mean age was 57 years, 53% of patients were men, BMI was 32 kg/m<sup>2</sup>, average duration of diabetes was 9.5 years, and mean

A1C was 9.0 ± 1.3%. Approximately 92% ( $n = 1,917$ ) of all patients were on an SFU, with the most common OAD combination being metformin plus SFU (64%;  $n = 1,339$ ).

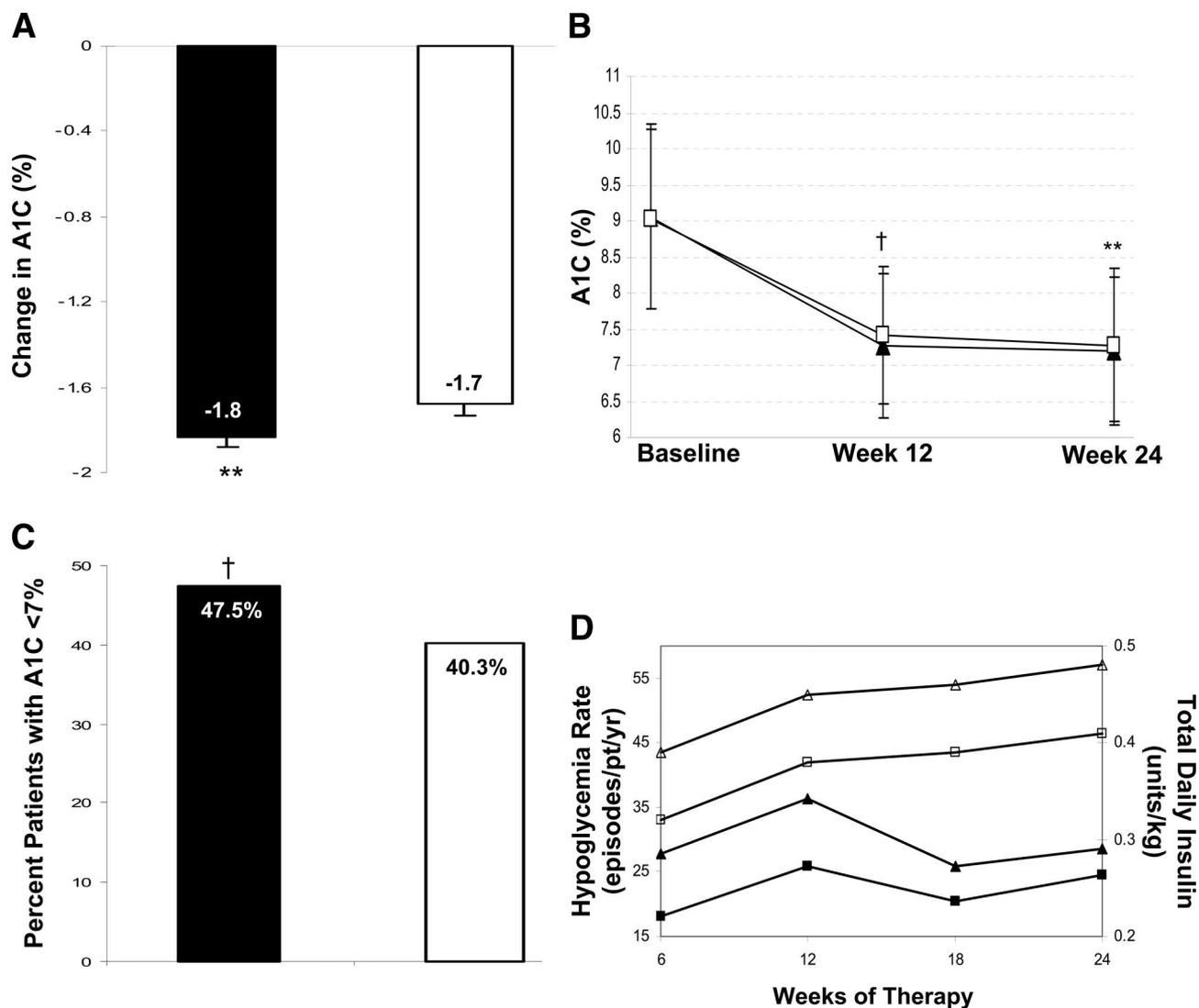
### Glycemic control

The change in A1C from baseline to end point was greater for the LM75/25 group compared with the GL group ( $-1.8 \pm 1.3$  vs.  $-1.7 \pm 1.3\%$ ,  $P = 0.005$ ) (Fig. 2A). Mean A1C decreased in both groups with therapy ( $P < 0.0001$  for comparison of baseline to 24 weeks) (Fig. 2B). At end point, A1C was lower for LM75/25 compared with glargine ( $7.2 \pm 1.1$  vs.  $7.3 \pm 1.1\%$ ,  $P = 0.005$ ). After adjusting for baseline A1C, country of origin, SFU use, and TZD use, end point A1C (least-squares mean ± SE) values were  $7.0 \pm 0.1\%$  for LM75/25 and  $7.1 \pm 0.1\%$  for GL ( $P = 0.005$ ). As shown in Fig. 2C, a higher percentage of patients in the LM75/25 group were able to reach target A1C <7.0% by end point compared with the GL group (47.5 vs. 40.3%,  $P < 0.001$ ). There was no difference between groups in the percentage of patients who achieved A1C ≤6.5% (LM75/25 24.6%, GL 22.2%;  $P = 0.174$ ).

Comparison of baseline and end point seven-point SMPG profiles (online appendix Fig. A1) showed that therapy with either LM75/25 or GL lowered plasma glucose values at all time points ( $P < 0.0001$ ). At end point, fasting plasma glucose was higher in the LM75/25 group than in the GL group ( $134 \pm 35$  vs.  $122 \pm 33$  mg/dl,  $P < 0.001$ ). Patients in the LM75/25 group had lower 2-h postprandial plasma glucose after morning ( $167 \pm 49$  vs.  $172 \pm 49$  mg/dl,  $P < 0.05$ ) and evening ( $163 \pm 47$  vs.  $176 \pm 49$  mg/dl,  $P < 0.001$ ) meals, as well as lower premeal plasma glucose before the noon meal ( $130 \pm 42$  vs.  $137 \pm 44$  mg/dl,  $P < 0.001$ ). There were no differences between therapies for plasma glucose values at the noon 2-h postprandial, evening premeal, or 3:00 A.M. time points.

### Insulin dose and weight gain

At end point, the TDI dose (mean ± SD) was higher for patients in the LM75/25 group than in the GL group ( $0.47 \pm 0.23$  vs.  $0.40 \pm 0.23$  units/kg,  $P < 0.001$ ). Patients on LM75/25 gained more weight than did patients on GL ( $3.6 \pm 4.0$  vs.  $2.5 \pm 4.0$  kg,  $P < 0.001$ ).



**Figure 2**—A: Change in A1C from baseline to end point for patients treated with LM75/25 (■) versus glargine (□). \*\* $P < 0.01$ . B: A1C values at each visit for patients treated with LM75/25 (▲) versus glargine (□). \*\* $P < 0.01$ ; † $P < 0.001$ . C: Percent of patients achieving A1C target  $<7.0\%$  at end point for patients treated with LM75/25 (■) versus glargine (□). † $P < 0.001$ . D: Observed mean overall hypoglycemia rate (episodes  $\cdot$  pt $^{-1} \cdot$  year $^{-1}$ ) and TDI dose (units/kg) at each visit between 6 and 24 weeks of therapy for patients treated with LM75/25 (▲, hypoglycemia rate; △, TDI) or glargine (■, hypoglycemia rate; □, TDI).

**Hypoglycemia**

At end point, a higher ( $P = 0.016$ ) percentage of patients on LM75/25 experienced at least one episode of hypoglycemia (incidence of overall hypoglycemia) than patients on GL (Table 2). Additionally, patients on LM75/25 had a higher ( $P = 0.007$ ) rate of overall hypoglycemia than did their GL-treated counterparts. Patients on LM75/25 had a lower ( $P = 0.009$ ) rate of nocturnal hypoglycemia compared with patients on GL (Table 2). The majority of patients in the GL treatment group administered their daily dose before breakfast ( $n = 396$ ; 39%), before the evening meal ( $n = 139$ ; 14%), or at bedtime ( $n = 458$ ; 45%); among these groups, nocturnal hypoglycemia rates did

not differ between groups ( $P > 0.05$  for all comparisons). There were no statistically significant differences between groups in the incidence or rate of severe hypoglycemia (Table 2). As shown in Fig. 2D, the observed mean hypoglycemia rate continued to increase in association with increasing insulin dose through week 12 for both treatment groups. After week 12, the overall hypoglycemia rate comparatively decreased, even with gradual continued upward titration of insulin dose.

**Safety**

Overall, 65 (6.2%) patients in the LM75/25 group and 45 (4.3%) patients in the GL group experienced at least one SAE ( $P = 0.051$ ); the percentage of car-

diovascular system–related SAEs was similar between treatment groups (LM75/25: 29%; GL: 26%;  $P = 0.716$ ). There were 15 adverse events (AEs) leading to discontinuation in the LM75/25 group and 6 AEs in the GL group ( $P = 0.077$ ) (Fig. 1). Five deaths occurred in the LM75/25 group and one death occurred in the GL group ( $P = 0.218$ ) (Fig. 1). In addition, an SAE in two GL-treated patients led to death after discontinuation from the study.

**CONCLUSIONS**

The 24-week initiation phase of the DURABLE study compared two common starter insulin regimens (LM75/25 twice daily versus GL once daily) in a large multinational pop-

Table 2—Incidence and rate of hypoglycemia\*

	LM75/25 group	GL group	P
Hypoglycemia incidence			
Overall	586 (57.1)	530 (51.8)	0.016
Documented symptomatic (plasma glucose $\leq$ 70 mg/dl [3.9 mmol/l])	454 (44.2)	345 (33.7)	<0.001
Documented symptomatic (plasma glucose <60 mg/dl [3.3 mmol/l])	388 (37.2)	295 (28.2)	<0.001
Documented symptomatic (plasma glucose <50 mg/dl [2.8 mmol/l])	210 (20.1)	120 (11.5)	<0.001
Documented asymptomatic (plasma glucose $\leq$ 70 mg/dl [3.9 mmol/l])	265 (25.8)	289 (28.2)	0.194
Nocturnal	348 (33.9)	351 (34.3)	0.834
Severe†	22 (2.1)	12 (1.2)	0.080
Hypoglycemia rate (episode $\cdot$ pt <sup>-1</sup> $\cdot$ year <sup>-1</sup> )			
Overall			
Median (interquartile range)	8.7 (0.0–42.1)	7.0 (0.0–27.2)	0.007
Observed mean	28.0	23.1	0.007
Documented symptomatic (plasma glucose $\leq$ 70 mg/dl [3.9 mmol/l])			
Median (interquartile range)	0.0 (0.0–20.9)	0.0 (0.0–8.9)	<0.001
Observed mean	17.83	11.80	<0.001
Documented symptomatic (plasma glucose <60 mg/dl [3.3 mmol/l])			
Median (interquartile range)	0.0 (0.0–31.3)	0.0 (0.0–13.0)	0.006
Observed mean	23.00	18.07	0.006
Documented symptomatic (plasma glucose <50 mg/dl [2.8 mmol/l])			
Median (interquartile range)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	<0.001
Observed mean	15.30	9.29	<0.001
Documented asymptomatic (plasma glucose $\leq$ 70 mg/dl [3.9 mmol/l])			
Median (interquartile range)	0.0 (0.0–7.3)	0.0 (0.0–7.9)	0.117
Observed mean	7.13	8.48	0.117
Nocturnal			
Median (interquartile range)	0.0 (0.0–8.7)	0.0 (0.0–9.9)	0.009
Observed mean	8.9	11.4	0.009
Severe†			
Median (interquartile range)	0.00 (0.0–0.0)	0.0 (0.0–0.0)	0.167
Observed mean	0.10	0.03	0.167

Data are *n* (%) or median (interquartile range), unless otherwise indicated. \*Hypoglycemia was recorded any time a patient experienced symptoms of hypoglycemia or had an SMPG  $\leq$ 70 mg/dl (3.9 mmol/l), and the event was deemed severe if it required assistance. For all nonsevere hypoglycemia, values were calculated at end point (using LOCF) for the period between the previous office visit and end point office visit. †For severe hypoglycemia, incidence and rate were calculated over the entire study duration due to the rare occurrence of severe hypoglycemia.

ulation of patients with type 2 diabetes who were concurrently receiving two to three OADs, including SFUs. Although both regimens demonstrated significant A1C reduction from baseline, some important differences were observed between therapies. Compared with GL, LM75/25 therapy resulted in slightly lower end point A1C and a moderately higher percentage of patients reaching A1C target of <7.0% but with more weight gain and higher rates of overall hypoglycemia. Nocturnal hypoglycemia rates were lower with LM75/25, and there were no differences in the frequency or rate of severe hypoglycemia between the groups.

The rationale for use of premixed insulin analogs in the management of type 2 diabetes is based on the need for basal and postprandial glucose-lowering activity to more closely mimic physiological insulin secretion. In the DURABLE study,

LM75/25 demonstrated better postprandial glycemic control after the morning and evening meals compared with GL (with over 90% SFU use across treatment groups). There is evidence that improvement in postprandial glycemic excursions may be beneficial, as elevated postprandial glucose levels have been suggested as an independent risk factor for many diabetes-related complications, including macrovascular disease (15–19). Additionally, at A1C values approaching lower targeted goals, the need to address postprandial glucose control becomes increasingly important (20).

Efficacy findings from our study are consistent with those described for the first phase of the 4-T study (9), which reported 1-year results for three different analog insulin initiation therapies (basal, biphasic premixed, and prandial). Both studies compared insulin initiation regimens in the setting of continued prestudy

OADs, including SFU. The 24-week initiation phase of the DURABLE study evaluated a similar question to the 4-T study, comparing use of biphasic and basal insulin as starter insulin therapy but did so in a larger, more diverse population. In contrast to the 4-T study, which allowed for the use of an additional insulin formulation as rescue therapy during the first year of treatment, the initiation phase of the DURABLE study did not allow rescue therapy.

The DURABLE study, like the 4-T study, required insulin dose titration according to prespecified algorithms. Despite this, only 40–50% of DURABLE patients, regardless of treatment regimen, achieved the American Diabetes Association–recommended A1C target of <7.0%; though these results were more favorable than the 1-year percent to target A1C  $\leq$ 7.0% in the 4-T study (biphasic: 41.7%; basal: 27.8%). In the DURABLE study,

the majority of the A1C reduction occurred during the first 12 weeks, which corresponded to the phase of the most frequent insulin dose adjustments and the largest increase in total daily dose. This highlights the need for ongoing assessment and adjustment of insulin doses over time in an effort to improve and maintain glucose control while managing the risk of hypoglycemia. The majority of DURABLE investigative sites were in community-based clinics, and these real-world findings may, in part, reflect the challenge of limited time for plasma glucose review and adjustment of insulin regimens, as well as the treatment barrier of symptomatic hypoglycemia.

An increased occurrence of hypoglycemia with the combination of insulin and SFU could have limited insulin dose adjustments in both studies. This rationale is suggested by a TDI dose of 0.40–0.47 units · kg<sup>-1</sup> · day<sup>-1</sup> for patients in our study and, similarly, a TDI dose of 0.49–0.53 units · kg<sup>-1</sup> · day<sup>-1</sup> in basal and biphasic insulin-treated patients in the 4-T study. This is somewhat lower than the reported TDI dose in previous insulin initiation studies using basal or premix insulin without concomitant SFU (7,8).

Additionally, in the DURABLE study, investigators were instructed to adjust the insulin dose to prevent recurrent hypoglycemia but were not allowed to alter the SFU dose. This was done in an effort to control for factors impacting medication-induced glycemic control other than the two specific insulin regimens under investigation. Thus, when patients experienced hypoglycemia in the setting of improving glucose control, physicians may not have had the flexibility needed to further individualize the insulin plus OAD regimen. In clinical practice, it may be more practical to allow adjustment of either insulin dose or SFU in order to continue to optimize glycemic control while limiting hypoglycemia.

In light of recent published studies reporting on cardiovascular outcomes in patients with type 2 diabetes (21,22), it is important to note that this study was not designed to compare these end point measures (e.g., no stratified randomization based on cardiovascular risk factors, no data collection of past medical history or concomitant nondiabetes medications, and no adjudication of events). Withdrawals due to AEs, SAEs, and deaths did not differ significantly between treatment groups, even in this large study popula-

tion; however, there were numerically more events in the LM75/25 group. Because of the aforementioned trial design limitations, it is difficult to draw substantive conclusions from these observations other than the importance of considering the need for risk factor assessment when designing future clinical trials in type 2 diabetes.

In a predominately community-based setting, in 11 countries across five continents, type 2 diabetic patients initiating insulin with either twice-daily LM75/25 or once-daily GL, in combination with OADs, had a clinically meaningful reduction of A1C. At 24 weeks, LM75/25 demonstrated modestly greater efficacy, with a 0.1% greater absolute A1C reduction and 7.2% more patients treated to reach the American Diabetes Association–recommended A1C goal of <7.0% in the setting of more overall hypoglycemia but less nocturnal hypoglycemia. Clinicians will need to weigh the significance of these findings within their own algorithms of care as they strive to achieve glycemic goals and meet the standards of disease management programs evaluating quality of care (17,23,24). An important unanswered question—the long-term durability of starter insulin therapy—is being evaluated in the ongoing 2-year maintenance phase of the DURABLE study.

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