ORIGINAL RESEARCH

A Japanese Study Assessing Glycemic Control with Use of IDegAsp Co-formulation in Patients with Type 2 Diabetes in Clinical Practice: The JAGUAR Study

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ABSTRACT

Introduction: The aim of this study was to evaluate the glycemic control and safety of insulin degludec/insulin aspart (IDegAsp) co-formulation in Japanese patients with type 2 diabetes (T2D) in a real-world clinical setting, including elderly patients (aged > 75 years).

Methods: Patients ($\geq$ 18 years) diagnosed with T2D, previously treated with insulin were included from the Japanese Medical Data Vision database. Baseline data were taken at the index date, defined as the first IDegAsp prescription claim. Change in glycated hemoglobin (HbA_{1c}) at 12 months was estimated using a mixed model repeated measures analysis. The proportion of patients achieving target $HbA_{1c} < 8.0\%$ without experiencing hypoglycemia (identified by International Classification of Disease codes) was calculated at 12 months (365 $\pm$ 90 days) after baseline.

Results: Overall, 10,798 patients were included, 3940 were aged > 75 years, and 913 had baseline HbA_{1c} values available. Switching to IDegAsp was associated with significantly improved HbA_{1c} values at 12 months ($- 1.23\%$ $[- 1.43, - 1.02]_{95\%CI}$, $p < 0.001$) versus baseline. Moreover, relative to baseline, a significantly greater proportion of patients achieved $HbA_{1c} < 8.0\%$ without hypoglycemia at 12 months, relative rate (RR) 1.30 [1.15, 1.45]$_{95\%CI}$, $p < 0.001$. Results were similar for patients aged $\leq$ 75 years and aged > 75 years; 66% and 64% of patients, respectively, achieved $HbA_{1c} < 8.0\%$ without hypoglycemia at 12 months.

Conclusion: Switching from insulin to IDegAsp co-formulation was associated with significantly improved glycemic control and a reduction in hypoglycemia rate during 12 months of follow-up in Japanese patients with T2D, including those aged > 75 years.

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Key Summary Points

Why carry out this study?

Achievement of optimum glycemic control and prevention of diabetic complications are key goals of type 2 diabetes (T2D) management, which often require insulin treatment.

Older patients may need treatment intensification, which can increase the risk of hypoglycemia.

This study aimed to investigate glycemic control and incidence of hypoglycemia in Japanese patients with T2D who initiate insulin degludec/insulin aspart (IDegAsp) co-formulation in a real-world clinical setting, including elderly patients (aged > 75 years).

What was learned from the study?

Switching from insulin to IDegAsp co-formulation was associated with significantly improved glycemic control and a reduction in hypoglycemia rate during 12 months of follow-up in Japanese patients with T2D.

Results were similar for patients aged ≤ 75 years and aged > 75 years.

DIGITAL FEATURES

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INTRODUCTION

The objectives of diabetes management are to achieve optimum glycemic control and to prevent the progression of diabetic complications [1]. Older age and higher glycated hemoglobin (HbA_{1c}) levels are among the established risk factors for macro- and microvascular complications in type 2 diabetes (T2D), and their association has been confirmed in Japanese people with T2D [2]. As a result of the progressive nature of T2D, insulin treatment can often be a requirement for people of all ages to achieve glycemic control [3, 4].

Compared with younger people, older people (aged ≥ 75 years) with T2D typically have more comorbidities, which can impair their ability to perform diabetes self-care [5]. A further consideration when treating older patients is that many will have had a longer duration of diabetes than younger patients and may therefore require more intensified, complex regimens, which may increase the risk of hypoglycemia [6]. In addition, the symptoms of hypoglycemia can be particularly debilitating in older people because of frailty, which can result in increased risk of bone fracture, head injuries, hospital admissions, and long-term care placements due to falls [7].

Insulin degludec/insulin aspart (IDegAsp) is a co-formulation of insulin degludec (degludec, 70%) and insulin aspart (IAsp, 30%), in a single injection, and is administered once or twice daily with main meals [8]. The basal component, degludec, has a flat pharmacokinetic profile over 24 h at steady state, and provides a stable, long-lasting, glucose-lowering effect. The bolus component, IAsp, has a rapid onset and short duration of action and reduces glucose excursions at mealtimes immediately after injection [9].

The efficacy and safety profiles of IDegAsp have been demonstrated in people with T2D through the BOOST clinical trial program [10–13]. IDegAsp once daily has been evaluated in insulin-naïve Japanese patients with T2D, in which a significant estimated treatment difference in HbA_{1c} of − 0.28% ($p < 0.01$) and comparable rates of overall and nocturnal hypoglycemia were observed compared with insulin glargine 100 U/mL [12]. In a recent post hoc analysis in a subgroup of patients aged ≥ 65 years from two phase 3 BOOST trials, IDegAsp twice daily (BID) was found to provide effective glycemic control comparable with the

effects of biphasic insulin aspart 30 (BIAsp 30) BID [14]. Furthermore, no significant differences were observed between the treatment groups in overall confirmed or nocturnal hypoglycemic events. Similar findings were observed in the Japanese cohort of BOOST INTENSIFY ALL [14].

Randomized controlled trials (RCTs), and the findings from those described above, are, however, limited by their study design and patient inclusion criteria [15]. Therefore, it is important to determine whether the clinical effects of IDegAsp demonstrated in RCTs are generalizable to the real-world clinical setting. The aim of this study was to investigate glycemic control and incidence of hypoglycemia in Japanese patients with T2D who initiate IDegAsp in a real-world clinical setting. In addition, this study aimed to evaluate the glycemic control and incidence of hypoglycemia in elderly patients with T2D (aged > 75 years) using IDegAsp, an age group for which there are limited RCT data. To our knowledge, no real-world data on the effects or safety of IDegAsp in elderly Japanese patients have been published, despite older people (aged ≥ 65 years) accounting for 28.1% of the population in Japan and this proportion having been predicted to increase in the future [16]. Finally, elderly patients form an important population as they are more susceptible to hypoglycemia because of an increased risk of impaired counter-regulatory responses to hypoglycemia, and they have a lower threshold of autonomic symptoms of hypoglycemia, resulting in hypoglycemia unawareness [17].

METHODS

Study Design

This was a retrospective database study using secondary data obtained from a medical and pharmacy claims database provided by the Medical Data Vision Co Ltd (MDV; Tokyo, Japan) in October 2018. The MDV database comprises inpatient and outpatient administrative data from more than 300 hospitals in Japan, as well as selected laboratory test results [18]. Overall, at the time of study (October

2018) the database comprised data from 2,325,288 patients with a diagnosis of T2D [18].

Hypoglycemic events were taken from the administrative database and identified by the billable International Classification of Diseases (ICD), tenth edition, clinical modification (CM) (ICD-10-CM) codes (see Supplementary Material).

Study Population

People considered eligible for inclusion in the analysis were aged ≥ 18 years and had a diagnosis of T2D (ICD code E11 subtypes thereof [Supplementary Material]), with no diagnosis of type 1 diabetes. People were required to have started treatment with IDegAsp (at the index date; defined as the first IDegAsp prescription claim) and have had at least one prescription claim for insulin within the period 180 days prior to the index date. There were no restrictions on the use of concomitant antidiabetic medication.

Ethical Consideration

For this retrospective database study, all data for analysis were extracted from a pre-existing anonymized database and permission was granted to access the data and to use them for publication purposes. For the usage of de-identified secondary data, ethical approval and informed consent do not apply according to the Japanese Ethical Guidelines for Medical and Health Research Involving Human Subjects [19].

Outcomes

Change from baseline (index date) in HbA_{1c} at 12 months after IDegAsp initiation was estimated for patients with at least one follow-up measurement in addition to their baseline HbA_{1c}. Baseline values of HbA_{1c} and body mass index (BMI) were taken in the 180 days prior to the index date; if multiple assessments were available, the value closest to the index date was selected as the baseline value.

The proportion of patients with an HbA_{1c} of $< 8.0\%$, $< 7.5\%$, or $< 7.0\%$ at the 12-month time point was calculated for patients with available baseline and follow-up data. The 12-month data were defined as data recorded 365 ± 90 days after the index date. This range was used to allow for a sufficient number of patients with measurements recorded for inclusion in the analysis. Hypoglycemia outcomes included the proportion of patients experiencing at least one hypoglycemic event, and the difference in rates of hypoglycemic events after switching to IDegAsp, comparing baseline data with the available 12-month data. The hypoglycemia events included in the analysis were those identified by billable ICD-10-CM codes [20] (see Supplementary Material for list of codes and their descriptions). These hypoglycemic events justified admission to an acute care hospital.

The proportion of patients achieving $HbA_{1c} < 8.0\%$, $< 7.5\%$, or $< 7.0\%$ without experiencing hypoglycemia was also assessed. The proportion of patients with at least one hypoglycemic event in the 365 days after the index date (12-month data) was compared with the available data 365 days prior to the index date.

Statistical Analysis

Least-squares (LS) mean differences from baseline in HbA_{1c} at 12 months were calculated using a mixed model repeated measurements (MMRM) analysis, for which time was included as a fixed factor in months after the index date; an unstructured covariance matrix was used in the analyses. Covariates included in the MMRM analysis were baseline HbA_{1c}, time from baseline (grouped by month), previous insulin treatment, age, gender, duration of T2D, and body weight.

The binary outcomes were analyzed by calculating the risk ratio and associated 95% confidence intervals using a normal distribution approximation. In cases of zero cell count in the calculations of estimates of risk ratios, 0.5 was added to all cell frequencies. All other analyses

were as observed, with no imputation of missing data.

For the analysis of hypoglycemia at 12 months, the number of events 365 days post index were compared with the number of events 365 days prior to the index.

Stratified analysis was conducted to assess all outcomes in patients aged ≤ 75 years and patients aged > 75 years.

RESULTS

Demographics and Baseline Characteristics

Of the 2,325,288 patients with T2D in the MDV database, 10,798 were previously treated with insulin and therefore included in the study (see Fig. S1 in the Supplementary Material). In total, 6858 patients (63.5%) were aged ≤ 75 years and 3940 (36.5%) were aged > 75 years.

Demographics and baseline characteristics are shown in Table 1. The mean (standard deviation [SD]) age was 70.4 (11.4) years and the mean (SD) duration of T2D at baseline was 8.9 (8.3) years.

Overall, 73.3% of the population had a history of hypertension. Other recorded comorbidities were a history of dyslipidemia (66.3%), a history of nephropathy (41.1%), a history of retinopathy (39.8%), and a history of neuropathy (25.3%). Comorbidities were balanced between the age groups, except for hypertension (a greater proportion in patients aged > 75 years) and retinopathy (a smaller proportion in patients aged > 75 years; Table 1). Previous insulin treatments were pre-mixed insulin (44.9%), basal–bolus insulin (40.7%), and basal insulin (14.4%). Demographics and baseline characteristics of patients by previous insulin treatments are presented in Table S1 in the Supplementary Material. Mean (SD) duration of T2D was shorter for patients receiving basal–bolus insulin (6.4 [7.7] years) compared with patients receiving pre-mix (10.9 [8.5] years) or basal insulin (9.5 [7.7] years; Table S1). There was a greater proportion of inpatients in the basal–bolus therapy subgroup (80.8%)

Table 1 Patient demographics and baseline clinical characteristics

	Aged ≤ 75 years ($n = 6858$)	Aged > 75 years ($n = 3940$)	Total population ($n = 10{,}798$)
Age, mean ± SD (years)	64.1 ± 9.4	81.4 ± 4.0	70.4 ± 11.4
Female, n (%)	2685 (39.2)	1940 (49.2)	4625 (42.8)
Inpatient setting, n (%)	3507 (51.1)	2701 (68.6)	6208 (57.5)
BMI, mean ± SD (kg/m^2)[a]	24.1 ± 4.8	22.5 ± 4.2	23.4 ± 4.6
Duration of type 2 diabetes, mean ± SD (years)	8.5 ± 7.7	9.5 ± 9.3	8.9 ± 8.3
HbA$_{1c}$, mean ± SD (%)[b]	8.4 ± 1.9	8.4 ± 1.7	8.4 ± 1.9
History of hypertension, n (%)	4783 (69.7)	3135 (79.6)	7918 (73.3)
History of dyslipidemia, n (%)	4635 (67.6)	2525 (64.1)	7160 (66.3)
History of nephropathy, n (%)	2870 (41.8)	1573 (39.9)	4443 (41.1)
History of retinopathy, n (%)	2937 (42.8)	1359 (34.5)	4296 (39.8)
History of neuropathy, n (%)	1757 (25.6)	975 (24.7)	2732 (25.3)
Total number of concomitant medications, mean ± SD	13.3 ± 9.9	16.0 ± 9.6	14.3 ± 9.8
Insulin therapy, n (%)			
Pre-mixed insulin	3142 (45.8)	1705 (43.3)	4847 (44.9)
Basal–bolus insulin	2575 (37.5)	1825 (46.3)	4400 (40.7)
Basal insulin	1141 (16.6)	410 (10.4)	1551 (14.4)

BMI body mass index, *SD* standard deviation

[a] Baseline BMI measurements: total population ($n = 4928$); patients aged ≤ 75 years ($n = 2755$); patients aged > 75 years ($n = 2173$)

[b] Baseline HbA$_{1c}$ measurements: total population ($n = 913$); patients aged ≤ 75 years ($n = 571$); patients aged > 75 years ($n = 342$)

compared with the pre-mix (44.4%) or basal insulin (32.5%) subgroups (Table S1).

Of the total population, 913 patients had a baseline HbA$_{1c}$ measurement; the mean (SD) baseline HbA$_{1c}$ was 8.4 (1.9)%. Demographics and baseline characteristics for patients with a baseline HbA$_{1c}$ measurement were similar to those of the total population (Table S2).

Glycemic Control

Switching to IDegAsp was associated with statistically significantly improved HbA$_{1c}$ values

comparing the estimated change from baseline data at 12 months (-1.23% $[-1.43, -1.02]_{95\%CI}$, $p < 0.001$; Fig. 1). Improvements in glycemic control appeared numerically similar for patients aged ≤ 75 years and for patients aged > 75 years (Fig. 1).

There were numerical differences in the improvement in HbA$_{1c}$ by baseline insulin regimen at 12 months (Table S3); however, statistical analyses were not conducted because of the small numbers of patients in each subgroup.

The proportion of patients with an HbA$_{1c}$ < 8.0% was statistically significantly greater in
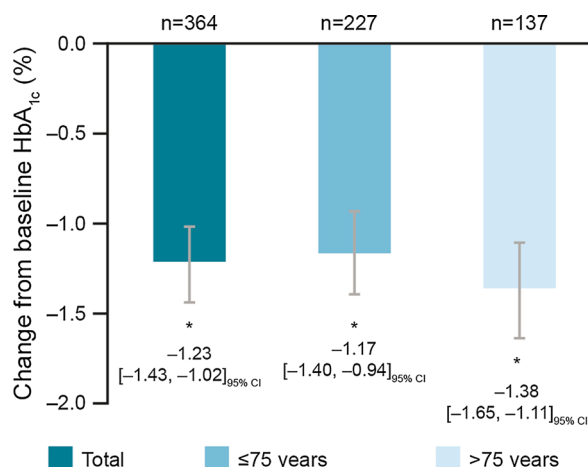
Fig. 1 Estimated mean difference from baseline in HbA_{1c} (%) at 12 months. LS mean differences were calculated using an MMRM analysis with the following covariates: baseline HbA_{1c}, time (grouped by month), previous insulin treatment, age, gender, duration of T2D, and body weight. *$p < 0.001$ versus baseline. CI confidence interval, LS least-squares, MMRM mixed model repeated measurements, T2D type 2 diabetes

IDegAsp-treated patients with 12-month data compared with baseline values (relative rate 1.28 [1.15, 1.43]$_{95\%CI}$, $p < 0.001$; Fig. 2a). The increased proportion of patients with an $HbA_{1c} < 8.0\%$ with IDegAsp treatment compared with baseline values was observed for patients aged ≤ 75 years and for patients aged > 75 years at 12 months (Fig. 2a).

The proportions of patients with an $HbA_{1c} < 7.5\%$ and $< 7.0\%$ are presented in Fig. 2b and Fig. 2c; similar trends were observed as for the proportion of patients with an $HbA_{1c} < 8.0\%$.

Hypoglycemia

At 12 months, the proportion of patients experiencing at least one hypoglycemic event was statistically significantly smaller after IDegAsp treatment compared with baseline (2.1% vs 2.6%; relative risk 0.80 [0.67, 0.95]$_{95\%CI}$, $p = 0.011$). When assessed by baseline insulin regimen, the proportions of patients experiencing at least one hypoglycemic event at 12 months versus baseline were 1.8% versus 2.5% (pre-mixed insulin), 2.8% versus 3.0%
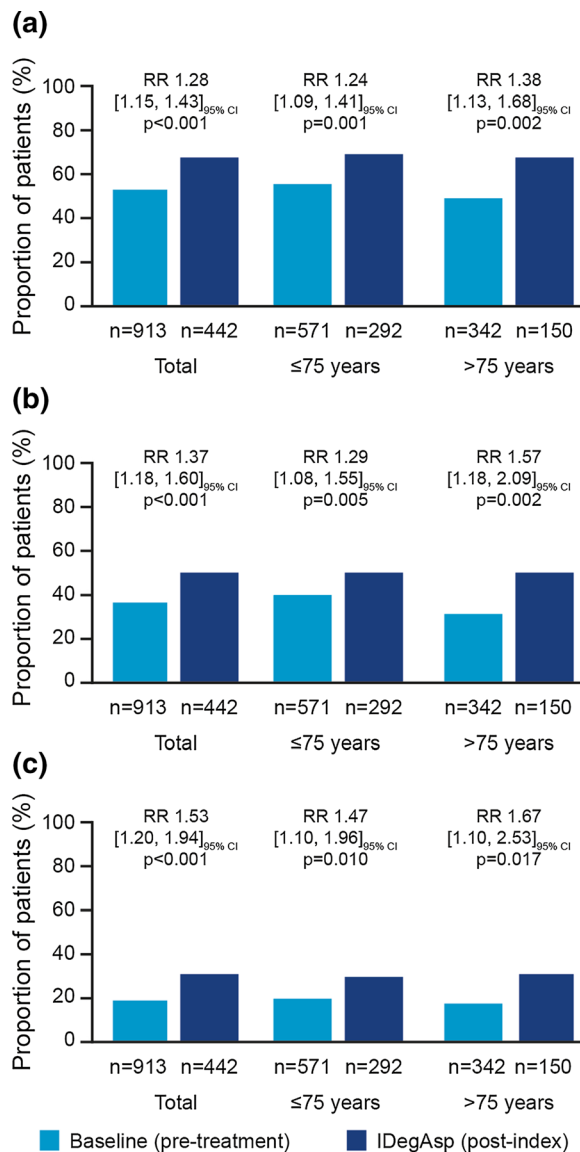
Fig. 2 Proportion of patients and relative rate of achieving an $HbA_{1c} < 8.0\%$ (**a**), $< 7.5\%$ (**b**), and $< 7.0\%$ (**c**) at baseline and 12 months. CI confidence interval, IDegAsp insulin degludec/insulin aspart, *n* number of people with an HbA_{1c} measurement, RR relative rate versus baseline (pre-treatment)

(basal–bolus insulin), and 1.0% versus 2.1% (basal insulin).

Switching to IDegAsp treatment was associated with a significantly lower rate of hypoglycemia compared with baseline in patients with 12-month data (rate ratio 0.83 [0.75, 0.91]$_{95\%CI}$, $p < 0.001$; Fig. 3). A similar trend

	N	Number of events after IDegAsp treatment	Rate after IDegAsp treatment [events per participant-year]	Number of events at baseline	Rate at baseline [events per participant-year]	Rate ratio IDegAsp vs previous insulin [95% CI]	p-value
Total	10,798	659	0.09	1005	0.10	0.83 [0.75, 0.91]	<0.001
≤75 years	6858	290	0.06	436	0.07	0.81 [0.70, 0.94]	0.006
>75 years	3940	369	0.15	569	0.17	0.87 [0.76, 0.99]	0.041

Fig. 3 Rate ratios of hypoglycemia. Hypoglycemia rate ratios at 12 months were based on the total number of hypoglycemic events in the 365 days after the index date (12-month data) compared with the available data 365 days prior to the index date. Rate ratios were calculated using a generalized linear model with negative binomial distribution. CI confidence interval, IDegAsp insulin degludec/insulin aspart

was observed for patients aged ≤ 75 years and for patients aged > 75 years (Fig. 3). Descriptive data for the rate of hypoglycemia, at baseline and 12 months, by baseline insulin regimen are presented in Table S4.

Composite Endpoints

Switching to IDegAsp treatment was associated with a significantly greater proportion of patients achieving $HbA_{1c} < 8.0\%$, $< 7.5\%$, or $< 7.0\%$ without experiencing hypoglycemia when comparing the available 6-month data and 12-month data with baseline values (Fig. 4). This was observed for the dual composite endpoint with all three HbA_{1c} cutoffs: $< 8.0\%$ (66% vs 51% at 12 months), $< 7.5\%$ (49% vs 36% at 12 months), and $< 7.0\%$ (28% vs 19% at 12 months). Similar results were observed for patients aged ≤ 75 years and for patients aged > 75 years (Fig. 4).

Concomitant Medication

In the overall population, the proportion of people receiving at least one prescription of glucagon-like peptide 1 (GLP-1) receptor agonists, dipeptidyl peptidase 4 (DPP4) inhibitors, sulfonylureas, or sodium/glucose co-transporter 2 (SGLT2) inhibitors was similar 365 days before, and 365 days after, the index date (Fig. S2). The most commonly received concomitant medications were DPP4 inhibitors: 56% of patients were receiving at least one prescription of DPP4 inhibitors 365 days prior to the index date and 61% were receiving at least one prescription 365 days after the index date (Fig. S2). The total numbers of concomitant medications received at 12 months are presented in Table S5.

DISCUSSION

This study provides the first real-world evidence of the effects of IDegAsp in elderly Japanese patients, using inpatient and outpatient administrative data from the MDV database. The study demonstrated that, in Japanese patients with T2D previously receiving insulin, switching to IDegAsp treatment was associated with significant reductions in HbA_{1c} and rates of hypoglycemic events based on the differences between 12-month data and baseline data. These results were observed both for patients aged < 75 years and for patients aged ≥ 75 years.

In the current study, the mean baseline HbA_{1c} was 8.4%, reflecting that many patients in this cohort had suboptimal glycemic control on their original insulin treatment, which would have been one of the reasons for being switched to IDegAsp. The reduction in HbA_{1c} in
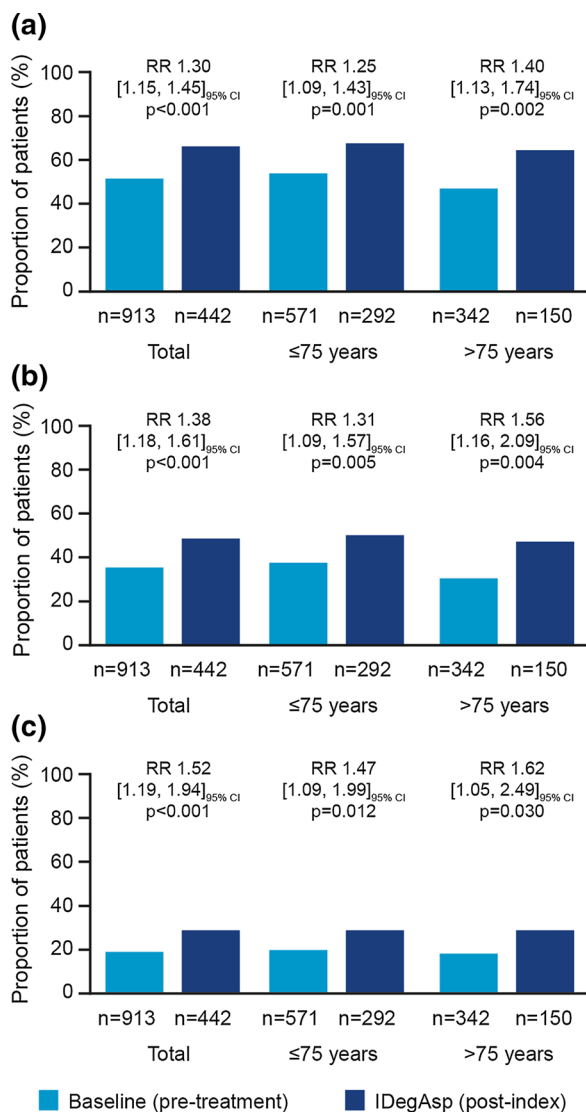
Fig. 4 Proportion of patients and relative rate of achieving the dual composite outcome of an $HbA_{1c} < 8.0\%$ (**a**), $< 7.5\%$ (**b**), and $< 7.0\%$ (**c**), without experiencing hypoglycemia. Hypoglycemia events as defined in the Supplementary Material. CI confidence interval, IDegAsp insulin degludec/insulin aspart, RR relative rate

the current real-world study at 12 months (− 1.23%) was similar to that observed in a subgroup of Japanese patients from a 6-month treat-to-target RCT conducted in patients with T2D inadequately controlled on insulin when treated with IDegAsp (− 1.40%) [21]. The baseline HbA_{1c} (8.3%) in that RCT was similar to that in our study; however, the proportion of patients achieving an $HbA_{1c} < 7.0\%$ was 29.9%

in our study compared with 52.5% in patients treated with IDegAsp in the study by Taneda et al. [21]. These differences are likely due to both the treat-to-target study design and the fact that the population in the RCT was younger, and therefore expected to achieve this target more easily. Overall, the results of this real-world study show that the potential benefits demonstrated in an RCT setting translate into clinical benefits in the real world.

Patients switched from either pre-mixed insulin, basal–bolus insulin, or basal insulin. Considering basal–bolus insulin is efficacious in reducing HbA_{1c} [22], the substantial improvement in glycemic control despite many patients switching from this regimen may not be expected. However, patients included in this real-world study had likely been switched because their regimen was not adequate for their requirements. It is likely that patients receiving basal–bolus insulin in this cohort found their regimen problematic, possibly as a result of adherence [23] and/or hypoglycemia [24].

The magnitude of HbA_{1c} reduction in elderly patients should always be carefully considered. Indeed, the Japan Diabetes Society (JDS)/Japan Geriatrics Society (JGS) Joint Committee report recommends an HbA_{1c} target of < 8.0% (lower limit, 7.0%) for patients aged ≥ 75 years with intact cognitive function and no impairment of activities of daily living who use medication potentially associated with severe hypoglycemia (e.g., insulins, sulfonylureas, or glinides) [25]. This follows the findings of the ACCORD study, which evaluated patients with T2D who had either established cardiovascular disease or additional cardiovascular risk factors [26]. Intensive insulin therapy (HbA_{1c} target of < 6.0%) for 3.5 years increased mortality compared with standard therapy (HbA_{1c} target of 7.0–7.9%) [26]. One possible factor affecting this association was the higher rate of hypoglycemia with intensive insulin therapy compared with standard therapy [26]. However, in the current study, despite the decrease in HbA_{1c}, statistically significant reductions in the rate of hypoglycemia at 12 months were observed compared with baseline in both people aged ≤ 75 years and those aged > 75 years.

Furthermore, a significantly greater proportion of people achieved an $HbA_{1c} < 8.0\%$, $< 7.5\%$, or $< 7.0\%$ without experiencing hypoglycemia at month 12 compared with baseline. This was observed for all HbA_{1c} cutoffs ($< 8.0\%$, $< 7.5\%$, and $< 7.0\%$) and for people aged ≤ 75 years and people aged > 75 years.

There are challenges when assessing hypoglycemia in real-world studies. In elderly patients, symptoms of hypoglycemia are not always apparent and are typically under-reported by patients and healthcare professionals [17]. In this study, only events of hypoglycemia identified by an ICD-10 code were included in the analyses; these were the hypoglycemic events that justified admission to an acute care hospital. The recorded events are therefore likely to be the most severe in nature. The frequency of hypoglycemia observed, as per this definition, in the current real-world study was 2.6% at baseline (pre-index) and 2.1% at 12 months post-index; these values are similar to those observed in real-world studies and RCTs. In the EUropean TREsiba AudiT (EU-TREAT) study, the proportion of patients experiencing at least one severe hypoglycemic event whilst receiving basal insulin was 3.6%. During the 12 months after switching basal insulin to insulin degludec, the proportion of patients experiencing at least one severe hypoglycemic event was 0.2% [27], although it should be noted that the data collection method differed from that of the current study. The Step-by-Step study was a randomized, treat-to-target trial in adults with T2D, previously treated with basal insulin ± oral antidiabetic drugs [28]. Over the 38-week treatment period (which included the option of intensification from once-daily IDegAsp to twice-daily IDegAsp), the proportion of patients experiencing at least one severe hypoglycemic event was 1.9%. As only the most severe events of hypoglycemia were recorded in this study, the results may not accurately represent the impact of the decrease in HbA_{1c} on hypoglycemia in this elderly population. Nevertheless, the study findings contribute to the currently available IDegAsp evidence in the literature.

This is the largest real-world study to date in any population assessing the impact of IDegAsp on glycemic control ($n = 10{,}798$); previous real-world reports have included much smaller numbers of patients ($n = 5$ [3], $n = 22$ [29], $n = 48$ [30]). The inclusion criteria were intentionally broad to reflect routine clinical practice and the Japanese population with T2D as closely as possible. The results are therefore intended to be more informative and relevant to clinicians than RCT data, which tend to reflect narrow inclusion criteria and have limited external validity. A further strength of this study was that the sample allowed for a sub-analysis of patients aged > 75 years. Considering the increased risk of hypoglycemia in elderly patients and the ageing population of Japan [16], the opportunity to evaluate the safety and effectiveness of IDegAsp in this population was particularly relevant for Japanese clinical practice.

This study had limitations commonly associated with real-world, retrospective studies, including selection bias and the inability to establish temporal relationships. A further limitation of the study was the relatively low proportion of people with HbA_{1c} recorded at baseline ($n = 913$). The outcomes of difference in HbA_{1c}, proportion of patients with $HbA_{1c} < 8.0\%$, $< 7.5\%$, or $< 7.0\%$, and proportion of patients achieving the dual composite outcomes were assessed using this subset of patients. This potentially limits the generalizability of the results and the number of possible confounders to include in the statistical model. However, demographics and baseline characteristics were assessed for those patients with a baseline HbA_{1c} measurement and were relatively similar to those of the total population.

The proportion of patients with at least one prescription of concomitant medication was similar after initiation of IDegAsp compared with before switching to IDegAsp. However, the data do not describe how much concomitant medication was used. Similarly, the dose of IDegAsp and previous insulin treatments was not recorded. Lastly, the duration of T2D was calculated on the basis of the first diagnosis of T2D in the database.

CONCLUSIONS

In this real-world study of Japanese patients with T2D, switching from a previous insulin regimen to IDegAsp was associated with significantly improved glycemic control and a reduction in the rate of hypoglycemia when comparing differences between 12-month follow-up data and baseline data. These findings indicate that IDegAsp may be a suitable treatment option for Japanese patients with T2D, including elderly patients.

ACKNOWLEDGEMENTS

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