

Dipeptidyl peptidase-4 inhibitors as preferable oral hypoglycemic agents in terms of treatment satisfaction: Results from a multicenter, 12-week, open label, randomized controlled study in Japan (PREFERENCE 4 study)

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ABSTRACT

Aims/Introduction: To compare the treatment satisfaction of four classes of oral hypoglycemic agents (OHAs): dipeptidyl peptidase-4 (DPP-4) inhibitors, α -glucosidase inhibitors (α GI), biguanides (BG) and sulfonylureas (SU), which are common initial treatments for type 2 diabetes mellitus patients in Japan, and to identify the best oral hypoglycemic agent in terms of treatment satisfaction.

Materials and Methods: In this 12-week, randomized, controlled, open-label study, Japanese outpatients with type 2 diabetes mellitus who were naïve to pharmacological treatment were randomly assigned a DPP-4 inhibitor, a BG, an α GI or a SU. The primary end-point was the Oral Hypoglycemic Agent Questionnaire (OHA-Q) total and subscale scores (treatment convenience, somatic symptoms and satisfaction) at week 4. Adherence, glycated hemoglobin (HbA1c) level and safety were also evaluated.

Results: The DPP-4 inhibitor group scored highest in the OHA-Q total and all subscale scores at week 4. The total score was significantly higher in the DPP-4 inhibitor group than in the BG or α GI groups ($P = 0.0084$ and 0.0147 , respectively). The mean total score at week 12 was also highest in the DPP-4 inhibitor group, with a significant difference compared with the α GI group ($P = 0.0293$). The mean HbA1c decreased from baseline to week 12 in all groups. The DPP-4 inhibitor group had the highest adherence at weeks 4 and 12. A total of 11 patients reported adverse events, including one hypoglycemic event in the SU group.

Conclusions: The DPP-4 inhibitor was the most preferable option in terms of treatment satisfaction.

INTRODUCTION

For the management of type 2 diabetes mellitus, various oral hypoglycemic agents (OHAs) are available, such as dipeptidyl peptidase-4 (DPP-4) inhibitors, α -glucosidase inhibitors (α GI), biguanides (BG), sulfonylureas (SU), thiazolidine insulin sensitizers and glinides, which differ in dosage, administration, side-effects and cost^{1,2}. Of this widening array of options, the

American Diabetes Association and the European Association for the Study of Diabetes guidelines designate metformin as the first-line treatment for type 2 diabetes¹. Conversely, the Japan Diabetes Society does not specify an OHA as the first-line drug, but recommends that the treatment be selected according to the pathophysiological condition of each patient³.

Given the heterogeneity of type 2 diabetes and of patients themselves, the most appropriate OHA should be selected on a case-by-case basis taking into consideration the advantages and

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disadvantages of each option, the practical aspects of the treatment and disease conditions, and the patient's preference^{1,4}. Treatment satisfaction is an important factor that should be considered during treatment selection. Type 2 diabetes management requires long-term and complex self-management, which has a great impact on a patient's daily life; therefore, successful treatment heavily depends on patient adherence. Patients who are dissatisfied with their treatment are less likely to adhere to that treatment^{5,6}, and non-adherence to treatments for type 2 diabetes can result in poor glycemic control^{7–10}, which increases the risk of complications and can lead to disease deterioration. Treatment selection should not solely stand on an objective efficacy assessment or disease conditions, but rather it should be a comprehensive consideration that encompasses the patient's view. Therefore, treatment satisfaction should be involved in the decision for selection of the optimal OHA.

To determine the treatment satisfaction with currently available OHAs, we developed and validated the patient-administered Oral Hypoglycemic Agent Questionnaire (OHA-Q). The OHA-Q assesses treatment satisfaction with adequate reproducibility and validity, specifically for OHAs for type 2 diabetes patients^{11,12}. Using the OHA-Q, this randomized, controlled, open-label study aimed to compare the treatment satisfaction among four OHAs (PREFERENCE 4 study) that are widely prescribed as an initial treatment for type 2 diabetes in Japan (DPP-4 inhibitors, BGs, α GI and SUs). We also aimed to identify the best OHA in terms of treatment satisfaction. Considering the lack of studies that directly compare the treatment satisfaction of major OHAs, we expect that the present study will contribute to improving patient-centered drug selection for type 2 diabetes patients.

METHODS

This was a 12-week, prospective, randomized, controlled, open-label, multicenter study, carried out from July 2012 to March 2015 at 19 sites in Japan. The protocol was approved by the ethics committee of each participating site.

Patients

Inclusion criteria were as follows: Japanese type 2 diabetes outpatients (aged 20–79 years) who were naïve to pharmacological treatments (including OHAs), and had suboptimal glycemic control (6.9–9.4%) after ≥ 4 -week diet and exercise therapy. The exclusion criteria included a history of severe ketosis, diabetic coma, liver dysfunction (alanine aminotransferase > 3 times the upper limit of normal), pregnancy/possibility of pregnancy, history/presence of cancer, or the judgment by the attending physicians that participation for this study was inappropriate based on medical evidence. Written informed consent was obtained from all patients before study participation.

Randomization and treatment

Patients were randomly assigned at a 1:1:1:1 ratio to receive either a DPP-4 inhibitor, a BG, an α GI or an SU by a central

registration system using minimization methods to ensure a well-balanced allocation in terms of age, sex, body mass index, disease duration and glycated hemoglobin (HbA1c) at baseline.

The four OHAs were selected according to the typical prescriptions in Japan. The assigned single OHA was administered, and the doses were adjusted at the physician's discretion. Changes in diet and exercise therapy, and concomitant drugs were not permitted.

Assessment

Treatment satisfaction with the assigned OHA was assessed using the OHA-Q at weeks 4 and 12. In addition, adherence to the assigned OHA, HbA1c levels and dosages were assessed at the same assessment points. HbA1c was also assessed at baseline. Data on adverse events (AEs) were also recorded.

The primary end-point was OHA-Q total and subscale scores at week 4. The OHA-Q consists of 20 items categorized into three subscales: treatment convenience (9 items), somatic symptoms (8 items) and satisfaction (3 items). Each item score ranges from 0 (worst) to 3 points (best)¹¹. Patients received the questionnaire at weeks 4 and 12, and sent the completed questionnaire back by post.

The level of adherence to the assigned OHA was assessed through interviews by physicians. Patients stated their level of adherence by describing how frequently they missed a dose from the following four options: (i) never; (ii) once a month; (iii) once a week; or (iv) more than once a week.

Statistical analysis

OHA-Q scores and HbA1c levels were analyzed for patients who received the assigned OHA and completed the OHA-Q at week 4. Baseline characteristics, adherence and safety data were summarized for patients who received the assigned OHA at least once.

OHA-Q total and subscale scores were analyzed using a pairwise comparison of the least square means of the OHA-Q scores with the corresponding 95% confidence intervals (CIs). The scores were calculated under the assumption of an equal interval between the response choices. Descriptive statistics were used to summarize the baseline demographics, adherence, HbA1c levels, dosages and safety data by OHA group. HbA1c values at weeks 4 and 12 were evaluated by pairwise comparison of the least square means for the OHA groups.

In the present study, missing data were not imputed. The analysis was not adjusted for multiplicity because of the exploratory nature of this study. Statistical analyses were carried out using SAS 9.3 (SAS Institute Inc., Cary, North Carolina, USA). All statistical tests were two-tailed, and the significance level was set at 0.05. We did not carry out a sample size calculation for this study.

RESULTS

A total of 64 patients were randomized to four groups (16 patients per group; Figure 1). After randomization, four

patients withdrew from the study (one in the DPP-4 inhibitor group withdrew consent; and two patients in the BG group and one patient in the SU group were withdrawn for not taking the assigned OHA). The remaining 60 patients received the assigned OHAs. Eight patients were excluded for not completing the OHA-Q at week 4 (3, 1, 3, and 1 patient in the DPP-4 inhibitor, BG, α GI and SU groups, respectively), leaving 52 patients for inclusion in the OHA-Q and HbA1c analyses.

Demographic and baseline characteristics are summarized in Table 1. The four OHA groups did not differ notably. Overall, women accounted for 41.7%. The mean (SD) age, body mass index and duration of type 2 diabetes were 63.1 years (11.1 years), 25.8 kg/m² (4.2 kg/m²) and 3.6 years (4.2 years), respectively.

OHA-Q total and subscale scores at week 4

The mean OHA-Q total score was highest in the DPP-4 inhibitor group and lowest in the BG group (48.2, 95% CI: 44.1–52.3 and 40.4, 95% CI: 36.4–44.3, respectively). OHA-Q total score was significantly different not only between the DPP-4 inhibitor and BG groups ($P = 0.0084$), but also between the DPP-4 inhibitor and α GI groups ($P = 0.0147$; Figure 2. The DPP-4 inhibitor group also scored highest in the treatment convenience, somatic symptom and satisfaction subscales (23.6, 95% CI: 21.1–26.1; 18.4, 95% CI: 16.0–20.8; and 6.2, 95% CI: 5.4–6.9, respectively). The lowest scores among subscales were as

follows: α GI (treatment convenience 19.6, 95% CI: 17.2–22.0), BG (somatic symptom 14.1, 95% CI: 11.8–16.4) and SU (satisfaction 5.0, 95% CI: 4.3–5.7). The scores in the DPP-4 inhibitor group were significantly different from the groups that scored the lowest in the respective subscales ($P = 0.0246, 0.0109$ and 0.0232 , respectively).

OHA-Q item scores at week 4

Table 2 shows the mean OHA-Q item scores at week 4. Compared with the scores of the DPP-4 inhibitor group, the other groups scored lower by ≥ 0.5 points in the following items. For the treatment convenience subscale: BG ([2] difficulty swallowing, [7] compliance with treatment schedule and [8] number of doses) and α GI ([1] missed dose, [3] carrying and preparing for taking the agent, [7] compliance with treatment schedule, and [8] number of doses). For the somatic symptom subscale: BG ([11] rumbling stomach, [12] diarrhea, [13] constipation, [14] increased bodyweight and [15] tendency to become hungry easily), α GI ([11] rumbling stomach and [12] diarrhea) and SU ([14] increased bodyweight). For the satisfaction subscale: BG, SU ([19] glycemic control).

OHA-Q total and subscale scores at week 12

Figure 2 shows the OHA-Q scores at week 12 by group. The mean total score was highest in the DPP-4 inhibitor group and lowest in the α GI group (46.9, 95% CI: 42.4–51.4 and 40.1,

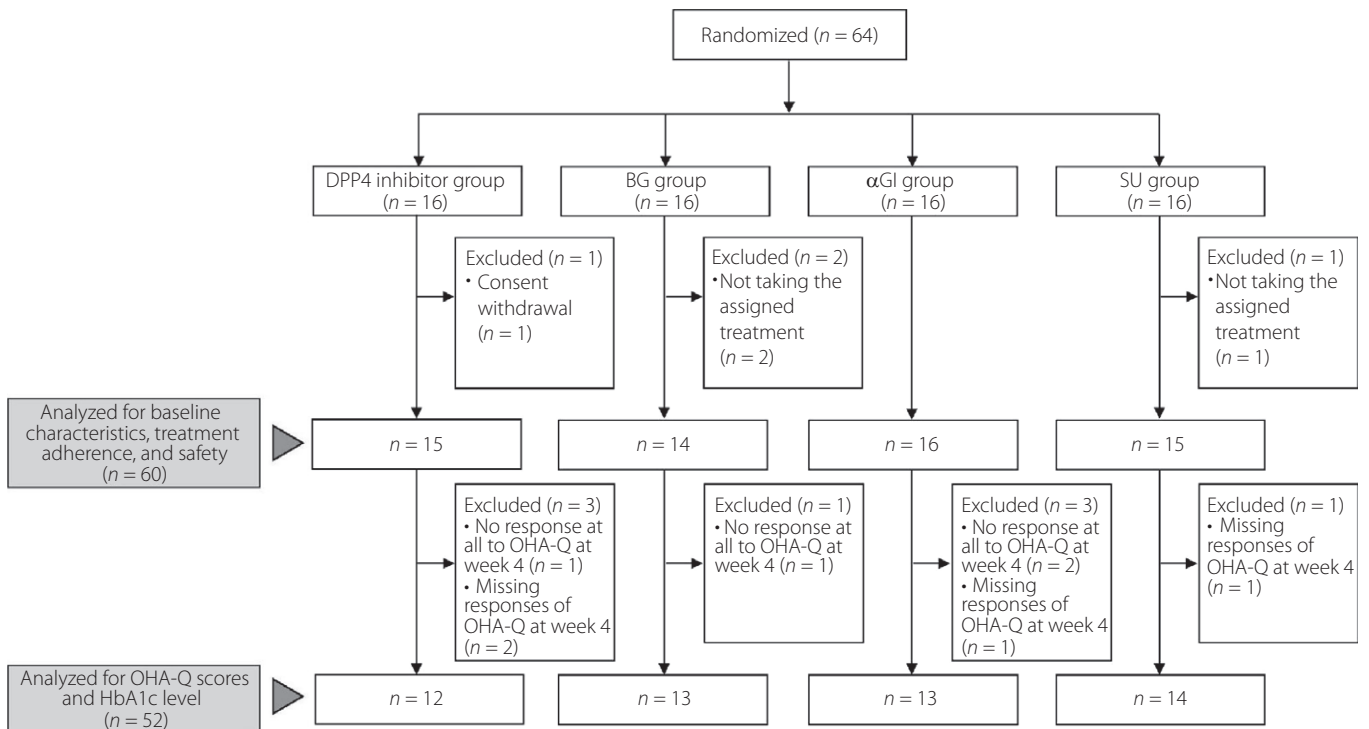


Figure 1 | Patient disposition. α GI, α -glucosidase inhibitor; BG, biguanide; DPP-4, dipeptidyl peptidase-4; HbA1c, glycated hemoglobin; OHA-Q, Oral Hypoglycemic Agent Questionnaire; SU, sulfonylurea.

Table 1 | Baseline demographic and clinical characteristics of the patients

	DPP-4 inhibitor (<i>n</i> = 15)	BG (<i>n</i> = 14)	α GI (<i>n</i> = 16)	SU (<i>n</i> = 15)	Total (<i>n</i> = 60)
Sex					
Men, <i>n</i> (%)	9 (60.0)	9 (64.3)	9 (56.3)	8 (53.3)	35 (58.3)
Women, <i>n</i> (%)	6 (40.0)	5 (35.7)	7 (43.8)	7 (46.7)	25 (41.7)
Mean age, years (SD)	63.1 (12.1)	63.6 (13.4)	64.4 (9)	61.2 (10.7)	63.1 (11.1)
Mean weight, kg (SD)	65.4 (15.5)	67.9 (11.6)	64.0 (12.1)	70.6 (10.6)	66.9 (12.5)
Mean body mass index, kg/m ² (SD)	25.1 (4.8)	26.0 (3.9)	25.4 (3.7)	26.7 (4.7)	25.8 (4.2)
Mea duration of disease, years (SD)	3.5 (4.8)	3.7 (4.1)	3.4 (4.3)	3.7 (4.1)	3.6 (4.2)
Smoking, <i>n</i> (%)	3 (20.0)	5 (35.7)	2 (12.5)	4 (26.7)	14 (23.3)
Drinking habit, <i>n</i> (%)	8 (53.3)	7 (50.0)	8 (50.0)	8 (53.3)	31 (51.7)
Comorbidities, <i>n</i> (%)	7 (46.7)	7 (50.0)	8 (50.0)	10 (66.7)	32 (53.3)
Hypertension	4 (26.7)	3 (21.4)	5 (31.3)	7 (46.7)	19 (31.7)
Hyperlipidemia	5 (33.3)	6 (42.9)	3 (18.8)	6 (40.0)	20 (33.3)
Fatty liver	1 (6.7)	2 (14.3)	0 (0.0)	0 (0.0)	3 (5.0)
Retinopathy	1 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
Diabetic nephropathy	1 (6.7)	0 (0.0)	0 (0.0)	2 (13.3)	3 (5.0)

Data are presented as *n* (%) or mean (SD). α GI, α -glucosidase inhibitors; BG, biguanides; DPP-4, dipeptidyl peptidase-4; SU, sulfonylureas.

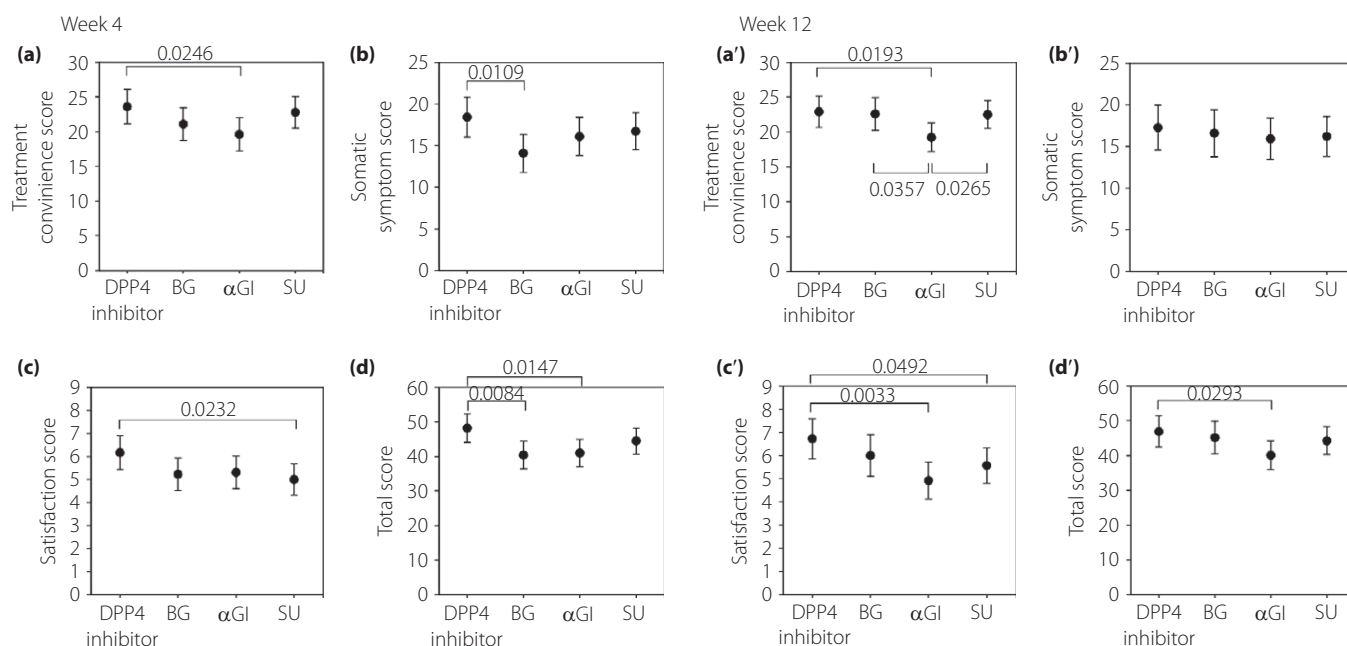


Figure 2 | Mean OHA-Q total and subscale scores at weeks 4 and 12. Pairwise comparison of least square means of Oral Hypoglycemic Agent Questionnaire scores with the corresponding 95% confidence intervals. The treatment convenience, somatic symptom, and satisfaction subscales consist of nine, eight and three items, respectively. Each item score ranges from 0 (worst) to 3 points (best); the higher score indicates better treatment satisfaction. α GI, α -glucosidase inhibitor; BG, biguanide; DPP-4, dipeptidyl peptidase-4; OHA-Q, Oral Hypoglycemic Agent Questionnaire; SU, sulfonylurea.

95% CI: 35.9–44.2, respectively), with a significant difference between the groups ($P = 0.0293$). Scores for treatment convenience, somatic symptom and satisfaction were all highest in the DPP-4 inhibitor group (22.9, 95% CI: 20.7–25.2; 17.3, 95% CI: 14.6–20.0; and 6.7, 95% CI: 5.9–7.6, respectively) and lowest in the α GI group (19.2, 95% CI: 17.2–21.3; 15.9 95% CI:

13.4–18.4; and 4.9 95% CI: 4.1–5.7, respectively). A statistically significant difference was detected between the following groups: α GI and DPP-4 inhibitor, α GI and BG, and α GI and SU for treatment convenience subscale scores ($P = 0.0193$, 0.0357 and 0.0265, respectively). Significant differences were similarly found between DPP-4 inhibitor and α GI, and DPP-4

Table 2 | Item scores for the OHA-Q at week 4

Subscales and items	DPP-4 inhibitor	BG	α GI	SU
Treatment convenience subscale				
1. Missed dose	2.6 (0.8)	2.3 (0.9)	1.8 (0.9)	2.7 (0.5)
2. Difficulty swallowing	3.0 (0.0)	2.4 (0.8)	2.8 (0.4)	2.8 (0.4)
3. Carrying and preparing for taking the agent	2.8 (0.4)	2.5 (0.7)	2.0 (1.0)	2.5 (0.9)
4. People around the patient	2.8 (0.6)	2.8 (0.6)	2.6 (0.5)	2.6 (0.8)
5. Following the meal schedule	2.2 (0.8)	2.3 (0.9)	2.0 (0.7)	2.2 (1.0)
6. Interval between taking the agent and a meal	2.2 (0.8)	2.0 (0.9)	2.1 (0.8)	2.1 (0.9)
7. Compliance with treatment schedule	2.7 (0.7)	2.2 (0.8)	2.0 (0.8)	2.4 (1.0)
8. Number of doses	2.8 (0.4)	2.3 (0.9)	1.8 (0.9)	2.9 (0.4)
9. Taking the agent at a place other than home	2.6 (0.5)	2.4 (0.7)	2.4 (0.7)	2.6 (0.9)
Somatic symptom subscale				
11. Rumbling stomach	2.3 (0.8)	1.7 (1.1)	1.7 (0.6)	2.0 (0.9)
12. Diarrhea	2.6 (0.5)	1.8 (1.0)	1.9 (1.0)	2.5 (0.7)
13. Constipation	2.5 (1.0)	1.5 (1.2)	2.2 (0.9)	2.2 (0.9)
14. Increased bodyweight	1.9 (1.1)	1.4 (1.1)	1.7 (0.9)	1.3 (0.7)
15. Tendency to become hungry easily	2.2 (0.7)	1.7 (0.9)	2.3 (0.5)	1.8 (0.6)
16. Nausea	2.3 (0.8)	1.9 (1.1)	2.1 (1.0)	2.5 (0.7)
17. Bodily swelling	2.5 (0.7)	2.2 (1.1)	2.2 (0.8)	2.4 (0.8)
18. Hypoglycemia	2.3 (0.9)	1.9 (1.1)	2.1 (0.6)	2.1 (0.9)
Satisfaction subscale				
10. Desire to continue the treatment	1.8 (1.0)	1.5 (0.7)	1.5 (0.5)	1.5 (0.7)
19. Glycemic control	2.1 (0.5)	1.6 (0.8)	1.8 (0.4)	1.6 (0.5)
20. Satisfaction with the current agent	2.3 (0.6)	2.1 (0.5)	1.9 (0.5)	1.9 (0.4)

Data are presented as mean (SD). Each item score ranges from 0 (worst) to 3 points (best); a higher score indicates better treatment satisfaction. α GI, α -glucosidase inhibitors; BG, biguanides; DPP-4, dipeptidyl peptidase-4; OHA-Q, Oral Hypoglycemic Agent Questionnaire; SU, sulfonylureas.

inhibitor and SU for satisfaction subscale scores ($P = 0.0033$ and 0.0492 , respectively).

HbA1c values

The mean (\pm SD) HbA1c decreased from baseline to week 12 in all groups (at baseline, week 4 and week 12: $7.6 \pm 0.5\%$, $7.2 \pm 0.3\%$ and $6.9 \pm 0.7\%$ in the DPP-4 inhibitor group; $7.7 \pm 0.9\%$, $7.3 \pm 0.8\%$ and $7.1 \pm 0.8\%$ in the BG group; $7.6 \pm 0.5\%$, $7.5 \pm 0.6\%$, and $7.1 \pm 0.6\%$ in the α GI group; and $7.5 \pm 0.5\%$, $7.0 \pm 0.6\%$ and $6.7 \pm 0.5\%$ in the SU group, respectively). The mean HbA1c was lowest in the SU group at both weeks 4 and 12. There was a statistical difference between SU and α GI groups at week 4 ($P = 0.0419$), and no other statistical differences were found between groups at weeks 4 or 12. The mean change in HbA1c values from baseline to week 12 was -0.74% (95% CI: -1.38 to -0.11), -0.68% (95% CI: -0.91 to -0.44), -0.49% (95% CI: -0.79 to -0.20) and -0.74% (95% CI: -1.05 to -0.42) in the DPP-4 inhibitor, BG, α GI, and SU groups, respectively.

Treatment adherence

A larger proportion of patients in the DPP-4 inhibitor group took all the assigned medication, followed by the SU, α GI and BG groups at week 4 (92.9% [13/14], 86.7% [13/15], 64.3% [9/14] and 61.5% [8/13], respectively). Similarly, the DPP-4 group

had the highest proportion of patients who took all the assigned medication at week 12, followed by SU, BG and α GI groups (100% [14/14], 93.3% [14/15], 66.7% [8/12] and 64.3% [9/14], respectively). One patient in the DPP-4 inhibitor group and two or more patients in the other groups missed their medication more than once a month.

Daily dosage

Of the 60 patients included in the analysis, 50 (83.3%) patients started the OHA treatment at or below the lowest standard dosage (Table 3)³. The dosage at week 12 was the same as the initial dosage for 49 patients (81.7%).

Reported AEs

A total of 11 patients reported AEs as follows: abdominal distension and dry mouth (each $n = 1$) in the DPP-4 inhibitor group; diarrhea, constipation, nausea and rash (each $n = 1$) in the BG group; diarrhea and abdominal distension ($n = 3$ and 1 , respectively) in the α GI group; and cold sweat ($n = 1$) in the SU group. A total of 10 of the AEs were considered to be related to the assigned OHAs. Four patients discontinued the treatment because of OHA-related AEs (abdominal distension and diarrhea each in one patient in the α GI group, dry mouth in one patient in the DPP-4 inhibitor group, and rash in one patient in the BG group). No serious AEs were reported.

Table 3 | Dosages at baseline and week 12, and standard dosage

Generic name	<i>n</i>	Dosage at baseline (mg/day)	Dosage at week 12 (mg/day)	Standard dosage (mg/day) ³
DPP-4 inhibitor (<i>n</i> = 15)				
Sitagliptin	1	25	50	50–100
	8	50	50	
Teneligliptin	1	10	10	20–40
	1	20	20	
Linagliptin	1	5	5	5
Alogliptin	3	25	25	25
BG (<i>n</i> = 14)				
Metformin (Glycoran)	2	500	500	500–750
Metformin (Metgluco)	1	250	250	500–1500
	6	500	500	
	2	500	750	
	1	750	750	
	2	1000	1000	
α GI (<i>n</i> = 16)				
Miglitol	2	50	50	150–225
	1	100	150	
	1	150	100	
	4	150	150	
Voglibose	4	0.6	0.6	0.6–0.9
	4	0.9	0.9	
SU (<i>n</i> = 15)				
Glimepiride	1	0.25	0.5	0.5–4
	1	0.5	0.25	
	3	0.5	0.5	
	3	0.5	1	
	1	1	0.5	
	2	1	1	
	1	10	10	
Gliclazide	1	10	10	20–120
	3	20	20	

α GI, α -glucosidase inhibitors; BG, biguanides; DPP-4, dipeptidyl peptidase-4; SU, sulfonylureas.

DISCUSSION

In the present study, we compared the treatment satisfaction using the OHA-Q between four classes of OHAs: DPP-4 inhibitors, BGs, α GIs and SUs, which are commonly prescribed in Japan. The mean total and the three subscale scores at week 4 suggested that patients were most satisfied with the DPP-4 inhibitor treatment. Furthermore, greater satisfaction sustained with high adherence, HbA1c improvement, and few AEs over 12 weeks reflect the actual popularity of DPP-4 inhibitors in Japan for their ability to ameliorate β -cell dysfunction with limited risk of hypoglycemia^{13,14}. Without previous studies that comprehensively compare several OHAs that are frequently prescribed, and that incorporate patient's perspectives, the present study could help to optimize the drug selection for patients with type 2 diabetes.

The findings support the well-documented association among treatment satisfaction, treatment adherence^{5,6}, and the association between adherence and glycemic control^{7–10}. The ranking of the OHA-Q total scores corresponded to the actual adherence level for each treatment. Furthermore, adherence level

further corresponded to HbA1c level improvement. The DPP-4 inhibitor might provide higher treatment satisfaction, because it is less frequently administered and causes less concern over AEs, which could motivate patients to adhere to the treatment, eventually leading to improved glycemic control. The previous report of the association between treatment adherence, glycemic control and quality of life¹⁵ might further suggest the possibility that DPP-4 inhibitors could even improve the whole quality of life.

Alternatively, treatment that raises some concerns in patients might reduce satisfaction and weaken motivation for them to adhere, eventually falling short of successful glycemic control, as reflected in the BG and α GI groups. The BG and α GI groups scored significantly lower than the DPP-4 inhibitor group in OHA-Q total, and somatic symptoms and treatment convenience subscales, respectively. The item score showed that the BG group was particularly concerned regarding gastrointestinal AEs, and the α GI group regarding administration frequency, which are typical issues in BG^{2,16,17} and α GI, respectively. Such concerns might contribute to

treatment dissatisfaction and eventually to smaller HbA1c improvement.

However, patients in the SU group were less satisfied with their treatment despite the HbA1c being maintained as low as in the DPP-4 inhibitor group. OHA-Q results suggest that patients in the SU group might have been particularly concerned about weight gain, which is a well-known adverse effect of SUs^{1,2,16}. This concern for SUs' influence on bodyweight might have surpassed the appreciation for glycemic improvement to suppress the overall satisfaction with SU.

Interestingly, from week 4 to 12, treatment satisfaction largely improved only in the BG group in terms of OHA-Q total and somatic symptom subscale scores. Some of the adverse gastrointestinal symptoms might subside with continued treatment¹⁸. Alternatively, lower actual incidence of gastrointestinal AEs than expected during the early stage of the treatment could have resolved the pre-existing anxiety.

Consistent with the present results, previous long-term studies reported maintenance or further improvement in treatment satisfaction with DPP-4 inhibitors over 26 and 52 weeks^{19–21}. Furthermore, DPP-4 inhibitors improved some aspects of quality of life including urinary frequency and paresthesia of the extremities²². These observations might suggest the DPP-4 inhibitor as an option from patients' perspectives. Whereas, the more expensive cost of DPP-4 inhibitors^{1,3} is a concern for some patients. Given that lifelong self-management in patients' daily lives is required for successful control of type 2 diabetes, patient-centered care advocated as an approach for 'providing care that is respectful of and responsive to individual patient preferences, needs and values, and ensuring that patient values guide all clinical decisions'^{23,24} is imperative. Reflecting the patients' perspectives in terms of self-reported treatment satisfaction with each OHA, the present study adds important information for deciding the appropriate treatment based on patient-centered care. Treatment should be selected by weighing a broad spectrum of important factors ranging from efficacy, safety, and patient pathophysiology to cost effectiveness and quality of life, in addition to the treatment satisfaction shown in the present study.

Some methodological limitations might require consideration on interpretation of the results. First, only a small number of patients were recruited in the present study (60 patients from 18 participating sites), which limits the generalizability of the findings. Larger-scale studies are warranted to confirm the findings. Second, the study period of 12 weeks might be relatively short. However, based on the previous studies^{25–30}, we considered 12 weeks sufficient to detect the effect of newly-initiated OHA treatment on OHA-Q score. Third, the present study did not include all the OHAs currently available, and did not designate the dosages, as the aim lay in capturing the daily clinical practice. There might be the possibility that inclusion of other OHAs and at fixed doses could result in a different conclusion. Fourth, full OHA-Q data could not be obtained for more than 10% of the recruited patients. Finally, we could not infer the

relationships between OHA doses and OHA-Q scores, as treatment was initiated at the lowest recommended dosage or lower³, and the initial dosages were continued until the end of the study for most of the patients, possibly driven by safety concerns of physicians. Nevertheless, the results show that even the low dosages can substantially improve HbA1c with few AEs.

In conclusion, among the four classes of OHAs in the present study, DPP-4 inhibitors were the most preferable option in terms of treatment satisfaction. Patients might be satisfied with the DPP-4 inhibitor treatment and thus be motivated to adhere to the treatment, which would likely result in better glycemic control. Patient-centered treatment selection, including treatment satisfaction, as well as other important factors, could be a key driver for optimal selection of type 2 diabetes treatments.

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DISCLOSURE

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