

Association Between Patient Preference for Inhaler Medications and Asthma Outcomes

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Purpose: Asthma guidelines recommend considering the patient preference to optimize medication choices. Patient preference for inhaler medication may affect asthma outcomes, but evidence regarding this is lacking. This study investigated the associations between patient preference for inhaler medications and asthma outcomes.

Patients and Methods: A multicenter questionnaire survey was conducted among 351 adult patients with asthma treated with regular inhaled corticosteroids. Agreement between patients' preferences and current medication was evaluated using two questions: matched preference was defined as patients answering that the current inhaler medication was the most preferred treatment and they were satisfied with it. Mismatched preference was defined as when patients reported that the current inhaler medication was not the most preferred treatment and/or they were not satisfied with it. We investigated the factors associated with patient preference for asthma inhaler medications.

Results: In total, 269 (76.6%) patients were classified into the matched preference group and 82 (23.4%) patients into the mismatched preference group. Multivariate analyses showed that matched preference was independently associated with higher asthma control test scores ($P<0.001$), fewer exacerbations ($P=0.009$), less regular oral corticosteroid use ($P=0.009$), and better inhaler adherence ($P=0.006$) than the mismatched preference group. In subgroup analysis, younger age was associated with matched preference in patients using dry powder inhalers but not in those using pressurized metered dose inhalers.

Conclusion: The use of preference-matched inhaler medication was associated with better asthma outcomes. Evaluation of patients' preference for inhaler medication might provide useful information for individualized treatment with asthma inhaler medications.

Keywords: patient preference, asthma control, inhaled corticosteroids, inhaler adherence, shared decision-making

Plain Language Summary

The use of asthma inhaler medication that matches patient preference may be associated with better clinical outcomes; however, to date, evidence is lacking.

This study shows that preference-matched inhaled medication was associated with better asthma control, fewer exacerbations, less oral corticosteroid use, and better adherence in a real-world clinical setting.

Introduction

Inhaled corticosteroids (ICS) are the mainstay treatment for asthma and can lead to improved symptom control and reduced exacerbations.¹ Various inhaler devices exist for asthma treatment, and device selection, as well as the choice of active drug, are important to achieve significant positive clinical response.²⁻⁴ Previous studies have shown that inhalation

technique and treatment adherence can be influenced by inhaler device type and patient background characteristics.^{5–7} Moreover, to optimize the patient-level medication choices, asthma guidelines recommend consideration of patient preference.^{1,8,9} However, evidence on the influence of patient preference for inhaler medication on asthma outcomes is lacking. In this study, we evaluated patient preference for inhaler medication using self-reported questionnaires and investigated the associations of the answers with asthma control, exacerbation rate, regular oral corticosteroid (OCS) use, and adherence to treatment.

Materials and Methods

Patients

A multicenter cross-sectional study was conducted among adult patients with persistent asthma to investigate their preferences for inhaled asthma medications. Four hundred and seventy-two patients at five hospitals and clinics were enrolled from April 2018 to March 2019. Patients were eligible if they were aged ≥ 20 years and had physician-diagnosed persistent asthma that required regular administration of ICS. Asthma exacerbations were defined as worsening of asthma with patients requiring administration of systemic corticosteroids. The annual rate of exacerbations in the 2 years before study entry was evaluated using medical records. Patients with less than 2 years of clinical follow-up data before enrollment and those with incomplete data were excluded from the study. Overall, 351 patients were analyzed (Figure 1). All the participants were informed about the study aims, and their participation was voluntary and anonymized. The Medical Ethics Committee of Hiroshima University approved this study (E-1128) and waived the requirement for obtaining signed informed consent as this was a non-invasive questionnaire survey.

Questionnaires

This study evaluated patient preference for asthma inhaler medication using two questions. One question required the patient to choose the most preferred asthma inhaler medication from the full list of asthma control inhalers with their names and photographs. The other question asked whether the patients were satisfied with their inhaler medication. Matched preference was defined as patients answering that their current inhaler medication was their preferred medication and that they were satisfied with it (Figure 2). Patients were considered to have mismatched preferences when they answered that their preferred inhaler did not match the current inhaler and/or were not satisfied with it. Asthma symptom control was assessed using the asthma control test (ACT); uncontrolled asthma was defined as ACT score ≤ 19 . Self-reported inhaler adherence was ascertained by participant responses to the question, “How frequently do you use your inhaler presently?”. Self-reported inhaler adherence score was rated on a 5-point scale (5 indicating always and 1

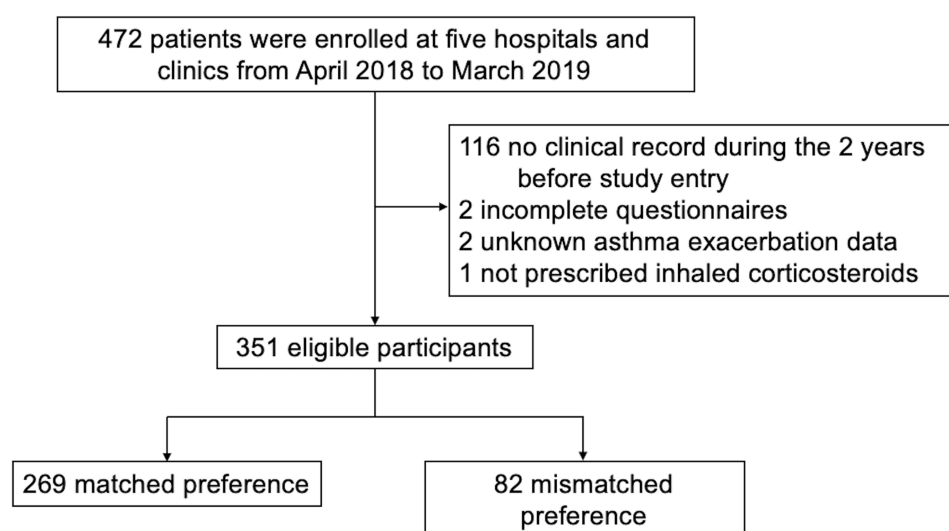


Figure 1 Study flow.

		Preferred inhaler matched the current inhaler medication	
		YES	NO
Satisfied with the current inhaler medication	YES	N = 269	N = 55
	NO	N = 9	N = 18

Matched preference group (n = 269)
 Mismatched preference group (n = 82)

Figure 2 Definition of patient preference for inhalers.

indicating never). It was classified as good ($\geq 75\%$ of medication taken) or poor ($< 75\%$ of medication taken). We also sought information regarding reasons for dissatisfaction with the current inhaler using a multiple choice and free response questionnaire.

Measurements

Pre-bronchodilator pulmonary function was measured using spirometry, and the percentage of predicted values was calculated using the Japanese reference values.¹⁰ Fractional exhaled nitric oxide (FeNO) was analyzed using NIOX VERO[®] from an aerocrine system, following the recommendations of the European Respiratory Society/American Thoracic Society.¹¹

Statistical Analysis

The results are expressed as mean \pm standard deviation. Comparisons of the two groups were made using the chi-square test, Fisher's exact test, and Mann–Whitney *U*-test. Univariate and multivariate linear regression model analyses were performed to investigate the clinical predictors of uncontrolled asthma and the number of exacerbations. Logistic regression analysis was performed to determine the predictors of adherence to treatment and regular OCS use. Sex, age, body mass index (BMI), smoking pack years, treatment step, and type of inhaler (dry powder inhaler [DPI] or pressurized metered dose inhaler [pMDI]) were used as independent variables in the multivariate analyses. For multivariate analysis of regular OCS use, the treatment step was not included as an independent variable because all patients with OCS were on step five of treatment, and these two indices were highly correlated. All statistical analyses were performed using the JMP[®]14 software (SAS Institute Inc., Cary, NC, USA). Results with *P*-values ≤ 0.05 were considered statistically significant for all the analyses.

Results

Among the 351 patients with asthma, 269 (76.6%) were divided into the matched preference group and 82 (23.4%) into the mismatched preference group (Figure 2). Table 1 compares patient characteristics between the matched and mismatched preference groups. There were no significant differences in age, BMI, smoking history, disease duration of asthma, asthma treatment step, and type of inhaler device between the matched and mismatched preference groups. Regular OCS use was significantly less frequent in the matched preference group than in the mismatched group (3.7% vs 13.4%; $P=0.003$). The number and types of controller inhaled medications ever used were slightly but significantly lower in the matched-preference group than in the mismatched group (2.06 vs 2.46, $P=0.004$). The patients achieving $> 75\%$ adherence were higher in the matched preference group. Significantly fewer patients with uncontrolled asthma and fewer exacerbation rates were observed in the matched preference group than in the mismatched group (Figure 3).

Tables 2 and 3 show the results of univariate and multivariate regression analyses of the factors associated with uncontrolled asthma symptoms, exacerbation rate, inhaler adherence, and OCS use. Multivariate analyses revealed that matched preference was independently associated with a lower prevalence of patients with uncontrolled asthma, fewer exacerbations, better adherence to medication, and a lower rate of regular OCS use.

Table 1 Patient Characteristics

	Matched Preference n = 269	Mismatched Preference n = 82	p-value
Age (year)	59.2 ± 15.1	61.2 ± 15.2	0.294
≥65 years old, n (%)	110 (40.9)	38 (46.3)	0.382
Number of females/males	171/98	46/36	0.223
Body mass index (kg/m ²)	23.6 ± 3.8	23.5 ± 4.8	0.607
Patients with smoking history, n (%)	91 (33.8)	32 (39.0)	0.687
Use of inhaled corticosteroids, n (%)	269 (100)	82 (100)	1.000
Type of inhaler device DPI/pMDI	194/75	54/28	0.275
(DPI device: Elipta/Turbohaler/Accuhaler/Twisthaler, n)	(64/94/29/7)	(22/25/6/1)	0.604
Use of LABA, n (%)	219 (81.4)	63 (76.8)	0.361
Use of LAMA, n (%)	25 (9.2)	9 (11.0)	0.652
Use of regular oral corticosteroids, n (%)	10 (3.7)	11 (13.4)	0.003*
Use of any biologics, n (%)	4 (1.5)	2 (2.4)	0.560
GINA treatment step, n	0/19/98/128/24	0/10/23/34/15	0.033*
FEV ₁ % of predicted ^a	97.4 ± 20.7	96.5 ± 20.2	0.880
FeNO ^b	33.7 ± 35.2	47.5 ± 56.9	0.202
Disease duration (year)	11.0 ± 12.0	10.9 ± 10.8	0.840
Number of types of controller inhaler medications ever used	2.06 ± 1.20	2.46 ± 1.26	0.004*
Adherence ≥75%, n (%)	246 (91.5)	66 (80.5)	0.006*
ACT score	22.9 ± 3.0	20.6 ± 4.6	<0.001*
Uncontrolled asthma (ACT≤19), n (%)	36 (13.4%)	25 (30.5%)	<0.001*
Exacerbation rate rate (/year)	0.38 ± 1.27	0.88 ± 1.73	0.003*

Notes: *P < 0.05, chi-square test, Fisher's exact test, or Mann-Whitney U-test. ^an=253. ^bn=238. Values are mean ± SD unless otherwise indicated.

Abbreviations: DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler; LABA, long-acting β-agonist; LAMA, long-acting muscarinic antagonist; GINA, global initiative for asthma; FEV₁, forced expiratory volume in 1 s; FeNO, fractional exhaled nitric oxide; ACT, asthma control test; SD, standard deviation.

Additionally, we asked about the points of dissatisfaction with the current inhaler in the mismatched preference group. Twenty-nine (35%) patients in the mismatched group had a reason for dissatisfaction: No feeling of effect (n = 16), Upper respiratory tract discomfort (n = 6), Difficult to inhale (n = 3), Difficult to handle the device (n = 3), Too much numbers of inhalation (n = 1). On the other hand, 65% did not have any reason for dissatisfaction.

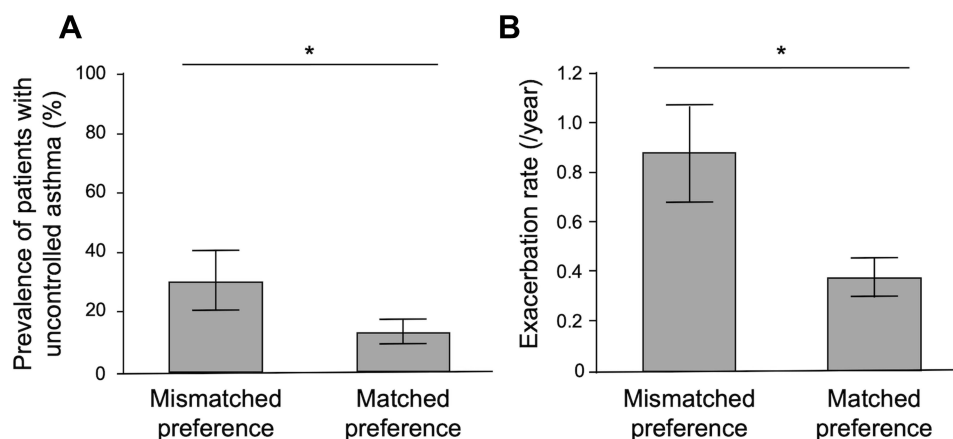


Figure 3 Comparison of (A) prevalence of uncontrolled asthma and (B) exacerbation rate between patients of matched and mismatched groups. Error bars represent (A) 95% score confidence intervals and (B) 95% confidence intervals. *P<0.05.

Table 2 Univariate and Multivariate Linear and Logistic Regression Analyses for Uncontrolled Asthma, Exacerbation Rate, and Adherence

	ACT Score ≤ 19 (Versus ACT Score ≥ 20)			Exacerbation Rate (/Year)			Good Adherence (Versus Poor Adherence)		
	Odds Ratio	95% CI	P-value	Regression Coefficient	95% CI	P-value	Odds Ratio	95% CI	P-value
Univariate analysis									
Matched preference (versus Mismatched)	0.352	0.196–0.637	<0.001*	0.497	0.149–0.846	0.005*	2.593	1.278–5.162	0.009*
Age	1.000	0.982–1.019	0.999	0.009	–0.011–0.029	0.366	1.005	0.983–1.027	0.667
Male (versus female)	0.469	0.243–0.860	0.018	0.137	–0.169–0.443	0.379	1.913	0.900–4.064	0.053
Body mass index	1.031	0.964–1.100	0.371	0.016	–0.058–0.090	0.673	0.989	0.914–1.075	0.794
Smoking (pack-year)	1.012	1.001–1.023	0.027*	–0.001	–0.014–0.012	0.885	1.015	0.995–1.046	0.242
GINA treatment step	2.168	1.474–3.266	<0.001*	0.496	0.124–0.868	0.009*	1.021	0.668–1.551	0.924
DPI (versus pMDI)	0.687	0.386–1.244	0.212	–0.221	–0.548–0.105	0.183	2.031	1.029–4.008	0.041*
Multivariate analysis									
Matched preference (versus Mismatched)	0.331	0.175–0.629	<0.001*	0.494	0.143–0.846	0.006*	3.007	1.457–6.208	0.003*
Age	0.993	0.973–1.013	0.492	0.008	–0.012–0.028	0.412	1.005	0.982–1.028	0.672
Male (versus female)	0.278	0.131–0.592	<0.001*	0.128	–0.190–0.447	0.429	1.955	0.840–4.549	0.107
Body mass index	1.023	0.954–1.097	0.518	0.008	–0.064–0.082	0.819	1.000	0.920–1.087	1.000
Smoking (pack-year)	1.017	1.004–1.030	0.010*	–0.007	–0.021–0.007	0.315	1.009	0.986–1.034	0.377
GINA treatment step	2.125	1.418–3.279	<0.001*	0.498	0.123–0.872	0.009*	1.049	0.678–1.623	0.829
DPI (versus pMDI)	0.759	0.404–1.427	0.366	–0.280	–0.605–0.044	0.090	1.906	0.931–3.905	0.082

Note: *P < 0.05.

Abbreviations: ACT, asthma control test; GINA, global initiative for asthma; DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler; CI, confidence interval.

Table 3 Univariate and Multivariate Logistic Regression Analyses for Regular Oral Corticosteroid

	Odds Ratio	95% CI	P-value
Univariate analysis			
Matched preference (versus mismatched)	0.249	0.102–0.610	0.002*
Age	1.006	0.976–1.036	0.707
Male (versus female)	2.807	1.131–6.964	0.026*
Body mass index	0.948	0.843–1.065	0.353
Smoking (pack-year)	1.016	1.003–1.029	0.012*
DPI (versus pMDI)	1.352	0.482–3.792	0.567
Multivariate analysis			
Matched preference (versus mismatched)	0.287	0.113–0.734	0.009*
Age	0.993	0.962–1.026	0.678
Male (versus female)	2.280	0.850–6.115	0.099
Body mass index	0.939	0.834–1.057	0.283
Smoking (pack-year)	1.011	0.995–1.027	0.177
DPI (versus pMDI)	1.502	0.517–4.363	0.443

Note: * $P < 0.05$.

Abbreviations: DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler; CI, confidence interval.

In the subgroup analyses by type of inhaler device, the prevalence of younger patients was significantly higher in the matched preference group among patients using DPI ($P < 0.05$); among patients using pMDI, the prevalence of older patients tended to be higher in the matched group ($P = 0.087$) (Table 4). There was no difference in other variables between patients using DPI and those using pMDI. Patients using DPI and pMDI used regular OCS less frequently and had fewer asthma exacerbations, lower prevalence of uncontrolled asthma, and better adherence in the matched preference group than in the mismatched group.

Table 4 Comparison of Patient Characteristics Between Matched and Unmatched Groups Regarding DPI or pMDI Usage

	Patients Using DPI (n = 248)			Patients Using pMDI (n = 103)		
	Matched Preference n = 194	Mismatched Preference n = 54	P-value	Matched Preference n = 75	Mismatched Preference n = 28	P-value
Age (year)	58.1 ± 15.1	63.5 ± 14.0	0.020*	62.1 ± 14.8	56.8 ± 16.7	0.108
≥ 65 years old, n (%)	69 (35.6)	28 (51.9)	0.030*	41 (54.7)	10 (35.7)	0.087
Number of females/males	124/70	29/25	0.184	47/28	17/11	0.856
Body mass index (kg/m ²)	23.4 ± 3.8	24.0 ± 5.2	0.614	24.0 ± 4.0	22.6 ± 3.9	0.092
Patients with smoking history, n (%)	61 (31.4)	24 (44.4)	0.204	30 (40.0)	8 (28.6)	0.555
Use of LABA, n (%)	165 (85.1)	47 (87.0)	0.714	54 (72.0)	16 (57.1)	0.151
Use of LAMA, n (%)	17 (8.8)	7 (13.0)	0.356	8 (10.7)	2 (7.1)	0.591
Use of regular oral corticosteroids, n (%)	8 (4.1)	8 (14.8)	0.005*	2 (2.7)	3 (10.7)	0.114
Use of any biologics, n (%)	4 (2.1)	1 (1.9)	0.888	0 (0.0)	1 (3.6)	0.100
GINA treatment step, n 1/2/3/4/5	0/16/83/76/19	0/3/17/23/11	0.124	0/3/15/32/52/5	0/7/6/11/4	0.003*
Disease duration (year)	10.5 ± 10.7	11.3 ± 10.6	0.360	12.3 ± 14.5	9.9 ± 11.2	0.337
Exacerbation rate (/year)	0.88 ± 2.89	2.04 ± 3.78	<0.001*	0.49 ± 1.24	1.22 ± 2.69	0.648
ACT score	23.0 ± 2.8	20.9 ± 4.6	<0.001*	22.5 ± 3.3	20.1 ± 4.7	0.010*
Uncontrolled asthma (ACT ≤ 19), n (%)	25 (12.9%)	14 (25.9%)	0.020*	11 (14.7%)	11 (39.3%)	0.007*
Adherence ≥ 75%, n (%)	180 (92.8)	46 (85.2)	0.511	66 (88.0)	20 (71.4)	0.044*

Note: * $P < 0.05$. Values are mean ± SD unless otherwise indicated.

Abbreviations: DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler; LABA, long acting β -agonist; LAMA, long-acting muscarinic antagonist; GINA, global initiative for asthma; ACT, asthma control test; SD, standard deviation.

Discussion

We demonstrated that agreement between patients' preferences and their prescribed inhaler medication was associated with fewer patients with uncontrolled asthma symptoms, fewer exacerbations, and a lower rate of regular OCS use irrespective of background characteristics, including the type of inhaler device. Matched preference for inhalers was also positively correlated with treatment adherence. The present results indicate that patient preference may significantly impact asthma outcomes, and investigating patient preference using simple questions could provide useful information for individualized treatment with asthma inhaler medications.

One important finding of this study is that using preference-matched inhalers is independently associated with lower rates of uncontrolled asthma symptoms, exacerbation, and regular OCS use, as well as better adherence to treatment. There have been inconsistent results regarding the association between patient satisfaction with inhaler medication and adherence to treatment and/or asthma outcomes. Small et al showed that patient satisfaction scores evaluated using 13 questions about inhalers were significantly associated with physician-perceived adherence to treatment, while Price et al showed that patient satisfaction scores evaluated using 12 questions were correlated with asthma outcomes but not with adherence scores.^{2,12} Plaza et al also reported that patients with higher scores on ten questions regarding the extent of satisfaction with an inhaler (FSI-10) had higher adherence and better symptom control.¹³ This study evaluated the agreement between patients' preferences and current medication using two questions about their preferred medication and their satisfaction with the current inhaler. Our results showed that more than half of the patients in the mismatched group did not express dissatisfaction with the current inhaler. The reason for this discrepancy is unclear, but we speculate that it may be difficult for patients to identify specific problems, even when they do not prefer inhaler medications. The present results indicate that simple questions regarding patients' preferences may provide valuable information for selecting asthma inhaler medications. Since asthma is a prevalent disease, many patients are treated by a non-specialist.^{1,2} Therefore, a simple method to evaluate patient preference would be useful in clinical practice. Further studies are needed to clarify whether switching to preference-matched inhalers can provide useful information for shared decision-making and improve asthma outcomes.

In the present study, subgroup analysis showed that the prevalence of younger patients was higher in the matched preference group among patients using DPI, and the prevalence of older patients tended to be higher in the matched group among patients using pMDI. The former result agrees with a previous report that younger patients showed a higher satisfaction score for inhalers, predominantly (91.2%) consisting of DPI.¹³ Moreover, Welch et al showed that patient satisfaction score was higher in Turbuhaler users than in pMDI users, primarily in younger patients (mean age, 38.7 years). Consistent with the latter result, Muraki et al showed that among older adult patients (mean age, 62.1 years), 57.4% of the individuals preferred pMDI and 35.3% preferred DPI.¹⁴ DPI does not need to be synchronized with breathing and is widely available; however, a thorough understanding of the wide variety of DPI devices available and their techniques and sufficient inspiratory flow rates is necessary.^{15–17} These device characteristics of DPIs may affect patient preference in older patients,¹⁸ and the present results suggest that attention should be paid to patient preference, particularly among older patients using DPIs.

This study has some limitations. First, inhaler handling error was not evaluated in this study. Although patient education was provided by respiratory physicians and non-physician medical staff, handling errors in some patients may have contributed to poor palatability and/or asthma control. Second, we did not include a broad range of patients with asthma during spirometry and FeNO administration in real-world clinical settings. Missing data can potentially decrease the ability to detect differences in these indices. Third, self-reported adherence to inhaler medication could be over-estimated, and FSI-10 or electronic monitoring devices could help obtain more accurate information for treatment adherence.^{13,19} Fourth, three-fourths of the patients did not provide reasons for dissatisfaction with their current inhalers. This could imply that our questionnaire is imprecise and does not cover the entire preference issue. An inhaler-specific questionnaire, such as the FSI-10, might have picked up additional dissatisfaction. Finally, this was a cross-sectional survey; therefore, we did not have data on treatment change after this study and its effect on the patient's preference and disease outcomes.

Conclusion

In summary, we demonstrated that agreement between patient preference and inhaler medication was associated with fewer patients with uncontrolled symptoms, fewer exacerbations, better adherence to treatment, and less use of regular OCS treatment. Evaluation of patients' preference for inhaler medication might provide useful information for individualized treatment with asthma inhaler medications.

Abbreviations

ACT, asthma control test; BMI, body mass index; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroids; OCS, oral corticosteroids; DPI, dry powder inhaler; pMDI, pressurized metered dose inhaler.

Ethics Approval and Informed Consent

The study was approved by the Medical Ethics Committee of Hiroshima University and waived the requirement for obtaining signed informed consent (E-1128). All the participants were informed about the study aims, and their participation was voluntary and anonymized. This study was conducted in accordance with the Declaration of Helsinki.

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Disclosure

Dr Hiroshi Iwamoto reports personal fees from Astrazeneca, Glaxosmithkline, and Kyorin Pharmaceutical, outside the submitted work. Dr. Yojiro Onari reports personal fees from GlaxoSmithKline, AstraZeneca, Novartis Pharma, Kyorin Pharmaceutical, outside the submitted work. Dr Yasushi Horimasu reports personal fees from Boehringer Ingelheim, outside the submitted work. Dr. Yoshinori Haruta reports personal fees from GlaxoSmithKline, AstraZeneca, Novartis Pharma and Kyorin Pharmaceutical, outside the submitted work. Dr. Soichiro Hozawa reported personal fees from GlaxoSmithKline, AstraZeneca, Novartis Pharma, Kyorin Pharmaceutical, outside the submitted work. Dr Noboru Hattori reports grants from Teijin Pharma and Kyorin Pharmaceutical and personal fees from GlaxoSmithKline, AstraZeneca, Novartis Pharma, and Kyorin Pharmaceutical, outside the submitted work. The authors report no other conflicts of interest in this work.

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