**openheart**

# Patient perception and treatment convenience of dabigatran versus vitamin K antagonist when used for stroke prophylaxis in atrial fibrillation: Real-world Evaluation of Long-term Anticoagulant Treatment Experience (RE-LATE) study

Young-Soo Lee,[1] Yong Seog Oh [ID],[2] Eue-Keun Choi [ID],[3]
Alan Koay Choon Chern,[4] Panyapat Jiampo,[5] Aurauma Chutinet,[6,7]
Dicky Armein Hanafy,[8,9] Prabhav Trivedi,[10] Dongmei Zhai[11]

Check for updates

## ABSTRACT

**Purpose** Dabigatran is a direct thrombin inhibitor approved for stroke prophylaxis in patients with non-valvular atrial fibrillation (NVAF). Real-world data about patient preference, satisfaction and convenience in patients in Asia are not available. The study aimed to explore the perception of patients with newly diagnosed NVAF regarding dabigatran versus vitamin K antagonists (VKAs), when used for stroke prevention.

**Patients and methods** This was a multinational, multicentre, non-interventional study involving 49 sites across 5 countries in South East Asia and South Korea where 934 patients newly diagnosed with NVAF were initiated on either dabigatran (N=591) or VKA (N=343). Data were collected at baseline and over two follow-up visits across 6 months. Treatment satisfaction and patient convenience were evaluated using the Perception on Anticoagulant Treatment Questionnaire-2 (PACT-Q2).

**Results** The mean age of the patients was 65.9±10.4 years, and 64.2% were male. Mean $CHA_2DS_2$-VASc score was 2.4±1.5, and mean HAS-BLED score was 1.2±0.9. At baseline, patients initiated on dabigatran had higher stroke risk, bleeding risk, creatinine clearance and proportion of patients with concomitant illnesses compared with patients initiated on VKAs. Treatment convenience was perceived to be significantly better with dabigatran versus VKAs at visits 2 and 3 (p=0.0423 and 0.0287, respectively). Treatment satisfaction was significantly better with dabigatran compared with VKAs at visit 3 (p=0.0300).

**Conclusion** In this study, dabigatran is associated with better patient perception in terms of treatment convenience and satisfaction compared with VKAs when used for stroke prevention in newly diagnosed NVAF patients from South East Asia and South Korea.

**Trial registration number** NCT02849509.

**Plain language summary** Patient satisfaction with dabigatran versus VKAs in South East Asia. Patients

## Key questions

### What is already known about this subject?

► Non-vitamin K antagonist oral anticoagulants (NOACs) are increasingly used for stroke prophylaxis in patients with non-valvular atrial fibrillation (NVAF). The safety and efficacy of NOACs as well as the advantages they provide in terms of lower drug–drug and drug–food interactions over vitamin K antagonists (VKAs) are well established. However, data on patient-reported outcomes (such as treatment convenience and satisfaction) and factors influencing patients' perception of NOACs when given for stroke prophylaxis in NVAF patients are not well characterised.

### What does this study add?

► This study evaluates the influence on the perception and satisfaction of treatment-naïve NVAF patients when they are started with either VKA or dabigatran etexilate in routine clinical practice.

► Patients initiated on dabigatran had higher stroke risk, bleeding risk, creatinine clearance and proportion of patients with concomitant illnesses when compared with patients initiated on VKAs. The study provided insights showing that when treatment-naïve patients are started on dabigatran, their perception of treatment convenience and treatment satisfaction are better than matched patients who are started on VKAs.

with atrial fibrillation are at high risk of stroke and require anticoagulants for stroke prevention. Two such anticoagulants are dabigatran and VKAs. We wanted to compare the extent of satisfaction and treatment convenience among newly diagnosed patients with atrial fibrillation from the South East Asian region when they

## Key questions

### How might this impact on clinical practice?
► Patient preferences are an important part of clinical decision making.
► The differential scores of patient perception and satisfaction for treatment-naïve patients when started on VKAs or NOACs should form an integral part of patient–physician dialogue and will allow more informed decision making for treatment of NVAF patients for stroke prevention.

were given either dabigatran or VKAs. Consenting patients filled out a standardised questionnaire called the PACT-Q2 over three visits after they were started on either dabigatran (591 patients) or VKAs (343 patients). We found that satisfaction and convenience were significantly higher when patients received dabigatran than when they received VKAs.

## INTRODUCTION

Atrial fibrillation (AF) is shown to increase the risk of stroke by five times.[1] The severity of AF-related stroke is generally greater than stroke not related to AF.[2] Stroke prevention by using anticoagulants is an essential part of the management of non-valvular AF (NVAF), and is associated with an improved quality of life (QoL) in these patients.[3] Though the traditionally used vitamin K antagonists (VKAs) such as warfarin, phenprocoumon and acenocoumarol effectively prevent thromboembolism by providing optimal anticoagulation, they are associated with several food and drug interactions and require regular monitoring, both of which result in poor patient adherence and QoL.[4] Since 2008, many non-VKA oral anticoagulants (NOACs) such as the direct thrombin inhibitor (dabigatran) and the factor Xa inhibitors (rivaroxaban, apixaban and edoxaban) have been introduced as alternatives to VKA for stroke prevention in patients with AF, after their efficacy and safety was demonstrated in comparison with warfarin in four landmark clinical trials.[5–8] The direct thrombin inhibitor dabigatran etexilate (Pradaxa, Boehringer Ingelheim) was approved by the European Medicines Agency in 2008 and by the US Food and Drug Administration (FDA) in October 2010 for the prevention of stroke and systemic embolism in adult patients with NVAF.[9] The drug subsequently obtained US FDA approval for the prevention and treatment of deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), and for venous thromboembolism prophylaxis after total hip arthroplasty and total knee arthroplasty.[10]

A 2014 meta-analysis concluded that NOACs result in a lower risk of stroke, haemorrhage or death, but a higher risk of gastrointestinal bleeding than the VKAs.[11] The NOACs also have fewer food and drug interactions than the VKAs.[12] Reversal agents have been developed for dabigatran and direct factor Xa inhibitors.[13 14] On the other hand, NOACs are not recommended for patients with stages 4 and 5 chronic kidney disease, as per the 2017 consensus statement by the Asia Pacific Heart Rhythm Society.[15] Further, NOACs are more expensive than VKAs.[12]

While NOACs have some distinct advantages over VKAs with respect to clinical outcomes, whether these advantages translate to improvement of QoL and better patient satisfaction and convenience has been studied less thoroughly. QoL in patients receiving anticoagulants can be measured by generic tools such as EQ-5D, or by specific tools such as the Perception of Anticoagulant Treatment Questionnaire (PACT-Q).[16] PACT-Q is a validated tool to assess patient expectation before treatment initiation (PACT-Q1, seven items) and treatment convenience and treatment satisfaction with ongoing anticoagulation therapy (PACT-Q2, 20 items) in patients with AF, and also in DVT and PTE (see online supplemental table 1).[17] Higher scores in PACT-Q2 indicate better convenience and higher treatment satisfaction.[16] Two recent studies, one conducted in Europe and Israel and the other in South East Asia and South Korea, showed significant improvements in treatment convenience and satisfaction scores in patients who switched from a VKA to dabigatran for stroke prevention.[18 19] In this study, PACT Q2 was used to evaluate patient perception of anticoagulation with dabigatran versus VKAs when used for stroke prevention in patients with newly diagnosed AF in South East Asia and South Korea.

The objective of our study was to describe the treatment expectations prior to commencing therapy and the perception of NVAF patients regarding dabigatran, in comparison with VKAs, when used for stroke prevention, in terms of treatment satisfaction and convenience.

## METHODS

### Patients

This was a non-interventional, multi-centre study which prescribed both VKAs and dabigatran for stroke prevention in NVAF patients, according to the approved label of the respective country. Consenting patients of either sex, aged ≥18 years, who were newly diagnosed with NVAF were recruited. Patients having any contraindication for the use of dabigatran, patients already receiving any VKA or dabigatran for any other indication apart from stroke prevention in AF, patients participating in any registry (such as the GLORIA-AF registry programme), patients participating in any other clinical trial at the same time, and non-consenting patients were excluded from the study.

### Treatment groups

The patients were initiated with anticoagulation therapy with either dabigatran (dabigatran group) or a VKA (VKA group). The decision for therapy initiation was taken prior to and independently of enrolment into the study. The dosing of dabigatran (either 110 mg two times per day or 150 mg two times per day), and the choice of VKA, were based on the clinician's discretion and according to

the approved country label. All concomitant medications were prescribed based on the underlying medical condition and on the discretion of the treating physician. No treatment was withheld from the patients.

## Data collection

Patients were followed up for a median of 6 months with data collection at three time points: baseline, 7–124 days and 125–365 days. At the baseline visit, demographic details, HAS-BLED score for bleeding risk and $CHA_2DS_2$-VASc score for stroke risk were recorded. Patients were also administered the PACT-Q1 questionnaire to evaluate their treatment expectations at baseline (prior to starting treatment with dabigatran or VKA). At the two subsequent visits, the patients were administered the PACT-Q2 questionnaire to capture the progressive changes in the patient convenience, burden and treatment satisfaction. Validated translations of the PACT-Q2 questionnaires were provided to the patients in their language (namely, Indonesian, Korean, Chinese, Mandarin, English, Malay, Tamil and Thai). Adverse reactions as reported by the patients were also recorded. Details of concomitant illness and therapies, creatinine clearance and weight were recorded at all the three visits.

## Data analysis

All data were recorded electronically. Baseline demographic data, $CHA_2DS_2$-VASc score, HAS-BLED score and creatinine clearance of both the groups were analysed using standardised difference. Scores of the individual items of the PACT-Q1 questionnaire at baseline were summarised descriptively. For comparison of PACT-Q2 scores, the patients in the two treatment groups were first matched based on comparability using propensity scores; subsequently, the mean PACT-Q2 scores were compared between matched patients at visit 2 and visit 3 using paired t-test. All statistical analyses were performed using SAS v9.4 software. At least one of the authors had full access to all the data in the study and takes responsibility for data integrity and the analysis of data.

## RESULTS

A total of 49 participating sites from across the 5 countries were involved in the study, which recruited a total of 952 anticoagulation-naïve patients over a period of 18 months (from June 2016 to December 2017). A total of 934 patients were found to be eligible for the study, out of which 600 (64.2%) were male. Of patients who discontinued from the study, the most frequently reported reason in the dabigatran and VKA groups was 'lost to follow-up' (11.5% and 10.5%, respectively), followed by 'other' (8.8% and 9.0%) and 'other adverse event (AE)' (7.1% and 2.3%). Less frequent reasons were 'refused to continue in the study' (3.0% and 3.8%), 'worsening of disease under study' (0.2% and 0.3%) and 'worsening of other pre-existing disease' (0.2% and 0.6%).

The baseline demographic details are summarised in table 1. Patients recruited in the dabigatran group had higher mean values of $CHA_2DS_2$-VASc score, HAS-BLED score and creatinine clearance when compared with the patients recruited in the VKA group. A total of 343 patients (58.0%) in the dabigatran group received dabigatran at the lower dose (110 mg two times per day), while the rest (42.0%) received the standard dose (150 mg two times per day).

The scores for the PACT-Q1 items (based on 920 patients with valid data) were very similar for dabigatran and VKA patients with differences in mean scores between 0 and 0.2. Most patients rated importance of independence (mean (SD) score 3.7 (1.0)) and ease of use (3.6 (0.9)) highly and also expected that their treatment would prevent blood clots (3.4 (1.0)) and relieve symptoms (3.4 (0.9)), whereas concerns about costs (2.7 (1.2)), making mistakes (2.5 (1.2)), or expectations of side effects (2.6 (1.0)) played a minor role in treatment expectations.

Based on the PACT-2 questionnaire, treatment convenience was perceived to be significantly better with dabigatran compared with VKAs at visits 2 and 3 (p=0.0423 and 0.0287, respectively). Treatment satisfaction was also perceived to be significantly better with dabigatran compared with VKAs at visit 3 (p=0.0300) (table 2 and figure 1).

Adverse drug reactions (ADRs) were reported by 57 patients (6.1%) overall, out of which 45 patients were from the dabigatran group. Most patients with any ADR were reported with non-serious ADRs (51/57), of which gastrointestinal disorders were most frequent. Serious ADRs were observed in seven patients (0.7%) overall, out of which six were from the VKA group. ADRs led to treatment discontinuation in 35 patients, out of which 30 patients were from the dabigatran group.

## DISCUSSION

This study aimed to describe the treatment expectations and perception of convenience and satisfaction of NVAF patients with their anticoagulant treatment for stroke prevention with either dabigatran or a VKA in a real-world setting across five countries in South East Asia using the PACT-Q1 and PACT-Q2 questionnaires. To the best of our knowledge, no study in the past has described the patient perception in newly diagnosed and treated NVAF patients in this geographical region.

The population of this study was younger and had slightly higher male predominance than the population in the Global Anticoagulant Registry in the Field-Atrial Fibrillation (GARFIELD) registry,[20] the Prevention of Thromboembolic Events—European Registry in Atrial Fibrillation (PREFER) registry[21] and the Global Registry on Long-Term Oral Antithrombotic Treatment in Patients with Atrial Fibrillation (GLORIA-AF) registry.[22] The average $CHA_2DS_2$-VASc scores in this study were lower than the three registries. Patients who were initiated with dabigatran were older, had higher stroke and bleeding risk, and had a higher proportion of patients

**Table 1** Baseline demographic details of patients recruited in the study

| Parameter | Dabigatran group | VKA group | Total | Standardised difference |
|---|---|---|---|---|
| Eligible patients | 591 | 343 | 934 | |
| Sex, n (%) | | | | |
| Female | 228 (38.6) | 106 (30.9) | 334 (35.8) | 0.1617 |
| Male | 363 (61.4) | 237 (69.1) | 600 (64.2) | −0.1617 |
| Mean age (years) | 67.3±9.8 | 63.4±10.9 | 65.9±10.4 | 0.3797 |
| Age group, n (%) | | | | |
| <65 years | 196 (33.2) | 184 (53.6) | 380 (40.7) | −0.4223 |
| 65–75 years | 256 (43.3) | 101 (29.4) | 357 (38.2) | 0.2914 |
| ≥75 years | 139 (23.5) | 50 (16.9) | 189 (20.2) | 0.1651 |
| Region, n (%) | | | | |
| Region 1 | 124 (21.0) | 32 (9.3) | 156 (16.7) | 0.3293 |
| Region 2 | 467 (79.0) | 311 (90.7) | 778 (83.3) | −0.3293 |
| $CHA_2DS_2$-VASc stroke risk score, mean±SD | 2.6±1.4 | 2.0±1.6 | 2.4±1.5 | 0.3659 |
| $CHA_2DS_2$-VASc stroke risk score class, n (%) | | | | |
| Low risk (score=0) | 29 (4.9) | 50 (14.6) | 79 (8.5) | −0.3305 |
| Intermediate risk (score=1) | 78 (13.2) | 106 (30.9) | 184 (19.7) | −0.4372 |
| High risk (score ≥2) | 482 (81.6) | 187 (54.5) | 669 (71.6) | 0.6058 |
| Missing | 2 (0.3) | 0 (0.0) | 2 (0.2) | 0.0824 |
| HAS-BLED bleeding risk score, mean±SD | 1.3±0.9 | 1.1±1.1 | 1.2±0.9 | 0.2624 |
| HAS-BLED bleeding risk score class, n (%) | | | | |
| Low risk (score <3) | 540 (91.4) | 306 (89.2) | 846 (90.6) | 0.0729 |
| High risk (score ≥3) | 49 (8.3) | 37 (10.8) | 86 (9.2) | −0.0851 |
| Missing | 2 (0.3) | 0 (0.0) | 2 (0.2) | 0.0824 |
| Creatinine clearance (mL/min), mean±SD | 75.4±29.0 | 73.0±29.2 | 74.6±29.1 | 0.0807 |
| Creatinine clearance class, n (%) | | | | |
| <50 mL/min | 66 (11.2) | 42 (12.2) | 108 (11.6) | −0.0335 |
| 50 to <80 mL/min | 210 (35.5) | 78 (22.7) | 288 (30.8) | 0.2844 |
| ≥80 mL/min | 140 (23.7) | 69 (20.1) | 209 (22.4) | 0.0864 |
| Not available | 175 (29.6) | 154 (44.9) | 329 (35.2) | −0.3202 |
| No of patients with at least one prespecified concomitant disease, n (%) | 343 (58.0) | 162 (47.2) | 505 (54.1) | 0.2177 |
| Concomitant diseases, n (%) | | | | |
| Hypertension | 224 (37.9) | 89 (25.9) | 313 (33.5) | 0.2586 |
| Hyperlipidaemia | 147 (24.9) | 68 (19.8) | 215 (23.0) | 0.1214 |
| Diabetes mellitus (type 1 or 2) | 91 (15.4) | 34 (9.9) | 125 (13.4) | 0.1655 |
| Congestive heart failure | 52 (8.8) | 31 (9.0) | 83 (8.9) | −0.0084 |
| Stroke | 25 (4.2) | 25 (7.3) | 50 (5.4) | −0.1316 |
| Comorbidities, n (%) | | | | |
| Malignancy | 28 (4.7) | 11 (3.2) | 39 (4.2) | 0.0784 |
| GI disease | 31 (5.2) | 18 (5.2) | 49 (5.2) | −0.0001 |
| Concomitant therapies, n (%) | | | | |
| P-gp inhibitors | 50 (8.5) | 24 (7.0) | 74 (7.9) | 0.0548 |
| Antithrombotic agent | 56 (9.5) | 68 (19.8) | 124 (13.3) | −0.2959 |
| NSAIDs | 17 (2.9) | 6 (1.7) | 23 (2.5) | 0.0750 |
| Type of hospital or practice, n (%) | | | | |

**Table 1** Continued

| Parameter | Dabigatran group | VKA group | Total | Standardised difference |
|---|---|---|---|---|
| Public and other | 282 (47.7) | 142 (41.4) | 424 (45.4) | 0.1273 |
| Private | 309 (52.3) | 201 (58.6) | 510 (54.6) | −0.1273 |

GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; P-gp, P-glycoprotein; SD, standardised difference; VKA, vitamin K antagonists.

with concomitant illnesses than those who were initiated with VKAs. Such a trend where NOACs are prescribed to patients with higher bleeding and stroke risk has also been reported previously in studies from Taiwan[23] and Spain.[24] Among patients who were initiated on dabigatran, a higher proportion of patients received the lower dose of 110 mg two times per day (58.0%) compared with the standard dose of 150 mg two times per day (42.0%). This is consistent with the practice pattern previously reported in real-world studies from Taiwan[23] and Korea.[25]

We found that among patients newly initiated on anticoagulation for stroke prevention, treatment convenience and satisfaction were perceived to be significantly better with dabigatran compared with VKAs. This supports the findings from the RE-SONANCE study in which dabigatran treatment was shown to be associated with improved patient treatment convenience and satisfaction, with larger separation in PACT-Q2 scores compared with VKA therapy in a large, mostly European, cohort.[18] The lack of food and drug interactions, and the non-requirement of frequent monitoring with dabigatran when compared with the VKAs might have contributed to these results.

Concerns about the impact on health-related QoL (HRQoL) with VKAs have been well documented.[26] Recent studies have examined the impact of long-term VKA therapy on HRQoL in NVAF patients and concluded that VKAs are well tolerated and do not seem to significantly impact patient perception or treatment satisfaction scores compared with the general population.[27 28] However, these studies did not compare the outcomes of treatment with VKAs with those of NOACs.

Earlier comparative studies published at the time when NOACs were freshly introduced for clinical practice have not consistently demonstrated the beneficial impact of these drugs on HRQoL when compared with the VKAs. A 2013 study reported that over a 1-year observation period, the HRQoL of patients with AF was not significantly different between those receiving dabigatran and warfarin for anticoagulation; however, the tool used in this study was EQ-5D, which was a generic tool, and only those patients who did not experience an event were included.[26] The PREFER in AF registry substudy, which collected data between 2012 and 2013, observed that NVAF patients who switched from VKA to NOACs had poorer treatment satisfaction, and more often reported bruising, bleeding, mobility problems, and anxiety and depressive states, when compared with patients on stable treatment with VKAs.[29] It may be that in the PREFER in AF registry substudy, complaints about bruising/bleeding, treatment dissatisfaction and anxiety/depression may have influenced the switching from VKAs to NOACs. Multiple studies published subsequently have consistently observed that the NOACs, in comparison with the VKAs, have higher treatment satisfaction, convenience and perceived benefits, and lower perceived disease and treatment burdens in patients suffering from NVAF[18 19 24 30–32] and also from other conditions where the NOACs are indicated.[33 34] Consistent with recent studies, our study also shows higher treatment convenience and satisfaction scores with dabigatran compared with VKAs and adds to a growing wealth of data. The findings along with other studies are important especially considering the increasing role of patient participation and patient preference in treatment decision making.

Serious and non-serious ADRs to dabigatran and VKA and fatal AEs were collected systematically. The safety data collected in this study are consistent with the known safety profile of dabigatran and do not give rise to any new safety concerns.

**Table 2** Comparison of PACT-Q2 scores of dabigatran group versus VKA group

| PACT-Q2 dimensions | No of matched patient sets | Dabigatran group (mean±SD) | VKA group (mean±SD) | P value (dabigatran vs VKA) |
|---|---|---|---|---|
| Convenience dimension score | | | | |
| Visit 2 | 217 | 78.4±14.6 | 75.1±19.6 | **0.0423** |
| Visit 3 | 157 | 80.4±13.6 | 76.0±18.9 | **0.0287** |
| Satisfaction dimension score | | | | |
| Visit 2 | 217 | 61.5±12.7 | 59.9±13.5 | 0.2226 |
| Visit 3 | 157 | 63.9±11.6 | 60.9±12.8 | **0.0300** |

Bold p value indicates significance.
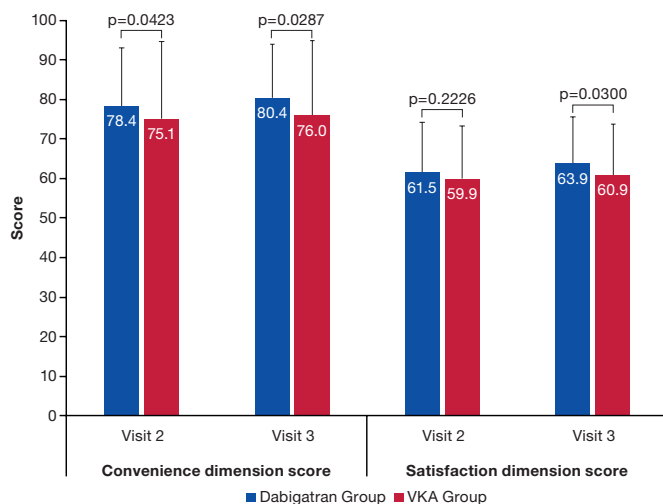PACT-Q2, perception on anticoagulant treatment questionnaire-2; VKA, vitamin K antagonists.

**Figure 1** Comparison of PACT-Q2 scores of dabigatran group versus VKA group between propensity score matched dabigatran and VKA patients. PACT-Q2, Perception of Anticoagulant Treatment Questionnaire-2; VKA, vitamin K antagonist.

This study has several strengths including the real-life setting, large numbers of patients with and without anticoagulant treatment experience, non-restrictive entry criteria that permitted the enrolment of a broad patient population, a study design that allowed the collection of cross-sectional data at baseline and longitudinal follow-up data, and the use of standardised and validated questionnaires. Furthermore, data from a real-life setting may better represent routine practice than the idealised conditions of a randomised controlled trial and may be used to complement the findings from randomised controlled trials; however, real-world studies have a number of inherent limitations. Among the limitations of this study, the baseline characteristics in both the groups were not balanced, which is likely the result of the real-world nature of the study and that choice of anticoagulant was at the discretion of the treating physician. However, to ensure that the comparability between the two treatment groups was reasonable, we followed a propensity score matching method that is commonly used in epidemiological studies for observational data. Statistical techniques, such as adjustment for covariates and propensity score matching, were used to correct for identified confounders. However, not all comorbidities may have been considered in the analyses, and so serious confounding may remain from unidentified confounders. Patient numbers might be considered small for a study conducted over 49 centres, which may have influenced the study findings, such as satisfaction dimension scores of PACT-Q2 that were not statistically conclusive at visit 2, and so these data should be interpreted with caution. The occurrence of selection bias at the site level cannot be ruled out completely, since a larger number of cardiologists rather than general practitioners or other specialists participated in the study. Finally, most patients included in this study came from reimbursed settings.

## CONCLUSIONS

The RE-LATE study evaluated the perception of NVAF patients towards anticoagulant treatment for prevention of stroke in the South East Asian region. Among patients newly initiated on anticoagulation for stroke prevention in AF, the perception of treatment in terms of treatment convenience and treatment satisfaction was significantly better among patients on dabigatran compared with patients on VKA.

**Author affiliations**
[1]Department of Internal Medicine, Daegu Catholic University College of Medicine, Daegu, Republic of Korea
[2]Department of Internal Medicine, Catholic University of Korea, Seoul, Republic of Korea
[3]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea
[4]Department of Cardiology, Columbia Asia Hospital, Taiping, Malaysia
[5]Department of Medicine, Bhumibol Adulyadej Hospital, Bangkok, Thailand
[6]Chulalongkorn Stroke Center, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
[7]Division of Neurology, Department of Medicine, Chulalongkorn University, Bangkok, Thailand
[8]Cardiology and Vascular Medicine, Pusat Jantung Nasional Harapan Kita, Jakarta, Indonesia
[9]Cardiology and Vascular Medicine, University of Indonesia Faculty of Medicine, Jakarta, Indonesia
[10]Boehringer Ingelheim Singapore Pte Ltd, Singapore
[11]Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, Connecticut, USA

participants fitting the inclusion criteria provided written informed consent prior to the initiation of the study.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available on reasonable request. To ensure independent interpretation of clinical study results, Boehringer Ingelheim grants all external authors access to relevant material, including participant-level clinical study data, as needed by them to fulfill their role and obligations as authors under the ICMJE criteria. Clinical study documents and participant clinical study data are available to be shared on request after publication of the primary manuscript in a peer-reviewed journal, and if regulatory activities are complete and other criteria met as per the BI Policy on Transparency and Publication of Clinical Study Data (see Medical & Clinical Trials|Clinical Research|MyStudyWindow). Bona fide, qualified scientific and medical researchers are eligible to request access to the clinical study data with corresponding documentation describing the structure and content of the datasets. Upon approval, and governed by a Legal Agreement, data are shared in a secured data-access system for a limited period of 1 year, which may be extended upon request. Prior to providing access, clinical study documents and data will be examined, and, if necessary, redacted and de-identified, to protect the personal data of study participants and personnel, and to respect the boundaries of the informed consent of the study participants. Researchers should use the https://vivli.org/ link to request access to study data and visit Medical & Clinical Trials|Clinical Research|MyStudyWindow for further information

**ORCID iDs**
Yong Seog Oh http://orcid.org/0000-0003-3567-6505
Eue-Keun Choi http://orcid.org/0000-0002-0411-6372

## REFERENCES

1 Rahman F, Kwan GF, Benjamin EJ. Global epidemiology of atrial fibrillation. *Nat Rev Cardiol* 2014;11:639–54.
2 January CT, Wann LS, Alpert JS, *et al*. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation* 2014;130:e199–267.
3 Reiffel JA. Atrial fibrillation and stroke: epidemiology. *Am J Med* 2014;127:e15–16.
4 Hanley CM, Kowey PR. Are the novel anticoagulants better than warfarin for patients with atrial fibrillation? *J Thorac Dis* 2015;7:165–71.
5 Connolly SJ, Ezekowitz MD, Yusuf S, *et al*. Dabigatran versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2009;361:1139–51.
6 Patel MR, Mahaffey KW, Garg J, *et al*. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med* 2011;365:883–91.
7 Granger CB, Alexander JH, McMurray JJV, *et al*. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2011;365:981–92.
8 Giugliano RP, Ruff CT, Braunwald E, *et al*. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;369:2093–104.
9 Muñoz-Corcuera M, Ramírez-Martínez-Acitores L, López-Pintor R-M, *et al*. Dabigatran: a new oral anticoagulant. Guidelines to follow in oral surgery procedures. A systematic review of the literature. *Med Oral Patol Oral Cir Bucal* 2016;21:e679–88.
10 Drugs.com. Pradaxa approval history, 2021. Available: https://www.drugs.com/history/pradaxa.html
11 Ruff CT, Giugliano RP, Braunwald E, *et al*. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. *Lancet* 2014;383:955–62.
12 Mas Dalmau G, Sant Arderiu E, Enfedaque Montes MB, *et al*. Patients' and physicians' perceptions and attitudes about oral anticoagulation and atrial fibrillation: a qualitative systematic review. *BMC Fam Pract* 2017;18:3.
13 Pollack CV, Reilly PA, van Ryn J, *et al*. Idarucizumab for dabigatran reversal - full cohort analysis. *N Engl J Med* 2017;377:431–41.
14 Connolly SJ, Crowther M, Eikelboom JW, *et al*. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. *N Engl J Med* 2019;380:1326–35.
15 Chiang C-E, Okumura K, Zhang S, *et al*. 2017 consensus of the Asia Pacific Heart Rhythm Society on stroke prevention in atrial fibrillation. *J Arrhythm* 2017;33:345–67.
16 Prins MH, Marrel A, Carita P, *et al*. Multinational development of a questionnaire assessing patient satisfaction with anticoagulant treatment: the 'Perception of Anticoagulant Treatment Questionnaire' (PACT-Q). *Health Qual Life Outcomes* 2009;7:9.
17 Prins MH, Guillemin I, Gilet H, *et al*. Scoring and psychometric validation of the Perception of Anticoagulant Treatment Questionnaire (PACT-Q). *Health Qual Life Outcomes* 2009;7:30.
18 Vinereanu D, Napalkov D, Bergler-Klein J, *et al*. Patient perception of anticoagulant treatment for stroke prevention (RE-SONANCE study). *Open Heart* 2020;7:e001202.
19 Choi E-K, Lee Y-S, Chern AKC, *et al*. Real-world evaluation of perception, convenience and anticoagulant treatment satisfaction of patients with atrial fibrillation switched from long-term vitamin K antagonist treatment to dabigatran. *Open Heart* 2020;7:e001343.
20 Kakkar AK, Mueller I, Bassand J-P, *et al*. Risk profiles and antithrombotic treatment of patients newly diagnosed with atrial fibrillation at risk of stroke: perspectives from the international, observational, prospective GARFIELD registry. *PLoS One* 2013;8:e63479.
21 Le Heuzey J-Y, Ammentorp B, Darius H, *et al*. Differences among western European countries in anticoagulation management of atrial fibrillation. Data from the PREFER in AF registry. *Thromb Haemost* 2014;111:833–41.
22 Huisman MV, Rothman KJ, Paquette M, *et al*. The changing landscape for stroke prevention in AF: findings from the GLORIA-AF registry phase 2. *J Am Coll Cardiol* 2017;69:777–85.
23 Chan Y-H, Yen K-C, See L-C, *et al*. Cardiovascular, bleeding, and mortality risks of dabigatran in Asians with nonvalvular atrial fibrillation. *Stroke* 2016;47:441–9.
24 Contreras Muruaga MDM, Vivancos J, Reig G, *et al*. Satisfaction, quality of life and perception of patients regarding burdens and benefits of vitamin K antagonists compared with direct oral anticoagulants in patients with nonvalvular atrial fibrillation. *J Comp Eff Res* 2017;6:303–12.
25 Cha M-J, Choi E-K, Han K-D, *et al*. Effectiveness and safety of non-vitamin K antagonist oral anticoagulants in Asian patients with atrial fibrillation. *Stroke* 2017;48:3040–8.
26 Monz BU, Connolly SJ, Korhonen M, *et al*. Assessing the impact of dabigatran and warfarin on health-related quality of life: results from an RE-LY sub-study. *Int J Cardiol* 2013;168:2540–7.
27 Kooistra HAM, Piersma-Wichers M, Kluin-Nelemans HC, *et al*. Impact of vitamin K antagonists on quality of life in a prospective cohort of 807 atrial fibrillation patients. *Circ Cardiovasc Qual Outcomes* 2016;9:388–94.
28 Escobar C, Barrios V, Prieto L, *et al*. Perception of patients regarding burdens and benefits of vitamin K antagonists among patients with nonvalvular atrial fibrillation. *Cardiovasc Hematol Agents Med Chem* 2018;16:106–13.
29 De Caterina R, Brüggenjürgen B, Darius H, *et al*. Quality of life and patient satisfaction in patients with atrial fibrillation on stable vitamin K antagonist treatment or switched to a non-vitamin K antagonist oral anticoagulant during a 1-year follow-up: a PREFER in AF registry substudy. *Arch Cardiovasc Dis* 2018;111:74–84.
30 Suárez Fernández C, Castilla-Guerra L, Cantero Hinojosa J, *et al*. Satisfaction with oral anticoagulants in patients with atrial fibrillation. *Patient Prefer Adherence* 2018;12:267–74.
31 Benzimra M, Bonnamour B, Duracinsky M, *et al*. Real-life experience of quality of life, treatment satisfaction, and adherence in patients receiving oral anticoagulants for atrial fibrillation. *Patient Prefer Adherence* 2018;12:79–87.
32 Larochelle J, Brais C, Blais L, *et al*. Patients' perception of newly initiated oral anticoagulant treatment for atrial fibrillation: an observational study. *J Gen Intern Med* 2018;33:1239–41.
33 Heidorn K, Haenschke J, Lindner T, *et al*. Health economic analysis of thromboprophylaxis with rivaroxaban and certoparin-sodium in patients after total hip or knee replacement. *Int J Orthop* 2014;1:15–18.
34 Keita I, Aubin-Auger I, Lalanne C, *et al*. Assessment of quality of life, satisfaction with anticoagulation therapy, and adherence to treatment in patients receiving long-course vitamin K antagonists or direct oral anticoagulants for venous thromboembolism. *Patient Prefer Adherence* 2017;11:1625–34.