Treatment Satisfaction and Convenience for Patients With Atrial Fibrillation on Edoxaban or Vitamin K Antagonists After Transcatheter Aortic Valve Replacement: A Post Hoc Analysis from the ENVISAGE-TAVI AF Trial

Christian Hengstenberg, MD[a,*], Nicolas M. Van Mieghem, MD, PhD[b], Rosa Wang, MHA[c], Xiaomei Ye, MS[d], Ling Shi, PhD[d], Shien Guo, PhD[d], Cathy Chen, MD[c], James Jin, PhD[c], Xin Ye, PhD[c], George Dangas, MD, PhD[e,f], and Martin Unverdorben, MD, PhD[c]

ENVISAGE-TAVI AF (Edoxaban versus Standard of Care and Their Effects on Clinical Outcomes in Patients Having Undergone Transcatheter Aortic Valve Implantation−Atrial Fibrillation; NCT02943785) was a prospective, randomized, open-label trial comparing non−vitamin K oral anticoagulant (NOAC) edoxaban with vitamin K antagonists (VKAs) in patients with atrial fibrillation after successful transcatheter aortic valve replacement (TAVR). The effect of edoxaban- or VKA-based therapy on patient-reported outcomes remains unknown, as most studies focus on efficacy and safety. Pre-TAVR patient-reported expectations and post-TAVR Treatment Satisfaction and Convenience with edoxaban or VKA treatment (at months 3 and 12) were analyzed using the Perception of Anticoagulation Treatment Questionnaire (PACT-Q). This analysis included randomized and dosed patients with an evaluable PACT-Q1 assessment at baseline and ≥1 postbaseline assessment (PACT-Q2). Subanalyses included patients stratified by pre-TAVR anticoagulant (NOAC, VKA, no NOAC/VKA). Edoxaban- (n = 585) and VKA-treated (n = 522) patients had similar baseline characteristics and treatment expectations. Pre-TAVR anticoagulant use did not affect treatment expectations. After TAVR, edoxaban-treated patients had significantly higher Treatment Satisfaction and Convenience scores compared with VKA-treated patients at all time points (p <0.001 for all). Among edoxaban-treated patients, those who received VKAs pre-TAVR were significantly more satisfied with treatment than those who received NOACs (p <0.001) or no NOACs/VKAs (p = 0.003); however, there was no significant difference in the perception of convenience (p = 0.927 and p = 0.092, respectively). Conversely, among VKA-treated patients, the type of anticoagulant used pre-TAVR did not affect Treatment Satisfaction or Convenience scores post-TAVR. In conclusion, patients with atrial fibrillation who received edoxaban post-TAVR reported significantly higher Treatment Satisfaction and Convenience scores compared with those who received VKAs, resulting in a clinically meaningful difference between treatment groups. **(Am J Cardiol 2023;209:212−219)**

Keywords: atrial fibrillation, edoxaban, TAVR, treatment satisfaction

Approximately 1/3 of patients who underwent transcatheter aortic valve replacement (TAVR) require chronic oral anticoagulation because of atrial fibrillation (AF).[1−7] While there are many clinical studies on oral anticoagulants in patients with AF after TAVR, they primarily evaluate efficacy and safety.[8−10] Patient-reported assessments assist physicians in understanding specific treatment impacts on patient well-being and potential treatment influence on factors such as medication adherence and persistence. Previous anticoagulation patient-reported outcomes analyses used the Perception of Anticoagulation Treatment Questionnaire (PACT-Q) to measure expectations of and satisfaction with anticoagulation treatment.[11−15] Overall, patients with AF were satisfied with their anticoagulation therapy; however, patients receiving non−vitamin K oral anticoagulants

[a]Division of Cardiology, Department of Internal Medicine II, Vienna General Hospital, Medical University, Vienna, Austria; [b]Department of Cardiology, Erasmus University Medical Centre, Thoraxcenter, Rotterdam, The Netherlands; [c]Daiichi Sankyo, Inc., Basking Ridge, New Jersey; [d]Clinical Outcomes Analytics, Evidera PPD, LLC, Bethesda, Maryland; [e]Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai Hospital, New York, New York; and [f]School of Medicine, National and Kapodistrian University of Athens, Athens, Greece. Manuscript received June 7, 2023; revised manuscript received and accepted September 24, 2023.

Funding: This study was funded by Daiichi Sankyo, Inc. (Basking Ridge, New Jersey).

See page 218 for Declaration of Competing Interest.

*Corresponding author: Tel: +43 (0)1 40400-46140; fax: +43 (0)1 40400-42160.

E-mail address: christian.hengstenberg@meduniwien.ac.at (C. Hengstenberg).

https://doi.org/10.1016/j.amjcard.2023.09.091

(NOACs) reported better quality of life than those receiving vitamin K antagonists (VKAs).[14] In recent real-world studies of patients with AF or venous thromboembolism, those receiving NOACs versus VKAs had significantly higher ($p < 0.001$) Treatment Satisfaction and Convenience scores, as reported by the PACT-Q.[13,15] However, these studies did not include patients with AF after TAVR. This post hoc analysis of the ENVISAGE-TAVI AF (Edoxaban versus Standard of Care and Their Effects on Clinical Outcomes in Patients Having Undergone Transcatheter Aortic Valve Implantation−Atrial Fibrillation; NCT02943785) trial assessed patient-reported Treatment Satisfaction and Convenience in patients with AF treated with edoxaban or VKAs after successful TAVR.

Methods

ENVISAGE-TAVI AF was a global, prospective, randomized, controlled, open-label, multicenter, adjudicator-masked trial that compared the efficacy and safety of edoxaban with VKAs in patients with prevalent or incident AF after successful TAVR.[16,17] The study design of the ENVISAGE-TAVI AF trial is published.[16] Adults with prevalent or incident AF indicated for chronic oral anticoagulation after successful TAVR were eligible. The trial was conducted in accordance with the Declaration of Helsinki, the International Conference on Harmonisation-Good Clinical Practice, and all applicable local laws and regulations pertaining to clinical research. All patients provided written informed consent before enrollment. Patients were enrolled from April 2017 through January 2020.

Patients were randomized 12 hours to 7 days after TAVR in a 1:1 ratio to receive edoxaban 60 mg once daily or a VKA. The edoxaban dose was adjusted to 30 mg once daily if ≥1 criteria were met: (1) creatinine clearance rate (Cockcroft-Gault formula) 15 to ≤50 ml/min, (2) body weight ≤60 kg, or (3) use of certain *P*-glycoprotein inhibitors (the latter 2 criteria applied only to non-US patients).[17] The target international normalized ratio for VKA-treated patients was 2.0 to 3.0 (1.6 to 2.6 for patients ≥70 years of age in Japan).

Patients who received ≥1 dose of edoxaban or a VKA after TAVR, had evaluable PACT-Q1 data at baseline, and had ≥1 postbaseline PACT-Q2 assessment were included in the PACT-Q analysis set. Evaluable patients in this analysis set included those with ≥50% of items completed in all PACT-Q assessments.

The PACT-Q is a validated patient-reported outcomes instrument used to assess patients' expectations, satisfaction, and perceived convenience with their anticoagulant treatment with 2 modules. The PACT-Q1 module assessed patient expectations relating to anticoagulation therapy before treatment initiation and consists of 7 items (each scored from 1 to 5). For the items "confidence in prevention of blood clots" (A1), "expectations of symptom relief" (A2), "importance of use" (A4), and "importance of managing medication independently" (A6), a higher score corresponds to higher expectations. Conversely, lower scores on "expectations of side effects" (A3), "worries about making mistakes" (A5), and "worries about cost" (A7) correspond to higher expectations.[11]

The PACT-Q2 module assessed patients at all postbaseline visits (months 3 and 12): "Convenience" (11 items), "Burden of Disease and Treatment" (2 items), and "Treatment Satisfaction" (7 items). "Convenience" and "Burden of Disease and Treatment" were combined to form the Convenience dimension, and Treatment Satisfaction constituted its own dimension. All Convenience and Treatment Satisfaction dimension items were answered on a 5-point Likert scale (scored from 1 to 5). The sum of the dimension items was calculated and rescaled to a score ranging from 0 to 100. Higher scores in either dimension indicated a better patient-reported outcome (i.e., the treatment was more convenient and less burdensome, and/or the patient was more satisfied with the anticoagulation treatment).

Baseline demographic and clinical characteristics were assessed by the treatment arm based on the PACT-Q analysis set. PACT-Q1 scores and the type of anticoagulant used before TAVR (pre-TAVR anticoagulant) were recorded at baseline. PACT-Q1 results were evaluated for the total population, stratified by type of pre-TAVR anticoagulant, and stratified by assigned study treatment. Patients in each treatment arm were assessed using the PACT-Q2 at months 3 and 12 after TAVR (or at the end of treatment, whichever came first). Clinical outcomes by PACT-Q2 were also assessed in patients receiving edoxaban or a VKA.

For baseline demographic and disease characteristics, continuous variables were summarized as mean ± standard deviation, whereas categorical variables were summarized as relative frequencies. Descriptive statistics for PACT-Q scores were summarized by the treatment arm based on the PACT-Q analysis set.

Linear mixed model repeated measures analyses evaluated differences in PACT-Q2 Treatment Satisfaction and Convenience dimension scores between edoxaban- and VKA-treated patients at months 3 and 12. Fixed effect covariates in the mixed model included treatment arm, time, stratification factors, and treatment-arm-by-visit interaction. The least squares mean difference (LSMD) estimated the difference between treatment arms. The overall treatment effect across months 3 and 12 was calculated as the average of the least square mean scores across all visits. Cohen's effect size evaluated whether differences could be labeled as clinically meaningful. It was defined as ≥0.2 based on a common distribution-based threshold for determining minimal clinically important differences. Additional subgroup analyses investigated differences in PACT-Q1 and PACT-Q2 scores stratified by the type of anticoagulant used before TAVR.

Results

Of patients (N = 1,426) enrolled in the ENVISAGE-TAVI AF trial, 1,107 (response rate, 77.6%; edoxaban, n = 585; VKA, n = 522) had evaluable PACT-Q data and were included in this analysis (Figure 1). Baseline demographic and clinical characteristics were similar between treatment arms (Table 1). The mean patient age was 81.9 years, and 53.8% were male. The mean CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age ≥75 [doubled], Diabetes, Stroke [doubled], Vascular disease, Age 65 to 74 years, and Sex category) score was 4.5; the mean HAS-BLED

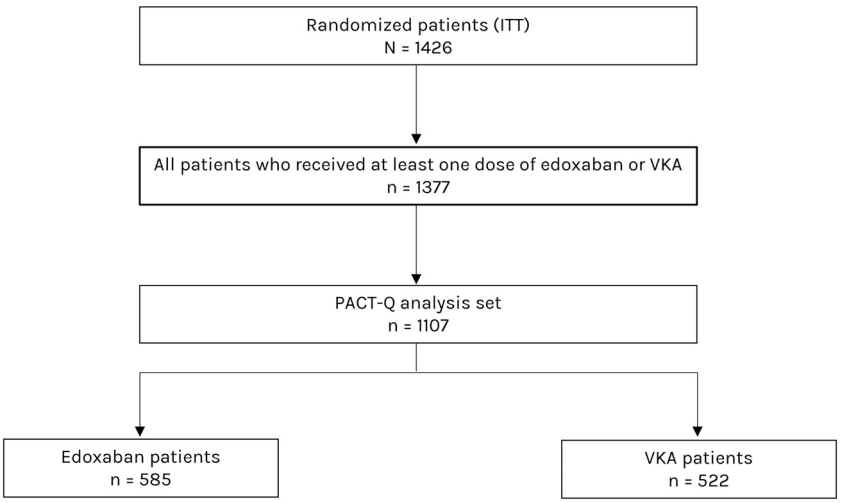


Figure 1. Patient disposition. ITT = intention-to-treat. PACT-Q = Perception Anticoagulant Treatment Questionnaire; VKA = vitamin K antagonist

(Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs/alcohol concomitantly) score was 1.6. Baseline PACT-Q1 scores were comparable between edoxaban- and VKA-treated patients (Table 1).

Patients had similar treatment expectations at baseline, regardless of the anticoagulant they received before TAVR (Figure 2). Overall, the 2 items with the highest scores were "importance of ease of use" (item A4; mean [95% confidence interval (CI)] 4.14 [4.08 to 4.20]) and "importance of managing medication independently" (item A6; mean [95% CI] 3.91 [3.84 to 3.98]; Figure 2). There were no significant differences between pre-TAVR anticoagulant groups, except edoxaban-treated patients who received NOACs before their TAVR reported higher expectations of symptom relief (item A2; i.e., leg pain or swelling, palpitations, shortness of breath, or chest pain) compared with those who previously received VKAs or no NOACs/VKAs ($p = 0.02$). VKA-treated patients who also received a VKA before TAVR reported higher confidence in the prevention of blood clots (item A1) compared with those who previously received NOACs or no NOACs/VKAs ($p = 0.05$).

Patients who received edoxaban versus VKAs after TAVR had significantly higher Treatment Satisfaction scores at months 3 and 12 and Convenience scores at month 12 ($p < 0.001$ for all; Figure 3). In the mixed model analysis, patients who received edoxaban had significantly higher overall scores compared with VKA-treated patients for Treatment Satisfaction (LSMD [95% CI], 6.1 [4.5 to 7.7]; $p < 0.001$) and Convenience (LSMD [95% CI], 6.9 [5.3 to 8.6]; $p < 0.001$; Figure 4). At month 3, scores for Treatment Satisfaction (LSMD [95% CI], 5.7 [3.9 to 7.5]; $p < 0.001$) and Convenience (LSMD [95% CI], 6.3 [4.6 to 8.1]; $p < 0.001$; Figure 4) were significantly higher in patients receiving edoxaban versus VKA; these differences were clinically meaningful (Treatment Satisfaction: effect size [95% CI], 0.4 [0.3 to 0.5]; Convenience: effect size [95% CI], 0.5 [0.3 to 0.6]). A similar difference was observed at month 12 ($p < 0.001$; Figure 4).

The LSMD (95% CI) edoxaban Treatment Satisfaction scores increased significantly from month 3 (67.6 [66.4 to 68.8]) to month 12 (70.1 [68.7 to 71.6]; $p = 0.02$); LSMD (95% CI) VKA Treatment Satisfaction scores also increased significantly from month 3 (61.7 [60.4 to 63.0]) to month 12 (64.6 [62.9 to 66.3]; $p = 0.01$). There was no statistically significant difference in Convenience within edoxaban-treated patients ($p = 0.07$) or VKA-treated patients ($p = 0.9$) across time points.

Compared with patients receiving a VKA after TAVR, patients receiving edoxaban after TAVR had significantly higher Treatment Satisfaction scores, regardless of pre-TAVR anticoagulant use (for pre-TAVR NOACs [$p = 0.007$]; for pre-TAVR VKAs [$p < 0.001$], and for no pre-TAVR NOACs/VKAs [$p = 0.001$]; Figure 5). Among patients treated with edoxaban after TAVR, those who received a VKA before TAVR were more satisfied with treatment than patients who previously received NOACs (LSMD [95% CI], 6.13 [3.53 to 8.73]; $p < 0.001$) or no NOACs/VKAs (LSMD [95% CI], 3.96 [1.33 to 6.59]; $p = 0.003$; Supplementary Figure 1). No statistically significant differences in Treatment Satisfaction were observed within the VKA arm across pre-TAVR anticoagulant groups (Supplementary Figure 1).

Patients receiving edoxaban after TAVR found treatment significantly more convenient, regardless of the type of pre-TAVR anticoagulant, compared with those receiving a VKA after TAVR ($p < 0.001$ for all; Figure 5). In both treatment arms, a trend of higher treatment Convenience was observed in patients who received pre-TAVR VKAs and pre-TAVR NOACs compared with no pre-TAVR NOACs/ VKAs (Supplementary Figure 1). No statistically significant differences in Convenience dimension scores were observed within either treatment group across patients who received pre-TAVR NOACs, pre-TAVR VKAs, or no pre-TAVR NOACs/VKAs (Supplementary Figure 1).

Discussion

In this analysis from the ENVISAGE-TAVI AF trial, patient-reported treatment expectations, satisfaction, and convenience were assessed in patients with AF treated with

Table 1
Baseline demographics and clinical characteristics

Variables	Edoxaban (n = 585)	VKA (n = 522)	Overall (N = 1107)
Age, years*	82.1 ± 5.3	81.7 ± 5.5	81.9 ± 5.4
Sex			
Male	305 (52.1%)	289 (55.4%)	594 (53.7%)
Female	280 (47.9%)	233 (44.6%)	513 (46.3%)
Race			
Asian	81 (13.8%)	77 (14.8%)	158 (14.3%)
Black or African American	1 (0.2%)	1 (0.2%)	2 (0.2%)
Other†	11 (1.9%)	12 (2.3%)	23 (2.1%)
White	484 (82.7%)	430 (82.4%)	914 (82.6%)
Missing	8 (1.4%)	2 (0.4%)	10 (0.95%)
Geographic region			
Asia	80 (13.7%)	75 (14.4%)	155 (14.0%)
Europe	432 (73.8%)	383 (73.4%)	815 (73.6%)
US/Canada	73 (12.5%)	64 (12.3%)	137 (12.4%)
Body mass index, kg/m^2*	27.5 ± 5.5	27.9 ± 5.6	
Indication for dose adjustment‡	272 (46.5%)	240 (46.0%)	512 (46.3%)
Creatinine clearance rate*,§	57.9 ± 23.7	59.8 ± 24.7	58.8 ± 24.2
Congestive heart failure	483 (82.6%)	449 (86.0%)	932 (84.2%)
History of stroke	101 (17.3%)	92 (17.6%)	193 (17.4%)
Diabetes mellitus	218 (37.3%)	195 (37.4%)	413 (37.3%)
Hypertension	528 (90.3%)	474 (90.8%)	1002 (90.5%)
CHA_2DS_2-VASc*	4.5 ± 1.4	4.5 ± 1.3	4.5 ± 1.4
HAS-BLED*	1.6 ± 0.8	1.6 ± 0.8	1.6 ± 0.8
Atrial fibrillation category			
Paroxysmal	248 (42.4%)	227 (43.5%)	475 (42.9%)
Persistent	67 (11.5%)	55 (10.5%)	122 (11.0%)
Long-standing persistent	47 (8.0%)	39 (7.5%)	86 (7.8%)
Permanent	219 (37.4%)	190 (36.4%)	409 (36.9%)
Atrial flutter with no plan to proceed with ablation therapy	4 (0.7%)	10 (1.9%)	14 (1.3%)
Pre-TAVR anticoagulant			
NOAC	172 (29.4%)	133 (25.5%)	305 (27.5%)
VKA	247 (42.2%)	258 (49.4%)	505 (45.6%)
No NOAC/VKA	166 (28.4%)	131 (25.1%)	296 (26.7%)
PACT-Q1 item scores*,‖			
A1, confidence in prevention of blood clots	3.8 ± 1.0	3.8 ± 1.0	3.8 ± 1.0
A2, expectations of symptom relief	3.0 ± 1.2	2.8 ± 1.2	2.9 ± 1.2
A3, expectations of side effects	2.6 ± 1.1	2.7 ± 1.2	2.6 ± 1.1
A4, importance of ease of use	4.2 ± 0.9	4.1 ± 1.0	4.1 ± 1.0
A5, worries about making mistakes	2.1 ± 1.3	2.3 ± 1.3	2.2 ± 1.3
A6, importance of managing medication independently	4.0 ± 1.1	3.8 ± 1.2	3.9 ± 1.2
A7, worries about cost	2.5 ± 1.4	2.5 ± 1.4	2.5 ± 1.4

Data presented as n (%) unless otherwise noted.

* Values are mean ± standard deviation.

† Includes patients of another race and those who chose not to report race.

‡ Indications for adjustment of the edoxaban dose included a creatinine clearance of ≤50 ml/min, a body weight of ≤60 kg (not used as an indication in US patients), and concomitant therapy with a *P*-glycoprotein inhibitor (not used as an indication in US patients).

§ Cockcroft-Gault formula.

‖ Scored on a 5-point scale. For items A1, A2, A4, and A6, higher scores indicate higher expectations for treatment; for items A3, A5, and A7, lower scores indicate higher treatment expectations.

CHA_2DS_2-VASc = Congestive heart failure, Hypertension, Age ≥75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65 to 74 years, and Sex category; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drug/alcohol concomitantly; NOAC = non−vitamin K oral anticoagulant; PACT-Q = Perception Anticoagulant Treatment Questionnaire; TAVR = transcatheter aortic valve replacement; VKA = vitamin K antagonist.

edoxaban or VKAs after successful TAVR. At baseline, patients had moderate to high expectations for their anticoagulant treatment (mean baseline response to A4 and A6 ≥4), regardless of assigned study treatment (edoxaban or VKA). Over the 12-month follow-up, patients treated with edoxaban after TAVR reported higher Treatment Satisfaction and Convenience scores when compared with VKA-treated patients.

Overall, patients had similar treatment expectations at baseline regardless of their pre-TAVR anticoagulant experience. In patients treated with edoxaban after TAVR, those who received pre-TAVR VKAs had significantly higher Treatment Satisfaction compared with patients who received pre-TAVR NOACs or no pre-TAVR NOACs/VKAs; this difference was not observed in those treated with VKAs after TAVR. There was no significant effect of

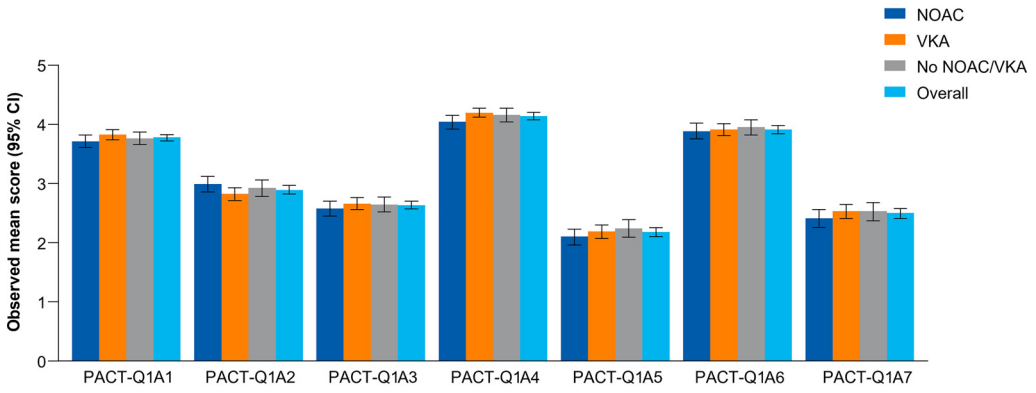


Figure 2. PACT-Q1 scores at baseline stratified by pre-TAVR anticoagulant. For items A1, A2, A4, and A6, the higher the score, the higher the patient's expectations for their treatment; for items A3, A5, and A7, the lower the score, the higher the expectations for their treatment. CI = confidence interval; NOAC = non-vitamin K oral anticoagulant; PACT-Q = Perception Anticoagulant Treatment Questionnaire; TAVR = transcatheter aortic valve replacement; VKA = vitamin K antagonist.

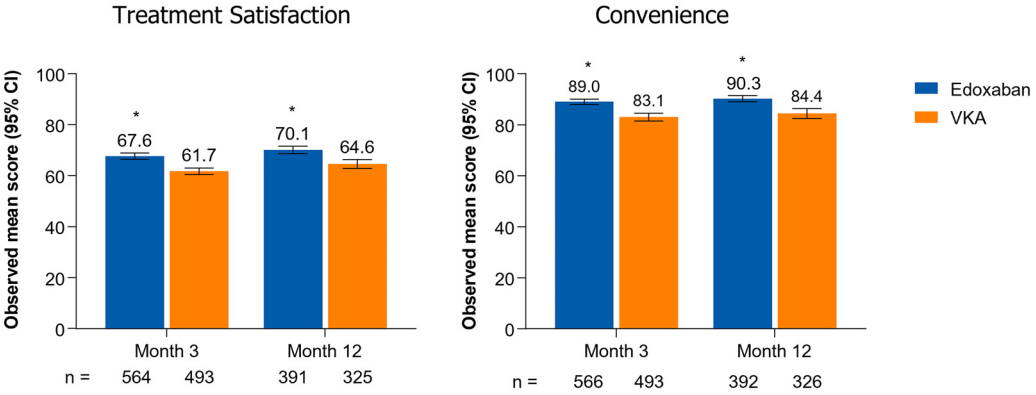


Figure 3. PACT-Q2 observed mean scores for Treatment Satisfaction and Convenience. *p <0.001 for edoxaban versus VKA. CI = confidence interval; PACT-Q = Perception Anticoagulant Treatment Questionnaire; VKA = vitamin K antagonist.

pre-TAVR anticoagulant on perceived treatment Convenience post-TAVR in either the edoxaban or VKA group.

Suboptimal adherence to oral anticoagulants, whether VKAs or NOACs, among patients with AF may negatively affect clinical outcomes.[18,19] In this study, patients with AF receiving edoxaban had higher Treatment Satisfaction and Convenience compared with patients receiving VKAs. Previous studies that explored if Treatment Satisfaction, Convenience, and adherence were connected found that higher Treatment Satisfaction and Convenience are associated with better treatment adherence, while experiencing adverse events and being dissatisfied with treatment were associated with lower adherence.[20,21] These results suggest an overall improved patient experience that may have clinical implications for treatment adherence and event rates in patients with AF receiving edoxaban versus VKA treatment after successful TAVR.

While there were no significant differences in Treatment Satisfaction or Convenience in VKA-treated patients based on the type of anticoagulant used before TAVR, these patients reported their treatment as less convenient than patients treated with edoxaban after TAVR. More patients

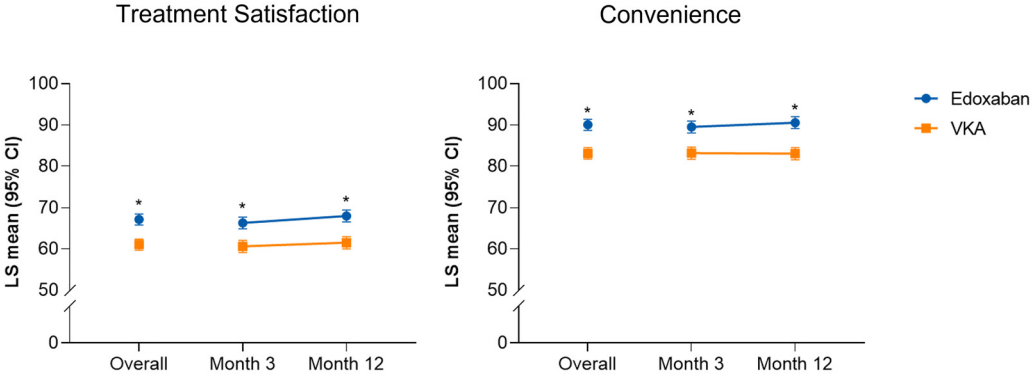
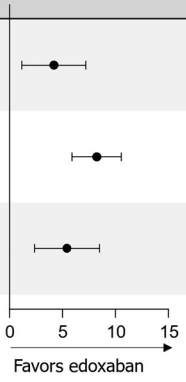


Figure 4. LS mean difference in the Treatment Satisfaction and Convenience dimension scores by time point. *p <0.001 for edoxaban versus VKA. CI = confidence interval; LS = least squares; VKA = vitamin K antagonist.

(a)

Pre-TAVR group	Edoxaban LS mean	VKA LS mean	LS mean difference (95% CI)	p-value
Pre-TAVR NOAC	65.07	60.88	4.19 (1.17, 7.21)	0.007
Pre-TAVR VKA	71.20	62.96	8.24 (5.90, 10.57)	<0.001
No pre-TAVR NOAC or VKA	67.24	61.81	5.43 (2.37, 8.49)	0.001



(b)

Pre-TAVR group	Edoxaban LS mean	VKA LS mean	LS mean difference (95% CI)	p-value
Pre-TAVR NOAC	90.29	82.96	7.33 (4.22, 10.45)	<0.001
Pre-TAVR VKA	90.17	83.34	6.83 (4.42, 9.23)	<0.001
No pre-TAVR NOAC or VKA	87.84	80.97	6.86 (3.71, 10.02)	<0.001

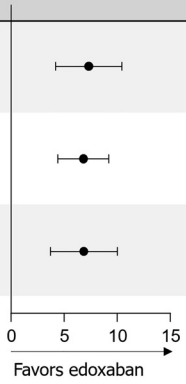


Figure 5. Overall LS mean in PACT-Q2 by pre-TAVR anticoagulant for the (*A*) Treatment Satisfaction and (*B*) Convenience dimensions. LS mean and p-values are estimated using MMRM models to calculate the between pre-TAVR group difference in LS mean within each treatment arm. CI = confidence interval; LS = least squares; MMRM = mixed model repeated measures; NOAC = non-vitamin K oral anticoagulant; PACT-Q = Perception Anticoagulant Treatment Questionnaire; TAVR = transcatheter aortic valve replacement; VKA = vitamin K antagonist.

in ENVISAGE-TAVI AF who received VKAs after TAVR discontinued treatment (40.5%) compared with those who received edoxaban (30.2%), suggesting that these patients were possibly driven to stop their VKA treatment, at least in part, by treatment inconvenience.[17] Among patients receiving edoxaban after TAVR, those previously taking a VKA or NOAC before the procedure found treatment numerically more convenient than those with no previous NOAC or VKA use. In patients treated with VKAs after TAVR, there was no difference in perceived treatment convenience between patients who used NOACs or VKAs pre-TAVR; patients who received VKAs before the procedure were more satisfied with post-TAVR VKA therapy when compared with patients who previously used NOACs or did not use NOACs/VKAs.

A major difference between VKAs and NOACs is that VKAs may require regular monitoring and multiple dose adjustments to ensure the patient's international normalized ratio stays within the therapeutic range.[22–26] Besides discontinuing treatment at a lower rate, significantly more patients with AF receiving edoxaban ($p < 0.001$) were not bothered by their anticoagulant treatment compared with patients receiving a VKA. Furthermore, significantly more patients in the edoxaban arm ($p < 0.001$) reported "Not at all" in difficulty for dose adjustment compared with those in the VKA arm. Those receiving edoxaban were significantly more satisfied ($p < 0.001$) with the form of anticoagulant treatment compared with those receiving a VKA across visits. In a recent observational epidemiological study, patients with AF receiving NOACs (dabigatran, rivaroxaban, or apixaban) reported significantly higher Treatment Satisfaction and Convenience on the PACT-Q2 assessment compared with patients receiving VKAs ($p < 0.01$ for both); higher satisfaction did not correlate with improved health-related quality of life, which may be influenced by a wide range of factors.[13] In a separate cross-sectional study of 208 patients with AF or venous thromboembolism on long-term anticoagulation therapy, patients receiving NOACs were significantly more satisfied with the treatment (as assessed by the PACT-Q2) than patients receiving warfarin ($p = 0.004$); Convenience scores were not significantly different between groups ($p = 0.2$).[15] Overall, the significantly higher and clinically meaningful (effect size >0.2) Treatment Satisfaction among patients receiving post-TAVR edoxaban versus VKAs in the current analysis from the ENVISAGE-TAVI AF trial is consistent with data from recent studies that compared NOAC and VKA use.

The randomized design of the ENVISAGE-TAVI AF trial may make it difficult to apply the results of this analysis to the general population of patients with AF in the real world. These patient-reported outcomes data are from a population of older adults with AF who underwent TAVR with intermediate and high surgical risk. Additionally, patients who did not want to change their anticoagulant post-TAVR may have chosen not to participate in this trial and, therefore, are not represented by the current data. Furthermore, patient-reported outcomes assessments are often difficult for patients with disabilities or low literacy skills, and these patients may not be fully represented in the evaluable population. Lastly, although the data from patient-reported outcomes analyses (i.e., data collected directly from patients) are subjective data and not objective data, patient-reported outcomes are considered valuable because they provide insights into the patient's perspective, which can be different from the observations made by healthcare professionals. As seen in the literature, patients receiving a direct oral anticoagulant had higher Satisfaction with their treatment, more improved quality of life, and better treatment adherence compared with VKAs.[14,27] This post hoc analysis shows that regardless of clinical outcomes, patients with AF after TAVR on edoxaban have an improved patient experience compared with VKAs. It is important for physicians to consider these factors when deciding on patient-centered treatment options. Additionally, the PACT-Q2, which is used to assess patients' satisfaction with their anticoagulant treatment and their opinions about convenience of treatment use, is a validated and reliable instrument appropriate for use in clinical research.[11]

In conclusion, patients with AF who were treated with edoxaban after TAVR had higher Treatment Satisfaction scores and considered treatment significantly more convenient than those who received VKAs. The results of this analysis demonstrate that treatment with edoxaban is associated with an improved patient experience compared with VKAs and may encourage more physicians to consider these factors when weighing the advantages and disadvantages of potential treatments.

Declaration of Competing Interest

Dr. Hengstenberg is a clinical proctor for Edwards Lifesciences and Boston Scientific; reports payment for speaker bureaus and support for attending meetings from Daiichi Sankyo, Inc.; and reports advisory board participation for Daiichi Sankyo, Inc. Dr. Van Mieghem reports grants or contracts from Abbott; Abiomed; Boston Scientific; Daiichi Sankyo, Inc.; Edwards Lifesciences; Medtronic; PulseCath BV; and Siemens. Ms. Ye and Drs. Shi and Guo are employees of Evidera PPD, LLC. Ms. Wang and Drs. Chen, Jin, and Ye are employees of Daiichi Sankyo, Inc. Dr. Dangas reports research grants to institution and support for attending meetings from Bayer and Daiichi Sankyo, Inc., and consulting fees from Daiichi Sankyo, Inc. Dr. Unverdorben is an employee of Daiichi Sankyo, Inc.

Acknowledgment

Writing and editorial support were provided by Kimberly Dent-Ferguson, MBS, MPH, of AlphaBioCom, a Red Nucleus company, and funded by Daiichi Sankyo, Inc.

Authors' Contributions

Christian Hengstenberg: conceptualization, visualization, methodology, investigation, writing – review & editing; Nicolas Van Mieghem: conceptualization, visualization, methodology, investigation, writing – review & editing; Rosa Wang: conceptualization, visualization, methodology, investigation, writing – original draft, data curation, formal analysis, investigation; Xiaomei Ye, Ling Shi, Shien Guo, and James Jin: methodology, software, validation, writing – review & editing; Cathy Chen: conceptualization, visualization, methodology, investigation, writing – review & editing; George Dangas: conceptualization, visualization, methodology, investigation, writing – review & editing; Martin Unverdorben: conceptualization, visualization, methodology, investigation, writing – review & editing, supervision.

Data Availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.09.091.

1. Adams DH, Popma JJ, Reardon MJ, Yakubov SJ, Coselli JS, Deeb GM, Gleason TG, Buchbinder M, Hermiller J Jr, Kleiman NS, Chetcuti S, Heiser J, Merhi W, Zorn G, Tadros P, Robinson N, Petrossian G, Hughes GC, Harrison JK, Conte J, Maini B, Mumtaz M, Chenoweth S, Oh JK, U.S. CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790–1798.
2. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S, PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–1607.
3. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ, PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–2198.
4. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG, PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–1620.
5. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP, SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321–1331.

6. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR, PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695–1705.
7. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL 3rd, Forrest JK, Tchétché D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ, Evolut Low Risk Trial Investigators. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;380:1706–1715.
8. Eikelboom JW, Connolly SJ, Hart RG, Wallentin L, Reilly P, Oldgren J, Yang S, Yusuf S. Balancing the benefits and risks of 2 doses of dabigatran compared with warfarin in atrial fibrillation. *J Am Coll Cardiol* 2013;62:900–908.
9. Fox KA, Piccini JP, Wojdyla D, Becker RC, Halperin JL, Nessel CC, Paolini JF, Hankey GJ, Mahaffey KW, Patel MR, Singer DE, Califf RM. Prevention of stroke and systemic embolism with rivaroxaban compared with warfarin in patients with non-valvular atrial fibrillation and moderate renal impairment. *Eur Heart J* 2011;32:2387–2394.
10. Giugliano RP, Ruff CT, Braunwald E, Murphy SA, Wiviott SD, Halperin JL, Waldo AL, Ezekowitz MD, Weitz JI, Špinar J, Ruzyllo W, Ruda M, Koretsune Y, Betcher J, Shi M, Grip LT, Patel SP, Patel I, Hanyok JJ, Mercuri M, Antman EM, ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med* 2013;369:2093–2104.
11. Prins MH, Guillemin I, Gilet H, Gabriel S, Essers B, Raskob G, Kahn SR. Scoring and psychometric validation of the Perception of Anticoagulant Treatment Questionnaire (PACT-Q). *Health Qual Life Outcomes* 2009;7:30.
12. Prins MH, Marrel A, Carita P, Anderson D, Bousser MG, Crijns H, Consoli S, Arnould B. 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.
13. Benzimra M, Bonnamour B, Duracinsky M, Lalanne C, Aubert JP, Chassany O, Aubin-Auger I, Mahé I. 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.
14. Keita I, Aubin-Auger I, Lalanne C, Aubert JP, Chassany O, Duracinsky M, Mahé I. 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;11:1625–1634.
15. Ng DL, Gan GG, Chai CS, Chee KH, Tan KL, Tan SB, Bee PC. Comparing quality of life and treatment satisfaction between patients on warfarin and direct oral anticoagulants: a cross-sectional study. *Patient Prefer Adherence* 2019;13:1363–1373.
16. Van Mieghem NM, Unverdorben M, Valgimigli M, Mehran R, Boersma E, Baber U, Hengstenberg C, Shi M, Chen C, Saito S, Veltkamp R, Vranckx P, Dangas GD. Edoxaban versus standard of care and their effects on clinical outcomes in patients having undergone transcatheter aortic valve implantation in atrial fibrillation-rationale and design of the ENVISAGE-TAVI AF trial. *Am Heart J* 2018;205:63–69.
17. Van Mieghem NM, Unverdorben M, Hengstenberg C, Möllmann H, Mehran R, López-Otero D, Nombela-Franco L, Moreno R, Nordbeck P, Thiele H, Lang I, Zamorano JL, Shawl F, Yamamoto M, Watanabe Y, Hayashida K, Hambrecht R, Meincke F, Vranckx P, Jin J, Boersma E, Rodés-Cabau J, Ohlmann P, Capranzano P, Kim HS, Pilgrim T, Anderson R, Baber U, Duggal A, Laeis P, Lanz H, Chen C, Valgimigli M, Veltkamp R, Saito S, Dangas GD, ENVISAGE-TAVI AF Investigators. Edoxaban versus vitamin K antagonist for atrial fibrillation after TAVR. *N Engl J Med* 2021;385:2150–2160.
18. Shehab A, Bhagavathula AS, Abebe TB, Abegaz TM, Elnour AA, Sabbour HM, Uzzafer M, Hersi A, Hamad AK. Patient adherence to novel oral anticoagulants (NOACs) for the treatment of atrial fibrillation and occurrence of associated bleeding events: a systematic review and meta-analysis. *Curr Vasc Pharmacol* 2019;17:341–349.
19. Wang Y, Kong MC, Lee LH, Ng HJ, Ko Y. Knowledge, satisfaction, and concerns regarding warfarin therapy and their association with warfarin adherence and anticoagulation control. *Thromb Res* 2014;133:550–554.
20. Barbosa CD, Balp MM, Kulich K, Germain N, Rofail D. A literature review to explore the link between treatment satisfaction and adherence, compliance, and persistence. *Patient Prefer Adherence* 2012;6:39–48.
21. Berhe DF, Taxis K, Haaijer-Ruskamp FM, Mulugeta A, Mengistu YT, Burgerhof JGM, Mol PGM. Impact of adverse drug events and treatment satisfaction on patient adherence with antihypertensive medication - a study in ambulatory patients. *Br J Clin Pharmacol* 2017;83:2107–2117.
22. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke* 1991;22:983–988.
23. Chugh SS, Blackshear JL, Shen WK, Hammill SC, Gersh BJ. Epidemiology and natural history of atrial fibrillation: clinical implications. *J Am Coll Cardiol* 2001;37:371–378.
24. Wilke T, Groth A, Mueller S, Pfannkuche M, Verheyen F, Linder R, Maywald U, Bauersachs R, Breithardt G. Incidence and prevalence of atrial fibrillation: an analysis based on 8.3 million patients. *Europace* 2013;15:486–493.
25. Casais P, Meschengieser SS, Sanchez-Luceros A, Lazzari MA. Patients' perceptions regarding oral anticoagulation therapy and its effect on quality of life. *Curr Med Res Opin* 2005;21:1085–1090.
26. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL, ESC Scientific Document Group. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021;42:373–498.
27. Afzal SK, Hasan SS, Babar ZU. A systematic review of patient-reported outcomes associated with the use of direct-acting oral anticoagulants. *Br J Clin Pharmacol* 2019;85:2652–2667.