

Clinical Study Synopsis for Public Disclosure

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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Pradaxa®			
Name of active ingredient: Dabigatran etexilate			
Report date: 27 June 2019	Study number: 1160-0286	Version/Revision: Version 1.0	Version/Revision date: 27 June 2019
Title of study:	Patients' Assessment of Satisfaction for Stroke Prevention in Atrial Fibrillation Impact of Conventional Oral Anticoagulant (OAC) Compared with Novel Oral Anticoagulant (NOAC)		
Keywords:	dabigatran etexilate, atrial fibrillation, patient satisfaction, real-world		
Rationale and background:	Non-interventional studies (NIS) observing patients treated with Pradaxa® for stroke prevention in atrial fibrillation (SPAF) to assess treatment satisfaction have not been conducted in Taiwan. Due to the limited data on patients' perception of conventional Vitamin K antagonist (VKA) or Pradaxa® treatment in real world experience (RWE), it remains an interesting topic to address. Therefore, the observational study was proposed to describe the perception of anticoagulant treatment according to the questionnaire—PACT-Q in the cohorts of patients switching from VKAs to Pradaxa® or newly initiating Pradaxa®/VKAs.		
Research question and objectives:	Objective 1 To describe the treatment perception from patients with non-valvular atrial fibrillation (NVAf) receiving Pradaxa® or VKA for stroke prevention by using the self-estimation questionnaire of PACT-Q during a 6-month study period Objective 2 To investigate the patient's characteristics		
Study design:	This non-interventional study enrolled patients in Taiwan with a previous VKA therapy, followed by switching to Pradaxa® OR patients being newly diagnosed with NVAF and initiated on Pradaxa® or VKA. The study was primarily based on questionnaire—PACT-Q.		
Setting:	It was planned to collect data of approximately 1,000 patients from approximately 20 medical centers or regional hospitals in Taiwan where Pradaxa® taken as one 110/150 mg capsule twice a day as the prescription of SPAF in hospital formulary. Patients diagnosed with NVAF before the patient's baseline (inclusion) visit were consecutively enrolled to minimize the selection bias in the real-world practice.		

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Patients were followed up over an observation period of 6 months. Data were collected at 3 time points during routine practice visits as below. No visit was conducted solely for study purposes. - Baseline (e.g., the enrollment date for Cohort A; the date of initiation on Pradaxa® or VKA for Cohort B). 0 to 45 days after baseline (initiation period). 150 to 210 days after baseline (continuation period).																	
Subjects and study size, including dropouts:		Planned: 1,000 subjects at the allocation as below. <table border="1"> <tr> <td>Cohort A—VKA switched to Pradaxa®</td> <td>300</td> </tr> <tr> <td rowspan="2">Cohort B—Newly initiator</td> <td>Pradaxa®</td> </tr> <tr> <td>VKA</td> </tr> <tr> <td></td> <td>200</td> </tr> </table> Actual: 1,315 subjects were enrolled and 1,252 were eligible for FAS: <table border="1"> <tr> <td>Cohort A—VKA switched to Pradaxa®</td> <td>139</td> </tr> <tr> <td rowspan="2">Cohort B*—Newly initiator</td> <td>Pradaxa®</td> </tr> <tr> <td>VKA</td> </tr> <tr> <td></td> <td>54</td> </tr> </table> *7 missing data in the Cohort B cannot be categorized into Pradaxa or VKA.		Cohort A —VKA switched to Pradaxa®	300	Cohort B —Newly initiator	Pradaxa®	VKA		200	Cohort A —VKA switched to Pradaxa®	139	Cohort B* —Newly initiator	Pradaxa®	VKA		54
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Variables and data sources:		Source data are collected from medical charts and the questionnaires (PACT-Q) completed by the enrolled subjects at approximately 20 medical centers or regional hospitals. A case report form will be designed for data collection. Primary outcome: <u>Cohort A</u> (patients switched from VKA to Pradaxa®) - Mean PACT-Q2 scores at the second (30-45 days) and the last assessment (150-210 days) compared to baseline assessment. <u>Cohort B</u> (patients newly initiated Pradaxa® or VKA) - Mean PACT-Q2 scores at the second (30-45 days) and the last assessment (150-210 days) compared between 2 treatment groups. Secondary outcome: <u>Cohort A</u> (patients switched from VKA to Pradaxa®) - Mean PACT-Q2 score at the last assessment (150-210 days) compared to the second assessment (30-45 days). <u>Cohort B</u> (patients newly initiated Pradaxa® or VKA) - Description of mean PACT-Q1 score at baseline. Characterization of patients from both cohorts according to:															

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	• Demographics: Age, gender, race, education level, height, weight, and BMI • Co-morbidities • Concomitant therapies • Stroke- and/or bleeding related risk factors in the medical history • CHA₂DS₂-VASc score • HAS-BLED score • Kidney function (creatinine clearance) • Dosing of Pradaxa® and the reasons for dose change • Duration of previous VKA treatment (for Cohort A only)		

Results:	Primary Endpoints <u>Cohort A (patients switched from VKA to Pradaxa®)</u> Treatment convenience was significantly increased by 5.0 ± 14.21 points at Day 30 – 45 and 7.7 ± 13.26 points at Day 150 – 210 ($P < 0.0001$ for both). Treatment satisfaction was significantly increased by 3.7 ± 14.33 points at Day 30 – 45 ($P = 0.0031$) and 7.0 ± 17.03 points at Day 150 – 210 ($P = 0.0001$). <u>Cohort B (patients newly initiated Pradaxa® or VKA)</u> Convenience was high overall, regardless of Pradaxa® or VKA treatment; however, it was noted that the score was slightly increased in long term for Pradaxa® users, but almost unchanged for VKA users over the treatment period. Overall, patients were very much satisfied with anticoagulation therapy, whether by Pradaxa or VKA. both of which demonstrated an increasing trend following 150 to 210 days of treatment. After propensity score matching, higher convenience (98.5 ± 2.18 points vs. 80.8 ± 9.79 points, respectively) and satisfaction (71.4 ± 0.00 points vs. 64.3 ± 2.02 points, respectively) scores were noted in the Pradaxa® cohort than the VKA cohort; however, due to the limited number of subjects, results should be interpreted with caution. Secondary Endpoints <u>Cohort A (patients switched from VKA to Pradaxa®)</u> An increase of 2.4 ± 8.10 points at Day 150 – 210 from Day 30 – 45 in the treatment convenience and an increase of 2.7 ± 15.03 points at Day 150 – 210 from Day 30 – 45 in the treatment satisfaction were noted. <u>Cohort B (patients newly initiated Pradaxa® or VKA)</u> PACT-Q1 was comparable between subjects using Pradaxa® and those using VKA. SAFETY Pradaxa® was safe and tolerable. ADRs were rarely reported. Over the study period, a total of 35 ADRs happened to 2.8% of subjects, with a higher incidence observed in the Cohort A (4.7%) than the Cohort B-Pradaxa® (2.6%). Among all ADRs, 3 were SAEs respectively reported by 1 subject in the Cohort A and 2 subjects in the Cohort B-Pradaxa®. Majority of ADRs were mild or moderate in severity and mostly were resolved at the end of study. The incidence of ADRs in MedDRA PT were all $< 1.0\%$, with no significant toxicities or safety issues observed. The ADRs related with other medications such as VKA were not included for records.
Discussion:	The two complementary parameters assessed in the present study (satisfaction with treatment and convenience of treatment) revealed generally satisfactory experience, whether of VKA or Pradaxa®. However, convenience seemed to be improved with Pradaxa®, which was evident in patients switching from VKA to Pradaxa® users. A long-term study will be of interest to assess the patients' perception after a long-term anticoagulant therapy.
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	10	[REDACTED]	[REDACTED], MD	
	11	[REDACTED]	[REDACTED], MD	
	12	[REDACTED]	[REDACTED], MD	
	13	[REDACTED]	[REDACTED], MD	
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2. LIST OF ABBREVIATIONS

ADR	Adverse Drug Reaction
AE	Adverse Event
AF	Atrial Fibrillation