Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

Name of Company: Boehringer Ingelheim		**Synopsis**	Boehringer Ingelheim
BI Proprietary Name: Pradaxa®		**EudraCT No.:** Not applicable	
BI Investigational Product: Dabigatran etexilate (mesilate)		**Page:** 1 of 5	
Report Date: 12 Feb 2016	**Trial No. / Doc. No.:** 1160.149	**Dates of Trial:** 12 Feb 2015 - 17 Aug 2015	**Date of Revision:** Not applicable

Title of Trial:	Post-authorisation study to evaluate the effectiveness of the risk minimisation activities in the treatment of SPAF
Principal/Coordinating Investigator:	Not applicable in this survey.
Trial Sites:	411 healthcare professionals in 8 European countries [58 in Bulgaria (BG), 64 in Czech Republic (CZ), 69 in Germany (DE), 1 in Denmark (DK), 62 in Spain (ES), 50 in France (FR), 46 in Slovakia (SK), and 61 in United Kingdom (UK)] .
Publications:	None.
Clinical Phase:	Not applicable. Survey
Objectives:	The objective of this survey was to evaluate the effectiveness of the risk minimization measure, the Pradaxa® educational package, and with this to evaluate the understanding of prescribers and patients of the information contained in the SPAF Prescriber Guide and Patient Alert Card in different regions of the European Union (EU)
Methodology:	Cross-sectional survey. Pradaxa® prescribing healthcare professionals and Pradaxa® treated patients were randomly selected and interviewed (face-to-face).
No. of Subjects:	
Planned:	Entered: 400 healthcare professionals (50 per country) and 800 patients with atrial fibrillation (100 per country)
Actual:	Enrolled: 411 healthcare professionals and 802 patients with atrial fibrillation
	Entered: 411 healthcare professionals and 802 patients with atrial fibrillation
Diagnosis:	Atrial fibrillation (applicable for patients only)
Main Criteria for Inclusion:	Physicians: Current prescribers of Pradaxa® for stroke prevention in patients with atrial fibrillation (AF).
	Patients: AF patients on treatment with Pradaxa®.
BI Investigational Product:	Pradaxa®; dabigatran etexilate (mesilate)
Dose:	Not applicable.

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Mode of Admin.:	Not applicable.
Batch No.:	Not applicable.
Comparator Product:	Not applicable.
Duration of Treatment:	Not applicable.
Criteria for Evaluation:	1. Physicians' knowledge and recommendations to their patients on appropriate dosing and minimizing the risk of bleeding when treated with Pradaxa®. The evaluation was based on the physicians' interview responses to questions regarding the "Prescriber Guide". 2. Patients' understanding of the disease, bleeding signs, what to do in case of bleeding and how to deal with emergency situations. The evaluation was based on the patients' interview responses to questions regarding the information received through the "Patient Alert Card".
Statistical Methods:	All analyses were descriptive. For both physician and patient surveys, all percentages and means were presented for the following groups: – The entire populations for physicians and for patients – Stratified by country (UK, DE, ES, FR, DK, BG, CZ and SK) – Patients stratified by those who had received the risk minimization materials and those who had not. – Physicians stratified for each country for the two medical specialty groups (i.e., general practitioners, cardiologists) Patients were further stratified by age groups (<75 years and ≥75 years). The results of this subgroup analysis are provided in Section 15, but are not presented in detail in this report, because only minor differences between the two subgroups were observed.
SUMMARY - CONCLUSIONS:	
Trial Subjects and Compliance with Trial Protocol:	A total of 411 physicians [124 primary care physicians (PCPs) and 287 cardiologists] and 802 AF-patients in 8 European countries participated in this survey. All of the participants were either prescribers (physicians) or current consumers (patients) of Pradaxa®. The proportion of male patients was slightly higher than that of females (54% vs. 46%) and 60% of the patients were less than 75 years old. Eighty-two

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	percent of the patients reported concomitant diseases other than AF, which required drug treatment. These were most frequently diabetes (36%), arterial hypertension (27%) and/or congestive heart failure (25%). In 42% of the patients, Pradaxa® was their first blood thinning medication for AF. In the total patient group, approximately half of them (49%) has taken Pradaxa® since 1-12 months. Shorter exposures were reported by only 5%. When considering the median exposure times, it was found that patients having received the Patient Alert Card had a 6-month shorter exposure than patients who had not or could not remember having received it (8.0 vs. 14.0 months). Besides this difference, the two patient groups were absolutely comparable with regard to demographics and medical history.
Efficacy / Clinical Pharmacology / Other Results:	<u>Physicians' knowledge and recommendations to their patients on appropriate dosing and minimizing the risk of bleeding when treated with Pradaxa®:</u> The majority of physicians (65%) stated that they had received the Patient Alert Card, mostly did this at start of the Pradaxa® treatment. Most of them (61%) handed it out to their AF-patients without selection of a certain patient group. The dispensing was the highest in UK (100%) and DE (99%) and the lowest (57%) in FR. As of September 2014 the Patient Alert Card was also distributed directly to the patient via the Pradaxa® trade pack. Overall, 71% of the physicians stated that they had received the Prescriber Guide (maximum: 97% in CZ, minimum: 36% in FR). More than 90% of the physicians who had received the educational pack in the different countries were satisfied with the information provided in the Prescriber Guide. Only in FR, 72% of those physicians who had received the Prescriber Guide were satisfied and the remaining 28% had not read it yet. All physicians were aware of the importance of determining and controlling of the patients' renal function for correct Pradaxa® dosing. The majority of physicians also knew about the correct dosing of patients. In risk patients, physicians tended to recheck the prescriber guide/literature first or would tend to prescribe lower doses than expected based on the patient profile. There was a high awareness of risk factors for bleeds. Only for specific risk factors like concomitant treatment with P-glycoprotein inhibitors or presence of bacterial endocarditis, the percentages of physicians replying "don't know" amounted to up to 34%. The physicians knew at least one suitable laboratory parameter [ecarin clotting time (ECT), thrombin time (TT), diluted thrombin time (dTT), and activated partial thromboplastin time (aPTT)], but nearly 20% of them were not aware of the unreliability of prothrombin time (international

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	normalized ratio; INR) in patients on Pradaxa®. Actions to be taken for surgeries or invasive procedures were more familiar. The answers regarding actions physicians would take in case of bleeds were variable and dependent on the physicians' routine and available technical equipment. Less than 50% would assess the patient's anticoagulation status first and/or would apply diuresis measurement (46% and 35%, respectively), but the physicians would discontinue Pradaxa® either immediately or in case of hemorrhagic complications (65% and 56%, respectively). Overall, some regional differences were observed, but across all countries, physicians were familiar with the content of the Prescriber Guide and applied the instructions as intended. In general, cardiologists appeared to be better informed than PCPs about the treatment of AF-patients with Pradaxa® and would less frequently check the Prescriber Guide than PCPs. <u>Patients' understanding of the disease, bleeding signs, what to do in the event of bleeding and how to deal with emergency situations:</u> Fifty-five percent of the interviewed patients had received the Patient Alert Card, had read it and understood its content. Most of the remaining patients, who had not received the Patient Alert Card, felt well informed by their treating physicians. The Patient Alert Card was completed with the patient-specific information in about 80% of the cases, and this was mostly done by the dispensing person. In general, all patients, irrespective of having received the Patient Alert Card or not, were well informed about their treatment and the actions to be taken in case of serious complications. The vast majority of patients knew about the anticoagulant effect of Pradaxa® (89%) and were well aware of the importance of the regular intake of the drug (>99%), potential side effects (bruising: 54%, bleeding: 52%), and the consequences associated with an arbitrary discontinuation. Patients having received the Patient Alert Card were even better informed, which confirms the patients' understanding of its content. In case of bleeding complications or surgery, most patients would behave correctly, irrespective of having received the Patient Alert Card or not.
Safety Results:	Safety data were not systematically collected in this survey. Spontaneous reports during the interviews were forwarded to the sponsor's pharmacovigilance unit for further processing.
Conclusions:	This survey in 8 preselected EU countries demonstrates a good educational

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level of prescribers and patients about the safety messages for Pradaxa® with some regional differences. The information given by the Prescriber Guide and the Patient Alert Card has been assessed by the study attendees as sufficiently informative and adequate.

Potential for improvements in the logistical distribution of the educational material to prescribers identified by this survey will be taken up by BI in the near future by adequate measures such as mailing and personal contacts to further improve the education and information related to key safety messages for Pradaxa®. The Patient Alert Card is directly distributed to the patient per Pradaxa® trade packs as of September 2014.