Evaluating Physician Knowledge of Risks and Safe Use of Xarelto (Rivaroxaban)

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CONFLICT OF INTEREST

L. Zografos, D. Wolin, B. Calingaert, E. Davenport, K. Hollis, and E. Andrews are full-time employees of RTI Health Solutions, which received funding from Bayer Pharma AG to conduct this study. The contract between RTI Health Solutions and the sponsor includes independent publication rights. RTI conducts work for government, public, and private organisations, including pharmaceutical companies.

K. Suzart, A. Horvat-Broecker, and M. Soriano-Gabarró are full-time employees of Bayer Pharma AG, the funder of this study.

BACKGROUND

- Rivaroxaban is an oral direct factor Xa inhibitor approved in the European Union (EU) for the prevention of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation in 2011 and for the treatment of deep vein thrombosis (DVT) and prevention of recurrent DVT and pulmonary embolism following an acute DVT in adults in 2012. These two indications were the focus of the study.
- Further indications are prevention of cardiovascular death, myocardial infarction, and stent thrombosis in patients after acute coronary syndrome (non-ST elevation, ST elevation myocardial infarction, or unstable angina) in combination with acetylsalicylic acid alone or with acetylsalicylic acid plus thienopyridines clopidogrel or ticlopidine (EU approval in 2013) and prevention of venous thromboembolism in patients undergoing major orthopedic surgery of the lower limbs (EU approval in 2008).
- A prescriber guide (PG) and patient alert card (PAC) were developed as risk minimisation measures and were distributed to physicians in the EU to provide education on key safety information. Subsequently, the PAC has been provided directly to patients through product packaging. The measurement of effectiveness of the educational materials is an additional pharmacovigilance activity required by the European Medicines Agency (EMA).

OBJECTIVE

- To measure whether prescribers received and used the PG and evaluate their knowledge of the key safety messages.

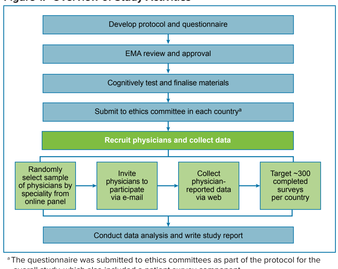
METHODS

Study Design

Overview

- The study was an observational, cross-sectional survey of knowledge, understanding, and self-reported behaviour among a sample of physicians and patients with recent rivaroxaban experience in four European countries (the United Kingdom [UK], Germany, France, and Spain). The information in this poster focuses on the physician survey.
- Figure 1 provides an overview of the study activities.

Figure 1. Overview of Study Activities



*The questionnaire was submitted to ethics committees as part of the protocol for the overall study, which also included a patient survey component.

Physician Selection and Recruitment

- The physician sampling frame was a physician panel made up of convenience samples of physicians derived from multiple sources (e.g., hospital books, medical directories, yellow pages, peer referrals).
- A stratified random sample of physicians was selected for recruitment such that the distribution of the specialities of the physicians that were invited was approximately proportional to the distribution of the specialities observed in country-specific prescribing patterns.
- Physicians were recruited via e-mail and quotas were set for each physician speciality to help ensure that the final distribution of respondents' specialities was similar to the prescribing patterns among specialities.
- The study aimed to recruit 300 physicians per country for a total of 1,200.
- Physicians were eligible to participate if they had prescribed rivaroxaban to at least one patient in the past 6 months for one of the following indications:
  - Prevention of stroke and systemic embolism in adults with nonvalvular atrial fibrillation (SPAF)
  - Treatment of DVT and prevention of recurrent DVT and pulmonary embolism following an acute DVT in adults

Survey Design and Administration

- The questionnaire was developed using best practices for instrument development and was tested through cognitive interviews with physicians in each country.
- The questionnaire included 27 closed-ended questions (e.g., multiple choice, true/false) with no free-text response fields.
- The following content areas were included: prescribing practices, knowledge of key safety messages outlined in the PG, sources of information about rivaroxaban and ratings of their helpfulness, experience with PACs, and physician and practice characteristics.
- The survey was conducted after physicians had received the educational material and had a chance to use the PG and the PAC in their practice.
- Physicians answered a screening question and provided consent before completing the questionnaire online.
- The online survey was programmed so that physicians were not able to go back to previous questions, thus prohibiting them from changing their answers based on subsequent questions.
- Data collection ran from 15 September 2014 to 20 November 2014.

Analysis

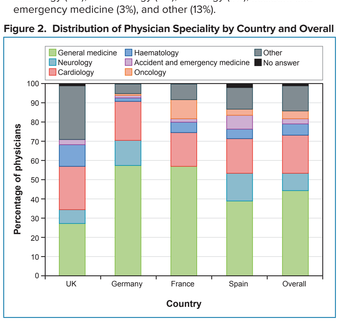
- Data analyses were descriptive and focused on summarising the questionnaire responses by country and overall.
- Six of the knowledge questions asked the respondent to "select all that apply" and included more than one correct response option. Correct responses to these questions were reviewed individually.

RESULTS

Demographics and Clinical Practice Characteristics

- A total of 1,224 physicians completed the survey out of 13,221 who were invited to participate, making an overall response rate of 9%. This rate is artificial because responses were not allowed once country- and speciality-quotas for responders were met; thus the true response rate, although unmeasurable, was higher.
- Most participants (74%) were male.
- Physician responses indicated they represented a range of specialities (Figure 2): general medicine (45%), cardiology (20%), neurology (9%), haematology (6%), oncology (4%), accident and emergency medicine (3%), and other (13%).

Figure 2. Distribution of Physician Speciality by Country and Overall



- A total of 63% of physicians reported that they practised in a general setting, and 43% of physicians reported that they practised at a hospital-based clinic.
- Physicians' experience (as measured by years in practice) was categorised into 5-year increments up to 25 years. More than 98% of physicians had been in practice more than 5 years, with durations fairly evenly distributed across the increments beyond 5 years. Approximately 1 in 5 physicians (20%) reported having been in practice more than 25 years.

Physician Prescribing Practices

- Most physicians (75%) had written a prescription for rivaroxaban within the last month.
- Almost all physicians (96%) had prescribed rivaroxaban for SPAF in the past 6 months, and most physicians (78%) had prescribed rivaroxaban for DVT treatment and secondary prevention in the past 6 months.
- Most physicians (85%) reported that they were responsible for initiating rivaroxaban treatment or converting from or to rivaroxaban, and more than half (63%) reported that they wrote follow-up (maintenance) prescriptions. (This was a "tick all that apply" question; thus, the sum of responses can be greater than 100%.)

Prescriber Guide and Patient Alert Card

- More than half (56%) of physicians reported that they used the PG as a source of information.
- Approximately half (47%) reported that they received PACs, and 80% of these reported that they provide it to most or all of their patients.

Knowledge Questions

Risks of Side Effects and Safe Use

- Almost all physicians (92%) correctly reported that the most important risk associated with taking rivaroxaban is bleeding.
- Overall, physicians' knowledge of patient populations at risk of experiencing serious side effects with rivaroxaban ranged from 66% to 91% correct for the individual response options; results were relatively consistent across countries.
  - Knowledge was highest among neurologists, cardiologists, and haematologists (Figure 3); knowledge levels of physicians responsible for initiating rivaroxaban treatment or converting treatment to or from rivaroxaban was, on average, 13% higher than for those responsible for maintenance prescriptions only; knowledge levels of physicians who reported receiving information from the Xarelto PG in addition to other sources (e.g., summary of product characteristics [SmPC], sales representative) was, on average, 8% higher than for those who did not report receiving information from the Xarelto PG.
- Overall, physicians' knowledge of patient groups for which rivaroxaban is contraindicated ranged from 80% to 90% correct for the individual response options; results were relatively consistent across countries.
  - Knowledge was highest among haematologists, neurologists, and cardiologists (Figure 4); knowledge levels of physicians responsible for initiating/converting rivaroxaban treatment was, on average, 12% higher than for those responsible for maintenance prescriptions only; knowledge levels of physicians who reported receiving information from the Xarelto PG in addition to other sources (e.g., SmPC, sales representative) was, on average, 9% higher than for those who did not report receiving information from the Xarelto PG.
- Most physicians (59%) correctly answered that rivaroxaban should be taken "with food/on a full stomach." There was some variation across countries with knowledge level among French physicians being slightly higher and knowledge level among physicians from the UK lower.
  - Knowledge was consistent across prescriber speciality with the exception of physicians who reported "general medicine" and "other" whose knowledge level was lower (Figure 5). Knowledge levels of physicians responsible for initiating/converting rivaroxaban treatment was 18% higher than for those responsible for maintenance prescriptions only; knowledge levels of physicians who reported receiving information from the Xarelto PG in addition to other sources (e.g., SmPC, sales representative) was 16% higher than for those who did not report receiving information from the Xarelto PG.
- Physicians were asked a series of five questions about monitoring and converting from another drug to Xarelto and from Xarelto to another drug.
  - Almost all physicians (95%) knew that routine coagulation monitoring is not required for patients taking rivaroxaban.
  - When asked about what situations cause there to be a need for international normalised ratio monitoring, 57% correctly indicated there was a need when converting from vitamin K antagonist (VKA) to rivaroxaban, and 75% correctly indicated there was a need when converting from rivaroxaban to VKA.
  - In two separate questions, physicians were asked about procedures for converting patients from VKA to rivaroxaban and from rivaroxaban to VKA; knowledge ranged from 30% to 63% for individual correct responses.
  - When asked about procedures for converting patients from parenteral anticoagulants to rivaroxaban, knowledge ranged from 48% to 54% for individual correct responses.
  - Knowledge varied by prescriber speciality. Knowledge levels of physicians responsible for initiating/converting rivaroxaban treatment was, on average, 14% higher than for those responsible for maintenance prescriptions only; knowledge levels of physicians who reported receiving information from the Xarelto PG in addition to other sources (e.g., SmPC, sales representative) was, on average, 9% higher than for those who did not report receiving information from the Xarelto PG.
- Physicians were asked up to three questions about Xarelto dosing depending on the indication(s) for which they prescribed.
  - Of the physicians who reported that they prescribed for SPAF, 71% correctly reported 20 mg taken once a day was the standard recommended dose of rivaroxaban for this indication, while 56% of physicians were aware that 15 mg taken once a day was the recommended dose of rivaroxaban for this indication for patients with moderate or severe renal impairment.
  - Of the physicians who reported that they prescribed rivaroxaban for DVT and secondary prevention, 61% correctly selected the response option for the standard recommended dose for patients receiving rivaroxaban for this indication.
  - Knowledge varied by prescriber speciality with higher knowledge among physicians who reported "cardiology" and lower knowledge among physicians who reported "oncology." Knowledge levels of physicians responsible for initiating/converting treatment was, on average, 23% higher than for those responsible for maintenance prescriptions only. Knowledge levels of physicians who reported receiving information from the Xarelto PG in addition to other sources (e.g., SmPC, sales representative) was, on average, 13% higher than for those who did not report receiving information from the Xarelto PG.

Figure 3. Correct Responses to Question: Which of the following populations are at an increased risk of experiencing serious side effect(s) associated with Xarelto?

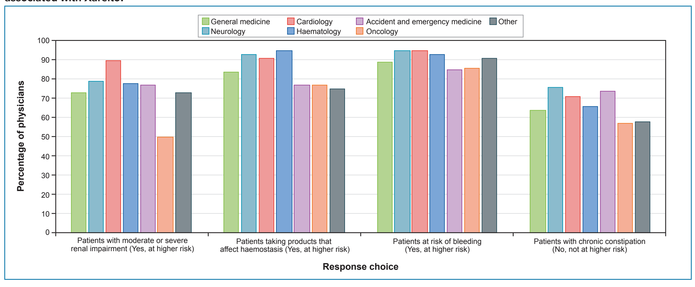
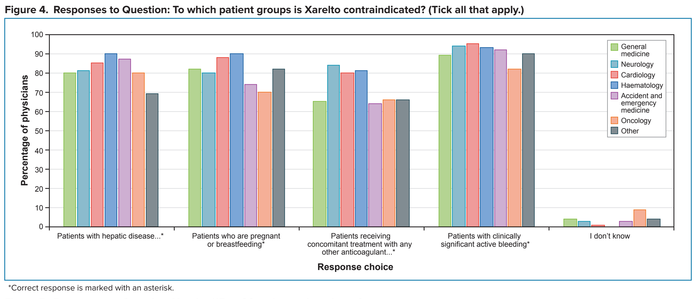
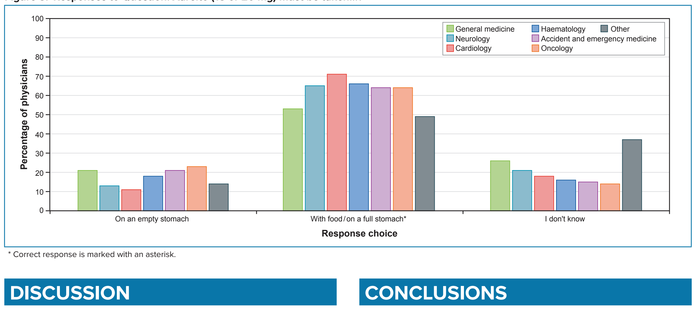


Figure 4. Responses to Question: To which patient groups is Xarelto contraindicated? (Tick all that apply.)



*Correct response is marked with an asterisk.

Figure 5. Responses to Question: Xarelto (15 or 20 mg) must be taken...?



* Correct response is marked with an asterisk.

DISCUSSION

- One of the most important factors when dealing with anticoagulation is understanding the risks associated with each product and how to mitigate these risks.
- In general, physicians' knowledge level of the key safety information in the Xarelto educational materials was high.
- The highest knowledge level was on overall risk of bleeding as well as the risks for populations with contraindications and populations that are at increased risk of serious side effects.
- A lower percentage of physicians were aware that rivaroxaban should be taken with food.
- As would be expected with all products, correct knowledge on specific details of individual patient scenarios was lower, in this case details associated with converting to and from VKA, monitoring, and dosing.
- Also, as would be expected, physicians who were responsible for initiating rivaroxaban treatment or converting treatment from or to rivaroxaban had a higher proportion of correct responses than those who were responsible only for maintenance treatment.
- In general, physicians who reported specialities in neurology, cardiology, and haematology had higher proportions of correct responses than physicians in other speciality categories on most of the knowledge questions.
- The PG was widely distributed to potential prescribers in all countries. More than half of physicians reported that they received information from the Xarelto PG in addition to other sources of information (e.g., SmPC, sales representative), and these physicians consistently provided more correct responses than those who did not report receiving information from this source.

CONCLUSIONS

- The discrepancy between the wide distribution of the PG and the level of reported receipt of the PG may reflect poor recall, poor recognition of the material, or barriers to the receipt of the material.
- In general, the observed patterns of knowledge among the physicians are as expected, with higher knowledge levels on the most important risks emphasised in the educational material and other product information and lower knowledge levels on more complex aspects of safe use (e.g., concepts related to dosing, converting to/from Xarelto, and patient monitoring) that lend themselves to consultation of the label and/or PG rather than reliance on recall.

ACKNOWLEDGMENTS

The authors thank Kim Davis of RTI Health Solutions for her assistance with poster development and Christine Tarenz, Jonas Schneider, Jacinta Carolina Reinikainen, and Suzanne Frankfort of Bayer Pharma AG for their assistance with review of study documents and other study activities.

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