STUDY REPORT SUMMARY

ASTRAZENECA CANADA INC.

FINISHED PRODUCT: Brilinta
ACTIVE INGREDIENT: Ticagrelor

Study No: D5130L00009

Knowledge and understanding survey of ticagrelor prescribers in Canada.

Developmental phase: Non-interventional study
Study Completion Date: 22 December 2014
Date of Final Report: 27 February 2015

OBJECTIVES:

Primary Objective:

- To evaluate the effectiveness of the current BRILINTA® risk minimisation strategy through a prescriber knowledge and understanding (KAU) survey of selected important identified safety concerns (i.e., bleeding, dyspnea and drug interactions) and ASA dosage.

Secondary Objective:

- To determine if there are differences in KAU across the key safety concerns.
- To explore the association between prescribers' characteristics and KAU of key safety concerns.

METHODS:

Study population

The survey targeted all interventional cardiologists or cardiologists in Canada who have prescribed BRILINTA® at least once.

Design

Cross-sectional survey of BRILINTA® prescribers was conducted in three waves. Wave 1 was completed in March 2013, Wave 2 in December 2013; Wave 3 in December 2014.

- The questionnaire included 4 eligibility screening questions (mandatory), 10 KAU questions (mandatory), 7 questions on physician or practice characteristics (optional).

- The questionnaire included closed questions only, took approximately 20 minutes to fill out, and was available both in English and French
- Both web-based and fax options were available.
- For each question, adequate KAU was defined as a correct answer to the question (dichotomous variable);
- For each safety concern, KAU was defined as: "adequate" when all questions pertaining to this safety concern have been answered correctly, otherwise it was categorized into "partially adequate" and "inadequate" (latter defined as incorrect answers to all questions.
- Response rate by region and specialty was determined.
- Frequency distributions were used to describe categorical variables .
- Estimates of adequate KAU were derived for each safety concern and 95% confidence intervals (CI) were obtained. Adequate KAU was defined by a lower bound of the 95% CI greater or equal to 65%.
- Percentage of adequate KAU was compared across physician sub-groups. As this is a descriptive component of the survey, no statistical testing was conducted.

RESULTS:

Demographics

The study included a total of 244 physicians across Canada who have prescribed ticagrelor at least once (53, 105, and 86 prescribers for Wave 1, 2 and 3, respectively).

Wave 1

The prescribers of BRILINTA had a very high understanding of 3 of the 4 key safety messages. More specifically, 98.1% (95% CI: 94.3-100%) of prescribers surveyed had adequate knowledge and understanding of the drug-drug interaction, 100% adequately understood ASA maintenance dose and 100% adequately understood the safety message pertaining to dyspnea.

For the risk of bleeding, 75.5% of respondents had partly adequate (2 out of 3 questions) or adequate (3 out of 3 questions) knowledge and understanding; however, the lower bound of the 95% CI included 65% (the pre-specified threshold). Comparisons across regions or sub-groups of prescribers (interventional cardiologists *vs*. cardiologists, rural *vs.* urban, *etc*.) did not reveal any marked differences.

Wave 2

The prescribers of BRILINTA had a high understanding of 2 of the 4 key safety messages (drug-drug interaction (83.8% KAU; 95%CI: 76.8-90.8%), and dyspnea (91.4% KAU; 95%CI: 86.1-96.7%)).

The percentage of prescribers with adequate (3 out of 3 questions) and partly adequate (2 out of 3 questions) knowledge of the bleeding risk has increased compared with Wave 1 (39.1% vs. 37.7%, and 46.7% vs. 37.7%, respectively), whereas fewer prescribers had inadequate knowledge (14.3% vs. 24.6%). Nevertheless, the knowledge and understanding of the safety messages pertaining to bleeding and ASA maintenance, did not meet the pre-determined threshold: 39.1%; 95% CI: 29.8-48.4%, and 69.5%; 95%CI: 60.5-78.5%, respectively.

Comparisons across regions or sub-groups of prescribers (interventional cardiologists *vs*. cardiologists, rural *vs.* urban, *etc*.) did not reveal any marked differences.

Wave 3

The prescribers of BRILINTA had a high understanding of 2 of the 4 key safety messages (drug-drug interaction (89.5% KAU; 95%CI: 83.1-96.0%), and dyspnea (95.3% KAU; 95%CI: 90.9-99.8%)).

The knowledge and understanding of the safety messages pertaining to bleeding and ASA maintenance did not meet the pre-determined threshold when considering only the adequate KAU (perfect answers to all questions). Knowledge and understanding for bleeding was 50.0% (95% CI: 39.4-60.6), and 69.8% (95% CI: 60.1-79.5) for ASA maintenance. However, the level became high (84.9% and 97.7%, respectively) when the data from the partly adequate was pooled. In addition, analysis of responses to individual questions demonstrates a very high knowledge and understanding pertaining to most clinically serious issues (e.g., 97.7% of respondents have correctly identified a history of intracranial haemorrhage as a contraindication to ticagrelor). Therefore, it appears that the communication strategy highlighting the risks of bleeding has been generally successful and the risks associated with ticagrelor are well understood.

In summary, based on the results of the KAU Survey (Waves 1-3), no changes to the Risk Minimisation and Pharmacovigilance activities for BRILINTA were deemed necessary.