Evaluating Physician Knowledge of Safety Information for Aflibercept (Eylea)

Laurie J Zografos,[1] Elizabeth Andrews,[1] Dan L Wolin,[1] Brian Calingaert,[1] Eric K Davenport,[1] Kelly A Hollis,[1] Paul Petraro,[2] Nada Djokanovic,[2] Vito S. Racanelli,[2] Zdravko Vassilev[2]

[1]RTI Health Solutions, Research Triangle Park, NC, United States; [2]Bayer U.S., Whippany, NJ, United States

CONFLICTS OF INTEREST

- L. Zografos, E. Andrews, D. Wolin, B. Calingaert, E. Davenport, and K. Hollis are salaried employees of RTI Health Solutions, which received funding from Bayer 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.
- N. Djokanovic, V. Racanelli, and Z. Vassilev are full-time employees of Bayer, the funder of this study. P. Petraro was employed by Bayer at the time the study was conducted.

BACKGROUND

- Aflibercept (Eylea), administered via intravitreal injection, is a fusion protein specifically designed to bind all forms of vascular endothelial growth factor A (VEGF-A) and placental growth factor, two proteins involved in the abnormal growth of new blood vessels.[1] Aflibercept is approved in Canada for the treatment of neovascular (wet) age-related macular degeneration (wAMD), visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO), visual impairment due to macular oedema secondary to branch retinal vein occlusion, diabetic macular oedema (DME), and myopic choroidal neovascularization.
- As part of the risk management plan for aflibercept, Bayer developed a vial preparation instruction card, an intravitreal injection procedure video, and a product monograph and distributed these materials to physicians to increase awareness and understanding about risks associated with aflibercept. The current study was conducted to evaluate the understanding and use of these materials.

OBJECTIVE

- To assess whether physicians received and used the aflibercept educational materials and to evaluate their knowledge of the key safety information.

METHODS

Study Design

Overview

- The study was an observational, cross-sectional survey of knowledge, understanding, and self-reported behaviour among a sample of physicians with recent aflibercept experience in Canada.
- Figure 1 provides an overview of the study activities.

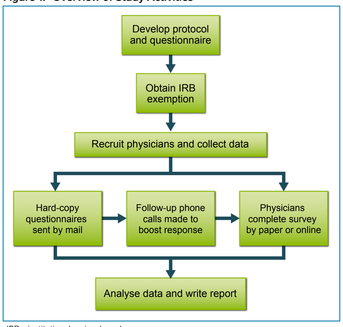
Physician Selection and Recruitment

- The sampling frame was constructed from a list of aflibercept prescribers provided by Bayer. The list included most physicians prescribing and/or administering aflibercept in Canada.
- Given the relatively small number of prescribers in Canada, all physicians on the list were invited to participate.
- A mailing that included a study invitation letter, a hard-copy questionnaire, and a prepaid/preaddressed envelope for returning the completed questionnaire was sent to all physicians.
- Physicians were given the option to complete and return the hard-copy questionnaire by mail or log on to a study website and complete the questionnaire online.
- Physicians eligible to participate were retinal specialists and ophthalmologists who had prescribed and/or administered aflibercept to at least 1 patient in the past 6 months.

Survey Design and Administration

- The questionnaire was developed using best practices for instrument development and consisted of questions that had been previously cognitively tested with physicians in the European study.[2]
- The questionnaire included primarily closed-ended questions (e.g., multiple choice, true/false) and a few that allowed free-text responses.
- The following content areas were included: physician experience with aflibercept; physician characteristics; and physician knowledge, receipt, use, and ratings of aflibercept educational materials.
- The survey was conducted after a sufficient amount of time for physicians to have received the educational materials and to have used them in their practice.

Figure 1. Overview of Study Activities



IRB = institutional review board.

- Physicians answered a screening question to confirm that they had prescribed and/or administered aflibercept to at least 1 patient in the past 6 months and provided consent before completing the questionnaire.
- Data were collected from 18 February through 31 March 2016.

Analysis

- Data analyses were descriptive and focused on summarising the questionnaire responses provided by the overall set of participants.
- The percentage of participants who answered each question correctly and exact 95% confidence intervals were calculated for each knowledge question.

RESULTS

Distribution of Participants

- A total of 308 physicians were invited to participate in the survey. Of those, 102 physicians responded to the invitation. Of the 102 physicians who responded, 1 was ineligible and 6 did not complete the consent question. The remaining 95 completed the questionnaire (26 online and 69 by paper). The overall response rate was 31%.

Physician Clinical Characteristics

- Most physicians (71%) indicated that their focus within ophthalmology was retina followed by general ophthalmology (59%), glaucoma (23%), and other (7%). (Physicians could select multiple focuses.)
- Most physicians (79%) reported having been in practice for more than 5 years.

Physician Prescribing Practices

- Most physicians (87%) reported that they had prescribed aflibercept in the past 6 months, and almost all (96%) reported that they had administered an aflibercept injection in the past 6 months.
- On average, most physicians (78%) administered more than 40 anti-VEGF intravitreal injections per month.
- Nearly all physicians (99%) reported they last administered an aflibercept injection less than 1 month ago.
- Physicians reported prescribing and/or administrating aflibercept for wAMD (94%), visual impairment due to macular oedema secondary to CRVO (81%), and visual impairment due to DME (93%). All indications were approved at the time the study was conducted.

Receipt and Review of the Aflibercept Educational Materials

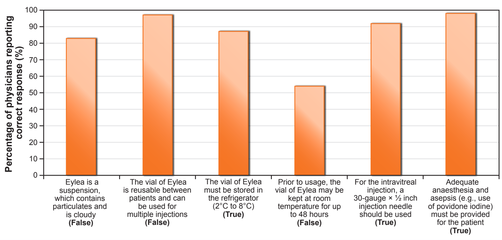
- Most physicians (79 of 95 [83%]) reported that they received the vial preparation instruction card. Of those who received it, 64 out of 79 (81%) reported that they reviewed it.
- Nearly half of physicians (44 of 95 [46%]) reported that they received the intravitreal injection procedure video. Of those who received it, 57% reported that they reviewed it.
- Nearly all physicians (93 of 95 [98%]) reported that they received the product monograph. Of those, 76% reported that they reviewed it.

Knowledge of Key Safety Information

Storage and Preparation

- Physicians' knowledge of proper storage and preparation of aflibercept was high, with the proportion of correct responses ranging from 83% to 98% for 5 of 6 questions on this topic. Approximately half of physicians (54%) correctly identified the remaining response "prior to usage, the vial of Eylea may be kept at room temperature for up to 48 hours" as inaccurate (the actual duration is up to 24 hours) (Figure 2).

Figure 2. Physicians' Responses to Questions on Storage and Preparation of (N = 95)



Dosing

- Physician knowledge was high on the recommended dose of aflibercept (91%) and questions related to dose preparation (91%-96%).
- Knowledge of dosing guidelines by indication varied by indication. Knowledge on the single dosing recommendation for wAMD was the highest, 95% followed by knowledge on the two dosing recommendations for DME (83%-84%). Knowledge on the four dosing recommendations for CRVO was the lowest (75%-89%) (Figure 3 and Figure 4).

Figure 3. Physicians' Response to Questions on Dosing Recommendations for DME (N = 95)

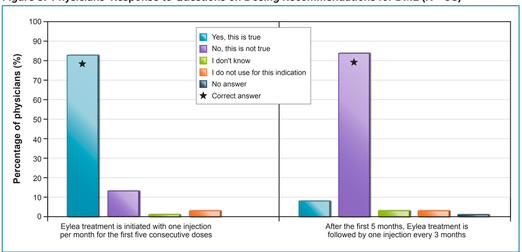
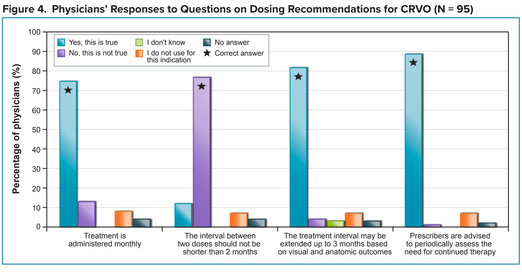


Figure 4. Physicians' Responses to Questions on Dosing Recommendations for CRVO (N = 95)



Safe Use

- Most physicians (89%) knew the contraindications for aflibercept use, with correct responses to the individual items ranging from 91% for active intraocular inflammation to 100% for known hypersensitivity to aflibercept, to any ingredient in the formulation, or to any component of the container.
- Sixty percent of physicians reported that aflibercept should not be used in pregnancy unless clearly indicated by medical need and unless the benefit outweighed risks. An additional 20% of physicians responded that aflibercept should never be used in pregnancy. Half of physicians (49%) selected the correct time frame for which women of childbearing potential must use effective contraception.

Injection Procedure

- In general, knowledge was high on questions about injection procedures (91%-99% on individual items); however, fewer physicians (24%) correctly reported that, before marking the scleral injection site, the eye should be covered with a sterile drape (Figure 5 and Figure 6).

Figure 5. Physicians' Response to Questions on Injection Procedures (N = 95)

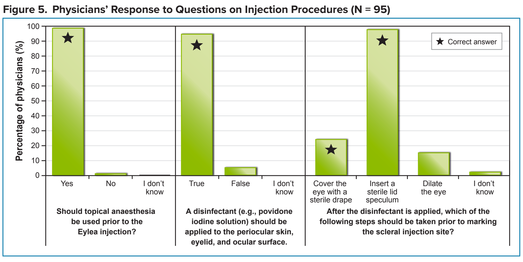
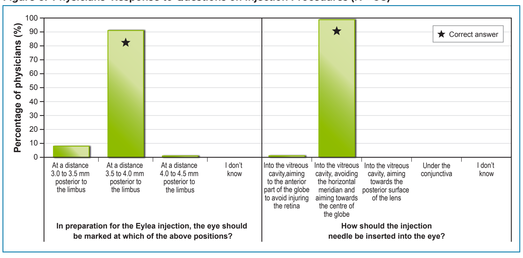


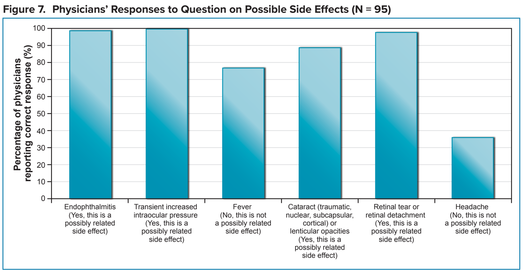
Figure 6. Physicians' Response to Questions on Injection Procedures (N = 95)



Possible Side Effects

- Knowledge was also high for possible side effects (ranging from 89% to 100% on individual items) (Figure 7).

Figure 7. Physicians' Responses to Question on Possible Side Effects (N = 95)



DISCUSSION

- In general, physicians' knowledge level of the key safety information in the aflibercept educational materials was high for most questions.
- Knowledge was lower on questions related to aflibercept use in pregnancy; however, in several cases, physicians who did not select the correct response chose another response outlining a more conservative approach to treatment.
- A quarter of physicians (24%) correctly reported that, before marking the scleral injection site, the eye should be covered with a sterile drape. This step is recommended as part of aseptic procedures; however, it is not common medical practice among ophthalmologists in Canada, as observed in the current study.[3]
- Almost all physicians (98%) reported receipt of the product monograph, and most physicians (83%) reported receipt of the vial instruction card. A lower proportion of physicians (46%) reported receipt of the intravitreal injection procedure video. The video was distributed on a USB drive with the card. The relatively low level of reported receipt of the video may reflect poor recollection of receiving the materials if the materials had indeed been received or various reasons for not receiving the educational materials.

CONCLUSIONS

- The study met its objectives to evaluate whether physicians received the educational materials for aflibercept and to assess physician knowledge and understanding of key safety information outlined in the materials. The reported receipt of the product monograph and instruction card was high (98% and 83%, respectively). The high level of knowledge among treating physicians also suggests that the key safety information is available to the treating physicians.
- In general, knowledge of most important topics was high. For example, knowledge of possible side effects ranged from 89% to 100%. Knowledge varied for topics that are less frequently encountered (e.g., use in women of childbearing potential) and for recommendations that are not part of standard medical practice (e.g., use of sterile drape).
- In general, the observed patterns of knowledge were as expected. The greatest physician knowledge was on the most important risks emphasised in the educational material. Physicians had less knowledge on aspects of safe use less relevant to the aflibercept patient population (e.g., use in pregnancy) for which one would assume that physicians would consult the safety information rather than relying on recall.

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CONTACT INFORMATION

Laurie Zografos, BS
Senior Survey Director

RTI Health Solutions
Phone: +1.919.485.2782
E mail: zografos@rti.org

Zdravko Vassilev
Director, Global Epidemiology

Bayer HealthCare Pharmaceuticals, Inc.
Phone: +1.973.487.2726
E-mail: zdravko.vassilev@bayer.com