Evaluation of Physician Knowledge of Safety and Safe Use Information for Aflibercept in Europe

Laurie J Zografos,[1] Brian Calingaert,[1] Eric K Davenport,[1] Zdravko P Vassilev,[2] Daniel L Wolin,[1] Elizabeth Andrews[1]

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

DISCLOSURES

- E. Andrews, B. Calingaert, E. Davenport, D. Wolin, and L. Zografos are full-time employees of RTI Health Solutions, which received funding from Bayer 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 organizations, including pharmaceutical companies. Z. Vassilev is a full-time employee of Bayer, the funder of this study.

BACKGROUND

- Aflibercept (Eylea), administered via intravitreal injection, is approved in Europe for the treatment of neovascular (wet) age-related macular degeneration (wAMD), visual impairment due to macular edema secondary to central retinal vein occlusion (CRVO), visual impairment due to macular edema secondary to branch retinal vein occlusion (BRVO), diabetic macular edema (DME), and visual impairment due to myopic choroidal neovascularization (myopic CNV).
- Risk minimization measures for aflibercept in Europe included:
  - A prescriber guide and injection procedure video
  - A patient booklet and audio CD

OBJECTIVE

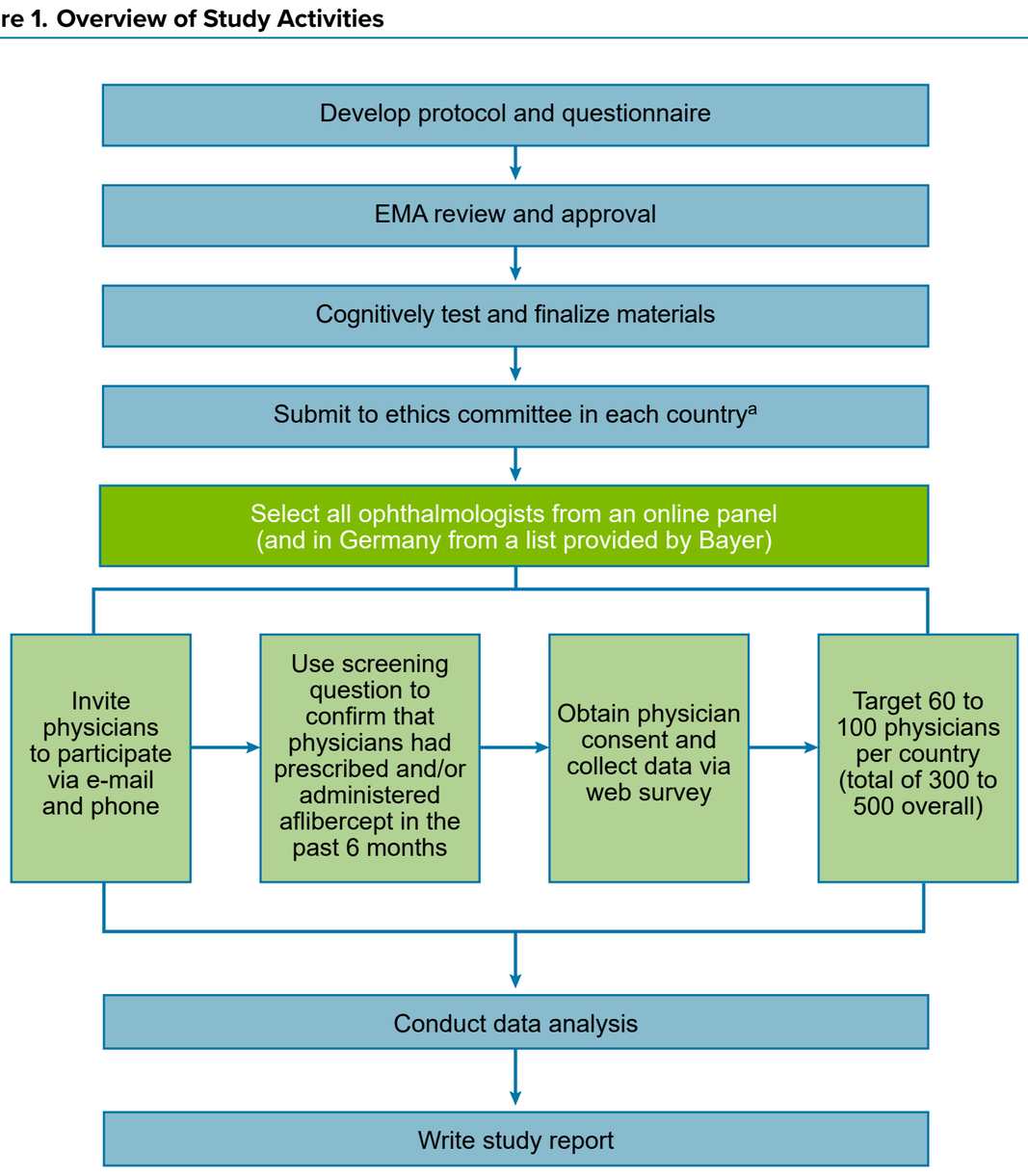
- To assess whether physicians received the aflibercept educational materials and evaluate their knowledge of key safety and safe use information.

METHODS

Overview of Study Design

- The study was an observational, cross-sectional survey of knowledge and understanding among physicians and patients with recent aflibercept experience in France, Germany, Italy, Spain, and the United Kingdom (UK). 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



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

Survey Design and Administration

- The questionnaire included 27 closed-ended items including the following content areas: (1) experience with aflibercept; (2) physician characteristics; (3) knowledge of aflibercept storage and preparation, dosing and monitoring, safe use, injection procedure, and side effects; (4) receipt and use of aflibercept educational materials; (5) ratings of aflibercept education materials; and (6) physician use of patient booklet.
- The questionnaire was developed using best practices for instrument development and was tested through cognitive interviews with physicians in each country.
- The survey was conducted after physicians had received the educational material and had a chance to use the prescriber guide and the patient booklet in their practice.
- 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 20 April 2016 to 24 October 2018.

Analysis

- Data analyses were descriptive and focused on summarizing the questionnaire responses by country and overall.
- The results for knowledge questions were reviewed individually and overall to assess the effectiveness of the educational material and identify any knowledge gaps.

RESULTS

Demographics and Experience

- Of 8,424 physicians who were invited to participate in the survey, 428 completed it, making an overall response rate of 5.1%. This rate is somewhat artificial because enrollment was stopped once the country quota for responders was met; thus the true response rate, although unmeasurable, would be higher.
- About three-quarters of physicians (73%) were male.
- Per the screening criteria, all physicians had either prescribed (91%) and/or administered (83%) aflibercept in the past 6 months for indications including wAMD (97%), DME (79%), CRVO (67%), and BRVO (58%).

Receipt and Review of Materials

- Most physicians reported that they received the SmPC (87%) and the prescriber guide (77%).[1] Approximately half of physicians reported that they received the intravitreal injection procedure video (50%) and the patient booklet (54%).

Knowledge Questions

Table 1 presents physicians' knowledge of key safety information contained in the aflibercept educational materials.

Table 1. Correct Responses to Questions on Key Safety Information for Aflibercept

Topic	Range of Proportion of Correct Responses Across Items: Point Estimate (Exact 95% CI)	
	Lower Bound	Upper Bound
Storage and preparation (5 of 6 items)[a]	74% (70%-78%)	97% (95%-99%)
Injection procedures (5 items)	83% (80%-87%)	96% (93%-97%)
Dosing requirements for wet AMD (4 items)	28% (24%-33%)[b]	94% (91%-96%)
Steps to prepare patients for treatment (3 items)	63% (58%-68%)	94% (91%-96%)
Contraindications for use (3 items)	85% (81%-88%)	95% (92%-97%)
Use in pregnancy (1 item)	59% (55%-64%)[c]	
Signs and symptoms of possible side effects (4 items)	78% (73%-81%)	89% (85%-92%)

[a] The remaining item was an inaccurate statement about storing aflibercept at room temperature for up to 48 hours (the actual duration is up to 24 hours). This item was answered correctly by 42% of physicians.

[b] The 28% knowledge level reflected a more conservative interpretation of monitoring requirements (i.e., 28% correctly responded "true" to there being no monitoring requirements between doses, while 68% responded "false").

[c] Fifty-nine percent of physicians correctly responded that aflibercept should not be used in pregnancy unless the potential benefit outweighs the potential risk, and an additional 27% (23%-31%) of physicians took a more conservative approach and responded that aflibercept should never be used in pregnancy.

Figure 2. Eylea is contraindicated in which of the following patients? Tick all that apply. (N = 428)

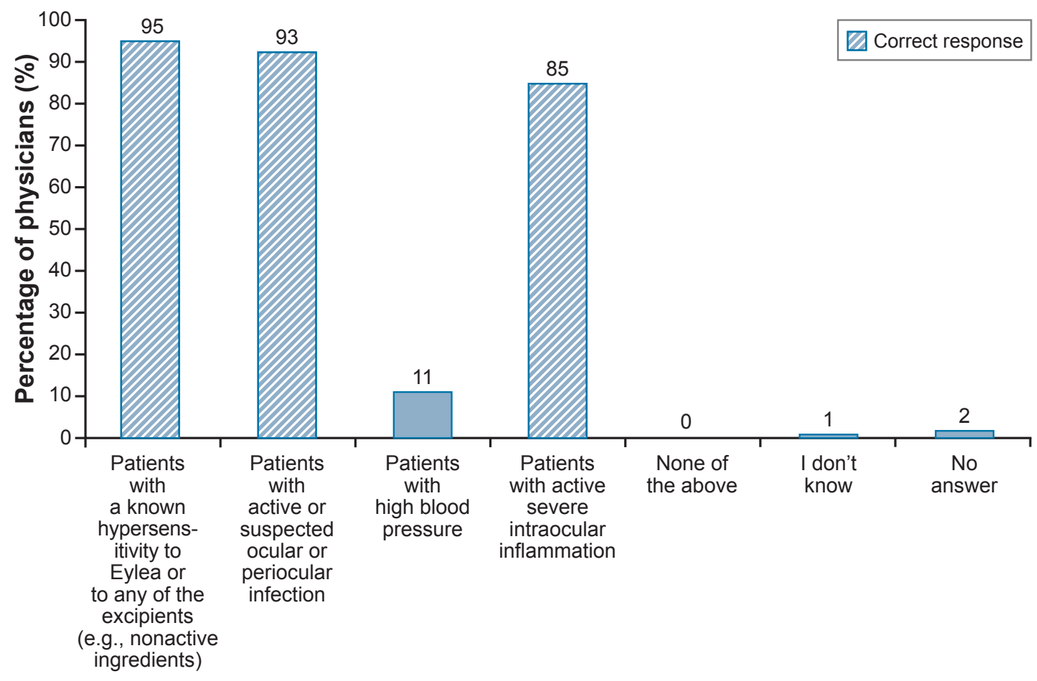
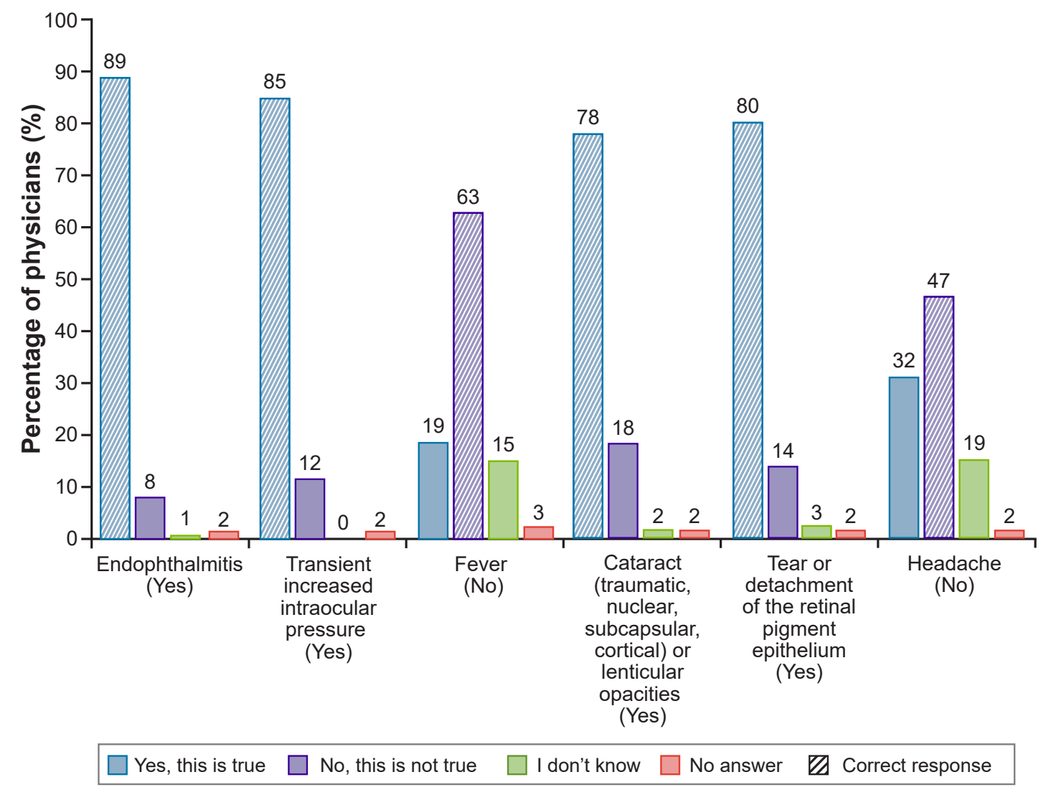


Figure 3. Which of the following signs or symptoms are known undesirable side effects of using Eylea? (N = 428)



DISCUSSION

- Most physicians reported that they received the SmPC and prescriber guide. The relatively low level of reported receipt of the video and booklet may be due to either poor recall, if the materials had indeed been received, or else various reasons if the materials actually were not received.
- In general, physicians' knowledge of storage and preparation guidelines, safe use, and injection procedures was high.
- Knowledge on dosing guidelines varied by indication, which may reflect knowledge and/or be a factor of the recency of indication approval and/or the status of drug reimbursement.
- Two-thirds of physicians responded incorrectly that monitoring is required during the first 12 months of aflibercept treatment for wAMD, demonstrating a more conservative approach to monitoring than is actually required.

CONCLUSIONS

- Reported receipt of the SmPC and prescriber guide was high, and the high level of knowledge suggests that the key safety information is available to the treating physicians.
- Some of the most important information communicated in the aflibercept educational materials is related to side effects. For most questions on this topic, more than 80% of physicians responded correctly.
- Knowledge was lower for topics less frequently encountered (e.g., use in women of childbearing potential) and for more complex aspects of safe use (e.g., dosing and monitoring) for which we assume that physicians would consult the label and/or prescriber guide rather than relying on recall.

REFERENCES

1. European Medicines Agency. Eylea summary of product characteristics. October 26, 2017. Available at: https://www.medicines.org.uk/emc/medicine/27224. Accessed June 12, 2018.

CONTACT INFORMATION

Laurie Zografos
Head, Surveys and Observational Studies

RTI Health Solutions
200 Park Offices Drive
Research Triangle Park, NC 27709

Phone: +1.919.485.2782
Fax: +1.919.541.7222
E-mail: zografos@rti.org

Presented at: 34th International Conference on Pharmacoepidemiology & Therapeutic Risk Management; August 22-26, 2018; Prague, Czech Republic