



Avastin and Lucentis: what do patients know? A prospective questionnaire survey

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DECLARATIONS

Competing interests

All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work

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Ethical approval

Not required as this is a patient survey

Summary

Objectives To assess patients' knowledge of their drug therapy for neovascular macular degeneration and to identify which aspects of the drug they considered most important if given the option of switching to an alternative drug.

Design Prospective questionnaire survey.

Setting Wolverhampton, England.

Participants A total of 126 patients attending our hospital service for intravitreal ranibizumab therapy for neovascular macular degeneration.

Main outcome measures Using a questionnaire, patients were asked questions pertaining to aspects of drug therapy in neovascular macular degeneration. Fields covered included drug names, knowledge of alternative drugs, cost of drugs and their views on switching to another drug.

Results Eighty (63.5%) had heard of Lucentis (ranibizumab) and 31 (24.6%) were aware of Avastin (bevacizumab). Of the latter 31 patients, 20 did not have a preference between Avastin and Lucentis. These patients felt that the factors they would consider important for them to consider switching were effectiveness (10, 50%), specialist recommendation (8, 40%), safety (2, 10%) and cost (0).

Conclusions Introducing a cheaper, off-label alternative in the therapy of macular degeneration in the presence of a licensed option has been extensively debated. Many patients have no knowledge of this controversial issue but it is likely that efficacy and recommendation by clinicians are more important than cost to patients who may consider switching to the off-label Avastin.

Introduction

The wet or neovascular form of age-related macular degeneration (nAMD) is the most common cause of blindness in the UK.¹ If untreated, visual loss is due to macular and central retinal

damage caused by exudation, leakage and haemorrhage from abnormal new vessels or choroidal neovascularization under the retina. Therapy is aimed at the control of neovascularization and leakage using biological, anti-angiogenesis agents targeting the vascular endothelial growth

Guarantor factor (VEGF) pathway in the pathogenesis of neovascularization.² Ranibizumab (Lucentis®; AM Genentech, South San Francisco, CA, USA) has been the only anti-VEGF drug to be appraised and approved by the National Institute for Health and Clinical Excellence (NICE)³ for use in patients with nAMD (TA 155). Although it has been shown to be very effective in preventing visual loss, it is required to be administered by the direct intraocular route involving an intravitreal injection performed at very frequent intervals for up to two or three years.^{4,5} Intravitreal injections are now becoming the most commonly performed procedure in hospital eye departments. We estimate that the NHS is spending in excess of £70 million per year on ranibizumab⁶ and with the projected increase in prevalence of nAMD, there is likely to be a greater impact on public health and also a heavier financial burden for healthcare providers.⁷

Contributorship Commissioners and healthcare providers are also faced with quite a unique and interesting situation over the choice of drug to use. Bevacizumab (Avastin®; Genentech), which is an anti-VEGF drug licensed for intravenous use in the treatment of colonic cancer is also produced by the same company as ranibizumab, but when divided into small aliquots for off-label use, it is considerably cheaper (£87.00 pre VAT per injection supplied by Moorfields Pharmacy) than ranibizumab (£742.17 pre VAT). This large cost differential coupled with the two-year results from the Comparison of Age Related Macular Degeneration Treatments Trial (CATT)⁸ and the one-year results of the IVAN trial⁹ which found that bevacizumab was non-inferior to ranibizumab may lead to a unique situation of an off-label drug being recommended over a licensed alternative despite caution expressed by professional bodies regarding systemic and ocular side effects.^{10–13} Given these continuing controversies and concerns, and the results of that UK-based head to head study, it is now an important time to understand patients' views and attitudes in order to facilitate patient education and counselling and involve patients in the decision-making process over choice of drug or over the switching of one drug to another.^{14,15}

Acknowledgements Our objective, in this study, was to survey patients undergoing intravitreal ranibizumab therapy to ascertain their views on the cost, safety and other aspects of their treatment.

Provenance Submitted; peer reviewed by Karen Wong

An understanding of the knowledge, views and attitudes of patients on this controversy may help ophthalmologists and other health care providers in counselling and management of expectations in treatment of nAMD in situations if a choice has to be made between bevacizumab and ranibizumab.

Methods

A specific questionnaire (Appendix 1) was designed to ascertain the knowledge and views of patients undergoing ranibizumab therapy in our department. The questionnaire contained two parts. Part 1 was designed to test specific knowledge of the drug they were receiving, its cost and also the availability of alternative options. In part 1, there were seven questions. Questions 1–3 covered biographical information and the number of intravitreal injections that patients had received. Question 4 was to determine whether our patients knew the name of the drug that they had been receiving (Lucentis). Question 5 tested their knowledge on the drug cost per injection with a range of £50–£1000. Questions 6 and 7 were to ascertain their knowledge of whether the drug they were receiving was the only approved option or if they were aware of alternatives. Five therapeutic products associated with macular therapy were presented in Question 7 to test if any were familiar to them. These included Avastin, Lucentis, Macugen (Pfizer Inc., a drug licensed for nAMD but not NICE approved), Ozurdex (Allergan Inc., recently licensed and NICE approved intravitreal dexamethasone implant for use in macular oedema) and ICAPs which is a popular dietary supplement containing lutein and multivitamins often recommended for macular degeneration. Part 2 was only completed by those who had heard of the bevacizumab (Avastin) and was designed to ascertain the patients' knowledge about its cost (Q1), where they had heard of Avastin (Q2), their preference, if any, between Avastin or Lucentis based on their own understanding (Q3 and Q4) and the information they would like about each drug if they had to make a choice between the two (Q5). The categories of information presented in Q5 for them to choose from included: (A) cost of each drug, (B) safety information on each, (C) information on safety of each drug and (D) recommendation by their eye specialist.

Patients attending our department for intravitreal ranibizumab therapy in the months of September and October 2011 were randomly invited to participate and were encouraged to complete the questions themselves but a doctor (TO or BN) was available to assist and clarify where necessary.

To minimize any influence on the patients' responses and views, we decided not to give them any prior information about bevacizumab or any aspects of the anti-VEGF debate. Instead, we used the same statement prior to every patient's interview explaining that we were doing a short survey of their awareness of treatment for wet macular degeneration. This allowed us to detect patients' own views formed from their own reading and understanding of any information that they may have gained from our departmental leaflet on ranibizumab therapy and other standard sources of information available to the general public.

Results

A total of 126 patients (89 (71%) women and 37 (29%) men) completed the questionnaires. Eight (6%) patients had had fewer than three prior intravitreal injections, 67 (53.2%) patients had between three and 10 prior injections and 51 (40.5%) patients had more than 10 prior intravitreal injections. Twelve (9.5%) patients were aged less than 70 years old, 47 (37.3%) patients were aged between 70 and 79 years old and 67 (53.2%) patients were aged over 80 years old. This indicated that this was a typical group of elderly patients who had had significant prior exposure to the treatment programme and had had time to absorb information and develop opinions about their treatment.

Despite this, only 80 (63.5%) patients had heard of Lucentis (ranibizumab) and only 52 (41%) of them knew that it was the only approved drug available. Eighty-two (65.1%) patients correctly identified the cost category of their treatment (£750–1000) indicating that there was a good level of awareness about the high cost of their intravitreal drugs.

Only 47 (37.3%) patients were aware of treatments other than ranibizumab. Avastin (bevacizumab) was the most commonly known alternative drug ($n=31$), followed by ICAPS

($n=15$), Macugen ($n=8$), and lastly Ozurdex ($n=1$).

Of the 31 patients who were aware of bevacizumab, only 17 (54.9%) estimated its cost correctly at £50–£250. The remaining patients estimated higher figures. Most patients had heard of bevacizumab from newspapers ($n=15$), from their doctor ($n=6$), from the internet ($n=4$), from other patients ($n=4$), from the television ($n=1$) and from family and friends ($n=1$).

Of the 31 patients who were aware of bevacizumab, 20 patients indicated that they had no preference between bevacizumab and ranibizumab, and 11 stated that they preferred to have ranibizumab. These 20 patients who had no preference were asked which of four factors they felt necessary to consider before deciding. Ten (50%) patients wanted more information about the effectiveness of bevacizumab and ranibizumab, eight (40%) patients wanted a recommendation from their ophthalmologist, two (10%) patients wanted information about the safety of bevacizumab and ranibizumab and none of the patients wanted information about the cost of bevacizumab and ranibizumab. This indicated that a large proportion of those who were aware of an alternative might accept a different choice of drug provided they could be reassured about its efficacy.

Discussion

Our results have revealed several interesting issues around the knowledge level of our patients about the standard therapy they were receiving and also around their views on the financial and non-financial reasons for considering alternative therapy. Although the majority of patients were able to correctly name the drug they were receiving and also correctly estimate the cost of ranibizumab, a significant proportion (63.5% of patients) could not name the drug that they were receiving regularly (ranibizumab) despite the provision, in our department, of patient information leaflets at the beginning of therapy in accordance with NICE guidance. We speculate that this may be because the patients' main concern is probably the procedure of intravitreal injection itself and the dosing regimen rather than the specific name of the drug. This highlights the need for continuing education of our patients so that they can be more informed and involved in

any decision-making process about choice of therapy in the future. However, nearly a quarter of our patients had heard of bevacizumab from information sources other than those provided by our department. Of particular note was that as many as two-thirds of those who had heard of bevacizumab were prepared to consider switching and felt that reassurance on efficacy and safety was the most important. This important message from our patient survey should encourage us to seek sufficient evidence to reassure our patients on safety and efficacy before we can contemplate switching to a cheaper alternative. As randomized trials like the CATT⁸ and IVAN⁹ studies are not powered to detect differences in uncommon events such as endophthalmitis or stroke, it is likely that continuing surveillance and data collection will be necessary to obtain evidence on the rare but severe side effects such as infective and non-infective endophthalmitis which is theoretically higher when using aliquots of bevacizumab.^{16–19}

Furthermore, none of the patients who were prepared to consider switching felt that knowledge regarding the cost of ranibizumab or bevacizumab was important to reach a decision to switch. This strongly suggests that any future information provided for patients to recommend the use of bevacizumab for nAMD should place much more emphasis on its efficacy and safety profile rather than its attractiveness as a cheaper alternative.

For convenience, the sampling method used was dependent on the interviewers (TO or BN) being available. Consequently, the sample was not randomized nor was it consecutive. However, we feel that the numbers of patients obtained was sufficient to offset any sampling error. Furthermore, patients were recruited in a very short timeframe, thereby reducing temporal bias.

This study, however, does not deal with another current issue concerning the use of an off-label drug in preference to a licensed one for the same indication. Currently, the GMC advises the use of unlicensed medicines only if the clinician is satisfied that an alternative licensed medicine would not meet the patient's needs.¹⁴ The proposed change in the wording of this guideline to allow off-label prescribing provided it is 'as safe and effective as an appropriately

licensed alternative'²⁰ would give clinicians more freedom to use bevacizumab for the treatment for nAMD.

The information transfer between patient and doctor is likely to become more complex as more therapeutic options such as off-label bevacizumab and the newer licensed drugs such as aflibercept (Eylea, Regeneron, Bayer)²¹ enter the arena. Coupled with an increasing evidence supporting the initiation of therapy earlier than the threshold recommended in the current NICE guidance,²² it is therefore conceivable that clinicians may be able to select different drugs for different patient scenarios and also switch from one drug to another in the future management of patients. It will become increasingly important to ensure that patients have a good understanding of how the decisions on the choice of their drug therapy have been made in order to maintain our patients' confidence and trust in our decision-making process for therapy for their challenging clinical needs. The findings from this simple survey further reaffirm the principles within the GMC guidelines governing the process of involving patients in decision making about therapy.

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Appendix 1

Patient survey – Part 1

You are currently receiving injection treatment for wet Age-related Macular Degeneration. We would be very grateful if you would spend a few minutes answering some questions about the treatment you receive.

1. **What is your age?**
 - A. Less than 50 years
 - B. Between 50–59 years
 - C. Between 60–69 years
 - D. Between 70–79 years
 - E. Over 80 years
2. **Are you Male/Female?** Please circle
3. **How many injections have you had into your eye so far?**
 - A. Less than 3
 - B. Between 3 and 10
 - C. More than 10
4. **Do you know the name of the drug that has been used for the injections so far?**
5. **Do you know how much money the drug costs each time you have an injection?** Please circle
 - A. About £50
 - B. About £250
 - C. About £500
 - D. About £750
 - E. About £1000
7. **Do you know if this is the only drug approved by the NHS for treatment of Age-related Macular Degeneration?** Yes/No
8. **Are you aware of any other drugs that are available that can be used for treatment of wet AMD?** Please circle
MACUGEN / LUCENTIS / OZURDEX / ICAPS / AVASTIN

Patient survey – Part 2

The drug you have been receiving with us is **Lucentis**. One of your answers for Question 7 was **Avastin**. We would like to ask you a few more questions about this drug.

1. **Do you know the cost of Avastin?** Please circle
 - A. About £50

- B. About £250
 - C. About £500
 - D. About £750
 - E. About £1000
2. **Where did you hear about Avastin?** Please circle
- A. Newspaper
 - B. Television
 - C. Radio
 - D. Internet
 - E. Family and friends
 - F. Other patients
 - G. Doctor
3. **Given the information you have, are you able to say whether you have a preference for either Avastin or Lucentis?** Yes/No
If Yes, please answer question 4, if No please answer question 5
4. **Would you prefer Avastin or Lucentis?**
5. **In question 3, you said that you do not have enough information to decide whether you would have Avastin or Lucentis. What further information would you like to have to be able to make this choice?**
- A. Cost of Avastin and Lucentis
 - B. Safety of Avastin and Lucentis
 - C. Effectiveness of Avastin and Lucentis
 - D. A recommendation by your Eye Specialist

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