Comments from Jennifer Nosek, Ophthalmic Nurse Specialist.

Appraisal Consultation Document on ranibizumab and pegaptanib for age-related macular degeneration

As a specialist nurse working in ophthalmology, I'm deeply troubled by some of the recommendations made by the appraisal committee. I'm absolutely convinced that the routine use of AntivegF drugs by retinal specialists to stabilise vision for all patients with wet AMD is fully justified by the evidence base that I have read and has been put to the committee.

I'm amazed to find that important elements of the evidence submitted by all the consultee's have been disregarded. I challenge the appraisal committee's recommendations and ask that the committee to give serious consideration to the points I raise in this reply.

Point 1

It is unethical and unacceptable to allow someone to go blind in one eye before being eligible for treatment in the second eye. Are the appraisal committee suggesting that only one functioning eye is required for normal life? This is patently untrue and there is enough literature available which describes this and the consequences of it. To limit these new treatments to 'second eyes' only would also be setting a disastrous precedent for other ophthalmic treatment areas such as cataract, diabetic retinopathy and glaucoma, all of which are bilateral in nature.

An ophthalmic clinician's goal is to prevent preventable loss of sight. This is also the aim of all national and international organisations concerned with vision and the notion that avoidable blindness should be allowed and indeed, encouraged is not something I'd expect an appraisal committee comprising of lead health care workers to recommend!

Point 2

The terminology 'no permanent structural damage' to the central fovea is misleading. How can you judge permanent damage unless you mean fibrosis that is long standing? The very fact that the patient has a subfoveal choriodal neovascular membrane (CNV) means there will be some damage in the foveal area. Therefore your recommendations are excluding the majority of patients with 'Wet AMD'!

Even patients with some central fibrosis at the fovea need treatment to control the disease process and prevent a large central scotoma that would grossly diminish their ability to self care and remain independent.

A study by Wagner (2006) using combined PDT and ranibizumab demonstrated that in patients with occult CNV, absolute scotoma decreased or remained stable in 83%. Severe relative scotoma also decreased or remained stable in 83% and mild relative scotoma had increased in 50% of patients. Areas of normal macular function improved or stabilized in 83%. In AMD patients this will enhance their ability in relation to visual rehabilitation and possibly preserve their dignity and independence.

Point 3

Not recommending the use of antiVegF treatment for minimal classic and occult CNV is to disregard a group of patients for whom currently there is no NHS treatment option and thus they will be forced to seek private health care or loose vision! To exclude these patients regardless of clinical need leaves them with no effective treatment and at high risk of increased dependence and injury. Therefore I can only reasonably infer that the Committee has not taken account of the available evidence of clinical need and national health priorities, focusing only on financial aspects of these therapies.

Point 4

By limiting treatment to only the predominantly classic subgroup of patients is adding to the moral dilemma and burden of NHS workers. Already we have to inform our patients that their wet AMD is treatable and there is a good chance that we can prevent further sight loss but unfortunately because they don't have a predominantly classic lesion we cannot provide their treatment on the NHS!. This causes distress to both parties and has an added burden on clinic time as these patients need time and empathy not only to except their diagnosis but understanding why there is no treatment available to them! In addition the costs to the individual, the family and the community are massive. We know from the vast evidence produced by the Royal National Institute for the Blind and the Macular Disease Society and my own clinical practice that visual impairment leads to loss of employment, dependency on state benefits, restricted mobility, family break-up and social exclusion. Surely the benefits of preventing blindness vastly outweigh the costs of treatment.

Point 5

The number of treatments used in the manufacturer's model is the number indicated in the licence indication for Ranibizumab based on the scientific findings of the PRONTO study. In this study, following an initial 3 injections over the first three months, retreatment with Ranibizumab was performed only if there was an increase in central OCT thickness of at least 100 µm, a loss of 5 letters in conjunction with recurrent fluid by OCT, new onset classic neovascularisation, or new macular hemorrhage. I feel based on this protocol, the number of treatments quoted in the model is a realistic guide on which to map costs to the NHS.

As a clinician I'm very aware that few interventions continue to be used in routine practice in precisely the same way as that reported in RCTs. However, this is more because RCTs are by their very nature are insufficiently flexible to allow for individualisation of treatment than because the treatment regimens evaluated in RCTs need to be entirely reconsidered.

The optimal treatment is likely to be patient dependent and appropriate treatment regimens for the individual patient can only be properly determined in routine clinical use. It's true that we don't know what the optimal regimen is at this point in time, but the right thing to do is to implement as close to the trial protocol as possible and then set up studies to answer questions on dosage regimen and also the effects of substituting lucentis with other agents in a graded manner.

This can be monitored under the clinical governance agenda of the providers. All routine practice is presently monitored through clinical audit and quality assurance outcome measures. The committee can be reassured that in the current climate all clinicians are painfully aware of their accountabilities to the NHS as well as their patients and therefore will make the best evidence based cost effective clinical decisions for all concerned.

Point 6

I note that you have estimated the cost these new treatments as a day case rather than an out patient procedure. The introduction of anti-VegF intravitreal treatments will mean a considerable increase in workload. In addition many units will need to provide additional services i.e. 'fast track' clinics, and because patients will potentially need monthly visits, staff numbers will need to increase to sustain demand. Therefore, despite the fact that the assessment and injection procedure takes no loner than that of photodynamic therapy (PDT), centres will need this additional funding as cost for day cases to develop services but the cost should be balanced against the fact that, over time as clinical experience and knowledge re- use of these treatments

grows, the number of treatments will be less as seen with PDT, and therefore cost to the NHS will decrease.

Point 7

You suggest that cost effectiveness is sensitive to uptake. I suggest that there will be a very high uptake in these new treatments in the NHS, therefore costs will be lower and outcomes for wet AMD patients better. Already our eye unit has seen an increase in referrals and enquiries as to whether or not we can offer treatment. Patients, relatives and carers are prepared to spend money travelling to clinics at frequent intervals and to remain under observation for years if we can save even a small amount of their sight. If this is the case surely we should not deny them the opportunity.

Point 8

I find it difficult to understand how a governing body whose remit is to examine evidence and recommend best practice, is recommending a head to head trial with a drug that is not licensed for use in the eye!

I welcome the fact that you recommend an investigation into the long term effects and optimal regimen of antivegF treatments but I strongly recommend that this be done via a national audit not as with PDT a ‘study’ that diverted necessary funding way from the clinical area .

Summary

I know the appraisal committee has a very difficult job reviewing numerous new therapies available to the NHS but I ask them to re-examine the evidence for antiVegF treatments for all wet AMD in the light of this response. I strongly believe, as do my colleagues that the evidence justifies the routine use of antiVegF treatments by retinal specialists to stabilise vision for all patients suffering the debilitating effects of wet AMD. We are already seeing dramatic results in our clinical practice. Our patients are not only getting stability but improvement in vision when VegFs are used. We owe it to these vulnerable elderly patients to allow them the dignity to remain as independent as possible by providing these treatments on the NHS.

Jennifer Nosek (Jul 2007)

(Wagner J, et al (2006) changes in functional mapping in patients with neovascular Age-related macular degeneration receiving combination of verteporfin and Randibizumab therapy Invest Ophthalmol Vis Sci 2006;47: E-Abstract 363)