Photodynamic therapy in age-related macular degeneration: missing information

SIR—We would like to add some elements of information and clarification to a commentary, entitled ‘Photodynamic therapy for age-related macular degeneration’ by Wendy Franks, that appeared in a recent issue [1].

In discussing conventional therapy for age-related macular degeneration (AMD), the leading cause of blindness in people over the age of 50, Dr Franks states that the only therapy in common use is argon laser. However, both the American Academy of Ophthalmology’s Preferred Practice Pattern for AMD [2] as well as published guidelines by retina experts [3] conclude that photodynamic therapy (PDT) with verteporfin
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(Visudyne®, Novartis AG, Switzerland) is now part of routine clinical care for AMD patients. PDT with verteporfin is a novel therapy that was first approved in 1999 and is now approved in more than 60 countries for the treatment of AMD associated with predominantly classic choroidal neovascularisation (CNV). To date, >170,000 patients have been treated with verteporfin therapy worldwide [4].

Dr Franks states that patients with large lesions who have experienced severe vision loss do not benefit from PDT with verteporfin. This statement is incorrect when these relative terms are defined more precisely. PDT with verteporfin was shown to reduce the risk of moderate and severe vision loss compared with a placebo therapy across a wide range of sizes of choroidal neovascular lesions associated with a wide range of visual acuities. Such results led experts [3], including policy makers for the Centers for Medicare and Medicaid Services [5], to conclude that verteporfin therapy should be considered as long as the physician and the patient judge that treatment would reduce the risk of further vision loss and impairment of quality of life, without a specific visual acuity or size cut-off.

Data from only one investigation with verteporfin (Verteporfin in Photodynamic Therapy (VIP) Trial) were presented in this commentary. However, several controlled clinical trials have been carried out in AMD patients, including the Treatment of AMD with PDT (TAP) Investigation (consisting of two concurrent randomised clinical trials with a total of 609 patients) and the VIP Trial (339 patients). PDT with verteporfin has been approved for the treatment of predominantly classic subfoveal CNV due to AMD based on the data from the TAP Investigation. As of August 2002, it has been approved in the European Union for occult with no classic lesions with presumed recent disease progression based on the data from the VIP Trial. In these indicated populations, a significantly lower proportion of treated patients experienced moderate vision loss (defined as <3 lines of vision) compared with the untreated control group at 2 years (41% versus 69%, P<0.001 for predominantly classic lesions and 55% versus 68%, P=0.032 for occult with no classic lesions) (6–8). Vision remained stable over the third year in an extension study of the predominantly classic lesions [6].

PDT with verteporfin usually requires multiple treatment courses involving an average of 5.6 treatments within the first 2 years. However, contrary to Dr Frank’s statement, AMD patients receiving laser photocoagulation may also need to be treated more than once. In fact, at least 50% of the patients treated with argon laser photocoagulation will need retreatment within 2 years which will be associated with further immediate vision loss in most of the cases [9].

The note of caution from the Cochrane reviewers cited in the commentary was based only on 12 months data of the TAP Investigation. These data, as well as the data at 24 months, have supported the significant treatment benefit of PDT with verteporfin in the total study population, without relying on subgroup analysis. However, there is an even stronger benefit in the subgroup of predominantly classic subfoveal CNV due to AMD. The Cochrane review also has not evaluated the published information from the occult with no classic lesions in the VIP Trial.

In contrast to £30,000 reported in the original commentary, our calculation of the cost of avoiding severe loss of vision with Dr Frank’s cost assumption (which we have taken to be in patients with predominantly classic lesions) is £24,225 per eye (using 4.76 as the Number Needed to Treat [NNT] for the predominantly classic form of AMD [10] and the cost of drug used by Dr Franks). In addition, our estimate of the total cost of drug for 2 years is £4,760 (5.6 treatments × £850): this calculation results in an even lower cost of £22,658 for blindness prevention. Since PDT with verteporfin is the first treatment proven to prevent blindness from AMD, we regret that the original commentary did not present either an accurate calculation of the cost-effectiveness data for PDT or the fact that untreated AMD causing blindness is itself associated with significant cost.

In conclusion, we hope that this letter will complement the overall clinical picture discussed in ‘Photodynamic therapy for age-related macular degeneration’ for the readers of Age and Ageing who may interact with patients at a time of early diagnosis of CNV due to AMD. In many cases the risk of moderate or severe vision loss can be reduced if patients presenting with reduced and distorted vision associated with a central blind spot are promptly referred to an ophthalmologist or retina specialist.

ANDREA WENKSTERN, JOHN STOKES
Novartis Ophthalmics AG, Grenzstrasse 10, CH-8180 Bülach, Switzerland
Fax: (+ 41) 1 862 0383
Email: andrea.wenkstern@pharma.novartis.com

1Novartis Ophthalmics, Australia


10. The NNT (number needed to treat) was calculated as follows: 1/(treatment responder rate- placebo responder rate). The absolute difference between treatment and placebo for predominantly classic patients, using severe vision loss as an outcome, in the TAP trial was 21%. Thus, the NNT is 1/0.21 = 4.76.