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EDITOR'S CHOICE

# Avastin versus Lucentis

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Drug treatment for age related macular degeneration is one of medicine's success stories. As Ning Cheung and colleagues explain (doi:10.1136/bmj.e2970), anti-vascular endothelial growth factors are preserving and restoring vision to millions around the world. But a related and less edifying story is stealing the limelight: ranibuzimab (Lucentis) versus bevacizumab (Avastin). It casts a shadow over this great medical advance and puts the world's drug development and licensing systems under the spotlight.

In its anti-cancer drug, bevacizumab, drug developer Genentech has created what may be the world's first "not me" (as opposed to "me too") drug, say Robert Campbell and colleagues (doi:10.1136/bmj.e2941). Despite evidence that it works in macular degeneration, the manufacturers and marketers (Roche in the US, Novartis in the UK and elsewhere) are actively discouraging its use for this condition, even going so far as taking legal action to prevent such off-label use. Why? Because they want people to use their other drug, ranibuzimab, which is licensed for treating macular degeneration.

The bottom line is that ranibuzimab is about 12 times more expensive: Cheung and colleagues report that the UK could save close to £300m (€368m; $485m) a year if it were standard treatment. So are Roche and Novartis simply fighting to protect their profits? They say no, that they are also protecting patients from the cheaper drug's higher risk profile. Although data from the publicly funded CATT trial in the US found similar effectiveness and safety for the two drugs in treating macular degeneration, the safety of bevacizumab remains a worry. Concerns relate to its greater systemic absorption and the fact that it has to be decanted into smaller quantities for intraocular injection, which introduces the risk of infection.

Whatever the motivation, the company has done all it can to limit the use of bevacizumab outside cancer, most notably by not applying for regulatory approval for use in patients with macular degeneration. Some health systems are finding ways round this, as Campbell and colleagues explain. But the combination of legal threats, safety concerns, and financial incentives to use ranibuzimab has maintained the more expensive drug's lucrative market. Sales in the US in 2010 topped $1.8bn.

In the UK, as Ingrid Torjesen reports (doi:10.1136/bmj.e3012), efforts are under way to get bevacizumab approved for use in macular degeneration despite resistance from Novartis. The National Institute for Health and Clinical Excellence has said it could appraise the drug if asked to by the Department of Health. Campbell and colleagues report that the department is waiting for the results of the IVAN trial in the UK, due to be published this month. But it is unlikely to resolve the safety concerns. Neither this nor the CATT trial was big enough to detect small but clinically relevant differences in adverse outcomes such as stroke, they say. Long term postmarketing surveillance is needed for that.

So what's to be done in the best interests of patients and the public purse? Campbell and colleagues call for clear guidance to use bevacizumab from professional organisations, a review of policies that discourage off-label use if there is good evidence for a drug's use, and better communication among health technology assessors in different parts of the world.

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