

## *Whither Avastin?*

Recently, both the Wall Street Journal and the New York Times ran articles regarding Genentech's decision to respond to eye doctors' use of Avastin over Lucentis by simply restricting Avastin's availability. The principle difference between the two is Lucentis' price, which is several hundred times higher per milligram than Avastin. The well informed realize that Lucentis is not a qualitatively different drug. It is essentially an altered fragment of Avastin with a different name and a different price. It is, if you will, the ultimate "me too" drug in that the original blockbuster was never suggested for ocular use while the "me too" version was promoted for what now seems a transparent reason.

To put this in perspective, if all 200,000 new cases of wet Macular Degeneration each year were treated with Lucentis according to the *approved* usage, it would cost 5.1 BILLION dollars per year **just for the drug**. This is more than the yearly Medicare budget for all of eye care. Consider also that if Genentech charged cancer patients for Avastin what they charge eye patients for Lucentis, it would cost each patient about \$500,000.00 every 2 weeks. The obvious question is, "Why is Lucentis' price so high?"

Another question is why Lucentis was developed in the first place. Genentech made a fantastic drug in Avastin and remarketed another version of the same molecule in Lucentis. Without any direct testing, they assumed (conveniently) that the Avastin molecule was too big to work in the eye. Contrary to this assumption, Avastin was independently found to work astonishingly well. The effectiveness and safety of Avastin have been corroborated repeatedly in peer reviewed reports ever since. This is no great surprise since both of these molecules have the same active site.

To summarize, Genentech knew that, in Avastin, they had a winner for cancer. They knew that it would be priced appropriately for cancer at doses of 500 to 1500 milligram every two weeks, guaranteeing them billions of dollars in revenue in the cancer market. They could deduce that if Avastin *would* work in the eye, doctors would only need 1 milligram or so, meaning that at the price fixed for cancer treatment, they wouldn't profit much from eye patients. This is in a world where competing drugs cost thousands of dollars per dose and don't even work that well.

This raises questions. Is it possible that the oncology pricing of Avastin could have been seen as a problem for ophthalmology marketing? As a for-profit company, what would have been Genentech's motivation to even see if Avastin worked for the eye? Might there have been greater motivation NOT to look at Avastin itself and simply assume that it was worthless for the eye? They could claim, for instance, that the Avastin molecule was just too big, creating a plausible reason to split the molecule. Might that have cleared the way to take a drug with an active site that they KNEW was good, split it, give it a new name, and bring it out as "something else", with a new price, guaranteeing billions in additional profit from a drug that had already become their cancer "blockbuster"?

These are not accusations *per se*, just musings on the seeming unlikelihood of the brilliant folks at Genentech missing something so obvious, and the odd coincidence that missing this could result in up to 5 billion per year in additional revenue.

There has been much recent coverage in the media and several recent authoritative books about the tactics used by the pharmaceutical industry to manipulate research, education, and regulation in the medical industry. The Lucentis story may define the current state of the art in this manipulation. Genentech dismissed Avastin for the eye, developed Lucentis, mobilized their paid medical promoters, and has refused to support any

comparative studies. In spite of this, a large and growing majority of retinal doctors prefer Avastin. In response to this, they now announce that they will restrict Avastin's availability, forcing doctors to use Lucentis, and forcing patients and payers to pay for it. They could have hoped for 5 billion per year from Lucentis just for one disease, and are now trying to make the safe, effective, affordable analog less available because they are only making 850 million in 2007. Even at this, Lucentis will break the bank for many seniors and possibly a few payers. Stories like this are the single biggest and most remediable factor in Medicare's drive toward bankruptcy.

Adding insult to injury, simultaneously with the announcement restricting Avastin's availability, retina doctors received an unvarnished bribe to use Lucentis in the form of a "gift certificate redeemable for medically related products ...- courtesy of Genentech" (quoting from the flyer).

Enough is enough. Hoodwinking the public for billions of dollars is immoral, but doing the same to government could be Medicare fraud on a massive scale. Situations like this demand action from doctors, from patient groups, or from congressional inquiry free of lobbyists and financially compromised medical minions.

Retinal specialty societies are responding to the latest events. Recently, the trend toward doctors accepting drug industry cash and support in exchange for promotional research, education, and patient care has reached crisis proportions. This is now being addressed in the press and in Congress, where the Sunshine Act has been introduced to shed light on these often covert financial relationships. Now is an opportune time for doctors and societies to decide and demonstrate whose side they are on.

In the November 2007 survey of retina care standards, Avastin is seen to be a true standard of care. The immediate need is to obtain relief from Genentech's attempts to prevent head to head comparisons between Avastin and Lucentis, from their efforts to limit the availability of Avastin, and from drug companies' attempts to control medical practice through control of research and education. At stake is no less than the solvency of Medicare, the credibility of patient care, and our seniors' medical and financial well-being.

Physicians for Clinical Responsibility