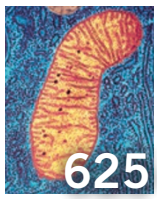
Disaster proofing: Researchers discuss ways to safeguard the lab against calamity



The organelle sell: Advocates urge new treatments for mitochondrial disease

Negative findings: Researchers tackle pathogenic Gram-negative bacteria

In vision trial, some researchers would rather see double

A government-sponsored clinical study of vision loss has come under fire for investigating a proprietary medicine without comparing it to a similar drug that costs a fraction of the price.

In late April, first year results from a two-year clinical study of about 700 individuals with a condition known as diabetic macular edema were reported by the Diabetic Retinopathy Clinical Research Network (DRCRnet), a multicenter collaborative group funded by the US National Eye Institute (NEI).

The researchers found that nearly half the people injected with the drug Lucentis (ranibizumab) into the eye, on its own or combined with laser therapy, gained two or more lines of vision on an eye chart after one year. By comparison, around 30% of those receiving only standard laser therapy experienced the same degree of improvement, and adding corticosteroid treatment did not seem to help (*Ophthalmology* doi:10.1016/j.ophtha.2010.02.031, 2010).

"This was a dream trial of mine to compare two different drugs head to head in the same study," NEI clinical director Frederick Ferris says in reference to Lucentis and the steroid treatment. "We did something in this trial that could not have been done if the government had not been involved."

But some researchers criticized the trial organizers for testing Lucentis without also evaluating another drug called Avastin (bevacizumab), both of which are made by South San Francisco–based Genentech. Lucentis is a truncated form of Avastin, a monoclonal antibody that inhibits a protein called vascular endothelial growth factor (*VEGF*).

Lucentis costs upward of $2,000 a dose and was approved in 2006 for a related eye disease, age-related macular degeneration. Avastin, meanwhile, is approved for some forms of cancer, but many eye doctors prescribe the drug off label for eye ailments, as it costs less than $100 per treatment.

A week before the DRCRnet study for diabetic macular edema was published, researchers at the Moorfields Eye Hospital in London reported the results of a £500,000 ($725,000) trial testing Avastin versus laser treatment in 80 individuals with the same eye condition. According to ophthalmologist and senior author Philip Hykin, the team chose Avastin instead of Lucentis at the urging of local health officials. "To them, cost was the overriding factor," he says.

In their study, the researchers showed that five times more people experienced a two-line improvement on the eye chart with Avastin compared to laser therapy (*Ophthalmology* doi:10.1016/j.ophtha.2010.03.045, 2010).

Taxing questions

Philip Rosenfeld, an ophthalmologist at the University of Miami Miller School of Medicine thinks that the NEI-backed researchers should have tested Avastin alongside its pricier derivative. "My frustration is that tax dollars were used to subsidize industry-sponsored research," he says. "The DRCRnet did a fabulous job, and they deserve credit for what they accomplished, but their talents were misdirected."

Several researchers contacted by *Nature Medicine* pointed to funding from the pharmaceutical industry as possibly swaying the decision not to include Avastin in the NEI-sponsored study. Organizers of the trial confirmed that the companies supplied free drugs and covered the costs associated with clinical care and testing, but, owing to a confidentiality agreement, they did not confirm or deny the reported $9 million provided by Genentech, as described by the *New York Times*, and they declined to specify how much financial support was supplied by Allergan, the Irvine, California biotech that made the steroid included in the trial. Both companies also declined to disclose the level of funding.

Neil Bressler of Johns Hopkins University School of Medicine in Baltimore, who led the trial, refutes claims of impropriety. The decision to use Lucentis, he says, "really was based on the science that we had at the time." Two major trials had shown that Lucentis is safe and effective for macular degeneration (*New Engl. J. Med.* **355**, 1419–1431 and 1432–1444, 2006); no comparable data existed for Avastin, he notes.

Paul Volberding, chief of the medical service at the San Francisco Veterans Affairs Medical Center, says the appearance of conflict could have been avoided had the NEI paid for the full cost of the drugs and the trial. However, Ferris notes that, with limited institute resources, doing so would have meant foregoing other studies. Plus, he stresses, the trial design went through external peer review and was not influenced by the company sponsors.

An eye on spending: Drug dispute in eye trial.

"It's ironic," Ferris says. "Virtually everybody is saying that government should be collaborating with industry. This network at least puts us in a position to do so. Those collaborations have allowed us to find things we wouldn't have been able to do otherwise."

Nikki Levy, a Genentech spokesperson, says the trial results are "encouraging," but the study will not form part of Genentech's regulatory filing. The company has two ongoing phase 3 trials comparing Lucentis to laser therapy; results are expected next year.

Although researchers have not tested Lucentis and Avastin side by side for macular edema, the two drugs are currently being compared in two separate trials of macular degeneration, sponsored by the NEI and the UK National Institute for Health Research, respectively.

The UK Diabetic Retinopathy Research Group now has a £1.5 million grant proposal under review to conduct a 300-person trial of Avastin and Lucentis, both alone and with laser, for macular edema, says Hykin, a member of the group. Meanwhile, the NEI will wait for the results of its head-to-head macular degeneration trial, expected next spring, before deciding whether to launch a trial formally comparing the drugs for macular edema, Ferris says.

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Correction

In the print version of the June 2010 issue of *Nature Medicine*, the byline was missing for the article entitled 'In vision trial, some researchers would rather see double' (*Nat. Med.* **16**, 611, 2010). The author was Elie Dolgin. The error did not appear in the HTML and PDF versions of the article.