

# Drug Shows Promise For Newborn Blindness

Treating Babies With Avastin Surpassed a Usual Therapy

By JENNIFER CORBETT DOOREN

An inexpensive drug therapy far surpassed a conventional laser procedure in fixing a leading cause of blindness in babies born prematurely, according to a new study.

The results of the study, to be published this week in the *New England Journal of Medicine*, were so significant that the 15 hospitals participating in the research have stopped using lasers in favor of the drug, Avastin, which is injected into the eyes of the affected newborns. Avastin, made by Roche Holding AG's Genentech unit, is designed to be used for treating cancer, and the company doesn't promote its use for any eye conditions.

Babies born before 30 weeks of gestation have immature eyes and are at high risk of developing a condition called retinopathy of prematurity that is caused by uncontrolled growth of blood vessels in the eye. The blood-vessel growth can lead to scarring and detachment of the retina, which causes blindness.

The study's lead researcher, Helen Mintz-Hittner, an ophthalmology professor at the University of Texas Health Science Center at Houston Medical School, says retinopathy of prematurity is traditionally treated with a laser procedure that requires general anesthesia. Some babies need several treatments over time, and in most cases peripheral vision can't be saved.

Dr. Mintz-Hittner estimates there are about 3,000 to 4,000 cases of retinopathy of prematurity in the U.S. each year. The numbers are increasing as more premature babies survive.

An injection of Avastin stopped blood-vessel growth. In many cases, the drug was able to successfully treat retinopathy in premature babies with just one

treatment. Babies get a small amount of anesthetic to numb the eye before being injected.

Avastin was designed to help treat cancer by choking off blood vessels to tumors, and doctors have been using it to treat some eye conditions. Genentech also markets a drug called Lucentis that's similar to Avastin and is approved by the Food and Drug Administration to treat age-related macular degeneration, which is the leading cause of blindness in older adults.

Dr. Mintz-Hittner says such a small dose of Avastin is used for premature babies that it costs about \$40 to treat both eyes. A comparable dose of Lucentis would be about \$2,500, she says. Avastin also is preferable to Lucentis for retinopathy in infants because of the way it's designed. Avastin is considered a large-molecule drug, so it can't easily travel outside the eye area. Dr. Mintz-Hittner said a theoretical concern with Lucentis, which is a smaller molecule, is that it might travel to other parts of the body and impact necessary blood-vessel growth in babies.

A Genentech spokesman said there's limited safety information about uses of Avastin in treating eye diseases. "We don't support or promote the off-label use of Avastin," he said, noting that Avastin is not approved for use in the eye.

About 150 premature babies were enrolled in the Houston-led study from March 2008 through August 2010. Half were randomized to receive Avastin and the other half received laser treatment. Seven babies died of causes unrelated to the eye treatments. The remaining 143 babies were followed for several weeks after their initial treatments to see if the retinopathy returned.

Overall, retinopathy recurred

in four infants treated with Avastin compared with 19 infants treated with the laser, which translates into a 20% reduction in the risk of recurrence. The results were even more significant for babies with a harder-to-treat form of the disease called zone 1, in which abnormal blood vessels form at the very back of the eye. Among infants with this form of the disease, the recurrence rate was 6% with Avastin compared with 42% for laser therapy.

James D. Reynolds, an ophthalmology professor at the University of Buffalo, wrote in an accompanying editorial that Avastin should be the treatment of choice for babies with zone 1 retinopathy of prematurity.

Bradley and Kelly Henry, who had two daughters born prematurely, saw first hand the outcomes of the different treatments. Their daughter Grace was born in 2004 at 24 weeks' gestation, weighing under two pounds. She was later diagnosed with retinopathy of prematurity and had several laser treatments under Dr. Mintz-Hittner's care. Grace's left eye eventually burst after she developed glaucoma, and it had to be replaced with a glass eye. She has enough vision in the right eye to attend regular school but is considered legally blind. "It's hard to watch your daughter walk into a flagpole because she can't see," Ms. Henry says.

By the time the Houston-area family's other daughter, Evelyn, was born early last year at 26 weeks' gestation, the Avastin study was under way. Evelyn wasn't enrolled but was able to receive Avastin after she was diagnosed with retinopathy.

Ms. Henry says she remembers being "elated" that Evelyn was able to receive Avastin. "I knew what the effects of laser treatment were," she says. Evelyn, now 13 months old, had just one treatment with Avastin and so far appears to be developing normally, Ms. Henry and Dr. Mintz-Hittner say.

The oldest children in the Avastin study are now nearly 3 years old and appear to be developing normally, Dr. Mintz-Hittner says, adding that so far she hasn't seen any significant side-effects from the drug. She says doctors need to be careful not to administer Avastin too early before the abnormal blood vessels fully develop, nor too late after the blood-vessel growth causes the retina to detach.



Among the early efforts to foolproof cars: replacing hand-crank starters with electric ones.

## Electric Fixes for Driver Error

By JOSEPH B. WHITE

The flap over sudden acceleration in Toyota cars gave automotive electronic systems a black eye. So what's in store now that a team of rocket scientists (literally) have concluded that people, not electronic throttles, are to blame for most accidents caused by runaway cars?

The answer: even more electronics in cars.

Specifically, drivers will see more electronics in vehicles

### YES ON THE ROAD

aimed at counteracting—or preventing—human error. What's more, there will be new electronics that take out of drivers' hands some of the responsibility of properly maintaining and in some cases, operating a vehicle.

In the future, the government is likely to require cars to have electronic systems that cut power to the car when drivers hit both the brake and gas pedals. Regulators could demand that the push-button, keyless ignition systems increasingly popular on new vehicles be redesigned to make it easier to shut down an out-of-control car. Cars could be required to carry "event data recorders," similar in concept to the black boxes installed on airliners, to record data on speed, braking and acceleration to help accident investigators reconstruct a crash.

### Response to Findings

The National Highway Traffic Safety Administration said it will pursue rules requiring these technologies in response to the findings from a nearly year-long investigation into the causes of a rash of sudden-acceleration incidents involving Toyota and Lexus cars. That investigation, which involved a team of engineers from NASA as well as NHTSA's own engineers, concluded that some of the crashes were the result of accelerators getting trapped under floor mats, but most of them were the result of drivers mistaking the gas pedal for the brake.

Safety regulators also have proposed that all new vehicles be equipped with cameras that would feed a real-time image of what's behind a vehicle moving in reverse. The goal of these systems is to prevent accidents in which people—often young children—are injured or killed by someone who can't see them when backing up.

Aside from safety, auto makers are pushing ahead on their own with increasingly sophisti-

cated electronics to monitor a vehicle's vital functions, diagnose potential trouble, and signal to a concierge service—or the customer's smartphone—when it's time to change the oil or go in for maintenance. The next evolution of these electronic concierges: Software updates pushed to the car remotely via a wireless link or through computers at the dealership.

BMW already can update information such as the phone number for its emergency-assistance service using wireless links to its cars, says Tom Baloga, chief engineer for BMW's North American operations.

"We will take it to the next level," he says. So "we can fix something before it goes wrong."

### An Eye on the Volt

General Motors Co. is monitoring the behavior of Chevrolet Volt plug-in hybrid vehicles using the wireless link that comes with the company's OnStar service. Data about how Volt batteries are performing in customer hands, and other information, flows anonymously to GM engineers, says OnStar's Steve Schwinke. The Volt system expands on the OnStar system's existing capability to transmit certain "trouble codes" to the system's operators when a customer calls in to report a problem.

All of this is aimed at transferring a greater share of the responsibility for properly maintaining and operating a car from the driver to either an automated system or human minders who can—via smartphone apps or a voice link—nudge customers to get the oil changed or have the brakes checked.

### Early Foolproof Move

The effort to foolproof vehicles goes back to the industry's beginnings. Early automobiles had hand crank starters that could break your arm if you didn't watch out. The solution: electric starters.

The next generation of foolproofing will venture along the boundary between what drivers should be expected to own as their responsibility, and what car makers or regulators should do to assure that driving is safe and convenient. Costs will be an issue. As will and trade-offs between what customers desire—throttle systems that feel peppy and responsive or the convenience of starting a vehicle with just a push of a button—and what regulators judge to be safe.

Some proposals that appear simple—such as NHTSA's suggestion that brake and gas pedals should be repositioned in future vehicles so they are harder to mix up—could be complicated.

Paul Green, a University of Michigan professor and expert on how drivers interact with cars, says changing the familiar layout of pedals could force car makers to make expensive changes to the body structure of vehicles.

If, for example, U.S. regulators decided brake and accelerator pedals should be an inch or two farther apart, that could compel car makers to reconfigure the floor of the car to accommodate the wider spacing.

If German or Chinese regulators took the view that a different pedal arrangement was better, that could force car makers to offer different pedal layouts for different countries—the exact opposite of the industry's goal of making cars more alike world-wide.

A NHTSA spokeswoman says the agency recognizes "pedal design is a delicate balance" plans to do more research before taking any action.

### Re-Learning to Drive

There's also the risk drivers will struggle to re-learn skills acquired over years of driving. There could be "enormous transfer of training issues" for motorists confronted with a dramatically different pedal layout, Dr. Green says.

Nobody in the auto business or the auto-safety regulation business likes to blame drivers for making dangerous mistakes. But the expanding push to foolproof vehicles speaks loudly about the lack of faith in the abilities of the average driver. And given auto makers' experience with drivers' lack of awareness, it may be for good reason.

For instance, a BMW owner called the company's call center to complain that his car wouldn't start, stranding him in an airport parking lot. The diagnosis, Mr. Baloga says, was delivered via the car's cellphone link after the call center worker assessed information relayed from the car: The vehicle had no gas. The owner realized he had forgotten to hit the off button on the keyless ignition, and left the vehicle running—very quietly—while he headed for the plane.

Read news, views and advice about cars at [blogs.wsj.com/drivers-seat](http://blogs.wsj.com/drivers-seat).



The Henry family (from left), Evelyn, Kelly, Brad and Grace. Both girls were born premature. Grace is legally blind while Evelyn (also pictured at top) received drug therapy and her eyesight is developing normally.

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