

THE WALL STREET JOURNAL.

Health & Family

Skin-Cancer Drug Uses Genetics

By Ron Winslow

729 words

3 June 2009

[The Wall Street Journal](#)

D3

English

(Copyright (c) 2009, Dow Jones & Company, Inc.)

ORLANDO, Fla. -- Results from a small, early-stage clinical trial suggest the burgeoning strategy of attacking tumors based on their genetic characteristics could soon yield effective drugs against advanced melanoma, one of cancer's most lethal and hard-to-treat conditions.

Researchers reported that nine of 16 patients with the malignant skin cancer experienced significant shrinkage of their tumors when given a drug known as PLX4032. Tumors in all of the patients had a mutation in a gene for a protein called BRAF that is believed to play a crucial role in up to 60% of patients with the cancer. Five other patients in the study whose cancers had a normal BRAF gene didn't respond to the treatment.

Melanoma experts said the findings were impressive, but cautioned that they need to be confirmed in larger, more rigorous studies. Excitement about positive data in a recent small study of another drug turned to disappointment when large studies failed to substantiate the early results.

Whatever the ultimate outcome for the drug, the findings reflect the broader potential of genetic information to help researchers and clinicians select for treatment patients with higher chances of benefiting from a drug and steering those unlikely to respond to other options. The hope is that this approach will speed drug development and enable doctors to deliver care more cost-effectively.

The drug, known as a BRAF inhibitor, is being developed by Roche Holding AG, the Swiss pharmaceutical giant, and **Plexikon** Inc., Berkeley, Calif., a closely held biotechnology company that discovered it. Novartis SA is among other companies pursuing BRAF inhibitors against melanoma and some other cancers where a mutated BRAF gene may drive tumor growth.

The study, sponsored by **Plexikon**, was among scores of reports looking at the interaction of genetic biomarkers and cancer treatments presented at the annual meeting of the American Society of Clinical Oncology, which ended here Tuesday. Overall, they added more support for the movement toward personalized medicine, in which treatments are tailored to individual patients based on genetics and other biomarkers that increase chances they will work.

"This is proof of principle that the target the drug is aiming at can be hit and lead to an important clinical result," said David F. McDermott, clinical director of the biologic therapy program at Beth Israel Deaconess Medical Center, Boston, who wasn't involved with the study.

But "we don't want to raise a sense of false hope," he added. Importantly, some of the patients who responded to the treatment relapsed soon afterward. "One of the big questions going forward is, do the effects last long enough to have a meaningful impact on survival?" Dr. McDermott said. Side effects included a rash and fatigue.

Melanoma, which afflicts about 160,000 people globally each year -- nearly half of them in the U.S. -- typically starts as an abnormal mole on the skin and is easily cured if caught and removed early. But once it spreads to the liver, lungs or other parts of the body, it is particularly deadly, and current treatments typically stave off progression by only a couple of months.

"We're about near zero in terms of our ability to treat the disease," said Keith Flaherty, an oncologist at the University of Pennsylvania's Abramson Cancer Center and principal investigator for the **Plexxikon** study.

The BRAF mutation was identified as a "smoking gun" for melanoma in 2002, but efforts to target the defect have so far come up short. Indeed, after an early-stage test of the drug Nexavar showed encouraging results against melanoma, it failed to benefit patients in two late-stage trials in combination with chemotherapy. BRAF is one of the targets of Nexavar, a drug approved for kidney and liver cancers and co-marketed by Onyx Pharmaceuticals Inc. and Bayer AG.

But patients in the Nexavar studies weren't tested for BRAF, Dr. Mcdermott said, and it wasn't determined whether those carrying the mutation fared any better.

Dr. Flaherty, who presented the **Plexxikon** findings at the cancer meeting late Monday, said the data so far indicate the drug prevents progression of the disease for six months. Current therapies keep it in check for just two months. Once the disease recurs, patients typically live only a few months.