Combo of Avastin, second drug shows promise fighting brain cancer, study finds

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The drug bevacizumab, also known by the trade name Avastin, shrinks tumors briefly in patients with an aggressive brain cancer known as glioblastoma multiforme, but then they often grow again and spread throughout the brain for reasons no one previously has understood. Now, Mayo Clinic researchers have found out why this happens. They have also discovered that pairing Avastin with another cancer drug, dasatinib, can stop that lethal spread. Dasatinib is approved for use in several blood cancers.

The findings, based on an animal study, are detailed in the Feb. 14 online issue of PLOS ONE. Based on those results, Mayo Clinic has already conducted a phase I clinical trial testing a combination of bevacizumab and dasatinib in glioblastoma patients whose other therapies failed. Mayo is now carrying out a randomized phase II study of 100 patients through Alliance for Clinical Trials in Oncology, a clinical trials network supported by the National Cancer Institute.

"We are very encouraged. This finding could potentially benefit many cancer patients," says co-author Panos Z. Anastasiadis, Ph.D., chair of the Department of Cancer Biology at Mayo Clinic in Florida. Working with him were researchers and oncologists from Mayo Clinic campuses in Florida and Minnesota.

The research began after Dr. Anastasiadis, a basic scientist who studies cell adhesion and migration, gave a seminar to a group of oncologists who treat brain tumors. The issue of bevacizumab-induced invasion was

brought up and a collaboration to study it was quickly set up and funded by the Mayo Clinic Specialized Program of Research Excellence (SPORE) grant for brain cancer, one of only four in the country.

The issue of bevacizumab's induced aggressiveness is not limited to brain cancer, Dr. Anastasiadis says.

"While Avastin offers clear benefit in some patients, oncologists have noted that when cancers of many types recur after use of Avastin, they become aggressive and invasive," he says.

The team discovered that as brain tumors become more aggressive after use of bevacizumab in mice, the cancers begin inducing a family of kinases known as Src, which then activate proteins found at the edge of brain tumors. These proteins essentially give the tumor cells "legs" upon which to crawl away and find a new source of nutrition, Dr. Anastasiadis says.

"Anti-angiogenesis drugs like Avastin deprive tumor cells of blood nutrients, so the tumors shrink initially, but we believe that this deprivation acts like a switch to turn on proteins that help the cancer cells migrate to other parts of the brain in search of blood," he says. "In short, if Avastin does not allow a tumor to make new blood vessels to feed it, the tumor will move to other existing blood vessels."

The researchers then tested dasatinib, a drug that inhibits Src kinases. They found that while use of bevacizumab or dasatinib alone did not provide much benefit in mouse models of human glioblastoma, use of both together shrank tumors and blocked any subsequent spread.

"If you block that migration, the cells are forced to stick together and hopefully die by lack of nutrition," Dr. Anastasiadis says.

Researchers next will work to identify which patients benefit the most from this new treatment, which do not, and why.

Provided by Mayo Clinic