New experimental treatment can stop growth of schwannoma tumors

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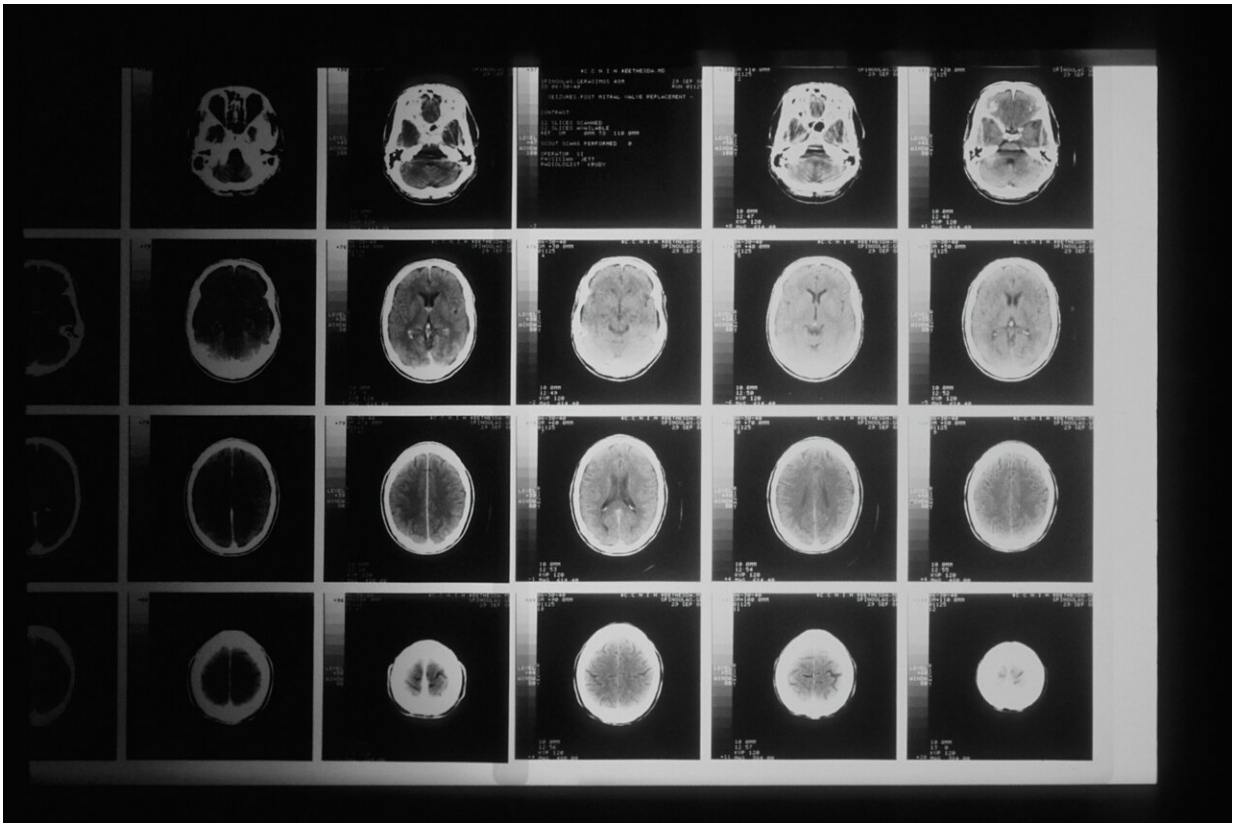

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Two novel and orally administered drugs can not only block the growth, but also shrink the size, of a tumor type found in the nervous system, new research has shown.

The tumors, schwannomas, most frequently grow on the nerves that bring hearing and balance information into the brain. Schwannomas are the most common nerve sheath tumor, and can occur in anyone but are also linked to a hereditary condition known as Neurofibromatosis Type II (NF2).

In NF2, where the function of the protein Merlin is lost in cells, patients frequently develop not only schwannomas, but also meningioma tumors associated with the brain and spinal cord.

The treatment of both tumor types is difficult, with surgery being the current mainstay but also carrying a high risk of damage to the surrounding normal nervous system tissue.

With an urgent need for new treatments, an international team of scientists focused on the Hippo signaling pathway, which normally controls organ size in human tissues and cells, but is dysregulated in multiple types of cancer.

Using a combination of patient-donor tumor cells from surgical resections and mouse models of schwannoma, the researchers showed that after just 21 days of the drugs being administered, tumor growth can be strongly and significantly reduced.

In addition, treatment with the Hippo pathway inhibitors (named VT1 and VT2 in the study) actually caused the death of tumor cells and an overall shrinkage of the tumor size.

Drugs from this new class of Hippo pathway inhibitors have also been shown to be effective in another tumor type, mesothelioma, and are presently in Phase 1 clinical trials.

Initial experiments with these new compounds show they also seem to

block the growth of meningioma tumor cells. As well as being a second tumor type seen in patients with NF2, meningioma is overall the most common tumor seen within the brain.

The impact of using these new therapies to hit both tumor types simultaneously has the potential to be highly clinically valuable.

The study is published in the November issue of the journal *Brain*, and was led by Research Fellow Dr. Liyam Laraba and Professor of Neuroscience David Parkinson from the University of Plymouth.

Dr. Laraba, who completed the work as part of his Ph.D. research, said, "We are really excited to show that blocking the Hippo pathway is highly effective in preventing schwannoma and meningioma growth. These drugs are well tolerated in our models and we hope that our work can stimulate and accelerate the use of these inhibitors in clinical trials."

Professor Parkinson, the study's senior author, added, "Our current study gives an early indication that we can potentially provide schwannoma patients with a successful alternative treatment to manage their condition. However, patients with Neurofibromatosis Type 2 often have both schwannoma and meningioma tumors in their nervous system. For those patients, the prospect of a single drug that could treat both tumor types without the need for intrusive and risky surgery is clearly an exciting prospect."

More information: Liyam Laraba et al, Inhibition of YAP/TAZ-driven TEAD activity prevents growth of NF2-null schwannoma and meningioma, *Brain* (2022). DOI: 10.1093/brain/awac342

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