

## Anti-angiogenesis treatment improves hearing in some NF2 patients

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Treatment with the angiogenesis inhibitor bevacizumab improved hearing and alleviated other symptoms in patients with neurofibromatosis type 2 (NF2). In a paper to appear in the July 23 *New England Journal of Medicine*, which is receiving early online release, researchers from Massachusetts General Hospital (MGH) report that bevacizumab treatment successfully shrank characteristic tumors in a small group of NF2 patients, the first reported successful NF2 treatment not involving surgery or radiation.

"This kind of treatment response is unprecedented," says Scott Plotkin, MD, PhD, of the Pappas Center for Neuro-Oncology in the MGH Cancer Center, lead author of the NEJM paper. "Our study is the first to provide evidence that a drug can shrink vestibular schwannomas - benign tumors on the balance and hearing nerves - and the first to show that patients' hearing can be improved."

NF2 is an inherited genetic disorder in which benign tumors develop throughout the nervous system. Vestibular schwannomas are the most common NF2-associated tumors, and although they grow slowly, they usually cause patients to lose all or most of their hearing by young adulthood or middle age. The tumors can be removed surgically or treated with radiation, but in patients with vestibular schwannomas on both sides, which is typical in NF2, such treatment usually leads to complete hearing loss. Growing vestibular schwannomas can also press on the brainstem, leading to headaches, difficulty swallowing and other serious neurologic symptoms.

Since vestibular schwannomas are benign tumors, it was believed that they did not stimulate formation of new [blood vessels](#) as malignant tumors do. However, when the researchers studied tissue samples from NF2-related schwannomas, sporadic tumors not caused by NF2 and normal spinal nerves, they found evidence of excess blood vessel development and increased expression of angiogenesis-related molecules in both NF2-associated and sporadic vestibular schwannomas. With this suggestion that angiogenesis was involved in these tumors, members of the research team offered treatment with bevacizumab (Avastin), which is FDA-approved for treatment of several forms of cancer, to NF2 patients in danger of complete hearing loss or other significant neurological damage.

Among the first ten NF2 patients to receive bevacizumab, treatment led to tumor shrinkage in nine, and six had 20 percent or greater reduction in tumor size. In those six patients, tumor shrinkage lasted from 11 to 16 months, longer than the four months typically seen in bevacizumab treatment of malignant brain tumors. Of seven patients who had started to lose their hearing before treatment, four experienced some hearing restoration - two returning to work or school as a result - improvement that has also lasted for up to 16 months. In one patient without significant tumor shrinkage or hearing improvement (he had lost all hearing prior to treatment), treatment alleviated headaches and nausea caused by brainstem compression, allowing him also to return to school.

"This study has opened a new approach to research and understanding of these tumors," says Emmanuelle di Tomaso, PhD, the study's senior author, formerly with the Steele Laboratory of Tumor Biology in the MGH Department of Radiation Oncology. "There had been a dogma that these tumors do not produce edema and are not angiogenic, concepts that now need to be reevaluated." She adds that the study also suggests that VEGF - the angiogenesis factor blocked by bevacizumab - may have a role in nerve physiology beyond the stimulation of blood vessel growth.

Plotkin notes, "Based on the results of this study, we have just opened the first formal clinical trial of a drug treatment for NF2. We are testing an exciting new, oral VEGF inhibitor that will be easier for [patients](#) to take - bevacizumab is administered intravenously - and may have fewer side effects."

Source: Massachusetts General Hospital ([news](#) : [web](#))

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