News Release

Chugai Files for Additional Indication of Avastin for the Treatment of Neurofibromatosis Type 2

- The filing is based on the results from an investigator-initiated Japanese phase II clinical study
- If approved, Avastin would become the world's first therapeutic drug for neurofibromatosis type 2, a rare intractable disease with limited treatment options

TOKYO, September 24, 2025 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it filed a regulatory application with the Ministry of Health, Labour and Welfare (MHLW) on August 29 for the anti-cancer agent/humanized anti-VEGF*1 monoclonal antibody Avastin® for Intravenous Infusion 100mg/4mL, 400mg/16mL [generic name: bevacizumab (genetical recombination)] for neurofibromatosis type 2 (NF2), a new indication for Avastin.

This filing is based on the results from a Japanese phase II BeatNF2 study initiated by investigators, which evaluated the efficacy and safety of Avastin for NF2.

About BeatNF2 study

BeatNF2 study (jRCT2080224914) is an investigator-initiated, Japanese Phase II, multicenter, placebo-controlled, double-blind, randomized study that evaluated the efficacy and safety of Avastin for NF2, a rare hereditary disease. The study enrolled 62 patients who were divided into an Avastin treatment group and a placebo group to compare the improvement in hearing at 24 weeks after treatment initiation. After 24 weeks and up to 48 weeks, both groups received Avastin. The primary endpoint was “the proportion of patients with improved hearing at 24 weeks after treatment initiation compared to baseline, based on the evaluation using maximum speech discrimination score*2.” Secondary endpoints included maximum speech discrimination score at weeks 12, 36, and 48, tumor volume, pure tone audiometry, auditory steady-state response, NF2 severity score, and the efficacy of retreatment in patients who experienced hearing deterioration following initial improvement.

*1 VEGF：Vascular Endothelial Growth Factor

*2 Maximum speech discrimination score is an indicator of speech comprehension ability. It refers to the percentage of correct answers in a monosyllabic word recognition test at

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the volume level that yields the highest accuracy while adjusting sound intensity. The higher this value, the better one's ability to accurately understand speech when sounds are audible. It also serves as a measure for evaluating the effectiveness of hearing aids.

About neurofibromatosis type 2 (NF2)[1]

NF2 is an autosomal dominant hereditary disease characterized by bilateral acoustic nerve tumors (vestibular schwannomas). Symptoms commonly associated with acoustic schwannomas include hearing loss, dizziness, unsteadiness, and tinnitus. Additionally, symptoms related to other manifestations such as spinal nerve schwannomas may include numbness in the limbs, reduced sensation, and weakness.

For acoustic neuroma, observation, surgery, and radiation therapy are performed. While it is a benign tumor that sometimes shows little growth, in cases where symptoms develop or tumor growth is evident, surgical removal may be performed, which can affect the long-term prognosis. Preservation of hearing through surgery is difficult, and there is a risk of postoperative neurological complications.

According to overseas reports, the incidence rate is a rare 1 in 25,000-60,000 people, and in Japan, approximately 800 people submitted clinical registry data between 2009-2013. Most cases are diagnosed in patients between 10 and 29 years of age.

About Avastin

Avastin is an antibody drug that specifically binds to VEGF[2], which plays an important role in angiogenesis necessary for tumor growth and metastasis, and inhibits its action. Since its launch in Japan in June 2007, it has been positioned as one of the standard treatments in treatment guidelines for various types of cancer. It has been approved for seven indications (unresectable advanced or recurrent colorectal cancer, unresectable advanced or recurrent non-small cell lung cancer excluding squamous cell carcinoma, inoperable or recurrent breast cancer, malignant glioma, ovarian cancer, advanced or recurrent cervical cancer, and unresectable hepatocellular carcinoma).

Sources

1. Japan Intractable Diseases Information Center. Neurofibromatosis type 2 (designated intractable disease 34) [Internet; cited September 2025].
   Partially modified from: https://www.nanbyou.or.jp/ (Japanese only)
2. Presta LG, Chen H, O'Connor SJ, Chisholm V, Meng YG, Krummen L, et al.
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