Phase II Study of Neratinib for Adolescents and Adults With Neurofibromatosis 2 and Progressive *NF2*-Related Neoplasms: A Substudy of the INTUITT-NF2 Platform-Basket Trial

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Condition: *NF2*-related schwannomatosis, previously known as neurofibromatosis 2

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INTUITT-NF2 is an open-label, multiarm, phase II adaptive, platform-basket screening trial designed to test safety, tumor responses, and clinical and pharmacodynamic activity of multiple experimental therapies simultaneously in patients with *NF2*-related schwannomatosis (SWN) and associated progressive tumors. Tumor types eligible for inclusion upon progression will include vestibular SWN (VS), non-vestibular SWN, meningiomas, and ependymomas.

The INTUITT-NF2 master study is being conducted as a basket study that may allow participants with multiple tumor types associated with *NF2*-related SWN to receive new drugs throughout the study. Embedded within the master study are individual drug substudies:

- Investigational drug substudy A: brigatinib
- Investigational drug substudy B: neratinib

Up to 40 participants with *NF2*-related SWN and associated progressive tumors will be enrolled and randomized to each of several experimental treatment arms. Treatment will continue until target tumor progression, unacceptable adverse event(s), intercurrent illness that prevents further treatment, patient withdrawal, or termination of the study by the sponsor. Periodic assessments of tumor response will be conducted by measuring progression using established criteria. Clinical and pharmacodynamic activity will be assessed by measuring changes in hearing test scores (VS only), quality of life (QoL), and biomarkers during the study. Safety will be monitored throughout.

Participants who complete treatment on one experimental arm will be permitted to enroll in a different experimental arm if they meet eligibility criteria. Subjects' target lesion may change between substudies. Participants with progression who are not eligible for enrollment in a different arm will be permitted to remain on the master study to contribute natural history data for potential use as historical controls.

Primary Objective:

- Determine the biological activity of systemic therapies in *NF2*-related tumors

The NCCN Oncology Research Program (ORP) strives to improve the quality of life for patients and reduce cancer-related deaths by advancing cancer therapies through research. Since the program's establishment in 1999, the NCCN ORP has brought millions of dollars in research grants to investigators at NCCN Member Institutions. Research grants are provided to NCCN through collaborations with pharmaceutical and biotechnology companies; these grants are in turn used to support scientifically meritorious cancer research efforts.

NCCN ORP studies typically explore new avenues of clinical investigation and seek answers to important cancer-related questions. All studies are approved and funded through a scientific peer-review process and are overseen by the ORP.

This feature highlights an NCCN study funded through the grant mechanism.

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For more information on specific trials, including patient selection criteria, use the contact information listed with each study.

For more information on the NCCN ORP, including a complete detailing of the clinical studies currently underway at NCCN Member Institutions, go to www.nccn.org/education-research/nccn-oncology-research-program/clinical-trials.

Secondary Objective:

- Assess safety and tolerability of systemic therapies in patients with *NF2*-related tumors

Exploratory Objectives:

- Assess hearing response rate (VS only)
- Assess tumor progression
- Assess QoL
- Assess relationship between biomarkers and clinical response
- Assess pharmacokinetics

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