NOW ENROLLING

Dabrafenib With Trametinib

in Children and Adolescent Patients With *BRAF* V600-Mutant Low-Grade Glioma or Relapsed or Refractory High-Grade Glioma

NCT02684058

A Phase II, Open-label, Global Study to Evaluate the Effect of Dabrafenib in Combination With Trametinib in Children and Adolescent Patients With *BRAF* V600 Mutation-Positive Low-Grade Glioma (LGG) or Relapsed or Refractory High-Grade Glioma (HGG)

An open-label, nonrandomized, two-cohort, Phase II study to investigate the activity of dabrafenib plus trametinib in children and adolescent patients with BRAF V600-mutant LGG or relapsed/refractory HGG

Study Design

Key Eligibility Criteria[a]:

- 1 to 17 years of age
- *BRAF* V600 mutation-positive tumor
- Confirmed measurable disease
- No prior treatment with dabrafenib, trametinib, other RAF inhibitor, other MEK or ERK inhibitor
- HGG: no cancer treatment within the past 3 weeks
- No stem cell transplant within the past 3 months
- No history of heart disease
- Pregnant or lactating females are excluded

HGG cohort

HGG that has relapsed, progressed or failed to respond to frontline therapy (N ≈ 40)

→ **Dabrafenib po BID + Trametinib po QD**

LGG cohort

Progressive disease post-surgical excision, or non-surgical LGG that requires systemic treatment (N ≈ 102)

Randomized 2:1

→ **IV Chemotherapy Carboplatin With Vincristine (n ≈ 34)**

Centrally confirmed radiological progression: Crossover to D+T arm

→ **Dabrafenib po BID + Trametinib po QD (n ≈ 68)**

→ **Safety and Survival Follow-up**

[a]Please refer to www.clinicaltrials.gov (NCT02684058) for additional inclusion/exclusion criteria.

Primary Endpoints

- **HGG cohort:** ORR as determined by central independent assessment based on MRI or CT scans using RANO criteria
- **LGG cohort:** ORR as determined by blinded central independent assessment based on MRI or CT scans using RANO criteria

Secondary Endpoints

- **HGG and LGG cohorts:** ORR by investigator assessment, duration of response, time to response, clinical benefit rate, and progression-free survival as assessed separately by investigator and central review based on MRI or CT scans using RANO criteria; overall survival, safety, pharmacokinetics of dabrafenib and trametinib, and palatability of dabrafenib oral suspension and trametinib oral solution
- **LGG cohort:** patient-reported outcomes

For More Information About the Study Design or Enrollment

- US residents can call our clinical trials hotline at 1-844-ONC-INFO
- For countries outside of the United States, please contact your local Novartis medical representative
- Visit www.clinicaltrials.gov for eligibility criteria

Acronyms:
BID=twice daily; CT=computed tomography; D+T=dabrafenib plus trametinib; ERK=extracellular signal-related kinase; HGG=high-grade glioma; IV=intravenous; LGG=low-grade glioma; MEK=mitogen-activated extracellular signal-regulated kinase; MRI=magnetic resonance imaging; ORR=overall response rate; po=per oral; QD=once daily; RAF=rapidly accelerated fibrosarcoma; RANO=Response Assessment in Neuro-Oncology.

REFERENCES: 1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02684058. Accessed February 27, 2019.
2. Data on file. CDRB436G2201 Protocol. Novartis Pharmaceuticals Corp; August 7, 2018.

The dabrafenib and trametinib combination as described in this trial is either investigational or being studied in new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

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