

## Phase II Pediatric Study With Dabrafenib in Combination With Trametinib in Patients With HGG and LGG

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. **A** [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:  
 NCT02684058

[Recruitment Status](#) ⓘ: Recruiting  
[First Posted](#) ⓘ: February 17, 2016  
[Last Update Posted](#) ⓘ: July 2, 2018

See [Contacts and Locations](#)

**Sponsor:**

Novartis Pharmaceuticals

**Information provided by (Responsible Party):**

Novartis ( Novartis Pharmaceuticals )

**Study Details**

[Tabular View](#)

[No Results Posted](#)

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### Study Description

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**Brief Summary:**

The purpose of this study is to investigate the activity of dabrafenib in combination with trametinib in children and adolescent patients with BRAF V600 mutation positive low grade glioma or relapsed or refractory high grade glioma.

<a href="#">Condition or disease</a> ⓘ	<a href="#">Intervention/treatment</a> ⓘ	<a href="#">Phase</a> ⓘ
Diffuse Astrocytoma	Drug: dabrafenib	Phase 2
Anaplastic Astrocytoma	Drug: trametinib	
Astrocytoma	Drug: Carboplatin with vincristine	
Oligodendroglioma, Childhood		
Anaplastic Oligodendroglioma		
Glioblastoma		
Pilocytic Astrocytoma		
Giant Cell Astrocytoma		
Pleomorphic Xanthoastrocytoma		

Anaplastic Pleomorphic Xanthoastrocytoma  
Angiocentric Glioma  
Chordoid Glioma of Third Ventricle  
Gangliocytoma  
Ganglioglioma  
Anaplastic Ganglioglioma  
Dysplastic Gangliocytoma of Cerebellum  
Desmoplastic Infantile Astrocytoma and  
Ganglioglioma  
Papillary Glioneuronal Tumor  
Rosette-forming Glioneuronal Tumor  
Central Neurocytoma  
Extraventricular Neurocytoma  
Cerebellar Poneurocytoma

## Study Design

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**Study Type** ⓘ: Interventional (Clinical Trial)

**Estimated Enrollment** ⓘ: 142 participants

**Allocation:** Non-Randomized

**Intervention Model:** Single Group Assignment

**Masking:** None (Open Label)

**Primary Purpose:** Treatment

**Official Title:** 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)

**Actual Study Start Date** ⓘ: December 28, 2017

**Estimated Primary Completion Date** ⓘ: February 11, 2021

**Estimated Study Completion Date** ⓘ: September 13, 2024

### Resource links provided by the National Library of Medicine

Drug Information available for: [Trametinib](#) [Dabrafenib](#) 

[Genetic and Rare Diseases Information Center](#) resources: [Glioma](#)

[Glioblastoma](#) [Anaplastic Astrocytoma](#)

[Pleomorphic Xanthoastrocytoma](#) [Gangliocytoma](#)

[Diffuse Astrocytoma](#) [Oligodendroglioma](#)

[Anaplastic Oligodendroglioma](#) [Ganglioglioma](#)

[Anaplastic Ganglioglioma](#) [Pilocytic Astrocytoma](#)



[Chordoid Glioma of the Third Ventricle](#)

[Desmoplastic Infantile Astrocytoma](#)

[Papillary Glioneuronal Tumors](#) [Central Neurocytoma](#)

[Neuroepithelioma](#)

[U.S. FDA Resources](#)

Arm 	Intervention/treatment 
<p>Experimental: HGG cohort: Dabrafenib and trametinib</p> <p>HGG cohort: All patients in the HGG cohort will receive DRB+TMT</p>	<p>Drug: dabrafenib dabrafenib oral, twice daily. Other Name: DRB436</p> <p>Drug: trametinib trametinib oral, once daily. Other Name: TMT212</p>
<p>Active Comparator: LGG cohort: Carboplatin with vincristine</p> <p>LGG cohort: Patients randomized 2:1 to either DRB+TMT or active comparator chemotherapy.</p>	<p>Drug: Carboplatin with vincristine Chemotherapy of carboplatin with vincristine - LGG only</p>
<p>Experimental: LGG cohort: Dabrafenib and trametinib</p> <p>LGG cohort: Patients randomized 2:1 to either DRB+TMT or active comparator chemotherapy.</p>	<p>Drug: dabrafenib dabrafenib oral, twice daily. Other Name: DRB436</p> <p>Drug: trametinib trametinib oral, once daily. Other Name: TMT212</p>

## Outcome Measures

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1. HGG cohort: Overall response rate (ORR) [ Time Frame: Within the first 32 weeks of treatment ]

HGG cohort: ORR as determined by investigator assessment based on Magnetic resonance imaging (MRI) or CT (CAT) scans using Response Assessment in Neuro-Oncology Criteria (RANO) criteria.
2. LGG cohort: Overall response rate (ORR) [ Time Frame: Within the first 32 weeks of treatment ]

LGG cohort: ORR as determined by blinded independent review based on MRI or CT scans using RANO criteria.

Secondary Outcome Measures 

1. HGG cohort: Overall response rate (ORR) [ Time Frame: Within the first 32 weeks of treatment ]

HGG cohort ORR as determined by central independent review based on Magnetic resonance imaging (MRI) or CT (CAT)scans using Response Assessment in Neuro-Oncology (RANO) criteria)
2. HGG and LGG cohorts: Duration of response (DOR) [ Time Frame: Within the first year of treatment ]

HGG and LGG cohorts: DOR as assessed separately by investigator and central review based on MRI or CT scans using RANO criteria

3. HGG and LGG cohorts: Time to response (TTR) [ Time Frame: Within the first year of treatment ]  
HGG and LGG cohorts: TTR as assessed separately by investigator and central review based on MRI or CT scans using RANO criteria
4. HGG and LGG cohorts: Overall survival (OS) [ Time Frame: 2 years from last patient dosed ]  
HGG and LGG cohorts: OS as defined as the time from first dose to death due to any cause
5. HGG and LGG cohorts: Progression free survival (PFS) [ Time Frame: Within 4 months of treatment ]  
HGG and LGG cohorts: PFS as assessed separately by investigator and central review based on MRI or CT scans using RANO criteria
6. Patients on DRB+TMT: Area under the curve (AUClast) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: Assessed from time zero to the last measurable sampling time
7. Patients on DRB+TMT: Area under the curve (AUCtau) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: Calculated to the end of a dosing interval at steady state (12 hours)
8. Patients on DRB+TMT: Maximum Plasma Concentration (Cmax) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: The maximum (peak) observed plasma drug concentration after a single dose
9. Patients on DRB+TMT: Time to reach maximum concentration (Tmax) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: The time to reach maximum (peak) concentration of study drug after a single dose
10. Patients on DRB+TMT: Elimination half-life (T1/2) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: The elimination half-life associated with the terminal slope of a semi-log concentration-time curve
11. Patients on DRB+TMT: Predose plasma concentration (Ctrough) [ Time Frame: Within the first month of treatment ]  
Patients on DRB+TMT: Measured concentration at the end of a dosing interval at steady state, taken directly before next study drug administration).
12. HGG and LGG cohorts: Adverse events [ Time Frame: From first dose to end of treatment (EOT) ]  
HGG cohort: Incidence of AEs and SAEs reported during treatment with dabrafenib and trametinib in this population. LGG cohort: Incidence of AEs and SAEs reported during treatment with dabrafenib and trametinib as compared to chemotherapy
13. HGG and LGG cohorts: Vital signs [ Time Frame: First dose to end of treatment ]  
HGG: Assess the safety of dabrafenib and trametinib in this population through monitoring changes in vital signs. LGG: Assess the safety of dabrafenib and trametinib in this population as compared to chemotherapy through monitoring changes in vital signs.

14. HGG and LGG cohorts: Abnormal lab values [ Time Frame: First dose to end of treatment ]

HGG: Assess the safety of dabrafenib and trametinib in this population through hematology, chemistry and urinalysis tests. LGG: Assess the safety of dabrafenib and trametinib in this population as compared to chemotherapy through hematology, chemistry and urinalysis tests

15. HGG and LGG cohorts: Changes in Electrocardiogram (ECG) [ Time Frame: First dose to end of treatment ]

HGG: Assess the safety of dabrafenib and trametinib in this population through changes in ECG values.

LGG: Assess the safety of dabrafenib and trametinib as compared to chemotherapy in this population through changes in ECG values

16. HGG and LGG cohorts: ECHO [ Time Frame: First dose to end of treatment ]

HGG: Assess the safety of dabrafenib and trametinib in this patient population through changes in ECHO results. LGG: Assess the safety of dabrafenib and trametinib in this patient population as compared to chemotherapy through changes in ECHO results.

17. LGG cohort: Overall response rate (ORR) [ Time Frame: Within the first 32 weeks of treatment ]

LGG cohort: ORR as determined by investigator assessment based on MRI or CT scans using RANO criteria

18. HGG and LGG cohort: Palatability of pediatric formulations [ Time Frame: Within the first 5 weeks of treatment ]

HGG and LGG cohort: Palatability questionnaire data for DRB suspension and TMT solution

19. LGG cohort: PROMIS Parent Proxy scale [ Time Frame: Within the first 32 weeks of treatment ]

LGG cohort only: PROMIS parent proxy scale to estimate differences between treatment groups

20. HGG and LGG Cohorts: Clinical benefit rate (CBR) [ Time Frame: Within the first 24 weeks of treatment ]

HGG and LGG cohorts: CBR as assessed separately by investigator and central review of MRI and CT scans per RANO criteria

21. LGG cohort: 2 year Overall survival (OS) [ Time Frame: 2 years from first dose ]

LGG cohort: OS as defined as the time from the first dose to death due to any cause

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## Eligibility Criteria

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### Information from the National Library of Medicine



*Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, [Learn About Clinical Studies](#).*

Ages Eligible for Study: 6 Years to 17 Years (Child)  
Sexes Eligible for Study: All  
Accepts Healthy Volunteers: No

#### Criteria

##### Inclusion Criteria:

- Diagnosis of BRAF V600 mutant High Grade glioma that has relapsed, progressed or failed to respond to frontline therapy
- Diagnosis of BRAF V600 mutant Low Grade glioma whose tumor is unresectable and who require treatment
- Confirmed measurable disease

##### Exclusion Criteria:

- Previous treatment with dabrafenib, trametinib, other RAF inhibitor, other MEK or ERK inhibitor
- Cancer treatment within the past 3 weeks
- Stem cell transplant within the past 3 months
- History of heart disease
- Pregnant or lactating females

## Contacts and Locations

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### Information from the National Library of Medicine



*To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.*

*Please refer to this study by its ClinicalTrials.gov identifier (NCT number): **NCT02684058***

#### Contacts

Contact: Novartis Pharmaceuticals 1-888-669-6682 [novartis.email@novartis.com](mailto:novartis.email@novartis.com)

Contact: Novartis Pharmaceuticals +41613241111 [novartis.email@novartis.com](mailto:novartis.email@novartis.com)

 [Show 30 Study Locations](#)

#### Sponsors and Collaborators

Novartis Pharmaceuticals

#### Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

## More Information

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Responsible Party: Novartis Pharmaceuticals  
ClinicalTrials.gov Identifier: [NCT02684058](#) [History of Changes](#)  
Other Study ID Numbers: CDRB436G2201  
2015-004015-20 ( EudraCT Number )  
First Posted: February 17, 2016 [Key Record Dates](#)  
Last Update Posted: July 2, 2018

## Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: Undecided

Plan Description: Novartis is committed to sharing with qualified external researchers, access to patient-level data and supporting clinical documents from eligible studies. These requests are reviewed and approved by an independent review panel on the basis of scientific merit. All data provided is anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

This trial data availability is according to the criteria and process described on [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com)

Studies a U.S. FDA-regulated Drug Product: Yes

Studies a U.S. FDA-regulated Device Product: No

## Keywords provided by Novartis ( Novartis Pharmaceuticals ):

Malignant glioma	Dabrafenib
BRAF mutant positive	Trametinib
High grade glioma	Pediatrics
Low grade glioma	Brain neoplasma

## Additional relevant MeSH terms:

Glioblastoma	Central Nervous System Neoplasms
Glioma	Nervous System Neoplasms
Astrocytoma	Neoplasms by Site
Oligodendroglioma	Brain Diseases
Ganglioglioma	Central Nervous System Diseases
Neurocytoma	Nervous System Diseases
Ganglioneuroma	Trametinib
Neoplasms, Neuroepithelial	Dabrafenib
Neuroectodermal Tumors	Carboplatin
Neoplasms, Germ Cell and Embryonal	Vincristine
Neoplasms by Histologic Type	Antineoplastic Agents
Neoplasms	Antineoplastic Agents, Phytogenic
Neoplasms, Glandular and Epithelial	Tubulin Modulators
Neoplasms, Nerve Tissue	Antimitotic Agents
Brain Neoplasms	Mitosis Modulators