PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

A Phase II, Open-label, Study in Subjects With BRAF V600E-Mutated Rare Cancers With Several Histologies to Investigate the Clinical Efficacy and Safety of the Combination Therapy of Dabrafenib and Trametinib

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

This is a Phase II, open-label, non-randomized, multi-center study of oral Dabrafenib in combination with oral Trametinib in subjects with rare cancers including anaplastic thyroid cancer, biliary tract cancer, gastrointestinal stromal tumor, non-seminomatous germ cell tumor/non-geminomatous germ cell tumor, hairy cell leukemia, World Health Organization (WHO) Grade 1 or 2 glioma, WHO Grade 3 or 4 (high-grade) glioma, multiple myeloma, and adenocarcinoma of the small intestine, with BRAF V600E positive-mutations. This study is designed to determine the overall response rate (ORR) of oral Dabrafenib in combination with oral Trametinib in subjects with rare BRAF V600E mutated cancers. Subjects will need to have a fresh or frozen tumor tissue sample provided to confirm the BRAF V600E mutation status. Only subjects with histologically confirmed advanced disease and no available standard treatment options will be eligible for enrollment. Subjects will undergo screening assessments within 14 days (up to 35 days for ophthalmology exam, echocardiogram or disease assessments) prior to the start of treatment to determine their eligibility for enrollment in the study.

Brief Summary in Scientific Language

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Organizational Data

- DRKS-ID: **DRKS00007132**
- Date of Registration in DRKS: **2014/12/15**
- Date of Registration in Partner Registry or other Primary Registry: **2013/12/05**
- Investigator Sponsored/Initiated Trial (IST/IIT): **no**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT02034110 (ClinicalTrials.gov)**
- Sponsor-ID: **117019 (GlaxoSmithKline)**

Health condition or Problem studied

- Free text: **Cancer**

Interventions/Observational Groups

- Arm 1: **Drug: Dabrafenib**
- Arm 2: **Drug: Trametinib**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Single arm study**
- Blinding: **[---]***
- Who is blinded: **[---]***
- Control: **Uncontrolled/Single arm**
- Purpose: **Treatment**
- Assignment: **Single (group)**
- Phase: **II**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Overall response rate (ORR); time frame: Possibly up to Week 208; To determine the ORR as measured radiographically via Response Evaluation Criteria in Solid tumors (RECIST) version 1.1 for solid tumor histologies or established response criteria for specific hematologic malignancies.

Secondary Outcome

- Duration of response; time frame: From the time of first documented evidence of CR or PR until the first documented sign of disease progression or death (approximately up to Week 208); Duration of response is defined as the subset of subjects who show a confirmed clinical response (CR) or partial response (PR), the time from first documented evidence of CR or PR until the first documented sign of disease progression or death.
- Investigator-assessed Progression-free survival (PFS); time frame: Possibly up to Week 208; PFS is defined as the time from the date of enrollment to the earliest date of progression or death.
- Overall Survival (OS); time frame: Until death or lost to follow-up (approximately up to Week 208); OS is defined as the time from the date of enrollment to the date of death due to any cause.
- Change from baseline in physical examination findings; time frame: Possibly up to Week 208; Examination will include assessments of the head and neck, eyes, ears, nose, throat, skin, thyroid, neurological, lungs, cardiovascular, abdomen (liver and spleen), lymph nodes, extremities and genitalia. Height (measured only at Screening) and weight will be measured and recorded. Complete physical examinations will also include thorough rectal and genitourinary (pelvic) examinations to assess secondary malignancies.
- Change from baseline in vital signs; time frame: Possibly up to Week 208; Vital sign measurements will include systolic and diastolic blood pressure, temperature, pulse rate and respiratory rate
- Number of subjects with Adverse events (AEs); time frame: Possibly up to Week 208; AE is any untoward medical occurrence in a subject or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
- Change from baseline in laboratory values; time frame: Possibly up to Week 208; Laboratory assessments include haematology, clinical chemistry, urinalysis, coagulation and histology-specific tests
- Change from baseline in cardiac assessments; time frame: Possibly up to Week 208; Cardiac assessments include Electrocardiogram (ECG) and Echocardiograms (ECHOs)

Countries of recruitment

- US **United States**
- AT **Austria**
- BE **Belgium**
- DK **Denmark**
- FR **France**
-

DE **Germany**

- IT **Italy**
- KR **Korea, Republic of**
- NO **Norway**
- SE **Sweden**

Locations of Recruitment

- **GSK Investigational Site, Freiburg**
- **GSK Investigational Site, Heidelberg**
- **GSK Investigational Site, Mannheim**
- **GSK Investigational Site, Tuebingen**
- **GSK Investigational Site, Berlin**
- **GSK Investigational Site, Hamburg**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2014/03/31**
- Target Sample Size: **135**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **International**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

- Signed, written informed consent.

- Sex: male or female.

- Age: >=18 years of age at the time of providing informed consent.

- Eastern Cooperative Oncology Group (ECOG) performance status: 0, 1 or 2.

- BRAF V600E mutation-positive tumor: Local testing - Local BRAF mutation test results obtained by a Clinical Laboratory Improvement Amendments (CLIA)

approved local laboratory may be used to permit enrollment of subjects with positive results. Local BRAF mutation test results will be subject to central verification; Central testing - Local BRAF mutation test results will be confirmed by central testing in a CLIA approved, designated central reference laboratory by the THxID BRAF assay or an alternate GSK designated assay. NOTE: For central testing, Formalin-fixed paraffin-embedded (FFPE) core bone marrow (BM) biopsies are not acceptable from subjects in the Multiple myeloma (MM) cohort.

- Able to swallow and retain orally administered medication. NOTE: Subject should not have any clinically significant gastrointestinal (GI) abnormalities that may alter absorption such as malabsorption syndrome or major resection of the stomach or bowels. For example, subjects should have no more than 50% of the large intestine removed and no sign of malabsorption (i.e., diarrhea).NOTE: If clarification is needed as to whether a condition will significantly affect the absorption of study treatments, contact the GSK Medical Monitor.

- Female Subjects of Childbearing Potential: Subjects must have a negative serum pregnancy test within 7 days prior to the first dose of study treatment and agrees to use effective contraception, throughout the treatment period and for 4 months after the last dose of study treatment.

- French subjects: In France, a subject will be eligible for inclusion in this study only if either affiliated to or a beneficiary of a social security category.

Exclusion criteria

- Prior treatment with: BRAF and/or MEK inhibitor(s); anti-cancer therapy (e.g., chemotherapy with delayed toxicity, immunotherapy, biologic therapy or chemoradiation) within 21 days (or within 42 days if prior nitrosourea or mitomycin C containing therapy) prior to enrollment and/or daily or weekly chemotherapy without the potential for delayed toxicity within 14 days prior to enrolment; Investigational drug(s) within 30 days or 5 half-lives, whichever is longer, prior to enrollment

- Previous major surgery within 21 days prior to enrollment.

- Prior extensive radiotherapy treatment within 21 days prior to enrolment.

NOTE:
Limited radiotherapy for palliative care is permitted within 14 days prior to enrollment as long as any radiation-related toxicity has resolved prior to enrollment.

- Prior solid organ transplantation or allogenic stem cell transplantation (ASCT).
NOTE: Previous autologous bone marrow transplant (ABMT) or autologous peripheral blood stem cell transplant (PBSCT) is permitted.

- History of: Interstitial lung disease or pneumonitis; Another malignancy.
NOTE:
Subjects with another malignancy are eligible if: (a) disease-free for 3 years, (b) had a history of completely resected non-melanoma skin cancer, and/or (c) have a indolent second malignancy(ies) defined as a slow growing second/concurrent malignancy which is characterized by slow growth, a high initial response rate and a relapsing , progressive disease course. For example, a previously untreated low grade and select intermediate-grade lymphoid malignancy would be allowed as per the available body of evidence. There are no available clinical alternatives to the proposed population. Consult a GSK Medical Monitor if unsure whether second malignancies meet requirements specified above.

- Presence of: cerebral metastases (except for subjects in the WHO Grade 1 or 2 Glioma or WHO Grade 3 or 4 Glioma histology cohorts). NOTE: Subjects with brain metastases may be included if: All known lesions have been previously treated with surgery or stereotactic radiosurgery, and Any remaining cerebral lesion(s) are asymptomatic and confirmed stable disease (i.e., no increase in lesion size) for >=90 days prior to enrollment as documented by two consecutive magnetic resonance imaging (MRI) or computed tomography (CT) scans with contrast, and No treatment with corticosteroids or enzyme-inducing anticonvulsants required for >=30 days prior to enrolment.
Approval received from GSK Medical Monitor.

- Presence of symptomatic or untreated leptomeningeal or spinal cord compression. NOTE:
Subjects who have been previously treated for these conditions and have stable central nervous system (CNS) disease (documented by consecutive

**imaging studies) for
>60 days, are asymptomatic and currently not taking corticosteroids, or have been on
a stable dose of corticosteroids for at least 30 days prior to enrollment, are
permitted.**

- Presence of pre-existing >= Grade 2 peripheral neuropathy.

**- Presence of unresolved treatment-related toxicity of >= Grade 2 (except alopecia) or
toxicities listed in the general and histology-specific adequate organ function
tables at the time of enrolment.**

**- Presence of any serious and/or unstable pre-existing medical disorder (aside from
malignancy exception above), psychiatric disorder, or other conditions that could
interfere with subject's safety, obtaining informed consent or compliance to the
study procedures.**

**- History or current evidence/risk of retinal vein occlusion (RVO) or central serous
retinopathy (CSR): History of RVO or CSR, or predisposing factors to RVO or CSR
(e.g., uncontrolled glaucoma or ocular hypertension, uncontrolled systemic disease
such as hypertension or diabetes mellitus, or history of hyperviscosity or
hypercoagulability syndromes); Visible retinal pathology as assessed by ophthalmic
examination that is considered a risk factor for RVO or CSR such as evidence of new
optic disc cupping, evidence of new visual field defects and intraocular pressure >21
mmHg.**

**- History or evidence of cardiovascular risk including any of the following: Acute
coronary syndromes (including myocardial infarction and unstable angina), coronary
angioplasty, or stenting within 6 months prior to enrolment; Clinically significant
uncontrolled arrhythmias NOTE: Subjects with controlled atrial fibrillation for >30
days prior to enrollment are eligible; Class II or higher congestive heart failure as
defined by the New York Heart Association (NYHA) criteria; Left ventricular ejection
fraction (LVEF) below the institutional lower limit of normal (LLN). NOTE: If a LLN
does not exist at an institution, then use LVEF <50%.; Corrected QT (QTc) interval
for heart rate using Bazett-corrected QT interval (QTcB) >=480 millisecond**

(msec);
Intracardiac defibrillator and/or permanent pacemaker; Treatment-refractory
hypertension defined as a blood pressure (BP) >140/90 millimeters of mercury (mmHg)
which may not be controlled by anti-hypertensive medication(s) and/or lifestyle
modifications; Known cardiac metastases.

- Current use of prohibited medication(s) or requirement of prohibited medications
during study. NOTE: Use of anticoagulants such as warfarin is permitted; however,
international normalization ratio (INR) must be monitored according with local
institutional practice.

- Positive for: Hepatitis B surface antigen or Hepatitis C antibody. NOTE: Subjects
with laboratory evidence of cleared hepatitis B virus (HBV) and hepatitis C virus
(HCV) infection will be permitted. NOTE: False positive subjects may be cleared for
enrollment based on RNA-based assays; Human immunodeficiency virus (HIV); testing not
required.

- Known immediate or delayed hypersensitivity reaction or idiosyncrasy to drugs
chemically related to study treatment, or excipients, or to dimethyl sulfoxide and/or
sulfonamides (structural component of dabrafenib).

- Female subjects: Pregnant, lactating or actively breastfeeding.

- Subjects enrolled in France: The French subject has participated in any study using
an investigational product (IP) within 30 days prior to enrollment in this study.

Addresses

■ **Primary Sponsor**

GlaxoSmithKline

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***

Primary Sponsor

GlaxoSmithKline

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Contact for Scientific Queries**

GlaxoSmithKline
GSK Clinical Trials

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

- **Contact for Public Queries**

US GSK Clinical Trials Call Center

Telephone: **877-379-3718**
Fax: **[---]***
E-mail: **GSKClinicalSupportHD at gsk.com**
URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

The parameters in ClinicalTrials.gov and DRKS are not identical. Therefore the data import from ClinicalTrials.gov required adjustments. For full details please see the DRKS FAQs.

- Translation on version: 46

- Last processed date by ClinicalTrials.gov: 2014/10/27

** This entry means the parameter is not applicable or has not been set.*

**** This entry means that data is not displayed due to insufficient data privacy clearing.*