KURZPROTOKOLL
BAY18239

Öffentlicher Titel	Phase I Studie zum IDH1-Inhibitor BAY 1436032 bei Patienten mit IDH1-R132X-Mutation und fortgeschrittenen soliden Tumoren
Wissenschaftl. Titel	An open-label, non-randomized, multicenter Phase I study to determine the maximum tolerated or recommended Phase II dose of oral mutant IDH1 inhibitor BAY 1436032 and to characterize its safety, tolerability, pharmacokinetics and preliminary pharmacodynamic and anti-tumor activity in patients with IDH1-R132Xmutant advanced solid tumors
Kurztitel	BAY18239
Studienart	multizentrisch, prospektiv, offen/unverblindet, einarmig, Pharma-Studie
Studienphase	Phase I
Erkrankung	Verdauung: Gallengangs-/Gallenblasenkrebs (maligne biliäre Tumoren): sonstige Therapiestudien Muskeln/Bewegungsapparat: Knochenkrebs (Sarkome): sonstige Therapiestudien Verdauung: Darmkrebs (Kolorektales Karzinom): sonstige Therapiestudien Geschlechtsorgane: Krebserkrankungen der männlichen Geschlechtsorgane: sonstige Therapiestudien Weichteile: Sarkome: sonstige Therapiestudien Kopf-Hals: Kopf-Hals-Tumoren: sonstige Therapiestudien Nervensystem: Gliome: sonstige Therapiestudien

Einschlusskriterien

- Male or female patients >= 18 years of age
- Patients with a histologically confirmed solid tumor:
- Tumor must harbor an IDH1-R132X mutation
- Disease must be evaluable as per RECIST 1.1 or RANO (for gliomas)
- Patients with advanced cancer who are refractory to, have demonstrated intolerance to, or have refused access to, available standard therapies
- Glioma patients must have completed chemoradiotherapy at least 12 weeks prior to screening and their baseline scan
- Patient must be able to provide a formalin-fixed and paraffin-embedded (FFPE) tumor tissue specimen prior to treatment. The specimen may have been taken at any time during the course of the disease and may be from the primary tumor or from a metastasis.
- Patient must be able to take oral medication and comply with protocol procedures and scheduled visits
- Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2
- Negative serum or urine pregnancy test must be obtained within 7 days prior to the first dose of study drug in women of childbearing potential. Negative results must be available prior to study drug administration.
- Sexually active women and men of reproductive potential must agree to use highly effective contraception. This applies for the period between signing of the informed consent and 3 months after the last administration of study drug. These procedures should be documented in source documents. The investigator or a designated associate is requested to advise the patient on how to achieve highly effective birth control. Highly effective contraception includes:
- Established use of oral, injected or implanted hormonal methods of contraception
- Placement of certain intrauterine devices (IUD) or intrauterine systems (IUS)
- Hysterectomy, or vasectomy of the partner (provided that partner is the sole sexual partner of the woman of childbearing potential trial participant and that the vasectomized partner has received medical assessment of the surgical success) In addition, the use of condoms for patients or their partners is required

- Ability to understand and the willingness to sign a written informed consent. A signed informed consent, including consent for biomarker analyses, must be obtained prior to any study-specific procedures.
- Adequate blood clotting as defined by international normalized ratio (INR) and partial thromboplastin time (PTT) 1.5 times ULN (patients on anticoagulation with an agent such as Coumadin or heparin or Xarelto will be allowed to participate provided that no prior evidence of underlying abnormality in these parameters exists). For patients on warfarin, close monitoring of at least weekly evaluations will be performed until INR is stable based on a measurement at pre-dose, as defined by the local standard of care
- Adequate bone marrow, liver, and renal functions as assessed bythe following laboratory requirements to be conducted within 7 days prior to the first dose of study drug:
- Hemoglobin >= 9.0 g/dL
- Absolute neutrophil count (ANC) >= 1.5*10^9/L
- Platelet count >= 100*10^9/L
- Total bilirubin <= 1.5 times the upper limit of normal (ULN). For intrahepatic cholangiocarcinoma (IHCC) patients only, total bilirubin <= 2.5 times ULN is acceptable.
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <= 2.5 times ULN (<= 5 times ULN for patients with impaired liver function due to metastatic disease)
- Estimated glomerular filtration rate (eGFR) >= 50 mL/min per 1.73 m² according to the Modification of Diet in Renal Disease Study Group (MDRD) formula

Ausschlusskriterien

- Known hypersensitivity to the study drug or excipients of the preparation or any agent given in association with this study
- History of cardiac disease, including congestive heart failure of New York Heart Association (NYHA) class >II, unstable angina (anginal symptoms at rest) or new-onset angina (within 6 months prior to study entry), myocardial infarction within 6 months prior to study entry, or cardiac arrhythmias requiring anti-arrhythmic therapy except for beta-blockers and digoxin; evidence for uncontrolled coronary artery disease (e.g. angina pectoris, myocardial infarction within 6 months prior to study entry, major regional wall motion abnormalities upon baseline echocardiography). Patients with a pacemaker are also excluded.
- Left ventricle ejection fraction (LVEF) < 40% as measured by echocardiography performed at Screening
- Uncontrolled hypertension defined as systolic blood pressure >= 160 mmHg or diastolic blood pressure >= 100 mmHg, despite medical management
- Patients who have an active clinically significant infection of the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) grade 2
- Previous or coexisting cancer(s) distinct in primary site or histology from the cancer evaluated in this study EXCEPT:
- Appropriately treated cervical cancer in-situ, non-melanoma skin cancers, or superficial bladder tumors (Ta and Tis)
- Any cancer that was curatively treated at least 3 years before entry into this study
- Unresolved specific chronic toxicity of previous treatment of grade > 1 except for alopecia or hemoglobin 9.0 g/dL (or 5.6 mmol/L).
- Major surgery, significant trauma, wide-field radiotherapy, or therapy with monoclonal antibodies within 4 weeks before the first dose of study drug

	- Investigational drug treatment within 4 weeks before the start of BAY1436032 treatment and during the study (glioma patients must have completed chemoradiotherapy at least 12 weeks prior to screening and their baseline scan; see inclusion criteria #2) - Pregnant women. Women of reproductive potential must have a negative serum or urine pregnancy test performed within 7 day - Prior treatment with any therapy targeting mutant IDH1 (including BAY1436032)
Alter	18 Jahre und älter
Molekularer Marker	IDH1
Fallzahl	10
Sponsor	Bayer Healthcare (Hauptsponsor)
Registrierung in anderen Studienregistern	EudraCT 2015-003483-37 ClinicalTrials.gov NCT02746081