KURZPROTOKOLL
BI 1336-0011

Öffentlicher Titel	Phase I Studie zu BI 836880 und BI 754091 bei fortgeschrittenen soliden Tumoren
Wissenschaftl. Titel	An open label phase Ib dose finding study of BI 836880 in combination with BI 754091 to characterize safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy in patients with locally advanced or metastatic non-squamous Non-Small Cell Lung Cancer and in other solid tumors
Kurztitel	BI 1336-0011
Studienart	multizentrisch, prospektiv, Therapiestudie, offen/unverblindet, einarmig
Studienphase	Phase I
Erkrankung	Nervensystem: Gliome: Glioblastom (WHO Grad IV) - Zweitlinie oder höher
Einschlusskriterien	- Part 1: - Of full age (according to local legislation, usually >= 18 years) at screening - Pathologically confirmed locally advanced or metastatic non-squamous NSCLC with PDL-1 expression available and >1% by IHC (as defined by the Pembrolizumab companion diagnostic test, determined by appropriate local pathology lab - No previous treatment with check-point inhibitor. Or patients with checkpoint inhibitor based treatment as last therapy before entering the trial - Documented disease progression or relapse (based on investigator's assessment) during or after completion of at least 2 cycles of platinum-based chemotherapy as first line treatment of Stage IIIB/IV non- squamous NSCLC or for checkpoint inhibitor experienced patients during or after completion of at least 2 cycles of platinum-based chemotherapy and a checkpoint inhibitor treatment (monotherapy or in combination with chemotherapy). This includes patients relapsing within 6 months of completing (neo)adjuvant/curative-intent chemotherapy/CPI or chemoradiotherapy - At least one target lesion (outside the brain) that can be accurately measured per Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 - Lesion with a diameter >= 2cm assessed by radiologist as suitable for DCE-MRI evaluation (Mandatory in Part 1, optional in Part 2) - Eastern Cooperative Oncology Group (ECOG) performance status <= 1 Life expectancy >= 3 months after start of the treatment in the opinion of the investigator - Recovery from all reversible adverse events of previous anti-cancer therapies to baseline or CTCAE grade 1, except for alopecia (any grade), sensory peripheral neuropathy , must be <= CTCAE grade 2 or considered not clinically significant - Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial - Availability and willingness to provide a fresh tumour tissue sample obtained at baseline, and after 2 cycles of treatment - Adequate organ function defined as all of the following (all screening labs should be performed at local lab within 10 days prior to treatment initiation) - Male or female patients. Women of childbearing potential (WOCBP)1 and men able to father a child must be ready and able to use highly effective methods of birth control per ICH M3 (R2) that result in a low failure rate of less than 1% per year when used consistently and correctly, starting with the screening visit and through 6 months after the last dose of BI 836880 and BI 754091 treatment, respectively. A list of contraception methods meeting these criteria is provided in the patient information Note: Female patients of childbearing potential must have a negative serum pregnancy test within 72 hours prior to taking study medication during the screening period. At the following visits according to the flowchart a urine and/or serum pregnancy test is required. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. The serum pregnancy test must be negative for the patient to be eligible - Part 1 & Part 2:

- Of full age (according to local legislation, usually >= 18 years) at screening
- At least one measurable target lesion outside the brain (excluding the glioblastoma patients), that can be accurately measured per RECIST 1.1
- ECOG performance status <= 1 (For glioblastoma cohort Karnofsky status is applicable; see below)
- Adequate organ function as all of the following (all screening labs should be performed at local lab within approximately 72 hours prior to treatment initiation)
- Availability and willingness to provide a fresh tumor tissue sample obtained after relapse or progression on or after prior therapy. For Part 2, In case a fresh biopsy cannot be obtained (e.g. inaccessible lesions or patient safety concern), an archived specimen obtained up to 6 months prior to cycle 1, visit 1 (C1V1) may be submitted in case no systemic antineoplastic therapy has been administered between the biopsy and C1V1 (except for cohort D). For cohorts E, F and G, a fresh on-treatment biopsy is mandatory at C3D1, if possible from the same lesion as the pre-treatment biopsy
- Life expectancy >= 3 months after start of the treatment in the opinion of the investigator
- Recovery from all reversible adverse events of previous anti-cancer therapies to baseline or CTCAE grade 1, except for alopecia (any grade), sensory peripheral neuropathy , must be <= CTCAE grade 2 or considered not clinically significant
- Signed and dated written informed consent in accordance with ICH-GCP and local legislation prior to admission to the trial
- Male or female patients. Women of childbearing potential (WOCBP)2 and men able to father a child must be ready and able to use highly effective methods of birth control per ICH M3 (R2) that result in a low failure rate of less than 1% per year when used consistently and correctly, for the entire duration of the trial treatment intake and for 6 months after the end of the trial treatment. A list of contraception methods meeting these criteria is provided in the patient information
- Note: Female patients of childbearing potential must have a negative serum pregnancy test within 72 hours during the screening period. At the following visits according to the flowchart, a urine and/or serum pregnancy test is required. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required. The serum pregnancy test must be negative for the patient to be eligible. - Further inclusion criteria apply

Ausschlusskriterien

- Part 1:
- Known hypersensitivity to the trial drugs or their excipients or risk of allergic of anaphylactic reaction to drug product according to Investigator judgement (e.g. patient with history of anaphylactic reaction or autoimmune disease that is not controlled by nonsteroidal anti-inflammatory drugs (NSAIDs), inhaled corticosteroids, or the equivalent of </= 10 mg/day prednisone)
- Known immunodeficiency virus infection or an active hepatitis B or C virus infection
- History of severe hypersensitivity reactions to other mAbs
- Immunosuppressive corticosteroid doses (> 10 mg prednisone daily or equivalent) within 4 weeks prior to the first dose of trial medication
- Current or prior treatment with any systemic anti-cancer therapy either within 28 days or a minimum of 5 half-lives, whichever is shorter before start of treatment
- Serious concomitant disease, especially those affecting compliance with trial requirements or which are considered relevant for the evaluation of the endpoints of the trial drug, such as neurologic, psychiatric, infectious disease or active ulcers (gastrointestinal tract, skin) or laboratory abnormality that may increase the risk associated with trial participation or trial drug administration, and in the judgment of the investigator would make the patient inappropriate for entry into the trial

- Major injuries and/or surgery or bone fracture within 4 weeks of start of treatment, or planned surgical procedures during the trial period
- Patients with personal or family history of QT prolongation and/or long QT syndrome, or prolonged QTcF at baseline (> 480 ms)
- Significant cardiovascular/cerebrovascular diseases (i.e. uncontrolled hypertension, unstable angina, history of infarction within past 6 months, congestive heart failure > NYHA II)
- Uncontrolled hypertension defined as: Blood pressure in rested and relaxed condition >= 140 mmHg, systolic or >= 90 mmHg diastolic (with or without medication), measured according to Appendix 10.2
- LVEF < 50%
- History of severe hemorrhagic or thromboembolic event in the past 12 months (excluding central venous catheter thrombosis and peripheral deep vein thrombosis)
- Known inherited predisposition to bleeding or to thrombosis in the opinion of the investigator
- Patient with brain metastases that are symptomatic and/or require therapy
- Patients who require full-dose anticoagulation (according to local guidelines). No Vitamin K antagonist and other anticoagulation allowed; LMWH allowed only for prevention not for curative treatment
- History of pneumonitis within the last 5 years
- Patients who are under judicial protection and patients who are legally institutionalized
- Patients unable or unwilling to comply with protocol
- Previous enrolment in this trial (Part 1 or Part 2)
- Chronic alcohol or drug abuse or any condition that, in the investigator's opinion, makes them an unreliable trial patient or unlikely to complete the trial
- Women who are pregnant, nursing, or who plan to become pregnant in the trial
- Part 2:
- Known hypersensitivity to the trial drugs or their excipients or risk of allergic of anaphylactic reaction to drug product according to Investigator judgement (e.g. patient with history of anaphylactic reaction or autoimmune disease that is not controlled by nonsteroidal anti-inflammatory drugs (NSAIDs), inhaled corticosteroids, or the equivalent of </= 10 mg/day prednisone)
- Not more than one CPI based treatment regimen prior to entering study (eg. anti-Programmed Death receptor-1 (PD-1), anti-Programmed Death-1 ligand-1 (PD-L1), anti-PD-L2, or anti-cytotoxic T lymphocyte associated antigen-4 (anti-CTLA-4) antibody) unless combination CPIs approved by the local regulatory agencies; For eg., Melanoma cohort (Cohort E)
- Known HIV infection
- Active hepatitis B virus (HBV) or hepatitis C virus (HCV) infection (exception for patients in HCC cohorts; Cohorts F& G)
- History of severe hypersensitivity reactions to other mAbs
- Immunosuppressive corticosteroid doses (> 10 mg prednisone daily or equivalent) within 4 weeks prior to the first dose of trial medication except for control of cerebral edema in case of recurrent glioblastoma (cohort D)
- Current or prior treatment with any systemic anti-cancer therapy (including radiotherapy) either within 28 days or a minimum of 5 half-lives, whichever is shorter before start of treatment

- Serious concomitant disease, especially those affecting compliance with trial requirements or which are considered relevant for the evaluation of the endpoints of the trial drug, such as neurologic, psychiatric, infectious disease or active ulcers (gastrointestinal tract, skin) or laboratory abnormality that may increase the risk associated with trial participation or trial drug administration, and in the judgment of the investigator would make the patient inappropriate for entry into the trial
- Major injuries and/or surgery or bone fracture within 4 weeks of start of treatment, or planned surgical procedures during the trial period
- Patients with personal or family history of QT prolongation and/or long QT syndrome, or prolonged QTcF at baseline (> 480 ms)
- Significant cardiovascular/cerebrovascular diseases (i.e. uncontrolled hypertension, unstable angina, history of infarction within past 6 months, congestive heart failure > NYHA II)
- Uncontrolled hypertension defined as: Blood pressure in rested and relaxed condition >= 140 mmHg, systolic or >= 90 mmHg diastolic (with or without medication), measured according to Appendix 10.2
- LVEF < 50%
- History of severe hemorrhagic or thromboembolic event in the past 12 months (excluding central venous catheter thrombosis and peripheral deep vein thrombosis)
- Known inherited predisposition to bleeding or to thrombosis in the opinion of the investigator
- Patient with brain metastases that are symptomatic and/or require therapy
- Patients who require full-dose anticoagulation (according to local guidelines)
- No Vitamin K antagonist and other anticoagulation allowed; LMWH allowed only for prevention not for curative treatment
- History of pneumonitis (non-infectious) within the last 5 years
- Patients who are under judicial protection and patients who are legally institutionalized
- Patients unable or unwilling to comply with protocol
- Previous enrolment in this trial
- Chronic alcohol or drug abuse or any condition that, in the investigator's opinion, makes them an unreliable trial patient or unlikely to complete the trial
- Women who are pregnant, nursing, or who plan to become pregnant in the trial
- UncontrolledSymptomatic pleural effusion, pericardial effusion, or ascites
- Prior treatment with any antiangiogenic treatment (e.g. bevacizumab, cediranib, aflibercept, vandetanib, XL-184, sunitinib, etc) except for sorafenib and lenvatinib in 2nd line HCC cohort (Cohort F)
- Has received a live vaccine within 30 days prior to the first dose of study drug
- Patients with known active second malignancy other than non-melanoma skin cancers, non-metastatic prostate cancer, in situ cervical cancer, and ductal or lobular carcinoma in situ of the breast. Patients are not considered to have a currently active malignancy if they have completed anticancer therapy and have been disease free for greater than 2 years prior to screening
- Further exclusion criteria apply

Alter	18 Jahre und älter
Sponsor	Boehringer Ingelheim Pharmaceuticals
Registrierung in anderen Studienregistern	ClinicalTrials.gov NCT03468426 (primäres Register) EudraCT 2017-001378-41