NintNivo

Feasibility and Safety of Nintedanib in Combination With Nivolumab in Pretreated Patients With Advanced or Metastatic NSCLC of Adenocarcinoma Histology

NCT-Nummer:
NCT04046614

Studienbeginn:
Mai 2018

Letztes Update:
06.08.2019

Wirkstoff:
nintedanib-nivolumab combination therapy
Indikation (Clinical Trials):
Adenocarcinoma, Adenocarcinoma of Lung

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
-

Sponsor:
AIO-Studien-gGmbH, AIO-Studien-gGmbH

Collaborator:
-

Studien-Informationen

Brief Summary:

Determination of a safe dose for nintedanib+nivolumab combination therapy and the generation of exploratory efficacy data in pretreated patients with advanced or metastatic NSCLC of adenocarcinoma histology.

Ein-/Ausschlusskriterien

Inclusion Criteria:

- Written informed consent and any locally-required authorization (EU Data Privacy Directive in the EU) obtained from the subject prior to performing any protocol-related procedures, including screening evaluations.

- Subject is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up.

- Age over or equal to 18 years at time of study entry.

- Histologically confirmed adenocarcinoma of the lung stage IIIB/IV according to UICC7

- One or two previous lines of systemic therapy including maintenance for advanced or metastatic NSCLC. Patients should be offered standard therapy regimens as recommended by current local Clinical Practice Guidelines. Neo-adjuvant and adjuvant therapies are permitted, provided that disease progression/relapse occurred more than 6 months after cessation of therapy.

- ECOG performance status 0-1.

- Expected life expectancy of at least 3 months.

- Patients with measurable disease (at least one uni-dimensionally measurable target lesion by CT-scan or MRI) according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) are eligible. If a potential target lesion has been irradiated previously, clear evidence of progression at target site must be documented.

- A formalin fixed, paraffin-embedded (FFPE) tumor tissue block (archival or recent) or approx. of 10-15 unstained slides of tumor sample (slices must be recent and collected on slides provided by the sponsor) must be available for PD-L1 and other biomarker evaluation. Biopsy should be excisional, incisional or core needle. Fine needle aspiration is insufficient.

- Prior therapies and surgeries are allowed if completed 2 weeks (for minor surgery) or 4 weeks (palliative radiotherapy for bone pain; major surgeries with complete wound healing), respectively prior to start of treatment and patient recovered from toxic effects.

- Adequate blood count, liver-enzymes, and renal function (obtained no later than 14 days prior to start of treatment)

- Women of childbearing potential (WOCBP) must use appropriate method(s) of contraception. WOCBP should use an adequate method to avoid pregnancy for 5 months (30 days plus the time required for nivolumab to undergo five half-lives) after the last dose of nivolumab. Since the effect of nintedanib on the metabolism and efficacy of contraceptives has not been investigated,

barrier methods should be applied as a second form of contraception, to avoid pregnancy.

- Women of childbearing potential must have a negative serum or urine pregnancy test within 24 hours prior to the start of study treatment and monthly throughout treatment until 5 months after last dose of IMP.

- Men who are sexually active with WOCBP must use any contraceptive method with a failure rate of less than 1% per year. Men receiving nivolumab and who are sexually active with WOCBP will be instructed to adhere to contraception for a period of 7 months after the last dose of investigational product. Women who are not of childbearing potential (ie, who are postmenopausal or surgically sterile) as well as azoospermic men do not require contraception.

Exclusion Criteria:

- More than one or two prior treatment lines for advanced or metastatic NSCLC

- Subjects with active CNS metastases are excluded. Subjects are eligible if CNS metastases are adequately treated and subjects are neurologically returned to baseline (except for residual signs or symptoms related to the CNS treatment) for at least 4 weeks prior to enrollment. In addition, subjects must be either off corticosteroids, or on a stable or decreasing dose of ≤ 10 mg daily prednisone (or equivalent).)

- Leptomeningeal disease, carcinomatous meningitis, chronic diarrhea or short bowel syndrome

- Known activating EGFR mutation or a known ALK translocation.

- Patients with symptomatic interstitial lung disease.

- Any previous treatment with nitedanib, ramucirumab, anti-tumor vaccines or other immuno-stimulatory antitumor agents exept checkpoint inhibitors.

- Ongoing toxicities attributed to prior anti-cancer therapy other than alopecia and fatigue that have not resolved to grade 1 (NCI CTCAE version 4.03) or baseline before administration of study drug.

- Major injuries within the past 4 weeks prior to start of study treatment with incomplete wound healing and/or planned surgery during the on-treatment study period.

- Patients should be excluded if they have an active, known or suspected autoimmune disease or history of allogeneic tissue/solid organ transplant. NOTE: Subjects are permitted to enroll if they have vitiligo, type I diabetes mellitus, residual hypothyroidism due to autoimmune condition only requiring hormone replacement, psoriasis not requiring systemic treatment, or conditions not expected to recur in the absence of an external trigger

- Patients should be excluded if they have a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days of study drug administration. NOTE: Inhaled or topical steroids and adrenal replacement doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease.

- Positive test for HBV sAg or HCV RNA indicating acute or chronic infection OR positive HIV test

- History of severe hypersensitivity reactions to other monoclonal antibodies or any excipient. Known hypersensitivity to nintedanib, peanut, soya or to any of the excipients or contrast media.

- Radiotherapy to the target lesion within the past 3 months prior to baseline imaging. (see also inclusion criterion 8)

- Radiographic evidence of cavitary or necrotic tumors

- Centrally located tumors with radiographic evidence (CT or MRI) of local invasion of major blood vessels

- Therapeutic anticoagulation with drugs requiring INR monitoring (except low-dose heparin and/or heparin flush as needed for maintenance of an in-dwelling intravenous devise) or anti-platelet therapy (except for low-dose therapy with acetylsalicylic acid < 325mg per day)

- History of clinically significant hemorrhagic or thromboembolic event in the past 6 months

- Known inherited predisposition to bleeding or thrombosis

- Significant cardiovascular diseases (i.e. uncontrolled hypertension, unstable angina, history of infarction within the past 12 months prior to start of study treatment, congestive heart failure > NYHA II, serious cardiac arrhythmia, pericardial effusion)

- Active alcohol or drug abuse

- Body Mass Index (BMI) exceeding 20 kg/m2

- Previous malignancy (other than NSCLC), which either progresses or requires active treatment.

- Subjects with previous malignancies (except non-melanoma skin cancers, and the following in situ cancers: bladder, gastric, colon, cervical/dysplasia, endometrial, melanoma, or breast) are excluded unless a complete remission was achieved at least 2 years prior to study entry AND no additional therapy is required or anticipated to be required during the study period.

- Female subjects who are pregnant, breast-feeding or male or female patients of reproductive potential who are not employing an effective method of birth control (failure rate of less than 1% per year)

- Receipt of the last dose of anti-cancer therapy (chemotherapy, immunotherapy, endocrine therapy, targeted therapy, biologic therapy, tumor embolization, monoclonal antibodies, other investigational agent) ≤28 days prior to the first dose of study treatment.

- Any other serious or uncontrolled medical disorder (e.g. active ulcers), active infection, physical exam finding, laboratory finding, altered mental status, or psychiatric condition that, in the opinion of the investigator, would limit a subject's ability to comply with the study requirements, substantially increase risk to the subject, or impact the interpretability of study results.

- Patient who might be dependent on the sponsor, site or the investigator.

- Patient who has been incarcerated or involuntarily institutionalized by court order or by the authorities § 40 Abs. 1 S. 3 Nr. 4 AMG.

Studien-Rationale

Primary outcome:

1. Safety and tolerability as determined by frequency and severity of adverse events (Time Frame - 47 months):
Safety and tolerability as determined by frequency and severity of adverse events

2. progression free survival (Time Frame - 6 months):
6-month progression free survival rate

3. progression free survival (Time Frame - 9 months):
9 month progression free survival rate

Secondary outcome:

1. Overall response rate (Time Frame - 35 months):
Determination of the overall response rate

2. Progression free survival (Time Frame - 47 months):
Determination of progression free survival

3. Time to progression (Time Frame - 35 months):
Determination of the time to progression

4. Overall survival (Time Frame - 47 months):
Determination of the overall survival

5. Adverse events (Time Frame - 47 months):
Determination of adverse events, sevier adverse events, treatment emergent adverse events according to common terminology criteria of adverse events version 4.03

6. Depth of response (Time Frame - 35 months):
Determination of depth of response defined by the maximal tumor shrinkage before progression. Depth of response will be assessed by tumor imaging (computed tomography or magnetic resonance tomography) evaluated according to Response Evaluation Criteria in Solid Tumors version 1.1

7. Time to response (Time Frame - 35 months):
Determination time to response

Geprüfte Regime

- nintedanib-nivolumab combination therapy:
Safety run-in - Dose finding stage The safety-run in phase will be designed as a standard 3+3 design for dose escalation/de-escalation and 3 to 6 patients will be enrolled in each cohort sequentially, depending on occurrence of dose limiting toxicities. The recommended phase 2 dose (RP2D) will be the highest dose in which the frequency of DLTs is less than

33% if no other safety or feasibility considerations prevail. Expansion phase: Nintedanib RP2D + nivolumab 240 mg Q2W until progression of disease.

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Studienlocations (1 von 1)

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Status: Rekrutierend

Quelle: ClinicalTrials.gov