Atezolizumab Plus 8 Gy Single-fraction Radiotherapy for Advanced Oligoprogressive NSCLC

NCT-Nummer:
NCT04549428

Studienbeginn:
Oktober 2020

Letztes Update:
24.02.2021

Wirkstoff:
Atezolizumab
Indikation (Clinical Trials):
Carcinoma, Non-Small-Cell Lung

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 2

Sponsor:
Oncology Institute of Southern Switzerland

Collaborator:
Ente Ospedaliero Cantonale, Bellinzona, Istituto Cantonale di Patologia, Clinical Trial Unit Ente Ospedaliero Cantonale,

Studien-Informationen

Detailed Description:

Atezolizumab will be administered at a fixed dose of 1,200 mg by intravenous infusion every

21 days on an outpatient basis according to the its approved prescribing information.

Palliative radiation therapy will be delivered concomitant to the 2nd dose of atezolizumab as

a single fraction of 8 Gy to all eligible metastatic and primary sites.

Ein-/Ausschlusskriterien

Inclusion Criteria:

- Signed Informed Consent Form

- Histologically or cytologically confirmed diagnosis of metastatic (Stage IV)

- NSCLC as per the American Joint Committee on Cancer (AJCC) 8th edition

- No sensitizing EGFR mutation (L858R or exon 19 deletions), ALK fusion oncogene or ROS1 rearrangement detected

- Progressing to one line of chemotherapy defined as follows:

1. A platinum-doublet.

2. In case of patients being ineligible for platinum-containing regimens but otherwise compliant with the other inclusion-exclusion criteria of the present study, at least one line of mono-chemotherapy is required.

3. As an exception, patients with oligoprogression to anti PD-1 agents alone for whom the investigator considers local treatment of metastases and continuation of immunotherapy appropriate (i.e. would not be eligible for 2nd line treatment) may be enrolled without a previous line of chemotherapy. In this case, approval by the Project Leader is necessary.

- Progressing to an anti-PD-1 agent, either associated to chemotherapy or as monotherapy (e.g., pembrolizumab or nivolumab)

- Patients with treated, asymptomatic central nervous system (CNS) metastases are eligible, provided they meet all of the following criteria:

1. Measurable disease outside CNS.

2. Only supratentorial and cerebellar metastases allowed (i.e., no metastases to midbrain, pons, medulla or spinal cord).

3. No ongoing requirement for corticosteroids as therapy for CNS disease; anticonvulsants at a stable dose allowed.

4. No stereotactic radiation within 7 days or whole-brain radiation within 14 days prior to initiating study treatment.

5. No evidence of interim progression between the completion of CNS-directed therapy and the screening radiographic study.

- Patients with new asymptomatic CNS metastases detected at the screening scan must receive radiation therapy and/or surgery for CNS metastases. Following treatment, these patients may then be eligible without the need for an additional brain scan prior to initiating study treatment, if all other criteria are met, including clinical confirmation of no evidence of interim disease progression

- Measurable disease by RECIST v1.1. Previously irradiated lesions can only be considered as measurable disease if disease progression has been unequivocally documented at that site since radiation and the previously irradiated lesion is not the only site of disease.

- Oligoprogressive disease defined as follows:

1. A minimum of 1 and a maximum of 4 progressing lesions (with up to 3 total organs and 3 lesions per organ, except skeletal lesions) as assessed by a Positron Emission Tomography-Computed Tomography (PET-CT) scan (contrast enhanced).

2. Definition of progression is made by RECIST 1.1 criteria (new lesions or increased pre-existing ones).

3. Patients with additional non-progressing lesions according to RECIST 1.1 are accepted, but non-progressing lesions according to RECIST 1.1 with 6% to 19% increase in diameter, should also be included in the radiation scheme, provided the limit of lesions/diameter/organs is observed.

- Adequate hematologic and end organ function, defined by the laboratory results obtained within 14 days prior to initiating study treatment (see §7.1 of the protocol

for full details).

- For female patients of childbearing potential agreement to remain abstinent (refrain from heterosexual intercourse) or to use highly effective form(s) of contraceptive methods that result in a failure rate of < 1% per year when used consistently and correctly during the treatment period and for at least 5 months after the last dose of atezolizumab.

Exclusion Criteria:

- Cancer-specific exclusion criteria
- Patients with an ECOG Peformance status >2
- Active or untreated CNS metastases as determined by Computed
- Tomography (CT) or magnetic resonance imaging (MRI) evaluation of the brain during screening and prior radiographic assessments
- Uncontrolled hypercalcemia (>1.5 mmol/L ionized calcium or >3 mmol/L of corrected serum calcium) or symptomatic hypercalcemia requiring continued use of bisphosphonate therapy or denosumab (see §7.1 of the protocol for exceptions).
- NCI CTCAE Grade 3 or higher toxicities due to any prior therapy (e.g., radiotherapy) (excluding alopecia), which have not shown improvement and are strictly considered to interfere with current study medication, with special focus on prior toxicity to anti-PD1 agents.

General medical exclusion criteria

- Women who are pregnant or lactating, or intending to become pregnant during the study. Women of childbearing potential including women who have had a tubal ligation, must have a negative serum pregnancy test result within 14 days prior to initiation of study drug.
- History of autoimmune disease (see §7.1 of the protocol for exceptions).
- Known positivity for human immunodeficiency virus (HIV) (see §7.1 of the protocol for further details).

- Known active hepatitis B (chronic or acute; defined as having a positive hepatitis B surface antigen [HBsAg] test at screening) or known active hepatitis C (see §7.1 of the protocol for further details).
- Severe infections within 4 weeks prior to initiating study treatment, including but not limited to hospitalization for complications of infection, bacteremia, or severe pneumonia.
- Significant cardiovascular disease, such as New York Heart Association (NYHA) cardiac disease (Class II or greater), myocardial infarction within 3 months prior to initiating study treatment, unstable arrhythmias, or unstable angina.
a) Patients with known coronary artery disease, congestive heart failure not meeting the above criteria, or left ventricular ejection fraction (LVEF) <50% must be on a stable medical regimen that is optimized in the opinion of the treating physician, in consultation with a cardiologist if appropriate.
- Major surgical procedure other than for diagnosis within 4 weeks prior to initiating study treatment or anticipation of need for a major surgical procedure during the course of the study.
- Prior allogeneic bone marrow transplantation or solid organ transplant.
Exclusion criteria related to atezolizumab
- History of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanized antibodies or fusion proteins.
- Oral or IV antibiotic treatment. Patients will thus need to have recovered from any infection requiring antibiotics. Patients receiving prophylactic antibiotics (e.g., for prevention of a urinary tract infection or to prevent chronic obstructive pulmonary disease exacerbation) are eligible.
- Administration of a live, attenuated vaccine within 4 weeks before initiating study treatment or anticipation that such a live attenuated vaccine will be required during the study

a) Influenza vaccination is allowed, but should be given during influenza season.

However, patients must not receive live, attenuated influenza vaccine (e.g., FluMist®) within 4 weeks prior to initiating study treatment, at any time during the study or within 5 months after the last atezolizumab dose.

- Prior treatment with CD137 agonists or anti-PD-L1 therapeutic antibodies.

- Patients who have had prior anti-cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) treatment may be enrolled, provided the following requirements are met:

1. Minimum of 6 weeks from the last dose of anti-CTLA-4

2. No history of severe immune related adverse effects from anti-CTLA-4 (NCI CTCAE Grade 3 and 4)

- Treatment with systemic corticosteroids or other immunosuppressive medications (including but not limited to prednisone, dexamethasone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumor necrosis factor [anti-TNF] agents)

- Patients with history of allergic reaction to IV contrast requiring steroid pretreatment should have baseline and subsequent tumor assessments done by MRI.

Exclusion criteria related to radiotherapy

- Previously irradiated lesions having received the maximum permissible dose.

Studien-Rationale

Primary outcome:

1. Objective Response Rate (Time Frame - 3 months):
Percentage of patients with a complete response or partial response

Secondary outcome:

1. Overall Survival (Time Frame - 12 months):
Time in months from the first day of study treatment to the date of death

2. Progression Free-Survival (Time Frame - 12 months):
Time in months from the first day of study treatment until the first evidence of tumour progression

Geprüfte Regime

- Atezolizumab (Tecentriq):
  Intravenous infusion every 21 days, until disease progression, intolerance or loss of clinical benefit.

Studienleiter

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Studienlocations (1 von 1)

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Status: Rekrutierend

Quelle: ClinicalTrials.gov