Pembrolizumab Alone versUs pembrolizumab-chemotherapy in first LInE NSCLC

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Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON20213

Bron
NTR

Verkorte titel
PAULIEN

Aandoening

Non-small cell lung cancer (NSCLC)

Ondersteuning

Primaire sponsor: None
Overige ondersteuning: Amsterdam UMC

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- to assess the effect of chemotherapy given concurrently with pembrolizumab on overall response rate (ORR) in NSCLC patients with high PD-L1 and high tumor burden

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: In stage 4 non-small cell lung cancer (NSCLC), there is sometimes a medically urgent situation in which a patient needs to have a quick shrinkage of the tumor, especially in patients with a high tumor burden. We hypothesized that, in NSCLC patients with high PD-L1 (TPS≥50%) expressing tumors, the combination of pembrolizumab with platinum-based chemotherapy will result in a higher tumor response, and possibly in a better progression free and overall survival as compared to pembrolizumab monotherapy.
Objective: to compare the response rate of chemo-pembro vs pembro alone
Study design: an open label, phase 3, randomized clinical trial
Study population: stage 4 NSCLC, with TPS≥50%, and at least a cTxNxM1c
Intervention: Arm 1: pembrolizumab alone (200mg fixed dose, 3 weekly) until progressive disease (PD); arm 2: pembrolizumab (200mg fixed dose, 3 weekly) with chemotherapy (carboplatin AUC 5 or cisplatin (75 or 80mg/m2) combined with either pemetrexed (500mg/m2, non-squamous) or paclitaxel (200mg/m2, squamous). Chemotherapy doublets will be given for 2-4 cycles depending on the tumor response, also, pemetrexed and pembrolizumab will continued as maintenance until PD or unacceptable toxicity in arm 2.
Main study endpoints: primary objective: ORR, secondary objectives: PFS-1, PFS-2 (to compare the PFS obtained with first line pembrolizumab and second line platinum doublet in arm 1 vs PFS obtained with first line chemo-pembro in arm 2), OS
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients will undergo one of two accepted routine first line therapies. As such, there are no additional risks nor is there an additional benefit associated with participation in this study, other than the benefit for future patients that will derived from the knowledge gained in this study.

Doel van het onderzoek

We hypothesized that, in high PD-L1 expressing patients with high tumor burden, the combination of pembrolizumab with platinum-based chemotherapy will result in a higher tumor response, and possibly in a better progression free and overall survival as compared to pembrolizumab monotherapy.

Onderzoeksopzet

Patients will be evaluated for study end points with follow-up at 6, 12 weeks and subsequently 3 month intervals with history and physical examination, imaging including CT of the chest and/or abdomen, and laboratory testing including complete blood cell counts and/or comprehensive metabolic panels as needed.

Onderzoeksproduct en/of interventie

Pembrolizumab alone versus pembrolizumab-chemotherapy in first line NSCLC

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Histologically confirmed NSCLC, negative for EGFR mutations and ALK fusions, no molecular testing is required in squamous NSCLCECOG Performance Scale 0-2
• Be willing and able to provide written informed consent for the trial
• Be 18 years or older of age on the day of signing informed consent
• Have measurable disease based on RECIST v1.1
• Must provide tissue from a histological tumor biopsy that was not yet irradiated
• High tumor PD-L-1 expression (≥50% TPS)
• High tumor burden (≥2 extrapulmonary metastases (M1c)) and not amenable for local consolidative therapies
• Must have adequate hematologic and organ function, defined by the following laboratory results:
• - Absolute neutrophil count (ANC) ≥ 1500 cells/µL
• - WBC count ≥ 2000 cells/µL

• - Platelet count ≥ 100.000/µL
• - Hemoglobin ≥ 5.6 mmol/L
• - AST and ALT ≤ 3 x ULN (≤ 5 x ULN if liver metastases are present)
• - Serum bilirubin ≤ 1.5 x ULN (except subjects with known Gilbert disease, who can have total bilirubin < 3.0 mg/dL)
• - Serum Creatinine ≤ 1.5 x ULN OR measured of calculated creatinine clearance (GFR can also be used in place of creatinine or CrCl) ≥ 40 mL/min for subject with creatinine levels > 1.5 x ULN.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Patients amenable for local consolidative therapies
• Use of steroids equivalent to >10 mg prednisolon per day prior to start of study or other immunosuppressive medications within 14 days prior. Inhaled or topical steroids, and adrenal replacement steroid >10 mg daily prednisone equivalent, are permitted in the absence of active autoimmune disease.
• Untreated brain metastases
• Uncontrolled active infections, HIV, active Hepatitis B or C
• Autoimmune diseases and interstitial lung diseases are to be excluded depending on physicians decision
• A known additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or in situ cervical cancer that has undergone potentially curative therapy.
• Known psychiatric or substance abuse disorders that would interfere with cooperation with the requirements of the trial.
• Is pregnant or breastfeeding, or expecting to conceive children within the projected duration of the trial, starting with the screening.
• Prior systemic therapy for the NSCLC using chemotherapy or immunotherapy with prior therapy with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CTLA-4 antibody, or any other antibody or drug specifically targeting T-cell co-stimulation or immune checkpoint pathways.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd

Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	03-02-2020
Aantal proefpersonen:	84
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8896
Ander register	METC Amsterdam UMC (VUmc): source ID, 2019.581 (A2020.138) - NL70714.029.19 : METC Amsterdam UMC (VUmc): source ID, 2019.581 (A2020.138) - NL70714.029.19

Resultaten