

Protocol NICOLAS (ETOP)

A Feasibility Trial Evaluating Anti-PD1 Nivolumab Consolidation After Standard First-line Chemotherapy and Radiotherapy in Locally Advanced Stage IIIA/B NSCLC.

This is the trial summary as assessed on clinicaltrials.gov on 12/09/2016.

Minor changes in the protocol may occur. You can check this on this direct link:

<https://clinicaltrials.gov/ct2/show/NCT02434081?term=NICOLAS&rank=4>

Trial Design :

Nivolumab Consolidation with standard first-line chemotherapy and radiotherapy in Locally Advanced Stage IIIA/B Non-Small Cell Lung Carcinoma.

Trial patients will receive nivolumab 3mg/kg as therapy after standard chemo-radiotherapy for as long as 1 year after start of nivolumab treatment unless they have unacceptable toxic effects, disease progression, or withdrew consent.

Inclusion Criteria :

Histologically or cytologically confirmed non-small cell lung cancer

Locally advanced stage IIIA or III B (T0-3 N2-3 or T4N0-3 M0) NSCLC, according to 7th TNM classification.

Nodal status N2 or N3 needs to be proven (by biopsy, EBUS, mediastinoscopy or thoracoscopy).

Whole body FDG-PET CT, if feasible including a contrast-enhanced CT of thorax and upper abdomen (incl. liver, kidney, adrenals)

brain MRI (preferred) or high-quality brain CT with intravenous contrast at the time of staging mandatory within 28 days before enrolment.

Measurable disease (according to RECIST v1.1 criteria)

Age \geq 18 years

Eastern Cooperative Oncology Group (ECOG) Performance Status 0-1 (see below*)

Life expectancy $>$ 3 months

Adequate haematological function:

WBC \geq 2000/ μ L

haemoglobin \geq 9 g/dL

neutrophil count \geq 1×10^9 /L

platelet count \geq 100×10^9 /L

Adequate liver function:

Total bilirubin \leq 1.5 x ULN (except patients with Gilbert Syndrome, who can have total bilirubin $<$ 3.0 mg/dl)

ALT $\leq 3 \times$ ULN

alkaline phosphatase $\leq 5 \times$ ULN.

Adequate renal function: Calculated creatinine clearance ≥ 30 ml/min (according to Cockcroft-Gault)

Pulmonary function FEV1 of 1.0 l or $> 40\%$ predicted value and DLCO $> 30\%$ predicted value

Patient capable of proper therapeutic compliance, and accessible to correct follow-up.

Women of childbearing potential, including women who had their last menstrual period in the last 2 years, must have a negative serum or urine pregnancy test within 7 days before beginning chemoradiotherapy (the test needs to be repeated within 24 hours before the start of nivolumab treatment).

Written Informed Consent (IC) for trial treatment must be signed and dated by the patient and the investigator prior to any trial-related evaluation and/or intervention.

Exclusion Criteria:

Patient with mixed small-cell and non-small-cell histologic features

Patient with pleural or pericardial effusions proven to be malignant

Prior chemotherapy, radiotherapy or molecular targeted therapy for NSCLC

Patient who has an active, known or suspected autoimmune disease. Patients are permitted to enrol 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.

Patient who has had in the past 3 years any previous or concomitant malignancy EXCEPT adequately treated basal or squamous cell carcinoma of the skin, in situ carcinoma of the cervix or bladder, in situ ductal carcinoma of the breast.

Patient with other serious diseases or clinical conditions, including but not limited to uncontrolled active infection and any other serious underlying medical processes that could affect the patient's capacity to participate in the study.

Ongoing clinically serious infections requiring systemic antibiotic or antiviral, antimicrobial, antifungal therapy.

Known or suspected hypersensitivity to nivolumab or any of its excipients

History of severe hypersensitivity reaction to any monoclonal antibody

Substance abuse, medical, psychological or social conditions that may interfere with the patient's participation in the study or evaluation of the study results.

Established pathological diagnosis of underlying interstitial lung disease or pulmonary fibrosis

Women who are pregnant or in the period of lactation

Sexually active men and women of childbearing potential who are not willing to use an effective contraceptive method (two barrier methods or a barrier method plus a hormonal method) during the study treatment and for a period of at least 12 months following the last administration of trial drugs.

Patients with any concurrent anticancer systemic therapy

HIV, active Hepatitis B or Hepatitis C infection

Previous radiotherapy to the thorax (prior to inclusion), including RT for breast cancer

Planned radiotherapy to lung of mean dose > 20 Gy or V20 > 35 %

Patient who received treatment with an investigational drug agent during the 3 weeks before enrolment in the trial

Metastatic disease (brain MRI or high-quality CT with intravenous contrast at the time of staging mandatory)

Prior treatment 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 costimulation or immune checkpoint pathways