Protocol STIMULI (ETOP)

A Randomised Open-label Phase II Trial of Consolidation With Nivolumab and Ipilimumab in Limited-stage SCLC After Chemo-radiotherapy.

This is the trial summary as assessed on clinicaltrials.gov on 30/06/2016.

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

https://clinicaltrials.gov/ct2/results?term=stimuli+etop&Search=Search

Trial Design :

The aim of the study is to investigate the efficacy (how well the treatment works) and tolerability (how severe the side effects are) of the standard treatment (chemotherapy and radiotherapy) alone, compared with the standard treatment followed by nivolumab and ipilimumab in patients with limited SCLC.

Inclusion Criteria for enrolment :

Histologically or cytologically confirmed small cell lung carcinoma

Untreated limited stage disease ((with the exception of one cycle of chemotherapy given prior to enrolment) as defined by stage I-IIIB based on 7th TNM classification (IASLC classification for SCLC proposal). M0 proven by

Whole body FDG-PET CT including a contrast-enhanced CT of thorax and upper abdomen (incl. liver, kidney, adrenals); OR contrast-enhanced CT of thorax and upper abdomen (incl. liver, kidney, adrenals) and bone scan; AND

Brain MRI (or contrast enhanced CT of the brain). . within 28 days before start of chemotherapy.

Age ≥ 18 years

ECOG performance status 0-1

Adequate haematological function:

haemoglobin > 9 g/dL

neutrophils count >1.5×109/L

platelet count > 100 × 109/L

Adequate liver function:

Total bilirubin < 2.5 × ULN

ALT and/or AST < 2.5 × ULN

alkaline phosphatase < 5 ULN.

Adequate renal function: Calculated creatinine clearance ≥ 30 mL/min (Cockroft-Gault)

Pulmonary function FEV1 of 1.0L or > 40% predicted value and DLCO > 40% predicted value.

Patient capable of proper therapeutic compliance, and accessible for 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 of chemotherapy.

All sexually active men and women of childbearing potential must 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.

Measurable or evaluable disease (according to RECIST 1.1 criteria). Not eligible: patients with only one measurable or evaluable tumour lesion which was resected or irradiated prior to enrolment.

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

- Chemo-radiotherapy treatment and PCI, and subsequent randomisation, including mandatory biological samples
- Optional biological material collection, long-term storage and future use of biological material for translational research

Inclusion Criteria for randomisation :

Chemo-radiotherapy completed per protocol: 4 cycles of chemotherapy, ≥85% of PTV of thoracic radiotherapy, as well as completed, mandatory PCI

non-PD after chemo-radiotherapy and PCI

ECOG performance status 0-2

Recovery of all adverse events to a grade ≤1, except for fatigue, appetite, oesophagitis and renal impairment (where ≤2 is allowed) and alopecia (any grade)

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 randomisation.

Exclusion Criteria for enrolment :

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

Patient with pleural or pericardial effusions proven to be malignant

Patients who have had in the past 5 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 (if no RT was involved).

Patients 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 ipilimumab or any of their excipients.

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

Documented history of severe autoimmune or immune mediated symptomatic disease that required prolonged (more than 2 months) systemic immunosuppressive (e.g. steroids) treatment, such as but not limited to ulcerative colitis and Crohn´s disease, rheumatoid arthritis, systemic progressive sclerosis (scleroderma), systemic lupus erythematosus, or autoimmune vasculitis (eg, Wegener's granulomatosis).

Subjects with an autoimmune paraneoplastic syndrome requiring concurrent immunosuppressive treatment.

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 during the study.

Patients with any concurrent anticancer systemic therapy (except for chemotherapy cycle 1).

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 %

Patients who received treatment with an investigational drug agent during the 3 weeks before enrolment in the study.

Prior chemotherapy or radiotherapy for SCLC. Exception: one cycle of chemotherapy (as specified to section 10.2) may be administered prior to enrolment.

<u>Exclusion criteria for randomisation</u>:

Less than 4 cycles of chemotherapy administered, less than 85% PTV of thoracic radiotherapy delivered, or PCI not completed

Progressive disease after chemo-radiotherapy and PCI