# An open-label, phase Ib, dose-escalation trial on the safety, tolerability, pharmacokinetics, immunogenicity, biological effects and antitumor activity of EMD 521873 in combination with local irradiation (20 Gy) of primary tumors or metastases in subjects with non-small cell lung cancer stage IIIb with malignant pleural effusion or stage IV with disease control (partial response or stable disease) after application of 4 cycles of platinum-based, first-line chemotherapy.

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Respiratory and mediastinal neoplasms malignant and unspecified |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON34011

**Source**
ToetsingOnline

**Brief title**
EMD 521873 plus Radiotherapy in NSCLC

## Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

**Synonym**
Lung cancer, non-small cell lung carcinoma

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Merck KGaA
**Source(s) of monetary or material Support:** Farmaceutische Industrie

## Intervention

**Keyword:** local irradiation, non-small cell lung cancer, phase Ib, Selectikine

## Outcome measures

### Primary outcome

The primary endpoint is the incidence of DLTs occurring during the first cycle of administration of any dose of EMD 521873 following radiotherapy. This endpoint will be used to determine the MTD of EMD 521873.

### Secondary outcome

Additional safety variables (AEs, laboratory parameters, vital signs); serum levels of anti-EMD 521873 antibodies to characterize the immunogenicity of EMD 521873; objective tumor response, change in circulating tumor cell numbers; progression-free survival and overall survival; changes in leukocyte subsets and molecular markers of immune activation

# Study description

### Background summary

Patients with stage IV NSCLC or stage IIIB NSCLC with malignant pleural effusion have a dismal prognosis with a median overall survival time of approximately 1 year after treatment with standard platinum-based first-line chemotherapy with or without monoclonal antibodies. In the present trial, active immunotherapy with EMD 521873 and radiation will be investigated as maintenance therapy in subjects with SD or partial remission after first-line chemotherapy. The combination of EMD 521873 with local tumor radiation is expected to induce or enhance a cellular immune response against various tumor antigens leading to control of tumor growth.

### Study objective

The primary objective will be to assess the safety and tolerability of this combination and to determine whether the MTD of
EMD 521873 is reached up to a dose of 0.45 mg/kg. Secondary objectives will be the evaluation of the PK, immunogenicity, biological effects and antitumor activity of EMD 521873 in this combination.

### Study design

This open-label, dose-escalation trial consists of a 4 week screening phase, a treatment phase, and a follow-up phase. After screening, eligible subjects will receive local irradiation (5 x 4 Gy) given over 5 consecutive days, prior to the first treatment cycle with EMD 521873. After a 2-day treatment-free interval, intravenous infusions of EMD 521873 will be given on 3 consecutive days in 3-week cycles until progression of disease (according to Investigator) or unacceptable toxicity. Subjects will be hospitalized on days 1-4 of cycle 1.

### Intervention

This is a trial with increasing doses of Selectikine in combination with radiation. Groups of 3-6 patients (cohorts) will enter the study. The first cohort will be treated at the dose level of 0.15 mg/kg and depending on the tolerability of the drug additional cohorts of patients will be treated at higher dose levels or , if the drug is not so well tolerated, at the same or even lower dose levels.The highest dose level to be studied in this trial will be 0.45 mg/kg. Before starting treatment of a new patient cohort at a higher dose level, all data from the previous dose level will be evaluated by an independent safety monitoring committee which includes the doctors involved in the study, representatives from the sponsor and an independent physician. Visits will take place on each day of radiation therapy (day -7 to day -3).

During treatment with EMD 521873 visits will take place on days 1-4, 8 and 15 of cycles 1 and 2; and on days 1-3 and 8 of all subsequent cycles.

**Study burden and risks**

The trial will be discontinued in the event of new findings that indicate a relevant
increase in risk or deterioration in the risk-benefit relationship. The careful selection of
trial sites with prior experience in managing patients with advanced NSCLC treated with
radiation is expected to enhance both the safety and comfort of subjects in this trial. In
addition, careful screening of subjects prior to enrolment is part of this protocol to avoid
the inclusion of subjects who can be expected to be at increased risk for developing severe
side effects after treatment with EMD 521873.

# Contacts

**Public**
Merck KGaA

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

• Male or female, aged >=18 years of age
• Signed written informed consent
• Effective contraception for male and female subjects of childbearing potential
• ECOG performance status 0 or 1
• Adequate hematological function defined by WBC >=3 x 109/L, neutrophils >=1.5 x 109/L, lymphocyte count >=0.5 x 109/L, platelet count >=100 x 109/L; hemoglobin >=9 g/L
• Estimated creatinine clearance >=50 mL/min according to the Cockcroft - Gault formula or 24-h urine sampling
• Adequate hepatic function defined by a total bilirubin level <=1.5 times the upper limit of normal (ULN), and aspartate aminotransferase (AST) and alanine aminotrasferase (ALT) <=5 x ULN

## Exclusion criteria

• Requirement for immunosuppressive treatment with the exception of inhalative corticosteroids or low-dose systemic corticosteroids (prednisone equivalent dose <=10 mg/day)
• Systemic autoimmune disease (e.g. lupus erythematodes, rheumatoid arthritis)
• Organ transplant recipients
• Active infections (including HIV, hepatitis B and C, tuberculosis)
• Known or clinically suspected brain metastases
• Active cardiovascular/cerebrovascular disease (e.g. symptomatic coronary vascular disease, congestive heart failure >= NYHA II, LVEF <50%, ventricular arrhythmia requiring medication, myocardial infarction or stroke) within previous 6 months
• Pericardial effusion
• Major impairment in pulmonary function: forced expiratory volume in 1 second (FEV1) <50% and diffusion capacity for carbon monoxide (DLCO) <50% of normal limit
• Any other significant disease that in the Investigator*s opinion would exclude the subject from the trial
• Known conditions associated with necroses of non-tumor bearing tissues (e.g. esophageal or gastroduodenal ulcers, ischemic bowel disease, chronic inflammations)
• Pregnancy or lactation
• Radiotherapy, chemotherapy, major surgery, biological therapy or any investigational drug within 30 days prior to the start of trial treatment
• Requirement for concurrent systemic anticancer treatment (chemotherapy, biological therapy)

• Pretreatment with anti-EGFR antibodies or tyrosine kinase inhibitors
• Participation in another interventional clinical trial within the past 30 days before start of trial treatment
• Known alcohol or drug abuse
• Any psychiatric condition that would prohibit the understanding or rendering of the informed consent
• Legal incapacity or limited legal capacity

# Study design

## Design

**Study type:** Interventional

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Treatment |

## Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 15-03-2009 |
| Enrollment: | 24 |
| Type: | Anticipated |

## Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Not applicable |
| Generic name: | Selectikine (other name NHS-IL2LT) |

# Ethics review

Approved WMO

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| Date: | 03-03-2009 |
| Application type: | First submission |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |

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| Approved WMO Date: | 24-08-2009 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 25-08-2009 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 01-12-2009 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 12-04-2010 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |
| Approved WMO Date: | 31-05-2011 |
| Application type: | Amendment |
| Review commission: | PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2008-007091-20-NL |
| CCMO | NL26310.031.08 |