A randomized, double-blind, placebo-controlled, phase III study evaluating the efficacy and safety of pembrolizumab plus platinum-based doublet chemotherapy with or without canakinumab as first line therapy for locally advanced or metastatic non-squamous and squamous non-small cell lung cancer subjects (CANOPY-1)

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Primary: Safety run-in part (part 1):• Recommended Phase 3 dose regimen (RP3R) of canakinumab in combination with pembrolizumab plus chemotherapy. Double-blind, randomized, placebo-controlled part (part 2):• Progressive free survival (PFS) between...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52694

Source
ToetsingOnline

Brief title
CACZ885U2301 (CANOPY-1)

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
Lung cancer; non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma B.V. (sponsor/verrichter van dit onderzoek)

Intervention

Keyword: Advanced, Canakinumab, Non-small cell lung cancer, Standard treatment

Outcome measures

Primary outcome

Part 1: RP3R.

Part 2: PFS, OS.

Secondary outcome

Part 1: pharmacokinetic parameters, adverse events, anti-drug antibodies of

canakinumab and pembrolizumab, ORR, DCR and DOR.

Part 2: ORR, DCR, TTR and DOR, adverse events, pharmacokinetic parameters,

anti-drug antibodies of canakinumab and pembrolizumab, questionnaires QLQ-C30,

QLQ-LC13 EQ-5D-5L.

Study description

Background summary

Pembrolizumab in combination with platinum-based doublet chemotherapy is recently been approved as first line treatment for locally advanced or metastatic non-small cell lung cancer (NSCLC) and will soon be taken up in the Dutch treatment guidelines as standard first line treatment.
Chronic inflammation plays an important role in the development of NSCLC. Key etiological risk factors such as smoking, second-hand smoke exposure, chronic infections, and exposure to environmental toxins cause a chronic inflammatory milieu that plays a critical role in carcinogenesis, particularly, in lung cancer. The cytokine interleukin-1β (IL-1β) is one of the mediators of pulmonary inflammation that promotes lung cancer.
Canakinumab is a human anti-IL-1β monoclonal antibody. Currently canakinumab is approved and marketed as Ilaris for the treatment of various IL*1β driven auto-inflammatory diseases, such as gouty arthritis and Systemic Juvenile Idiopathic Arthritis.
In the CANTOS study (a cardiovascular study) canakinumab reduced, in addition to the composite end point of stroke and myocardial infarction, the occurrence of lung cancer and lung cancer mortality compared to placebo in a dose-dependent manner. One hypothesis to explain these findings is that canakinumab reduced the rate of progression, invasiveness and metastatic spread of already existing tumors, which were too small to be detected at study entry.
This data along with the preclinical information that IL-1β supports tumorigenic inflammation provides the rationale to investigate the therapeutic role of canakinumab in non-small cell lung cancer (NSCLC).

Study objective

Primary:
Safety run-in part (part 1):
• Recommended Phase 3 dose regimen (RP3R) of canakinumab in combination with pembrolizumab plus chemotherapy.
Double-blind, randomized, placebo-controlled part (part 2):
• Progressive free survival (PFS) between the two treatment arms
• Overall survival (OS) between the two treatment arms.
Secondary:
Safety run-in part (part 1): pharmacokinetics, safety and tolerability, immunogenicity (anti-drug antibodies) of canakinumab and pembrolizumab, preliminary clinical anti-tumor activity (overall response rate (ORR), disease control rate (DCR) and duration of response (DOR)).
Double-blind, randomized, placebo-controlled part (part 2): ORR, DCR, time to response (TTR) and DOR, safety, pharmacokinetics, immunogenicity, patient reported outcomes.

Study design

The study consists of 2 parts: the safety run-in part (part 1, n=27) and a double-blind, randomized, placebo controlled part (part 2, n=600).

Part 1: open label part to determine RP3R of canakinumab in combination with pembrolizumab and chemotherapy.
Part 2: double-blind, randomized, placebo-controlled part to evaluate the efficacy and safety of canakinumab vs. placebo in combination with pembrolizumab plus chemotherapy.
First line treatment for advanced disease.
Treatment until disease progression or unacceptable toxicity.
Treatment cycles of 3 weeks.
Canakinumab: 200 mg S.C. every 3 (or 6) weeks. In part 2 randomization (1:1) to canakinumab 200 mg S.C. or placebo.
Pembrolizumab 200 mg I.V. infusions every 3 weeks (max. 35 cycles).
Chemotherapy part 1: 3 cohorts:
• Cohort A (for non-squamous NSCLC): carboplatin plus pemetrexed I.V.infusions
• Cohort B (for non-squamous NSCLC): cisplatin plus pemetrexed I.V. infusions
• Cohort C (for squamous or non-squamous NSCLC): carboplatin plus paclitaxel I.V. infusions.
Chemotherapy for part 2:
• For non-squamous NSCLC: carboplatin or cisplatin plus pemetrexed I.V. infusions
• For squamous NSCLC: carboplatin plus paclitaxel or nab-paclitaxel I.V. infusions.

Intervention

Part 1: Treatment with canakinumab, pembrolizumab and chemotherapy.
Part 2: Treatment with canakinumab or placebo, pembrolizumab and chemotherapy.

Study burden and risks

Risk: Adverse effects of study treatment.
Burden:
Screening 4 weeks.
Treatment:
Canakinumab (or placebo): subcutaneous injection (1 mL) every 3 weeks until disease progression.
Pembrolizumab: I.V. infusion 500 mL every 3 weeks (max. 35 cycles)
Chemotherapy: 2 agents I.V. infusion 500 mL every 3 weeks (max. 4 cycles).
Study procedures (based on treatment duration of 18 cycles):
Physical examination: 23.
Blood tests: 29, in total approx. 452 mL (part 1) and 674 mL (part 2).
Tumor biopsy: 0-1.
Pregnancy test (if relevant): 23.
ECG: 1-2.
CT/MRI scan(s): approx. 7 (in line with standard treatment).
Questionnaires: 19.
Optional: blood test cytokines (10 mL), blood test genetic research (6 mL),

tumor biopsy (1-2).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Written informed consent
• Males or females >= 18 years of age.
• Histologically confirmed locally advanced stage IIIB or IV NSCLC; in need for treatment in the
first-line setting, see protocol paragraph 5.1 item 3 for details.
• Known PD-L1 status determined by a Novartis designated central laboratory, see protocol
paragraph 5.1 item 5 for details.
• ECOG performance status (PS) of 0 or 1.
• At least 1 measurable lesion by RECIST 1.1.

• Adequate organ function. See protocol paragraph 5.1 item 9 for details

Exclusion criteria

• Previous immunotherapy, see protocol paragraph 5.2 item 1 for details.
• Prior treatment with canakinumab or other IL-1β inhibitor.
• EGFR sensitizing mutations and/or ALK rearrangement. Squamous subjects: neither EGFR or
ALK testing is required. see protocol paragraph 5.2 item 3 for
details.
• Known active central nervous system (CNS) metastases and/or carcinomatous meningitis, see protocol paragraph 5.2 item 5 for details.
• Active autoimmune disease that has required systemic treatment in the past 2 years prior to randomization, see protocol paragraph 5.2 item 7 for details.
• Suspected or proven immunocompromised state or infections, see protocol paragraph 5.2 item
8 for details.
• Live vaccination within 3 months prior to first dose of study drug.
• Pregnant or lactating women, females of childbearing potential and males not using adequate
contraception. See protocol paragraph 5.2 item 18-20 for details.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2019

Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Alimta
Generic name:	Pemetrexed
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	carboplatin
Generic name:	carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ilaris
Generic name:	canakinumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Keytruda
Generic name:	pembrolizumab
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Taxol
Generic name:	paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-10-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-01-2019
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-09-2020
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-10-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-09-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-10-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2018-001547-32-NL
ClinicalTrials.gov	NCT03631199
CCMO	NL67590.042.18