A randomized, double-blind, placebo-controlled, phase III study evaluating the efficacy and safety of canakinumab in combination with docetaxel versus placebo in combination with docetaxel in subjects with non-small cell lung cancer (NSCLC) previously treated with PD-(L)1 inhibitors and platinum-based chemotherapy (CACZ885V2301, CANOPY-2)

Published: 09-04-2019
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Primary: Safety run-in part (part 1):* to confirm tthe recommended Phase 3 dose regimen (RP3R) of canakinumab in combination with docetaxel. Double-blind, randomized, placebo-controlled part (part 2):* to compare the overall survival (OS) between...

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

Summary

ID

NL-OMON49205

Source
ToetsingOnline

Brief title
CACZ885V2301 (CANOPY-2)

Condition

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

Synonym
Lungcancer; 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.

Intervention

Keyword: Advanced, Canakinumab, Docetaxel, Non-small cell lung cancer

Outcome measures

Primary outcome

Part 1: RP3R.

Part 2: OS.

Secondary outcome

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

canakinumab and pembrolizumab, ORR, DCR and DOR.

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

anti-drug antibodies against canakinumab, ECOG score, questionnaires QLQ-C30,

QLQ-LC13 EQ-5D-5L.

Study description

Background summary

The current standard second line treatment for locally advanced or metastatic non-small cell lung cancer (NSCLC) is docetaxel.

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-1* (IL-1*) is one of the mediators of pulmonary inflammation that can promote lung cancer.
Canakinumab is a human anti-IL-1* monoclonal antibody. Currently canakinumab is approved and marketed as Ilaris for the treatment of various IL*1* 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-1* 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):
* to confirm tthe recommended Phase 3 dose regimen (RP3R) of canakinumab in combination with docetaxel.
Double-blind, randomized, placebo-controlled part (part 2):
* to compare the overall survival (OS) between the two treatment arms (canakinumab plus docetaxel vs. docetaxel).
Secondary:
Safety run-in part (part 1): pharmacokinetics, safety and tolerability, 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): progression free survival (PFS), ORR, DCR, time to response (TTR) and DOR, safety, pharmacokinetics, immunogenicity, ECOG performance status, patient reported outcomes.

Study design

The study consists of 2 parts: the safety run-in part (part 1, n=6-18) and a double-blind, randomized, placebo controlled part (part 2, n=226).
Part 1: open label part to determine RP3R of canakinumab in combination with

docetaxel.
Part 2: double-blind, randomized, placebo-controlled part to evaluate the efficacy and safety of canakinumab vs. placebo in combination with docetaxel.
Second 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.
* Docetaxel: infusion every 3 weeks. Duration of infusion 1 hour.

Intervention

Part 1: Treatment with canakinumab plus docetaxel
Part 2: Treatment with canakinumab or placebo plus docetaxel

Study burden and risks

Risk: Adverse effects of study treatment.
Burden:
Screening 4 weeks.
Treatment:
Canakinumab (or placebo): subcutaneous injection (1,5 mL) every 3 weeks until disease progression.
Docetaxel: I.V. infusion 500 mL every 3 weeks.
Study procedures (based on treatment duration of 18 cycles):
Physical examination: 23.
Blood tests: 31, in total approx. 300 mL (part 1) and 516 mL (part 2).
Pregnancy test (if relevant): 23.
ECG: 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)
Elderly (65 years and older)

Inclusion criteria

* Males or females * 18 years of age.
* Histologically confirmed locally advanced stage IIIB or IV NSCLC.
* One prior platinum-based chemotherapy and one prior PD-(L)1 inhibitor therapy for locally advanced or metastatic disease, see protocol paragraph 5.1 item 4 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 8 for details
* Written informed consent

Exclusion criteria

* Previous treatment with docetaxel, canakinumab or other IL-1* inhibitor or another 1st line treatment than chemotherapy plus PD(L)1 inhibitor.
* EGFR sensitizing mutations, see protocol paragraph 5.2 item 2 for details.
* Previously untreated or symptomatic central nervous system (CNS) metastases or lepto- meningeal disease, see protocol paragraph 5.2 item 7 for details.
* Suspected or proven immunocompromised state or infections, see protocol paragraph 5.2 item 6 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 19-21 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):	13-08-2019
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ilaris
Generic name:	Canakinumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	09-04-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-05-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-08-2019
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:	16-09-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-02-2020
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:	10-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-04-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	25-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-10-2021
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	EUCTR2018-002480-26-NL
ClinicalTrials.gov	NCT03626545
CCMO	NL68516.042.19