The influence of different diets on alectinib pharmacokinetics in NSCLC patients.

Published: 01-09-2021
Last updated: 15-05-2024

To investigate the effect of various dietary interventions and co-administration of subcutaneous semaglutide on the pharmacokinetics of alectinib in NSCLC patients.

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

Summary

ID

NL-OMON28490

Source
Nationaal Trial Register

Brief title
DIALECT study

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lungcancer

Health condition

Non-smalle cell lung carcinoma (NSCLC).

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Department of Medical Oncology
Source(s) of monetary or material Support: Erasmus MC, Department of Medical Oncology

Intervention

Keyword: semaglutide, Ozempic, alectinib

Explanation

Outcome measures

Primary outcome

"The primary outcome will be the change in Ctrough of alectinib during phase B or C compared to phase A." into "The primary outcome will be the change in Ctrough of alectinib during phase B, C and D compared to phase A.".

Secondary outcome

Toxicity and the mean the range of the macronutrients in the current intake and a pharmacokinetic model.

Study description

Background summary

Rationale: Alectinib (Alecensa) is a second generation small-molecule kinase inhibitor, registered for ALK-positive, metastatic non-small cell lung cancer (NSCLC). Because alectinib’s plasma trough concentration (Ctrough) is correlated with patients’ progression-free survival, it is important to optimize its bioavailability. Compared to fasted intake, alectinib’s exposure increases with >200% when taken with a high-fat meal. In daily practice, patients are therefore recommended to take alectinib twice daily with a (high-fat) meal. However, 37% of patients does not reach the vital Ctrough. Additionally, (extreme) weight gain is an important side effect of alectinib treatment. It is currently unknown if there are good (and healthy) alternatives for a high-fat meal to increase alectinib’s absorption and to optimize its treatment. Objective: To investigate the effect of different diet interventions on the pharmacokinetics of alectinib in NSCLC patients. Study design: This study is an interventional, randomized, three-period cross-over pharmacokinetic study in which alectinib will be taken twice daily (BID) for seven days in combination with: - in phase A (control phase): a normal diet, c.q. continental breakfast and normal dinner; - in phase B: a low-fat diet, c.q. 200 grams low-fat yoghurt as breakfast, and normal dinner; - in phase C: a normal diet with different intake times, c.q. lunch and dinner. After the 7th day of each phase,

patients are asked to withdraw blood in the morning, prior to alectinib intake to collect a Ctrough sample. Optionally, in phase A, patients are admitted for a 10-hour pharmacokinetic sampling of in total 13 samples. Study population: Adult patients with NSCLC who are treated with alectinib. Main study parameters/endpoints: The primary outcome will be the change in Ctrough of alectinib during phase B or C compared to phase A. Secondary outcomes will be the occurrence of (patient reported) toxicity, the current intake with alectinib and a pharmacokinetic model. Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The risk of blood withdrawal is negligible. In addition, the risk for altered alectinib concentrations in this short period is also considered to be negligible. The burden for patients is also limited as only a Ctrough sample is taken and the 10h PK-sampling is optional.

Study objective

To investigate the effect of various dietary interventions and co-administration of subcutaneous semaglutide on the pharmacokinetics of alectinib in NSCLC patients.

Study design

This study is an interventional, randomized, three-period cross-over pharmacokinetic study in which alectinib will be taken twice daily (BID) for seven days in combination with:

- in phase A (control phase): a normal diet, c.q. continental breakfast and normal dinner;

- in phase B: a low-fat diet, c.q. 200 grams low-fat yoghurt as breakfast, and normal dinner;

- in phase C: a normal diet with different intake times, c.q. lunch and dinner.

- in phase D: a normal diet, c.q. continental breakfast and dinner, with co-administration of semaglutide 2.4 mg s.c..

After the 7th day of each phase, patients are asked to withdraw blood in the morning, prior to alectinib intake to collect a Ctrough sample. Optionally, in phases A and D, patients are admitted for a 10-hour pharmacokinetic sampling of in total 13 samples.

Intervention

Different diatairy intake with alectinib.

- in phase B: a low-fat diet, c.q. 200 grams low-fat yoghurt as breakfast, and normal dinner;

- in phase C: a normal diet with different intake times, c.q. lunch and dinner.

- in phase D: a normal diet, c.q. continental breakfast and dinner, with co-administration of semaglutide 2.4 mg s.c..

Study burden and risks

The risk of blood withdrawal is negligible. In addition, the risk for altered alectinib concentrations in this short period is also considered to be negligible. The burden for patients is also limited as only a Ctrough sample is taken and the 10h PK-sampling is optional.

Contacts

Public
Erasmus MC
G.D. Marijn / D.A.C. Veerman / Lanser

010-70 41 937
Scientific
Erasmus MC
G.D. Marijn / D.A.C. Veerman / Lanser

010-70 41 937

Eligibility criteria

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

Inclusion criteria

- • Age: ≥18 years;
- • Able to understand the written information and willing to give informed consent;
- • Diagnosed with metastatic NSCLC and (are planned to) receive treatment with alectinib (Alecensa);
- • Use of alectinib of at least 14 days, to guarantee steady-state, and expected to continue treatment until end of study period;
- • WHO performance score with a maximum of 2; • Willing to follow dietary restrictions.

Exclusion criteria

- • Unable to draw blood for study purposes;
- • Pregnant or lactating women;
- • Not willing/able to not use medication which are a substrate for Pgp and have a small therapeutic window during study period, e.g. digoxine, dabigatran, sirolimus, everolimus, topotecan, nilotinib and lapatinib. Due to P-gp inhibition of alectinib;
- • Not willing/able to not use medication which are a substrate for Pgp and have a small therapeutic window during study period, e.g. rosuvastatine, sulfasalazine, methotrexaat, topotecan, lapatinib and mitoxantron. Due to BRCP inhibition of alectinib;
- • Unwillingness to abstain from any other food or drinks than the prescribed restrictions 1 hour before and 2 hours after intake of alectinib at the pharmacokinetic sampling day; • Patients with known impaired drug absorption (e.g. gastrectomy and achlorhydria); • Allergic to compounds in yoghurt.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-12-2023
Enrollment:	20
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Approved WMO Date:	08-08-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

ID: 54011
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9702
EudraCT	2022-003275-42
CCMO	NL78079.078.23
OMON	NL-OMON54011

Study results