Influence of Flavonoids on the Absorption of Nintedanib: a Randomized, Cross-Over Pharmacokinetic Study

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23987

Source
Nationaal Trial Register

Brief title
INFLATE study

Health condition

Interstitial Lung disease

Sponsors and support

Primary sponsor: Erasmus MC dept. of Medical Oncology and dept. of Pulmonology
Source(s) of monetary or material Support: Erasmus MC MRACE grant and dept. funding

Intervention

Outcome measures

Primary outcome

Change in nintedanib bioavailability, expressed in area under the plasma curve (AUC).

Secondary outcome

Change in other pharmacokinetic parameters i.e. maximal concentration (Cmax) and time to reach Cmax (Tmax) and a difference in occurrence of (patient reported) toxicity.

Study description

Background summary

Rationale: Tyrosine kinase inhibitors (TKIs) have become essential in the treatment of various diseases. Nintedanib (Ofev ®) is registered as first-line treatment of fibrotic interstitial lung disease (ILD). Nintedanib's bioavailability is 4.7% and is a substrate of the efflux pump P-glycoprotein (P-gP). P-gP can be inhibited by flavonoids, especially by epigallocatechin gallate (EGCG). ECGC is highly concentrated found in the popular beverage green tea. Hence, the flavonoid-drug interaction could potentially lead to higher nintedanib absorption by the gastro-intestinal tract. This would cause higher systemic bioavailability and lower local gastro-intestinal drug concentrations (which is thought to be causing most of nintedanib's toxicity). Furthermore, inter-patient variability could decrease.
Objective: to study the pharmacokinetic interaction between nintedanib and green tea extract (with > 60% ECGC) in fibrotic ILD patients.
Study design: A randomized, two-phase cross-over pharmacokinetic study in which nintedanib will be taken twice daily for seven days with water and a meal respectively with or without 500 mg green tea extract (with > 60% ECGC).
Study population: Adult patients who (are planned to) receive nintedanib for an ILD.
Main study parameters/endpoints: Primary outcome will be the change in nintedanib bioavailability, expressed in area under the plasma curve (AUC). Secondary objectives are the change in other pharmacokinetic parameters i.e. maximal concentration (Cmax) and time to reach Cmax (Tmax) and a difference in occurrence of (patient reported) toxicity.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The risk of the blood withdrawals is negligible.

Study objective

The flavonoid-drug interaction could potentially lead to higher nintedanib absorption by the gastro-intestinal tract. This would cause higher systemic bioavailability and lower local gastro-intestinal drug concentrations. Furthermore, inter-patient variability could decrease, as also seen with other SMKI's.

Study design

Interim analysis after four evaluable patients, full analysis of primary and secondary endpoints after last evaluable inclusion. Plasma drug concentrations are measured with LC/MS-MS.

Intervention

Seven days nintedanib taken with 500 mg green tea extract (with > 60% ECGC)

Contacts

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Eligibility criteria

Inclusion criteria

- Age ≥18 years;
- Able to understand the written information and able to give informed consent;
- Planned treatment with nintedanib for any fibrotic ILD according to standard of care.

Exclusion criteria

- unable to draw blood for study purposes
- usage of other strong P-gP or CYP3A4 interacting compounds
- patients with known impaired drug absorption (e.g. gastrectomy and achlorhydria)

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2020
Enrollment:	26
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL8913
Other	METC Erasmus MC : MEC 20-558

Study results