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

Gepubliceerd: 16-09-2020 Laatst bijgewerkt: 18-08-2022

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...

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|---|---|
| **Ethische beoordeling** | Niet van toepassing |
| **Status** | Werving nog niet gestart |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON23987

**Bron**
NTR

**Verkorte titel**
INFLATE study

**Aandoening**

Interstitial Lung disease

### Ondersteuning

**Primaire sponsor:** Erasmus MC dept. of Medical Oncology and dept. of Pulmonology
**Overige ondersteuning:** Erasmus MC MRACE grant and dept. funding

### Onderzoeksproduct en/of interventie

### Uitkomstmaten

**Primaire uitkomstmaten**

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

# Toelichting onderzoek

### Achtergrond van het onderzoek

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.

### Doel van het onderzoek

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.

### Onderzoeksopzet

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.

### Onderzoeksproduct en/of interventie

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

# Contactpersonen

## Publiek

Erasmus MC
G.D. Marijn Veerman

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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)

# Onderzoeksopzet

## Opzet

Type: Interventie onderzoek

| | |
|---|---|
| Onderzoeksmodel: | Cross-over |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Open / niet geblindeerd |
| Controle: | Geneesmiddel |

### Deelname

Nederland

| | |
|---|---|
| Status: | Werving nog niet gestart |
| (Verwachte) startdatum: | 01-10-2020 |
| Aantal proefpersonen: | 26 |
| Type: | Verwachte startdatum |

### Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nog niet bepaald

## Ethische beoordeling

Niet van toepassing

| | |
|---|---|
| Soort: | Niet van toepassing |

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

| Register | ID |
|---|---|
| NTR-new | NL8913 |
| Ander register | METC Erasmus MC : MEC 20-558 |

# Resultaten