Absolute bioavailability trial of oral imatinib (Glivec®) using a stable isotope labeled intravenous imatinib-d8 microdose

No registrations found.

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

Summary

ID

NL-OMON21434

Source
NTR

Health condition

Cancer, gastrointestinal stromal tumor, imatinib, absolute bioavailability

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek
Source(s) of monetary or material Support: Antoni van Leeuwenhoek

Intervention

Outcome measures

Primary outcome

To ascertain whether the absolute bioavailability of oral imatinib (Glivec®) at steady state can be calculated using LC-MS/MS after concomitant administration of a single 100 µg microdose of stable isotope labeled imatinib (imatinib-d8).

Secondary outcome

N/A

Study description

Background summary

The aim of this proof of concept study is to determine the ABA of imatinib using a SIL-microtracer trial design. Imatinib is chosen as a model compound because ABA trial results using a cross-over trial design are already available. (1) The results obtained from this new proof of concept study can be compared to the results obtained using the traditional cross-over trial design. When the results are comparable, this study provides proof that microtracer ABA trials are feasible in our institute, making it possible to reduce patient burden and saving costs and time in future trials where the ABA of oral anticancer agents needs to be investigated.

Study objective

The absolute bioavailability of oral imatinib (Glivec®) at steady state can be calculated using LC-MS/MS after concomitant administration of a single 100 µg microdose of stable isotope labeled imatinib (imatinib-d8).

Study design

Blood will be drawn for pharmacokinetic research at 16 time points at day 1: t=0 (predose), t=0.5h, t=1h, t=1.5h, t=2h, t=2.5h (pre IV microdose), t=3h, t=3.5h, t=4h, t=4.5h, t=5h, t=6h, t=8h, t=12h, t=24h, t=48h. The 48h timepoint will be collected in an outpatient setting. For each timepoint 4 mL of blood will be collected. In total, 64 mL of blood will be collected for the trial.

Intervention

Intravenous injection with stable isotople labeled imatinib and subsequent blood collection

Contacts

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Eligibility criteria

Inclusion criteria

1. Locally advanced or metastatic cancer;

2. On imatinib treatment at a stable dose of 400 mg once daily in the morning for at least 7 days (steady state plasma concentration)

3. Age ≥ 18 years;

4. Able and willing to give written informed consent;

5. WHO performance status of 0, 1 or 2;

6. Able and willing to undergo blood sampling for PK analysis

7. Minimal acceptable safety laboratory values
>
a. ANC of ≥ 1.5 x 109 /L

b. Platelet count of ≥ 100 x 109 /L

c. Hepatic function as defined by serum bilirubin ≤ 2 x ULN, ALAT and ASAT ≤ 5 x ULN

d. Renal function as defined by glomerular filtration rate (GFR MDRD) > 40 ml/min/1.73m2

8. Able and willing to get two lines for intravenous infusion (one for microdose infusion and one for PK sampling)

Exclusion criteria

Any treatment with investigational drugs within 30 days or 5 half-lives prior to receiving the investigational treatment;

2. Any treatment with inhibitors of CYP3A4 (e.g. boceprevir, claritromycine, erytromycine, indinavir, itraconazol, ketoconazol, ritonavir and voriconazol), inhibitors of Pgp (e.g. ciclosporine, kinidine and verapamil), inhibitors of BCRP (e.g. lapatinib), inductors of CYP3A4, Pgp or BCRP;

4. Woman who are pregnant or breast feeding;

5. Patients suffering from any known disease or dysfunction that might influence the dissolution and/or absorption of imatinib (e.g. inflammatory bowel disease)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2019
Enrollment:	6
Type:	Anticipated

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	NL6773
NTR-old	NTR7642
Other	: N18IBA

Study results

Summary results
N/A