Influence of an Acidic Beverage (Coca-Cola) on the exposure to Imatinib (GLIvec) after major gastrecTomY in patients with Gastrointestinal Stromal Tumors (ABILITY)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON41047

Source
ToetsingOnline

Brief title
ABILITY

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal therapeutic procedures

Synonym
Gastro-Intestinal Stromal Tumor/Gastro-intestinal Cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cola, gastrectomy, GIST, imatinib

Outcome measures

Primary outcome

To assess the effect of Coca*Cola on the exposure to imatinib in patients with

major gastrectomy.

Secondary outcome

To assess the effect of Coca*Cola on the frequency and severity of the adverse

events reported while on imatinib therapy

(safety parameter; study is not powered for a significant result)

Study description

Background summary

Imatinib is registered for patients with cKIT (CD 117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST) as well as for adjuvant treatment of adult patients who are at risk for relapse following resection of cKIT positive GIST.
Imatinib is well absorbed after oral administration with Cmax within 2*4 hours post*dose and with a bioavailability of 98%. The elimination half*live of imatinib is approximately 18 hours. Imatinib exposure (AUC) increases proportionally with increasing doses ranging from 25 *1000 mg.
The most common sites for GIST to occur are the stomach (60*70%) and proximal small intestines (20*25%). Therefore patients with GIST often have altered GI* tract due to tumor resection or palliative surgery which might affect imatinib exposure. Indeed, Yoo et al. showed that steady state imatinib trough levels in patients with advanced GISTs after major gastrectomy are lower compared to patients with a previous wedge resection or without gastric surgery. Patients that underwent major gastrectomy had an average imatinib plasma trough levels

below 1000 µg/L. This while imatinib trough levels above 1000 µg/L are correlated to more beneficial treatment outcomes (longer Progression Free Survival).

Study objective

Since imatinib easily and rapidly dissolves at pH 5.5 or less, a lack of gastric acid secretion might be causing the decreased exposure in the patients that underwent major gastrectomy. Therefore we would like to study if the exposure to imatinib in patients after major gastrectomy can be improved by creating a more acidic environment for absorption through combining imatinib intake with Coca*Cola.

Study design

Phase I post registration prospective, open*label, two*period, cross*over, randomised, intervention pharmacology study in patients with GIST

Intervention

For 1 week the patient will be asked to take their daily imatinib dosage with 150 mL of Coca-Cola instead of water.

Study burden and risks

Risk assessment is negligible.
Imatinib is well tolerated in doses up to 800 mg daily in the treatment of GIST. In this study we include patients who are currently treated with imatinib or who will start imatinib therapy at a standard dose.The dose will not be modified for study purposes. The only intervention in this study is the intake of imatinib with Coca*Cola, which might increase the exposure. Since these patients previously underwent major gastrectomy, their exposure after ingestion with Coca*Cola is not likely to be significant higher than the exposure to imatinib in the general population without major gastrectomy. Moreover, in the phase I studies dose limiting toxicities were only encountered at dosages > 1000mg imatinib. Participating patients will be monitored for adverse events, therefore we feel that it is safe to perform this study in this population.

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

1. Male or female patients >= 18 years of age
2. Patients with GIST, who previously underwent major gastrectomy
3. Eastern Cooperative Oncology Group (ECOG) performance
status (PS) of 0*1
4.Already selected to receive imatinib therapy in a dose of 400*800mg imatinib daily, as judged by the treating physician and with respect for and in agreement with the registration guidelines
5. Subject is able and willing to sign the Informed Consent Form prior to screening

Exclusion criteria

1. Concomitant administration of any anti*cancer therapies (e.g. chemo*therapy, other targeted therapy, experimental drug, etc) other than imatinib
2. Concomittant use of medication which strongly inhibits or induces CYP3A4
3. Refractory nausea and vomiting, malabsorption with other causes than gastrectomy or external biliary shunt that would preclude adequate absorption.
4. Unwillingness to use Coca*Cola
5. Inability to comply with the requirements of the protocol

6. Inability to understand the nature and extent of the study and the procedures required
7. Participation in a drug study within 60 days prior to the first day of this study

Study design

Design

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):	28-07-2014
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Gleevec
Generic name:	imatinib
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	04-06-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	28-07-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-02-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-02-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-06-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2014-001044-38-NL
CCMO	NL49001.091.14