Integrated pharmacokinetics of infliximab, adalimumab and golimumab in serum, tissue and faeces of patients with moderate to severe Ulcerative Colitis and Crohn's Colitis

Published: 22-09-2015
Last updated: 19-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON47648

Source
ToetsingOnline

Brief title
Three compartment PK study

Condition

- Gastrointestinal inflammatory conditions

Synonym
inflammatory bowel disease, ulcerative colitis/Crohn's colitis

Research involving
Human

Sponsors and support

Primary sponsor: Maag-, darm-, leverziekten
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: biologicals, inflammatory bowel disease, pharmacokinetics, ulcerative colitis

Outcome measures

Primary outcome

The primary endpoint of this exploratory study will be the relationship between

anti-TNF and TNF levels in serum, tissue and feces at different timepoints in

patients with moderate to severe colitis.

Secondary outcome

The correlation between primary response to those agents (clinical, biochemical

en endoscopic improvement) and drug levels in these three compartments.

Study description

Background summary

The mechanism why some patients with Inflammatory Bowel Disease do not respond to treatment with anti-tumor necrosis factor (TNF) agents such as infliximab (IFX), is largely unknown. Recent studies performed by Brandse et al.(Gastroenterology 2015) and Yarur et al (Gut 2014) investigated the role of the luminal (feces) and mucosal (tissue) compartments in the pharmacokinetics of IFX . It was shown that a significant proportion of IFX is lost through leakage from the gut in to the feces, especially in the acute phase of the disease, which led to impaired clinical outcome. As a consequence, patients with severe inflammation need higher doses of anti-TNF to achieve clinical effect. In order to fully understand the pharmacokinetics (PK) of three different anti-TNF agents (IFX, adalimumab and golimumab) in patients with moderate to severe Ulcerative Colitis or Crohn's colitis a mechanism -based PK model needs to be developed consisting of multiple physiological compartments. Therefore, we propose a PK study, focusing on anti-TNF and TNF levels in serum, tissue and feces. These levels will be combined in an integrated PK model

quantifying the relationship between the dose and concentrations of anti-TNF in the three compartments.

Study objective

The primary aim of this study is to develop a physiologically-based PK model for three different anti-TNF agents describing the relationship between dose and concentration in three physiological compartments in patients with moderate to severe colitis. Anti-TNF and TNF levels will be concomitantly measured in serum, tissue and feces.

Study design

Cohort study

Study burden and risks

Participating will result in additional blood sampling and additional stool sample collection (at 6 different time points). The first, baseline endoscopy can be considered as standard care before starting treatment. After this endoscopy, two additional endoscopies will be performed (day 14 and 42). This study is considered to be a low-risk trial; all subjects will receive anti-TNF treatment in accordance to standard care. The extra endoscopic procedures are also considered low risk, with a risk of perforation risk of 0,001% and a bleeding risk of 1%

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

Patients aged * 18 years, either male or female, moderate to severe Ulcerative Colitis or Crohns* colitis (respectively according to Mayo score (2 or 3) or SES-CD (*7) at baseline endoscopy), starting on Infliximab, adalimumab or golimumab at regular doses.

Exclusion criteria

Contra-indications to anti-TNF treatment, imminent need for surgery.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2016

Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	22-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL54078.018.15