Thioguanine therapy during pregnancy in inflammatory bowel diseases

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26685

Source
Nationaal Trial Register

Brief title
Thioguanine in pregnancy

Health condition

Inflammatory bowel diseases
Crohn's disease
Ulcerative colitis
Pregnancy
Offspring
Thioguanine
Congenital abnormalities
Mutagenic
Teratogenic

Sponsors and support

Primary sponsor: None
Source(s) of monetary or material Support: TEVA Pharmaceuticals BV

Intervention

Outcome measures

Primary outcome

The primary objective is to assess the safety of thioguaninein maternally exposed offspring. Efficacy variables will be the number and aspect of birth defects (minor and major) and rate of pre-term births, low-birth weights, (spontaneous) abortions and neonatal morbidity.

Secondary outcome

Secondary efficacy variables will be the number of complications during pregnancy and delivery, and the course after delivery. Furthermore, signs of myelosuppression or hepatotoxicity in the neonate and thiopurine metabolite measurements in the neonate (if applicable) will be assessed.

Study description

Background summary

Since 1962, the conventional thiopurines, mercaptopurine (MP) and its prodrug azathioprine (AZA), have been used in the treatment of ulcerative colitis and Crohn's disease, together known as inflammatory bowel diseases (IBD).1,2 In recent times, a third thiopurine-derivative named thioguanine (TG) is increasingly being used as a 'rescue' drug in IBD-patients who had to discontinue AZA or MP therapy due to intolerance or resistance (up to 50% in the first two years of treatment).3 Thioguanine treatment has shown promising short-term results with regards to safety and effectiveness in patients with IBD, and has recently been provisionally re-registered (name: Thiosix®) for IBD in The Netherlands.4-6

Ulcerative colitis and Crohn's disease predominantly affect young adults, including a significant number of female patients in their reproductive years.7 Active disease during pregnancy has been linked to poor reproduction capacity and pregnancy outcome (i.e. low birthweight and premature birth), emphasizing the importance of disease control prior to and throughout pregnancy. Azathioprine and MP are considered safe during pregnancy and breastfeeding, despite detectable metabolite concentrations in the newborn and breastmilk.8,9 Relatively less is known about the pharmacological aspects of TG therapy during pregnancy and its effects on maternally exposed offspring. In one descriptive case series consisting of 19 pregnancies, the relatively safe use of TG in pregnant IBD-patients was described.10 Larger studies are needed to confirm these findings and in order to counsel patients appropriately about conception and pregnancy during TG therapy for IBD. Additionally, knowledge about the long-term effects of maternally TG exposure is essential.

Therefore the objective of this study is to assess the safety of TG in maternally exposed offspring, as well as to collect data on the long-term development outcomes of these exposed

children.

Study objective

Based on a small cohort study of 19 pregnancies with healthy infants, we hypothesize that thioguanine exposure during pregnancy is relatively safe for the fetus.

Study design

Data will be collected after child birth

Intervention

None

Contacts

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Eligibility criteria

Inclusion criteria

Female patients with inflammatory bowel disease exposed to thioguanine during (a period of) the pregnancy.

Exclusion criteria

Patients with concomitant use of possible teratogenic drugs such as ACE inhibitors, angiotensin II antagonist, isotretinoin, cocaine, high doses of vitamin A, androgens, tetracycline, doxycycline, streptomycin, phenytoin, valproic acid, trimethadione, paramethadione, carbamazepine, lithium, methotrexate, penicillamine, thiouracil, carbimazole, thalidomide, warfarin, diethylstilbestrol, cocaine and alcohol.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2018
Enrollment:	30
Type:	Anticipated

Ethics review

Positive opinion

Date:	07-01-2019
Application type:	First submission

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	NL7466
NTR-old	NTR7708
Other	METC Amsterdam UMC, loc. VUmc : 2014.530 (A2016.473)

Study results

Summary results
van den Berg SA, de Boer M, van der Meulen-de Jong AE, et al. Safety of Tioguanine During Pregnancy in Inflammatory Bowel Disease. J Crohns Colitis 2016; 10(2): 159-65.