Thioguanine therapy during pregnancy in inflammatory bowel diseases

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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.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26685

Bron
Nationaal Trial Register

Verkorte titel
Thioguanine in pregnancy

Aandoening

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

Ondersteuning

Primaire sponsor: None
Overige ondersteuning: TEVA Pharmaceuticals BV

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

Data will be collected after child birth

Onderzoeksproduct en/of interventie

None

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-12-2018
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	07-01-2019
Soort:	Eerste indiening

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

Resultaten

Samenvatting resultaten
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.