VAART-onderzoek (VAccination in ARTritis).

Gepubliceerd: 03-07-2007 Laatst bijgewerkt: 18-08-2022

The primary objective of the study is to study the safety of MMR booster vaccination in JIA patients by measuring JIA disease activity and the occurrence of measles, mumps or rubella infection. The next primary objective is to evaluate the...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON26319

Bron
NTR

Verkorte titel
VAART

Aandoening

Juvenile Idiopathic Arthritis (JIA)
Measles, Mumps, Rubella
Vaccination

Ondersteuning

Primaire sponsor: N.M.Wulffraat
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Overige ondersteuning: Investigator driven investigation (fund = initiator = sponsor)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Safety of MMR vaccination, according to:
1. JIA disease activity (defined by internationally validated core set criteria, number of disease flares in the 12 months after MMR vaccination and medication use)
Measles, mumps or rubella infections
2. Efficacy of MMR booster, defined by specific antibodies against measles, mumps and rubella.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: The pathogenesis of autoimmune diseases (AID) is largely unknown. It is generally assumed that AID such as Juvenile Idiopathic Arthritis (JIA) arise in genetically predisposed patients after environmental triggers like infections or vaccinations. However, fail-safe mechanisms exist in our immune system. Among others, regulatory T-cells (Tregs) control the immune response and prevent destructive autoimmune responses. In order to develop AID after vaccination these regulatory T-cells and other homeostatic mechanisms must fail. Previous studies in JIA patients showed no increase in disease activity after immunization with dead vaccines. The MMR vaccination, a live attenuated vaccine, caused no increase in disease activity in JIA patients. However, a propspective trial was advised. In addition, it is unknown whether vaccination is effective, since the immune response to vaccination may be diminished due to immunosuppressive therapy for the underlying disease.
Objective: The primary goal of the current study is to study the safety and efficacy of MMR booster vaccination in JIA patients. Based on a retrospective analysis we hypothesize that MMR vaccination does not aggravate JIA disease and that patients with active JIA who are under immunosuppressive medication are still able to mount protective immunity in response to MMR booster. The secondary objective is to study immune regulatory mechanisms induced by vaccination. We hypothesize that Tregs are able to prevent relapse of JIA activity.
Study design: prospective randomized controlled open label vaccination study.
Study population: JIA patients, all subtypes, aged 4 to 8 years. Patients are treated by the pediatric rheumatology units from various University Medical Centers in the Netherlands.
Intervention: In the Netherlands, measles-mumps-rubella (MMR) vaccination is included in the National Vaccination Program and is normally administered at age 9. Included patients will be randomized for one extra MMR booster vaccination between the age of 4-8 years or no additional vaccination. Patients in both groups will also receive their usual MMR booster vaccine at age 9 according to the National Vaccination Program.
Main study parameters/endpoints: Primary outcome is disease activity, measured using

international validated core set criteria. During a 12 month follow-up period we will register disease activity and side-effects at different moments in time to determine safety of vaccination. The efficacy of the vaccine will be studied according to antibody levels against measles, mumps and rubella in the blood and presence of MMR neutralizing antibodies. Secondary endpoints are immunological changes. These are number of Tregs, capable to suppress proliferation in vitro; presence of anti-inflammatory cytokine profiles following MMR booster; number of MMR-specific T cells. Tregs will be isolated and their functionality will be determined using the blood cells collected during follow-up.

Doel van het onderzoek

The primary objective of the study is to study the safety of MMR booster vaccination in JIA patients by measuring JIA disease activity and the occurrence of measles, mumps or rubella infection.
The next primary objective is to evaluate the efficacy of the MMR booster vaccination in JIA patients by measuring protective immunity responses (specific anti measles, rubella, mumps antibodies by elisa) and functional antibody assays (measles neutralising antibodies) before and after MMR vaccination.
The secondary aim of the vaccination study is to analyse the influence on immune regulatory mechanisms capable of inducing JIA disease remission.

Onderzoeksproduct en/of interventie

Included patients will be randomized for one extra MMR booster vaccination (at age 4-8) or no additional vaccination (controls). Placebo vaccines will not be used in the control group.

N.B. In the Netherlands all children receive MMR booster vaccination at 9 years of age. Patients in both groups will also receive their usual MMR booster vaccine at age 9 according to the National Vaccination Program.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. All subtypes of JIA according to ILAR criteria;
2. Ages 4 to 8

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Use of Infliximab (Remicade, anti-TNF alpha therapy).
2. Use of Anakinra (Kineret, human interleukine-1-receptorantagonist)
3. Participation in another (drug) trial
4. Primary immunodeficiency
5. Fever less than 48 hour prior to vaccination (here the moment of vaccination will be postponed for 1 month)
6. Evidence of viral or bacterial infection less than 48hours prior to vaccination (here the moment of vaccination will be postponed for 1 month)
7. Methylprednisolon pulse therapy less than 1 month prior to vaccination (in these cases, the moment of vaccination will be postponed for 1 month)

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-08-2007
Aantal proefpersonen:	280
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

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	NL979
NTR-old	NTR1008
Ander register	:
ISRCTN	ISRCTN12271664

Resultaten

Samenvatting resultaten

(1) Wraith DC, Goldman M, Lambert PH. Vaccination and autoimmune disease: what is the evidence? Lancet 2003; 362(9396):1659-1666.

(2) Verhasselt V, Goldman M. From autoimmune responses to autoimmune disease: what is needed? J Autoimmun 2001; 16(3):327-330.
(3) Eden van W. Immunoregulation of autoimmune diseases. Hum Immunol 2006; 67(6):446-453.
(4) Bach JF. Protective role of infections and vaccinations on autoimmune
(5) Eden van W, Zee van der R, Koski CL et al. Balancing the immune system: Th1 and Th2. Ann Rheum Dis 2002; 61 Suppl 2:ii25-ii28.
(6) Update: vaccine side effects, adverse reactions, contraindications, and precautions. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 1996; 45(RR-12):1-35.
(7) Zonneveld-Huijssoon E, Ronaghy A, Van Rossum MA et al. Safety and efficacy of meningococcal c vaccination in juvenile idiopathic arthritis. Arthritis Rheum 2007; 56(2):639-646.
(8) Heijstek MW, Pileggi C, Zonneveld-Huijssoon E et al. Safety of measles, mumps and rubella vaccination in Juvenile Idiopathic Arthritis. Ann Rheum Dis 2007.
(9) Giannini EH, Ruperto N, Ravelli A, Lovell DJ, Felson DT, Martini A. Preliminary definition of improvement in juvenile arthritis. Arthritis Rheum 1997; 40(7):1202-1209.
(10) Andrews N, Pebody RG, Berbers G et al. The European Sero-Epidemiology Network: standardizing the enzyme immunoassay results for measles, mumps and rubella. Epidemiol Infect 2000; 125(1):127-141.