VAART-onderzoek (VAccination in ARTritis).

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26319

Source
NTR

Brief title
VAART

Health condition

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

Sponsors and support

Primary sponsor: N.M.Wulffraat
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Source(s) of monetary or material Support: Investigator driven investigation (fund = initiator = sponsor)

Intervention

Outcome measures

Primary outcome

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.

Secondary outcome

Secondary outcome measures are:
1. Number of Tregs, that are capable to suppress proliferation in vitro.
2. Presence of anti-inflammatory cytokine profiles following MMR booster
3. Number and function of MMR-specific T cells

Study description

Background summary

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.

Study objective

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.

Intervention

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.

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Eligibility criteria

Inclusion criteria

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

Exclusion criteria

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)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2007
Enrollment:	280
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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	NL979
NTR-old	NTR1008
Other	:
ISRCTN	ISRCTN12271664

Study results

Summary results

(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.