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PREVENT JIA-Study: Prevention of disease flares by risk-adapted stratification of therapy withdrawal in juvenile idiopathic arthritis (JIA)

Submission date
05/02/2013

Recruitment status
No longer recruiting

Registration date
21/03/2013

Overall study status
Completed

Last Edited
14/03/2022

Condition category
Musculoskeletal Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Juvenile idiopathic arthritis (JIA) is a type of arthritis that affects children, causing joint pain and inflammation. When the symptoms worsen, this is known as a flare. We have found that analysing patients' white blood cell proteins (biomarkers) allows us to detect low-level inflammation and identify when patients are at risk of flares after withdrawal of treatment. The aim of this study is test a treatment approach where patients with high levels of the biomarkers continue treatment, and treatment is stopped if the levels of biomarkers are low.

Who can participate?
Children with polyarticular JIA (affecting five or more joints), who are in a stable inactive condition without any symptoms.

What does the study involve?
Patients participate in the study for a maximum of 48 months. On visits every 3 months we carry out a clinical examination and a blood test. In the first 6 months of the study participants continue to take their medication. Treatment is then continued or withdrawn depending on the biomarker levels. The biomarker tests are performed every 3 months up to 18 months. If the biomarkers stay above the threshold at the end of this period the decision to continue or stop treatment is left to the doctors. The results are compared with matched patients who are treated without using the biomarkers.

What are the possible benefits and risks of participating?
This study does not test any new medications that could lead to new risks for patients. Stopping treatment earlier in the case of low biomarker levels reduces the risk of medication side effects but could increase the risk of a relapse. If a relapse occurs, the necessary treatment will be decided by the doctor.

Where is the study run from?
University Hospital of Muenster (Germany)

When is the study starting and how long is it expected to run for?
February 2013 to August 2019

Who is funding the study?
Interdisziplinäre Zentrum für Klinische Forschung (IZKF) at the Faculty of Medicine of the University of Muenster (Germany)

Who is the main contact?
1. Prof. Dr med. Dirk Foell
2. Dr med. Dirk Holzinger

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CRA04

Study information

Scientific Title
A trial to prevent disease flares by risk-adapted stratification of therapy withdrawal in juvenile idiopathic arthritis (JIA)

Acronym
PREVENT-JIA

Study objectives
The main hypothesis of this study is that JIA patients at risk of a flare due to subclinical inflammatory activity may be identified by analysis of the phagocyte activity marker S100A12 /hsCRP. The goal is a stratification of the therapeutic approach: Maintenance therapy for patients with elevated levels of the biomarkers, stop of therapy if both biomarkers are low.

The second major hypothesis of this study is that a risk-stratified decision on withdrawal of therapy is superior to treatment stop time point based solely upon the clinicians perspective (regarding the prevention of flares). An additional hypothesis is that the current definition of remission may be refined, adding immunological remission as a status that will be robust enough to last after discontinuing medication.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of the medical association of Westfalen-Lippe and of the medical school of Wesfälische Wilhelms-Universität- Münster, 21/12/2012, ref: 2011-079-f-S

Study design
This study will apply stratified therapeutic approaches based on a diagnostic test and hence cannot follow a randomized or blinded design for the intervention.

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Patients and parents will be provided with written information and receive an informed consent form.

Health condition(s) or problem(s) studied
Juvenile arthritis

Interventions
The study will involve at least 100 patients (male and female, age 2-18 years) in the intervention group and 200 matched controls, recruited at hospital visits from different countries.

Patients in the intervention group with biomarker driven withdrawal of therapy will be compared to matched controls with respect to the event-free interval, i.e. the time to first flare after therapy withdrawal. In the intervention group the stratification will be based upon S100A12/hsCRP levels measured in serum at each visit (i.e. every 3 months). After a watch and wait phase of 6 months in inactive disease, remission is confirmed according to the standard of care and patients will be stratified to stop therapy as soon as S100A12 is below 175 ng/ml and hsCRP is below 0.3 mg/dl. As long as any of the marker levels is above the respective threshold, patients will continue with maintenance therapy because a stable remission is not established. In the control group the duration of therapy with MTX/NSAID/Biologics is determined by the physician using any kind of clinical reasoning except the biomarker S100A12/hsCRP.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Event-free interval, i.e. the time to first flare after therapy withdrawal

Secondary outcome measures
The combined flare rate of all patients in the study will be compared to cohorts from previous studies providing robust data for a flare rate of 45%-50% after random withdrawal of therapy shown independently in several studies. As it can be expected from our trial published in JAMA and ARD that the flare rate will be only around 25%-30% with the stratified approach, we cannot withhold the chance of this superior approach from the patients included. The choice of comparisons was established in previous studies. The rationale for the biomarker to be tested, the units, and the cut offs at 175 ng/ml (S100A12) and 0.3 mg/dl (hsCRP) were established in published work.

Overall study start date
01/02/2013

Completion date
31/08/2019

Eligibility

Key inclusion criteria
Patients with polyarticular course of any JIA subcategory will be included at first confirmation of remission on medication, i.e. after clinically documented inactive disease for 6 months. At the time remission is documented, patients may be only on non-steroidal anti-inflammatory drugs (NSAIDs) plus DMARDs and/or biologics at a stable dose. Steroids must have beenwithdrawn at least 1 month before remission is documented. Intraarticular joint injections should not have been performed 6 months before remission is documented.

Participant type(s)
Patient

Age group
Child

Sex
Both

Target number of participants
100 in stratified protocol and 200 matched controls

Total final enrolment
114

Key exclusion criteria
Patients with persistent oligoarthritis subtype or systemic JIA having systemic features (within 1 year prior to inclusion) are excluded. In addition, patients may not have received treatment with steroids in the month before remission is first documented or treatment with intraarticular joint injections etc. in the 6 months before remission is first documented. Patient with a history of uveitis or macrophage activation syndrome are excluded. Patients may also not be included if withdrawal of any biological drug has ever been unsuccessful in the past.

Date of first enrolment
01/02/2013

Date of final enrolment
31/10/2018

Locations

Countries of recruitment
Germany

Italy

Netherlands

Russian Federation

United Kingdom

United States of America

Study participating centre
Roentgenstrasse 21
Muenster
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Sponsor information

Organisation
Interdisciplinary Center For Clinical Research Muenster (Interdisziplinäres Zentrum für Klinische Forschung) (Germany)

Sponsor details
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Sponsor type
University/education

Website
http://www.izkf.uni-muenster.de

ROR
https://ror.org/00pd74e08

Funder(s)

Funder type
University/education

Funder Name
Interdisciplinary Center For Clinical Research Muenster (Interdisziplinäres Zentrum für Klinische Forschung [IZKF]) at the Faculty of Medicine of the University of Muenster - CRA-04 (Germany)

Results and Publications

Publication and dissemination plan
Planned publication in 2020

Intention to publish date
30/06/2022

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/03/2022	14/03/2022	Yes	No