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The analysis of the predicting parameters related to the efficacy and safety of azathioprine given to Chinese patients with neuromyelitis optica spectrum disorders

Submission date
13/05/2017

Recruitment status
No longer recruiting

Registration date
22/05/2017

Overall study status
Completed

Last Edited
26/11/2020

Condition category
Nervous System Diseases

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

Plain English summary of protocol

Background and study aims
Neuromyelitis optica spectrum disorder (NMOSD) is a rate brain condition which involves episodes of optic neuritis (swelling of the optic nerve) and transverse myelitis (swelling of the spinal cord). The episodes are caused by the body's immune system (natural defence against illness and infection) mistakenly attacking the healthy nerve cells (autoimmune condition) in the optic nerve and spinal cord. This can lead to sudden vision loss or weakness in one or both eyes, and loss of sensation and bladder function. Azathioprine (AZA) is a drug which works by decreasing the effects of certain cells in the body's immune system, and is commonly used to treat autoimmune conditions such as arthritis. The success of treatment of NMOSD with AZA can be variable however, and there is currently no way of predicting the safety or effectiveness of the drug. The aim of this study is to explore the blood biomarkers (natural chemical indicators in the blood) in NMOSD patients treated with AZA.

Who can participate?
Adults with NMOSD who have been receiving AZA treatment for at least 12 months.

What does the study involve?
All patients receive treatment as usual with AZA. Participants attend regular study visits over the course of a year so that blood samples can be collected to assess the safety of the AZA treatment and what effects it is having on the body. Participants also complete a questionnaire about their levels of disability. In addition, at these clinic visits the number of participants to relapse (have their condition worsen) is recorded.

What are the possible benefits and risks of participating?
There are no direct benefits involved with participating. There is a small risk of pain or bruising when blood samples are collected.

Where is the study run from?
Beijing Tiantan Hospital (China)

When is the study starting and how long is it expected to run for?
September 2013 to September 2017

Who is funding the study?
Beijing Municipal Science & Technology Commission (China)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Z141107002514124

Study information

Scientific Title

An analysis of relations between thiopurines-methyltransferse (TPMT) genetic polymorphisms and TPMT activity, azathioprine metabolites, the clinical outcome after the azathioprine therapy in Chinese NMOSD patients

Study objectives
The aim of this study is to explore the relationship between thiopurines-methyltransferse (TPMT) genetic polymorphisms , TPMT activity, azathioprine metabolites, and the clinical outcome in Chinese NMOSD patients with the treatment of azathioprine, and to find valuable predicting parameters to guide the individualized therapy of azathioprine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee of Beijing Tiantan Hospital Affiliated to Capital Medical University, 29/01 /2016, ref: KY2015-031-02

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Neuromyelitisoptica spectrum disorders (NMOSD)

Interventions
Once patients are enrolled, blood samples for the TPMT genomic analysis, TPMT activity detection, AQP-4 IgG are routinely collected at the acute phase before any therapy, along with CSF samples for CSF cells, protein, CSF IgG and AQP4-IgG.

All patients then receive treatment as usual. This involves treatment an initial dosage of methylprednisolone 1000 mg for 3 days followed by tapering as 500 mg for 3 days, 250 mg for 3 days and 120 mg for 3 days. Participants then receive oral prednisone (60mg per day) which is altered and slowly withdrawn within 12 weeks. AZA therapy is added as oral prednisone starts. The initial dosage of AZA is 50 mg per day for the first 5 days. If no severe adverse reaction appears, the AZA is increased to 100 mg per day.

Blood samples (5 mL) are collected in vacuum tube (containing Ethylene Diamine Tetraacetic Acid) when the regular AZA therapy reaches 30 days (during the remission phase). After centrifugation and washing, the erythrocytes are stored at - 80 °C to detect the concentrations of erythrocyte 6-TGNs and 6-MMPNs by high-performance liquid chromatographic tandem mass spectrometry. Routine blood tests to assess hepatic and renal functions are completed regularly (every week for the first month of AZA intake, every two weeks for the second month and then monthly thereafter for one year). At the same timepoints, relapse rate (if occurring) is recorded and participants disability is assessed using the Expanded Disability Status Scale (EDSS).

Intervention Type
Genetic

Primary outcome measure
1. Annual relapse rate was calculated as the relapse times per year. The relapse time is assessed through patient interviews at monthly regular clinic visits and emergency circumstances (visit at the clinic because of the acute onset)
2. Disability is assessed using the Expanded Disability Status Scale (EDSS) at the acute stage (one month within the onset without any treatment), the remission stage (30 days after the AZA therapy) and the end of follow-up (more than a year of the AZA therapy)

Secondary outcome measures
Safety is assessed by recording adverse events by routine blood tests to assess white cell counts, hepatic and renal functions, which are regularly completed every week for the first month of AZA intake, every two weeks for the second month and then monthly thereafter for one year.

Overall study start date
01/09/2013

Completion date
01/09/2017

Eligibility

Key inclusion criteria
1. Fulfill the International Consensus Diagnostic Criteria for Neuromyelitis Optica Spectrum Disorder 2015
2. Aged 18 to 80 years
3. Never been exposed to any immunosuppressive agent
4. Without blood transfusion three months before sampling
5. More than 12 months with AZA treatment and, greater than 4 weeks since a dose change, to ensure a stable AZA metabolite profile

Participant type(s)
Patient

Age group
All

Sex
Both

Target number of participants
32

Total final enrolment
32

Key exclusion criteria
1. Intolerable to AZA treatment due to any severe adverse reaction such as the leukocyte counts less than 4×109/L, other severe cardiovascular disease or hepatopathy
2. Planned or current pregnancy and/or breast-feeding
3. Other unsuitable characteristics considered by the clinicians

Date of first enrolment
01/06/2014

Date of final enrolment
01/09/2016

Locations

Countries of recruitment
China

Study participating centre
Beijing Tiantan Hospital
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/003regz62

Funder(s)

Funder type
Government

Funder Name
Beijing Municipal Science & Technology Commission

Results and Publications

Publication and dissemination plan
Planned publication in a peer reviewed journal.

Intention to publish date
31/12/2017

Individual participant data (IPD) sharing plan
The current 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	results	05/07/2017	26/11/2020	Yes	No