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Phase I clinical trial of idiotypic DNA vaccination in patients with B-cell lymphoma

Submission date
12/11/2016

Recruitment status
No longer recruiting

Registration date
24/11/2016

Overall study status
Completed

Last Edited
28/07/2022

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
Vaccination against cancer can help the body's immune system to recognise and attack cancer cells, increasing patients' length and quality of life. An idiotype vaccine is personal and must be specifically made for each patient. The aim of this study is to test the effectiveness of two types of idiotypic DNA vaccine in patients with B-cell non-Hodgkin lymphoma, a type of cancer that affects white blood cells.

Who can participate?
Patients aged 18 to 75 with B-cell non-Hodgkin lymphoma

What does the study involve?
At the first assessment a standard biopsy (tissue sample) is performed – i.e. an enlarged lymph node is surgically removed. The biopsy is used for diagnosis as well as for vaccine production. After that, participants undergo standard treatment. 2-6 months after the completion of treatment, participants receive the vaccine by injection three times per month with an interval. After the whole course of vaccinations, participants visit the hospital several times (after 1 week, 1 month and 2 months) for standard tests and blood samples to test their immune response. If the first course of vaccination is not followed by an immune response, the vaccination course can be repeated with another form of the vaccine. Side effects are also recorded.

What are the possible benefits and risks of participating?
If the vaccination is successful, patients may be free of cancer symptoms (in remission) for longer. Risks of vaccination include some discomfort at the injection site for a day or two, and in rare cases weakness or fever may occur.

Where is the study run from?
1. N.N. Alexandrov National Cancer Centre of Belarus
2. Belarusian Research Center for Pediatric Oncology, Hematology and Immunology

When is the study starting and how long is it expected to run for?
April 2014 to December 2021 (updated 07/07/2021, previously: June 2019)

Who is funding the study?
Ministry of Health of the Republic of Belarus

Who is the main contact?
1. Dr Nadzeya Piatrouskaya (savitri@tut.by)
2. Dr Alexander Meleshko

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Protocol reg.# 20142755

Study information

Scientific Title
Phase I clinical trial of idiotypic DNA vaccine administered as a complex with polyethylenimine to patients with B-cell lymphoma

Acronym
Id-DNA/PEI vaccine

Study objectives
In this study Id DNA vaccine delivered as a DNA/PEI complex is evaluated in patients with B-cell non-Hodgkin lymphomas. First, two versions of immunostimulatory genes are compared: potato virus X coat protein (PVXCP) and human chemokine MIP3α. Second, the synthetic polymer linear PEI complexed with DNA vaccine is applied to enhance transfection efficacy in vivo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
National Cancer Centre of Belarus ethics committee, 17/03/2015, ref: 20142755

Study design
Non-randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the following contact details to request a participant information sheet: Nadzeya A. Piatrouskaya (savitri@tut.by)

Health condition(s) or problem(s) studied
Follicular lymphoma, small lymphocytic lymphoma/chronic lymphocytic leukemia, mantle cell lymphoma, nodal marginal zone B cell lymphoma, MALT lymphoma, lymphoplasmacytic lymphoma, diffuse large B-cell lymphoma

Interventions
After informed consent, patients underwent an excisional lymph node biopsy to confirm diagnosis and to provide the material for Id identification and cloning. Patients received standard therapy for their diagnosis (4-6 months), and then were not treated for 2 to 6 months

for immune recovery. Once the vaccine has been prepared, the patient received one or two courses of three vaccinations monthly. One of two vaccine constructions (scFv-PVXCP or MIP3A-scFv) was used per patient. Patients receive that form of the vaccine (scFv-PVXCP or MIP3A-scFv) which was first obtained by genetic engineering, so it is a random choice. However, this is not true randomization. After the last (3rd) vaccination in the course, immune response is observed at three time points: 1 week, 1 month and 2 months. If the first course of vaccination is not followed by immune response, they may be assigned a second course of vaccination with another form of the vaccine. Minimal residual disease (MRD) monitoring and at least one Magnetic Resonance Tomography (MRT) examination are performed for half a year after the last vaccination.

One dose included 500 µg of plasmid DNA solution in 1-2 ml sterile DPBS buffer. Linear PEI 8 kDa was used to prepare complexes with plasmid DNA with a ratio of N (PEI) to P (DNA) of 10/1. The required amount of 10 µg/µl solution PEI stock solution was diluted with 5% glucose to an equal volume of DNA solution added to it and rapidly mixed by pipetting. Mixture was kept for 10 minutes at room temperature to form complexes and administrated by intramuscular injection into the gluteal muscle.

The total duration of treatment is: standard chemotherapy (4-6 months) + recovery (2-6 months) + vaccination (2 months) + follow up (2 months – immune, 6 months – MRD, end of the study - survival).

Intervention Type
Biological/Vaccine

Phase
Phase I

Primary outcome measure
Safety and tolerability of vaccination; local and systemic adverse events are observed and symptoms are measured according to Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

Secondary outcome measures
Immunologic response to vaccination (anti-Id cellular and humoral immune response), measured using ELISPOT and ELISA at diagnosis (before treatment), before vaccination (after treatment), 1 week, 1 month and 2 months after the last vaccination

Overall study start date
03/04/2014

Completion date
31/12/2021

Eligibility

Key inclusion criteria
1. Surface immunoglobulin G or M isotype expression on tumor cells
2. Presence of tumor tissue biopsy before any treatment
3. The physical status scale ESOG 0 - 2
4. Life expectancy at least 24 months

5. Age 18 to 75 years
6. Adequate renal, hepatic, and bone marrow function
7. Signed written informed consent
8. The patient's ability to carry out the instructions of the doctor-researcher and comply with the treatment plan

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
30

Key exclusion criteria
1. Pregnancy and lactation
2. The presence of multiple primary cancer
3. History of autoimmune diseases (except Hashimoto's thyroiditis)
4. Severe diseases, including proceeding with symptomatic, untreated inflammatory and infectious processes
5. Social, economic or geographic circumstances which impede proper compliance with treatment protocols and follow-up
6. Polysensitisation
7. Positive tests for human immunodeficiency virus (HIV), hepatitis B or C

Date of first enrolment
03/04/2014

Date of final enrolment
01/10/2021

Locations

Countries of recruitment
Belarus

Study participating centre
N.N. Alexandrov National Cancer Centre of Belarus
Lesnoy
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223040

Study participating centre
Belarusian Research Center for Pediatric Oncology, Hematology and Immunology
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Sponsor information

Organisation
Ministry of Health of the Republic of Belarus (MH RB)

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Sponsor type
Government

Website
http://minzdrav.gov.by/en

ROR
https://ror.org/049840423

Funder(s)

Funder type
Government

Funder Name
Ministry of Health of the Republic of Belarus (MH RB)

Results and Publications

Publication and dissemination plan
At least two articles - the first in the near future to announce the start of the clinical trial, and the second
at the end of the study, in which the immunogenicity of the vaccine and other results will be described.

Intention to publish date
30/06/2022

Individual participant data (IPD) sharing plan
Not provided at time of registration

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?
Protocol article	protocol	03/06/2017		Yes	No
Results article		06/07/2022	28/07/2022	Yes	No