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WT1 immunity via DNA vaccination in haematological malignancies by intramuscular injection and electroporation

Submission date	Recruitment status	[_] Prospectively registered
21/01/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/01/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
25/10/2022	Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-new-vaccine-treat-leukaemia-win

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2009-017340-14

ClinicalTrials.gov (NCT)
NCT01334060

Protocol serial number

7339; EME 08/99/24

Study information

Scientific Title
WT1 immunity via DNA fusion gene vaccination in haematological malignancies by intramuscular injection followed by intramuscular electroporation: a multicentre interventional treatment open label single dose phase II study using genetic randomisation

Acronym
WIN

Study objectives
Open label, single dose level, phase II study in two patient groups (CML and AML) using genetic randomisation. Consented and eligible HLA A2+ve patients will be vaccinated with two DNA vaccines and HLA A2 -ve patients will be followed up with molecular monitoring only.

The objectives are to evaluate:
1. Molecular response following p.DOM-epitope DNA vaccination in patients with CML (BCR-ABL, WT1) and AML (WT1) at weeks 4, 8, 12, 16, 20 and at months 6, 12, 18 and 24
2. Time to disease progression, 2 year survival rate (patients with AML)
3. Correlation of molecular responses with immunological responses

Primary objective:
CML: Molecular response of BCR-ABL
AML: Time to disease progression

Secondary objective:
Molecular response of WT1 transcript levels, immune responses to WT1 and DOM, Toxicity, CML-Time to disease progression, next treatment and survival, AML-2 year survival, overall survival.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Gene Therapy Advisory Committee (GTAC) approved on 15/11/2010 (ref: 173)

Study design
Multicentre randomised interventional treatment open label single dose phase II study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Haematological Oncology; Disease: Leukaemia (acute), Leukaemia (chronic), Leukaemia (acute myeloid), Leukaemia (acute lymphoblastic), Leukaemia (acute promyelocytic)

Interventions

Current interventions as of 22/12/2011

Patients that are HLA A2+ will receive both vaccines as per below:

1. p.DOM-WT1-37:
Dosage: 1 mg
Method: intramuscular electroporation
Frequency of administration: 6 times at 4 weekly intervals - Responders (immunological but without molecular progression) may continue vaccination 3 monthly
Total duration of treatment: maximum of 24 months
Follow-up: 24 months post treatment

2. p.DOM-WT1-126:
Dosage: 1 mg
Method: intramuscular electroporation
Frequency of administration: 6 times at 4 weekly intervals - Responders (immunological but without molecular progression) may continue vaccination 3 monthly
Total duration of treatment: maximum of 24 months
Follow-up: 24 months post treatment

Patients that are HLA A2- will be monitored as the control group.

Measured in vaccinated patients only:
1. Autoimmune profile (together with other blood tests)
2. Bone marrow aspirate (all patients except HLA A2 negative CML patients)
3. Electrocardiogram (ECG), 1 before and after each vaccination
4. Immunological samples, samples for immunological analysis, blood (together with other blood tests)
5. Leukophoresis
6. Serum electrophoresis (together with other blood tests)
7. Skin biopsies (to be carried out if wherever feasible)

Measured in all patients:
8. Full blood count, biochemistry, (together with other blood tests)
9. Clotting (together with other blood tests)
10. HLA A2 test (together with other blood tests)
11. Infectious disease screen (human immunodeficiency virus [HIV], syphilis, Hepatitis, HTLV, CMV) (together with other blood tests)
12. Quantitative polymerase chain reaction (qPCR) (together with other blood tests)

Measured routinely:
13. Chest X ray

Previous interventions

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Measured routinely:
13. Chest X ray

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
p.DOM-epitope DNA vaccination

Primary outcome(s)
1. CML: Molecular response of BCR-ABL transcripts, measured at any time during follow up
2. AML: time to disease progression

Key secondary outcome(s))

1. AML: 2-year survival, overall survival, measured at any point during follow up
2. AML: Time to disease progression, measured at any point during follow up
3. Molecular response of WT1 transcripts, measured at any point during follow up

Completion date
31/07/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 02/07/2012

1. CML group:
1.1. Philadelphia chromosome positive CML in chronic phase
1.2. In complete cytogenetic response (CCyR) but with detectable BCR-ABL transcripts and maintained the CCyR on Imatinib monotherapy for a minimum of 24 months

2. AML group:
2.1. WT1+ AML in CR or morphologic CR with incomplete blood count recovery (CRi)
As the vast majority of AML express WT and evaluation in CR or CRi is technically not feasible, formal demonstration of WT1 expression in AML cells is not required. Where historical or relapsed samples become available, WT1 expression status will be evaluated post hoc.

3. All patients:
3.1. ≥ 18 years of age, written informed consent
3.2. Performance status of 0 or 1.
3.3. for vaccination groups: HLA-A0201 positive in at least one allele
3.4. for control groups: HLA A2 negative in both alleles
3.5. renal function and liver function (Creatinine <1.5 x upper limit of normal, liver function tests < 1.5 x upper limit of normal); Lymphocyte count > 1.0 x109/l*; normal clotting
3.6. HB>100 g/l
3.7. Adequate venous access for repeated blood sampling according to protocol schedule.
3.8. If sexually active and possibly fertile, patients must agree to use appropriate contraceptive methods during the trial and for six months afterwards.

* If the lymphocyte count is below 1.0 at the time of entry into the trial but has been over 1.0 in the last 6 months and has also not declined rapidly in the days and weeks preceding entry, then the patient is eligible.

Previous inclusion criteria

1. CML group:
1.1. Philadelphia chromosome positive CML in chronic phase
1.2. In complete cytogenetic response (CCyR) but with detectable BCR-ABL transcripts and maintained the CCyR on Imatinib monotherapy for a minimum of 24 months

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3. All patients:
3.1. Male and female, lower age limit of 18 years
3.2. Written informed consent
3.3. Performance status of 0 or 1
3.4. For vaccination groups: HLA-A0201 positive in at least one allele
3.5. For control groups: HLA A2 negative in both alleles
3.6. Renal function and liver function (creatinine less than 1.5 x upper limit of normal, liver function tests less than 1.5 x upper limit of normal); lymphocyte count greater than 1.0 x 10^9/l; normal clotting
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Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
21

Key exclusion criteria
1. CML patients:
1.1. CML in accelerated phase or blast crisis or having achieved CMR at any point during imatinib therapy
1.2. Imatinib dose modification in the previous year, imatinib interruption for more than 15 days in the previous 6 months to enrolment
1.3. Prior interferon-a therapy
1.4. Hypocellular bone marrow (less than 20%) (indicated by blood counts and most recent bone marrow (where available)
1.5. Complete molecular response (CMR)

2. AML patients:
2.1. AML in haematological relapse or eligible for allogeneic SCT
2.2. Hypocellular bone marrow (less than 20%)
2.3. AML patients with the "good-risk" abnormalities comprised by the core binding factor leukaemias (i.e., AML with the translocation [8;21] and inversion of chromosome 16, and acute promyelocytic leukaemia with the translocation [15;17])
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Performance status of 0 or 1.
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Previous exclusion criteria as of 22/12/2011

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3. All patients:
3.1. Systemic steroids or other drugs with a likely effect on immune competence are forbidden during the trial. The predictable need of their use will preclude the patient from trial entry
3.2. Major surgery in the preceding three to four weeks from which the patient has not yet recovered
3.3. Patients who are of high medical risk because of non-malignant systemic disease, as well as those with active uncontrolled infection
3.4. Patients with any other condition which in the Investigator's opinion would not make the patient a good candidate for the clinical trial, such as concurrent congestive heart failure or prior history of New York Heart Association (NYHA) class III/IV cardiac disease
3.5. Current malignancies at other sites, with the exception of adequately treated basal or squamous cell carcinoma of the skin. Cancer survivors, who have undergone potentially curative therapy for a prior malignancy, have no evidence of that disease for five years and are deemed at low risk for recurrence, are eligible for the study.
3.6. Patients who are serologically positive for or are known to suffer from Hepatitis B, C, Syphilis or HIV. Counselling will be offered to all patients prior to testing.

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Date of first enrolment
30/11/2010

Date of final enrolment
31/07/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Clinical Trials Unit, MP131
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
Southampton University Hospitals NHS Trust (UK)

ROR
https://ror.org/0485axj58

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC)/National Institutes of Health Research (NIHR) (UK) - Efficacy and Mechanism Evaluation (EME) Programme (ref: EME 08/99/24)

Funder Name
Leukaemia Research Foundation (UK)

Results and Publications

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

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2016		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			25/10/2022	No	Yes