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A Phase II Trial to Assess the Activity of NY-ES-O1 Targeted T Cells in Advanced Oesophagogastric Cancer

Submission date	Recruitment status	[X] Prospectively registered
10/09/2013	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
10/09/2013	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
05/03/2019	Cancer	[ ] Record updated in last year

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-t-cell-therapy-for-cancer-of-the-oesophagus-or-stomach

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

14133

Study information

Scientific Title
A Phase II Trial to Assess the Activity of NY-ES-O1 Targeted T Cells in Advanced Oesophagogastric Cancer

Acronym
ATTACK-OG

Study objectives
This is a trial of adoptive T cell therapy using autologous T cells genetically engineered to target the tumour associated antigen NY-ESO-1. Eligible patients will undergo leukapheresis to retrieve sufficient T cells which will be gene modified and expanded in the laboratory. Patients will undergo preconditioning chemotherapy with cyclophosphamide (60mg/kg) day -7 and day -6, followed by
fludarabine (25mg/m2) day -5 to day -1. The NY-ESO-1 gene modified cells will be re-infused on day 0 and the patients will receive up to 12 doses of intravenous IL2 (100000 U/kg) from day 0 to day 4.

Primary Objective:
To explore the activity of adoptive cell therapy targeted to NY-ESO-1 in oesophagogastric cancer patients who are NY-ESO-1 and HLA-A*0201 positive.

Secondary Objectives:
1. Evaluation of feasibility and tolerability of adoptive cell therapy targeted to NY-ESO-1 in oesophagogastric cancer patients who are NY-ESO-1 positive and HLA-A*0201 positive.
2. Evaluation of progression free survival.
3. Evaluation of the duration of response.
4. Assessment of overall survival.

Exploratory Objectives:
1. Laboratory analysis of gene modified T-cell survival and other immunological assessments.
2. Evaluation of response rate by immune related Response Criteria (irRC).
3. Evaluation of tumour marker responses.
4. Assessment of the cost of treatment.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=14133

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/SS/0041

Study design
Phase II open-label non-randomised interventional treatment trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Upper Gastro-Intestinal Cancer; Disease: Oesophagus, Stomach

Interventions
Interluekin 2, Patients will receive up to 12 doses of intravenous IL-2 (100000 U/kg) from day 0 to day 4
NY-ESO-1 T-cells, The NY-ESO-1 gene modified cells will be re-infused on day 0 Preconditioning chemotherapy, cyclophosphamide (60 mg/kg) day -7 and day -6
Preconditioning chemotherapy, fludarabine (25 mg/m2) day -5 to day -1

Intervention Type
Biological/Vaccine

Phase
Phase II

Primary outcome measure
Response rate according to RECIST 1.1; Timepoint(s): Week 6 post treatment, week 12 post treatment, and then 12 weekly until patient off study

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/09/2013

Completion date
01/05/2018

Eligibility

Key inclusion criteria
Prescreening:
1. Patients must be HLA-A0201 positive on pre-screen blood test

2. If confirmed HLA-A0201 positive, subjects tumour sample must stain positive by immunohistochemistry for NYES-O1 and/or LAGE (either diagnostic or more recent biopsy is acceptable. Subject may require additional biopsy if insufficient tumour material available form diagnostic sample).

Main Study:
1. Patients must have histologically confirmed oesophagogastric cancer and have received prior chemotherapy.
2. There must be measurable disease by Response Evaluation Criteria In Solid Tumors (RECIST) 1.1
3. Patients may have had any previous systemic therapies provided they are otherwise fit for treatment
4. Age equal to or greater than 18 years
5. World Health Organisation (WHO) performance status of 0 or 1
6. Patients must be human leukocyte antigen (HLA-A2) positive
7. Their tumour must stain positive by immunohistochemistry for NY-ESO-1 and/or LAGE (either diagnostic or more recent biopsy is acceptable)
8. Life expectancy >3months
9. Left ventricular ejection fraction (LVEF) > 50% as measured by ECHO or Multi Gated Acquisition (MUGA) and satisfactory stress ECHO (if over 60 or had previous cardiotoxic therapy)
10. Haematological and biochemical indices:
10.1. Haemoglobin (Hb) ≥ 8.0 g/dL
10.2. Neutrophils ≥ 1.0 x 109/L
10.3. Platelets (Plts) ≥ 100 x 109/L
11. Any of the following abnormal baseline liver function tests:
11.1. Serum bilirubin 1.5 x ULN
11.2. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) ≤ 3 x ULN unless patient has liver metastases when can be < 5 x ULN
11.3. Serum creatinine ≤ 150 µmol/L or creatinine clearance > 50 ml/min
These measurements must be performed prior to leukapheresis and again prior to commencing preconditioning chemotherapy.
12. The chemotherapy to be used in this trial is non-myeloablative, but where there is concern about a patients bone marrow reserves, for example due to multiple previous lines of myelosuppressive chemotherapy a backup stem cell harvest should also be obtained.
13. Female patients of child-bearing potential must have a negative serum or urine pregnancy test prior treatment and agree to use appropriate medically approved contraceptive precautions for four weeks prior to entering the trial, during the trial, and for six months afterwards.
14. Male patients must agree to use barrier method contraception during the treatment and for six months afterwards.
15. Full written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
Planned Sample Size: 28; UK Sample Size: 10

Key exclusion criteria
1. Those receiving radiotherapy, biological therapy, endocrine therapy, immunotherapy, systemic steroids, or chemotherapy during the previous four weeks (six weeks for nitrosoureas and MitomycinC)
prior to treatment or during the course of the treatment.
2. All toxic manifestations of previous treatment must have resolved. Exceptions to this are alopecia or certain Grade 1 toxicities, which an investigator considers should not exclude the patient.
3. Participation in any other clinical trial within the previous 30 days or during the course of this treatment.
4. Previous allogeneic transplant.
5. Clinically significant cardiac disease. Examples would include unstable coronary artery disease, myocardial infarction within 6 months or Class III or IV AHA criteria for heart disease
6. Patients who are high medical risks because of nonmalignant
systemic disease, including those with, uncontrolled cardiac or respiratory disease, or other serious medical or psychiatric disorders which in the lead clinicians opinion would not make the patient a good candidate for adoptive T-cell therapy
7. Concurrent systemic infections (CTCAE Grade 3 or more) within the 28 days prior to treatment.
8. Prior history of malignancies at other sites, with the exception of adequately treated cone-biopsied in situ carcinoma
of the cervix uteri and basal or squamous cell carcinoma of the skin.
9. Patients known or found to be serologically positive for Hepatitis B, C, HIV or HTLV.
10. History of systemic autoimmune disease which could be lifethreatening if reactivation occurred (for example hypothyroidism would be permissible, prior rheumatoid arthritis or SLE would not).
11. Evidence of CNS involvement.
12. Patients who are likely to require systemic steroids or other immunosuppressive therapy.
13. Pregnant and lactating women.
14. Radiotherapy to >25% skeleton.

Date of first enrolment
01/10/2014

Date of final enrolment
01/05/2018

Locations

Countries of recruitment
England

France

Italy

Netherlands

Sweden

United Kingdom

Study participating centre
Christie Hospital NHS Foundation Trust
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Sponsor information

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Sponsor type
Hospital/treatment centre

Website
http://www.christie.nhs.uk/

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme

Alternative Name(s)
EC Seventh Framework Programme, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No