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Dose escalation trial of Listeria monocytogenes based vaccine in patients with oropharyngeal squamous cell carcinoma

Submission date 31/10/2011	**Recruitment status** Stopped	[X] Prospectively registered [_] Protocol
Registration date 31/10/2011	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 02/09/2022	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-new-vaccine-treat-cancer-throat-that-may-be-caused-by-virus-hpv-realistic

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2010-019916-20

IRAS number

ClinicalTrials.gov number

NCT01598792

Secondary identifying numbers
11160

Study information

Scientific Title
A phase I, dose escalation trial of recombinant Listeria monocytogenes (Lm) based vaccine encoding human papilloma virus (HPV) serotype 16 target antigens (ADXS11001) in patients with HPV16 positive oropharyngeal squamous cell carcinoma

Acronym
REALISTIC

Study objectives
Human Papilloma Viruses (HPVs) are obligate human pathogens, some have the propensity to promote malignant transformations of their host cells. An example of this is HPV-16 in the oropharyngeal squamous cell carcinoma, which is seen in about 50-70% of cases although there is geographical variation.

Oropharyngeal squamous cell carcinoma (OPSCC) is on the increase in Europe and the United Kingdom, Cancer Research (UK) reported 953 new cases in 2005. If we accept that approx. 40-50% of these new cases may be due to HPV-16 infection, the resultant disease burden is about 380-480 new cases per annum in the UK. In contrast to other head and neck cancers, HPV related OPSCC occurs in younger patients, who are non-smokers and non-heavy drinkers.

ADXS11-001 (formerly Lovaxin C) is a bioengineered strain of living Listeria monocytogenes that induces a strong therapeutic immune response using multiple mechanisms of action. This vaccine secretes the tumour antigen HPV-16 E7 fused to an attenuated Lm virulence factor, Listeriolysin O (LLO), which has strong adjuvant properties.

If proved safe, there is a role for ADXS11-001 as a post-treatment adjuvant as part of a treatment de-escalation strategy in an attempt to reduce the adverse effects of current treatment strategies without compromising survival.

The REALISTIC trials' objective is to determine safety and to characterise the toxicity profile of ADXS11-001.

Ethics approval required
Old ethics approval format

Ethics approval(s)
First MREC, 20/09/2011, ref: GTAC 176

Study design
Non-randomised interventional screening treatment

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Head and neck cancer

Interventions
ADXS11-001 - the patient will recieve 3 vaccinations. The vaccine will be given on Day 1 of each cycle. An interval of at least 28 days should occur between any two vaccinations. To proceed to the next vaccination the previous vaccination(s) must have been well tolerated. At each recruiting centre, the infusion will take place in an area specifically designated for phase I clinical trial patients to receive their experimental treatments. Follow Up Length: 12 months

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ADXS11-001

Primary outcome measure
1. Safety
2. Occurrence of drug-related grade 3 or 4 systemic or local adverse events

Secondary outcome measures
1. Immunity
2. Demonstration by ELISPOT assay of the frequency of IFN secreting lymphocytes recognising MHC class

Overall study start date
01/01/2012

Completion date
01/01/2012

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. Histologically confirmed HPV-16 +ve, p16 +ve OPSCC
2. Patients in remission from disease, i.e. complete response (CR) or unconfirmed complete response (CRu) in the case of non-surgical treatment or complete macroscopic resection of tumour and associated cervical lymph nodes in patients undergoing surgery
3. Completion of standard therapy for malignancy at least 6 weeks before trial entry
4. A positive result following anergy testing
5. Written informed consent and the ability of the patient to co-operate with treatment and follow up must be ensured and documented
6. Age greater than 18 years
7. World Health Organisation (WHO) performance status of 0 or 1
8. Life expectancy of at least 12 months
9. Haematological and biochemical indices (these measurements must be performed within 8 days prior to the patient going on study)
10. Haematological:
10.1. Haemoglobin (Hb) > 10.0 g/dl
10.2. Neutrophils = 1.5 x 109/L
10.3. Platelets (Plts) = 100 x 109/L
11. Baseline liver function tests:
11.1. Serum bilirubin = 1.5 x upper normal limit
11.2. Serum alkaline phosphatase, alanine amino-transferase (ALT) and/or aspartate amino-transferase (AST) < 1.5 x ULN
12. Baseline renal function test: calculated creatinine clearance > 50ml/min (uncorrected value) or isotope clearance measurement > 50ml/min
13. Female patients of child-bearing potential are eligible, provided they have a negative serum pregnancy test prior to enrolment and agree to use appropriate medically approved contraception during the study up to six months after the last vaccination
14.. Male patients must agree to use appropriate medically approved contraception during the study up to six months after the last vaccination
15. Lower age limit 18

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 36; UK Sample Size: 36

Key exclusion criteria

1. Receiving, or having received, chemotherapy or radiotherapy within 6 weeks of trial entry.
2. Having undergone surgery +/- PORT within 6 weeks of trial therapy
3. A negative result following anergy testing
4. Known chronic active infection with Hepatitis B, Hepatitis C or Human Immunodeficiency Virus (HIV)
5. Current active autoimmune disease
6. Current active skin diseases requiring therapy (psoriasis, eczema etc)
7. Ongoing active infection
8. History of anaphylaxis or severe allergy to vaccination
9. Previous myeloablative therapy followed by an autologous or allogeneic haematopoietic stem cell transplant
10. Patients who have had a splenectomy or splenic irradiation, or with known splenic dysfunction
11. Receiving current immunosuppressive medication, including corticosteroids within 4 weeks of the first dose
12. Pregnant and lactating women
13. Ongoing toxic manifestations of previous treatment
14. Major thoracic and/or abdominal surgery in the preceding four weeks from which the patient has not yet recovered
15. Patients with any other condition which in the investigator's opinion would not make the patient a good candidate for the clinical trial
16. Concurrent congestive heart failure or prior history of class III/ IV cardiac disease

Date of first enrolment
01/01/2012

Date of final enrolment
01/01/2012

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Liverpool
Liverpool
United Kingdom
L3 9TA

Sponsor information

Organisation

University Hospital Aintree (UK)

Sponsor details
Fazakerley Hospital Lower Lane
Liverpool
England
United Kingdom
L9 7AL

Sponsor type
Hospital/treatment centre

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

ROR
https://ror.org/008j59125

Funder(s)

Funder type
Government

Funder Name
Clinical Trials Awards and Advisory Committee (UK) ref: C26837/A11920

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Plain English results			02/09/2022	No	Yes