

# Targeted radiotherapy for AL-Amyloidosis – TRALA

<b>Submission date</b> 08/02/2016	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 15/11/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 18/01/2023	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Amyloidosis is the name for a group of rare, serious condition in which an abnormal protein called amyloid is produced by the bone marrow (spongy tissue inside some bones where new blood cells are produced). Overtime, this protein builds up in tissues, affecting the way that organs work. There are several types of amyloid proteins, the most common being AL (A is for amyloid, L is for Light Chain). Chemotherapy (an anti-cancer drug treatment) and a stem cell transplant (a procedure where healthy cells, called stem cells are infused into the body to replace damaged or diseased bone marrow) can both be used to treat AL amyloidosis. In a stem cell transplant, special cells which have the ability to turn into different types of cell (stem cells), which are usually taken from that patient, are infused into the body to replace damaged or diseased cells. With a stem cell transplant, patients have very high doses of chemotherapy, (sometimes with whole body radiotherapy) to damage or destroy the abnormal cells in the bone marrow. The stem cells then replace these cells so the body can start making healthy blood cells again. In this study, doctors want to look at using targeted radiotherapy in place of high dose chemotherapy. Targeted radiotherapy means that the radiation is given directly to their bone marrow. This destroys the abnormal cells in the same way as high dose chemotherapy does. They have the radiation from a radiolabelled antibody (anti CD66 radiolabelled with Yttrium 90) which is as a single treatment into their vein. This treatment has been used alongside chemotherapy for people with different types of blood cancer. But this is the first time it is being used for people with amyloidosis. The aim of this study is to see how safe it is to use targeted radiotherapy as part of their stem cell transplant, learn more about the side effects and see how well it works.

### Who can participate?

Adults with amyloidosis

### What does the study involve?

Participants have stem cells collected using normal procedures before the study starts. As part of the study patients have a visit to the hospital to work out how much radiation they should have. They have a different radiolabelled drug (anti CD66 radiolabelled with Indium-111) to have this test. This is the dosimetry and imaging visit. This must be favourable before any treatment is given. About 1 week later they have their radiation treatment with radiolabelled drug anti CD66

radiolabelled with Yttrium-90. This is the study treatment. They have both the radiolabelled drugs as an injection into a vein. They might be also asked to have a bone marrow biopsy (sample taken) between 1 to 14 days after having the Yttrium-90. After the dose finding test, participants have scans 1, 3 and 4 days afterwards. 7 days before their transplant they go to their transplant centre. Their neutrophils (white blood cells that fight infection) are at their lowest so they are be antibiotics to help prevent an infection. They then have their stem cell transplant as they would normally. Participants see the study doctors 30 days after transplant to have a physical examination, blood tests and a bone marrow test. 100 days after their transplant they see the doctors at the National Amyloidosis Centre and have the same tests repeated.

What are the possible benefits and risks of participating?

There are no direct benefits involved with participating in this study. Most of the treatments and assessments the patients will receive/undergo will be standard of care (i.e. they will receive this anyway and so there are no risks other than those related to the standard procedures used.

Where is the study run from?

1. Southampton General Hospital (UK)
2. University College Hospital (UK)
3. The Queen Elizabeth Hospital (UK)
4. Freeman Hospital (UK)

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

December 2013 to July 2020

Who is funding the study?

Leukaemia and Lymphoma Research (UK)

Who is the main contact?

Mrs Yvanne Enever

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<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-targeted-radiotherapy-as-part-of-a-stem-cell-transplant-for-amyloidosis-trala>

## Contact information

**Type(s)**

Public

**Contact name**

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**Contact details**

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# Additional identifiers

**Clinical Trials Information System (CTIS)**

2015-002231-18

**Protocol serial number**

19732

## Study information

### Scientific Title

A Phase I/IIa Study of Targeted Radiotherapy alone for Stem Cell Transplant Conditioning in Systemic AL Amyloidosis

### Acronym

TRALA

### Study objectives

The aim of this study is to assess if targeted radiotherapy used as a sole conditioning treatment prior to autologous stem cell transplantation in patients with Systemic AL Amyloidosis is at least as safe and effective, if not better, than existing treatments for Systemic AL Amyloidosis.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

South Central - Hampshire B Research Ethics Committee, 13/11/2015, ref: 15/SC/0565

### Study design

Open labelled multi centre phase I/IIa study

### Primary study design

Interventional

### Study type(s)

Treatment

### Health condition(s) or problem(s) studied

Systemic AL-Amyloidosis

### Interventions

Three treatment levels with step-wise increase of the infused [90Y]-labelled anti-CD66 radiation activity. There will be 3 patients in each cohort (which can be expanded if required due to toxicities seen). A minimum of 12 patients maximum of 18 will be recruited.

All patients will undergo dosimetry using [111In]- CHX A"-DTPA anti-CD66 antibody (drug product). This is a one off dose and administered intravenously. All patients must have favourable dosimetry before they are treated with - CHX A"-DTPA anti-CD66 antibody (drug product)[90Y]. The conditioning treatment [90Y] again is a one off treatment administered intravenously.

There are three treatment levels, representing increasing infused radiation activity levels:

1. 30.0 MBq/kg lean body weight [90Y]-radio-labelled murine anti-CD66.
2. 40.0 MBq/kg lean body weight [90Y]-radio-labelled murine anti-CD66.
3. 45.0 MBq/kg lean body weight [90Y]-radio-labelled murine anti-CD66

After their conditioning treatment patients will undergo a stem cell transplant. They are then seen at day 30 and day 100 post stem cell transplant, after which they have completed the study.

The study would recruit patients with AL-amyloidosis due to undergo autologous stem cell transplantation.

## **Intervention Type**

Drug

## **Phase**

Phase I/II

## **Drug/device/biological/vaccine name(s)**

1. [111In]-radio labelled anti-CD66 (dosimetry)
2. [90Y]-radio-labelled anti-CD66 (conditioning treatment)

## **Primary outcome(s)**

1. Specific organ toxicity as measured, following patient review, using the CTCAE version 4.0
2. Adverse event rate is measured following patient review and interviews and is measured using the definitions of an adverse event under the clinical trials directive 2001/20/EC

## **Key secondary outcome(s)**

1. Disease response as determined by changes in the free light chain assay (FLCa) pre and post [90Y]-labelled anti-CD66 and post transplantation
2. Clonal plasma cell population as determined by FLOW cytometry pre and post transplantation (D100)
3. NT-proBNP levels are measured by taking blood samples pre and post transplant (D100)
4. Time to progression (TTP) is measured using the NCI definition of TTP which is the length of time from start of treatment with [90Y]-labelled anti-CD66 until Amyloidosis starts to get worse or spread to other parts of the body
5. Overall Survival (OS) is measured using the NCI definition of OS which is the percentage of people in the study who are alive five years after their start of treatment
6. To establish a dosimetry model to be used in AL-Amyloidosis patients by comparing organ dosimetry from previous trials using the same antibody vector
7. Platelet and neutrophil engraftment is assessed by measuring an increase in platelet and neutrophil counts by taking blood samples as per routine practice after transplantation
8. Detection of Human Anti-Mouse Antibodies (HAMA) is measured by taking blood samples at defined intervals post transplantation

## **Completion date**

07/07/2020

## **Eligibility**

### **Key inclusion criteria**

1. Aged  $\geq 18$  years
2. Diagnosis of systemic AL-amyloidosis, either as a new diagnosis or recurrent disease
3. Measurable clonal plasma cell dyscrasia
4. Amyloid related organ dysfunction or organ syndrome
5. Estimated life expectancy of at least 6 months (as defined at trial entry)
6. Sufficient stem cells for two transplant procedures
7. Bone Marrow (BM) cellularity  $>20\%$
8. Eligible for ASCT in AL amyloidosis defined as fulfilling all of the following criteria:
  - 8.1. ECOG Performance Status of 0 or 1
  - 8.2. Cardiac troponin-T  $<0.07 \mu\text{g/L}$
  - 8.3. NYHA heart failure class of  $<3$
  - 8.4. No more than 3 organs involved by amyloidosis by consensus guidelines
  - 8.5. Creatinine clearance or isotope GFR  $\geq 30\text{ml/min}$
  - 8.6. Bilirubin  $\leq 1.5$  times and alkaline phosphatase  $\leq 3$  x upper limit of normal
  - 8.7. AST or ALT  $<2.5$  x upper limit of normal range
  - 8.8. Mean left ventricular wall thicknesses of  $<16\text{mm}$  by echocardiography
  - 8.9. Absence of clinically important amyloid related autonomic neuropathy
  - 8.10. Absence of clinically important amyloid related gastro intestinal haemorrhage
9. Capable of providing written, informed consent
10. Women of child bearing potential should use adequate forms of contraception
  - 10.1. Intrauterine Device (IUD)
  - 10.2. Hormonal based contraception (pill, contraceptive injection etc.)
- 10.3. Double Barrier contraception (condom and occlusive cap e.g. diaphragm or cervical cap with spermicide)
- 10.4. True abstinence (this is defined as refraining from heterosexual intercourse after receiving [ $^{111}\text{In}$ ] at the Dosimetry and Imaging visit through to final study visit)

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Total final enrolment**

10

### **Key exclusion criteria**

1. Overt symptomatic multiple myeloma
2. Amyloidosis of unknown or non AL type
3. Localised AL-amyloidosis (in which amyloid deposits are limited to a typical single organ, for example the bladder or larynx, in association with a clonal proliferative disorder within that organ)

4. Trivial or incidental AL amyloid deposits in the absence of a significant amyloid related organ syndrome (e.g., isolated carpal tunnel syndrome)
5. NYHA Class III or IV heart failure
6. Liver involvement by amyloid causing bilirubin >1.5 times upper limit of normal
7. Concurrent active malignancies, except surgically removed basal cell carcinoma of the skin or other in situ carcinomas
8. Pregnant, lactating or unwilling to use adequate contraception
9. Intolerance / sensitivity to any of the study drugs
10. Known positive Human anti-murine antibodies (HAMA)
11. Unable to provide written informed consent

**Date of first enrolment**

08/07/2016

**Date of final enrolment**

30/09/2017

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Southampton General Hospital**

Tremona Road  
Southampton  
United Kingdom  
SO16 6YD

**Study participating centre**

**University College Hospital**

235 Euston Road  
Fitzrovia  
London  
United Kingdom  
NW1 2BU

**Study participating centre**

**The Queen Elizabeth Hospital**

Mindelsohn Way  
Edgbaston

Birmingham  
United Kingdom  
B15 2GW

**Study participating centre**  
**Freeman Hospital**  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

## Sponsor information

**Organisation**  
University Hospital Southampton NHS Foundation Trust

**ROR**  
<https://ror.org/0485axj58>

## Funder(s)

**Funder type**  
Charity

**Funder Name**  
Leukaemia and Lymphoma Research

**Alternative Name(s)**

**Funding Body Type**  
Private sector organisation

**Funding Body Subtype**  
Other non-profit organizations

**Location**  
United Kingdom

## Results and Publications

## Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

## IPD sharing plan summary

Other

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other unpublished results</a>		25/06/2021	22/08/2022	No	No
<a href="#">Participant information sheet</a>	version V2.1	08/03/2015	15/11/2016	No	Yes
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes