

A phase I study of lipoteichoic acid-T (LTA-T, Oncomycin™) in malignant pleural effusion

Submission date 17/06/2008	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 23/06/2008	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 07/09/2012	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
2.1

Study information

Scientific Title

Study objectives

The hypothesis that forms the basis for this study is that the intrapleural administration of lipoteichoic acid-T (LTAT-T) could reduce the recurrence of malignant pleural effusion and thereby alleviate a significant cause of morbidity in metastatic solid malignancies. The mechanism by which this might occur is not fully elucidated.

Pleural infection is characterised by fibrotic obliteration of the pleural cavity (pleurodesis) during an indolent illness, and therapeutic replication of this response could produce a clinically effective pleurodesis. Gram positive pathogens are immunologically recognised by the binding of their cell wall motifs to toll-like receptors (TLRs) on the cell surface. One such motif is LTA-T, which mediates its effects through TLRs.

We hypothesised that LTA-T may be capable of inducing a therapeutically effective pleurodesis for the control of malignant pleural effusion. We have performed a dose escalation study to assess the toxicity/tolerability of LTA-T administered into the pleural space, and to produce preliminary data assessing potential pleurodesis efficacy.

The purpose of this study is to confirm the favourable safety profile of LTA-T when administered intrapleurally and to define a maximum tolerated dose.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics approval received from the Central Oxford Research Ethics Committee in July 2004 (ref: 04/Q1606/53).

Study design

Single centre, open label phase I toxicity trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Hospital

Study type(s)

Treatment

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

Malignant pleural effusion

Interventions

An indwelling pleural catheter (PleurX, Denver, Colorado) was placed in the pleural effusion and the pleural space fully drained. After initial complete fluid drainage, 30 ml intra-pleural saline (saline control) was administered (day 1). The daily pleural fluid drainage was then recorded for seven days to quantify the rate of production of pleural fluid. On day seven, subjects received a single intra-pleural injection of LTA-T, according to an escalating dosing schedule. Over the next 7 days (days 7 - 14), daily pleural fluid volume drainage and pleural fluid cytology for malignant cells was performed unless pleural fluid flow ceased. On day 14, the intra-pleural catheter was flushed and closed (but left in situ) and not used again for the duration of the study unless recurrent pleural fluid caused dyspnoea.

The starting dose of LTA-T was 250 µg, with three patients planned at each dose and an increase in dose determined by side effects seen in these patients.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

Lipoteichoic acid-T (LTA-T, Oncomycin™)

Primary outcome measure

Adverse events (phase I toxicity trial), measured over the entire course of the study (i.e 12 weeks).

Secondary outcome measures

1. To compare the daily production of pleural fluid over days 5 to 10 after administration of intra-pleural LTA-T with that of the previous five days after the administration of intra-pleural saline, compared from week 1 (saline control) to week 2 (LTA-T)
2. To define the time to symptomatic pleural effusion recurrence - 'pleurodesis failure' following LTA-T administration and to estimate by comparison with the published time to recurrence after simple drainage, whether LTA-T reduces the requirement for later pleural effusion drainage, assessed at 1 month
3. To assess whether intra-pleural LTA-T alters the presence of cancer cells in drained pleural fluid and whether it induces a cellular inflammatory pleural fluid response, assessed at 2 weeks and whenever fluid available subsequently
4. To assess whether intra-pleural LTA-T influences the levels of pleural fluid cytokines known to be associated with pleural fluid production, assessed post LTAT administration (3 days)

Overall study start date

09/11/2004

Completion date

24/11/2005

Eligibility

Key inclusion criteria

1. Aged greater than or equal to 18 years, either sex
2. Histocytologically proven malignant pleural effusion
3. A Karnofsky Performance Status of greater than or equal to 60%
4. Life expectancy of more than three months
5. Written informed consent
6. Participants were required to be willing and able to comply with the protocol
7. Participants who were at least 4 weeks from their last chemotherapy cycle

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

Unknown initially as dose finding study - 14 patients recruited in total

Key exclusion criteria

1. Serious uncontrolled intercurrent infection
2. Proven infection in this episode of pleural effusion
3. Any bleeding diathesis such that chest tube insertion would be hazardous
4. Previous surgical pleurodesis for this pleural effusion
5. Any of the following abnormal laboratory results:
 - 5.1. Haemoglobin less than 8 g/dl (correction by transfusion allowed)
 - 5.2. Neutrophils less than $2.0 \times 10^9/l$
 - 5.3. Platelet count less than $100 \times 10^9/l$
 - 5.4. Serum creatinine greater than 3 x upper normal limit
 - 5.5. Serum bilirubin greater than 5 x upper normal limit
 - 5.6. Alanine transaminase or aspartate aminotransferase greater than 5 x upper normal limit
6. A known sensitivity to lipoteichoic acid (LTA-T)
7. If female patients were pregnant or lactating; to include all women of childbearing potential unless using a reliable and appropriate contraceptive method was used and a negative pregnancy test was confirmed
8. Any patient with organ allografts, significant cardiac disease, uncontrolled seizures, central nervous system disorders or psychiatric disability
9. Participation in any other investigational drug study within 4 weeks
10. Living too far from the study centre to attend for study follow up

Date of first enrolment

09/11/2004

Date of final enrolment

24/11/2005

Locations**Countries of recruitment**

England

United Kingdom

Study participating centre

Oxford Respiratory Trials Unit

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Sponsor information**Organisation**

Oxford University (UK)

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Sponsor type

University/education

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Funder(s)

Funder type

Other

Funder Name

Lunamed AG (Switzerland) - unrestricted grant

Funder Name

National Institute for Health Research (NIHR) (UK) - Biomedical Research Centre Programme (salary for Chief Investigator)

Funder Name

The funders had no role or influence on the study design, analysis or execution.

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?
Results article	results	01/10/2008		Yes	No