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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	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/06/2008	**Overall study status** Completed	
Last Edited 07/09/2012	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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)

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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 x10^9/l
5.3. Platelet count less than 100 x 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
United Kingdom

England

Study participating centre
Oxford Respiratory Trials Unit
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Sponsor information

Organisation
Oxford University (UK)

ROR
https://ror.org/052gg0110

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

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