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# Anti-mycobacterium treatment reverses cerebral radiation necrosis

**Submission date**
20/03/2013

**Recruitment status**
No longer recruiting

**Registration date**
18/04/2013

**Overall study status**
Completed

**Last Edited**
22/01/2019

**Condition category**
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Radiotherapy is used to treat a wide variety of head and neck tumors that arise in and around the skull base. Radiation-induced injury may occur when exposure of adjacent normal nervous system tissue to radiation is unavoidable. Acute injury is usually mild and transient, but the delayed radiation injury (DRI) of normal brain can be a devastating complication and generally occurs months to years after the initiation of therapy. DRI is generally progressive and irreversible, and have a tremendous negative impact on a patients quality of life. The mechanism of DRI is not well understood . DRI can occur even when the most stringent measures are taken to avoid exposing healthy tissue to harmful levels of radiation. To date, the treatment of DRI has typically been management of symptoms.
Nasopharyngeal carcinoma (NPC) is one of the most common malignant tumors that affects the southern Chinese population. Temporal lobe necrosis (TLN) is one of the most dreaded DRI complications in NPC after external radiation. Evaluation of the temporal lobes in patients previously treated for NPC can provide a better understanding of DRI in the brain unaffected by the underlying tumor outside of the planned field of radiation.
In 2008, we used anti-mycobacterium therapy (AMT) to treat a symptomatic TLN patient suffering headache and dysphasia, accompanied with pulmonary tuberculosis as evidenced by positive chest X-ray test. The AMT provided an unexpected symptom relief to TLN. Based on this experience, we have developed a trial protocol to evaluate whether AMT can reverse the disease in both symptoms and MRI abnormality.

Who can participate?
The study involves NPC patients who had undergone radiation therapy, suffering bilateral temporal lobe necrosis. The age ranges from 18 to 65 years old.

What does the study involve?
Participants belong to one of two groups: active treatment group or control group.
In the AMT active treatment group, all former treatments with corticosteroids were discontinued for patients prior to AMT initiation.
In the control group, treatments were conducted with routine practices.

What are the possible benefits and risks of participating?
The main risks of treatment group are injuries to liver function and stomach. The treatment is carried out under extensive observation.

Where is the study run from?
The study is conducted at the First Affiliated Hospital of Sun Yat-sen University, Guangzhou (China)

When is the study starting and how long is it expected to run for?
January 2009 to June 2014.

Who is funding the study?
Grants from the Guangdong Natural Science Foundation (China).

Who is the main contact?
Prof.Yanqing Feng
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# Contact information

### Type(s)
Scientific

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# Additional identifiers

### EudraCT/CTIS number

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
N/A

# Study information

### Scientific Title
Effects of anti-mycobacterium treatment on temporal lobe necrosis following radiotherapy for nasopharyngeal carcinoma: a prospective, controlled study

## Study objectives
The mechanisms of radiation-induced delayed brain injuries (DRI) remains poorly understood, and treatment with corticosteroids, surgery, and antioxidants is often ineffective. The aim of this study is to investigate whether temporal lobe necrosis, a severe type of DRI, can be reversed by anti-mycobacterium therapy (AMT).

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
The SUN Yat-sen university ethics committee approved the study. The approval number is 2012 (06). The date of approval is 18-Dec-2012. All patients were informed of the potential short- and long-term drug complications of AMT. Written informed consent was obtained from patients who agreed to participate in the study.

## Study design
Prospective non-randomized controlled single-center study

## Primary study design
Interventional

## Secondary study design
Non 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
Delayed brain radiation injury/temporal lobe necrosis/oncology

## Interventions
In the AMT active treatment group, all former treatments with corticosteroids were discontinued for patients prior to AMT initiation. Our initial treatment protocols (Treatment First Phase) comprised amikacin (600 mg/day) and mannitol 125 ml (bid) for 2 weeks, together with a three-drug AMT regimen (per day: isoniazid 8 mg/kg, rifampicin 10 mg/kg, pyrazinamide 25 mg/kg). Followed by treatment with a three-drug AMT regimen for nine months (Treatment Second Phase). And then by treatment with a combination of isoniazid and rifampicin with the same dosages that ceased after 24 months (Treatment Third Phase).
In the control group, treatments were conducted with routine practices including steroids, IVIG, Hyperbaric oxygen (HBO), nerve growth factor, and mannitol alone or combination during the observational period.

## Intervention Type

Other

### Phase
Not Applicable

### Primary outcome measure
The Activities of daily living (ADL) were adopted to assess subjects neurological status. ADL were assessed by the Barthel Index (BI) (0100 scale, with lower scores denoting less independence in activities of daily living)

### Secondary outcome measures
Evaluation by MRI tests

### Overall study start date
01/01/2009

### Completion date
30/12/2014

## Eligibility

### Key inclusion criteria
Patients who fulfilled the following eligibility criteria were recruited in this study:
1. Aged 18 to 65 years
2. Histopathologically proven cases of NPC who had undergone radiation therapy, with negative brain MR before RT
3. Patients must have received cranial irradiation ≥ 6 months prior to study entry
4. MRI evidence of bilateral temporal lobe edema and/or necrosis with
or without foci of contrast enhancement on MRI
5. Evidence of progressive neurologic signs or symptoms related with TLN

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
60

### Key exclusion criteria
Patients were excluded if they had:
1. Significant hepatic or renal insufficiency
2. Evidence of brain metastasis, brain abscess, any intracranial tumor, cerebral infarction,

demyelinating disease
3. Clinical manifestations such as fever, meningeal irritatation signs indicating meningitis

### Date of first enrolment
01/01/2009

### Date of final enrolment
30/12/2014

## Locations

### Countries of recruitment
China

### Study participating centre
**58, Zhongshan 2 Road**
Guangzhou
China
510080

## Sponsor information

### Organisation
Sun Yat-sen University (China)

### Sponsor details
No. 135, Xingang Xi Road
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### Sponsor type
University/education

### Website
http://www.sysu.edu.cn

### ROR
https://ror.org/0064kty71

## Funder(s)

### Funder type
Research organisation

### Funder Name
Guangdong Natural Science Foundation (Grant nos.2012B03180067), China

## 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 | 01/09/2014 | 22/01/2019 | Yes | No |