Partial oral antibiotic treatment for bacterial brain abscess: An open-label randomised non-inferiority trial.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON52080

Source
ToetsingOnline

Brief title
ORAL

Condition

- Bacterial infectious disorders
- Central nervous system infections and inflammations

Synonym
Brain abscsess, collection of pus in the brain

Research involving
Human

Sponsors and support

Primary sponsor: Aalborg University
Source(s) of monetary or material Support: Het betreft een investigator initiated studie

die vanuit de Novo nordisk foundation subsidie heeft gekregen.

Intervention

Keyword: Brain abcsess, Oral antibiotics, Treatment

Outcome measures

Primary outcome

Treatment failure at 6 months after randomisation, consisting of:

1. All-cause mortality

2. Intraventricular rupture of brain abscess

3. Unplanned re-aspiration or excision of brain abscess

4. Relapse or recurrence

Secondary outcome

1. Extended Glasgow Outcome Scale scores and all-cause mortality at end of

treatment as well as 3-, 6-, 12-months since randomisation

2. Completion of assigned treatment (oral vs. IV)

3. Line associated complications (infection, thrombosis, bleeding or need for

replacement)

4. Durations of admission and antibiotic treatment

5. Serious adverse events

6. Quality of life scores and cognitive evaluations.

Study description

Background summary

A brain abscess is a serious infection with a considerable impact on patients* lives. Treatment remains a challenge due to the precarious location of the

infection and the impenetrability of the blood-brain-barrier for most drugs. Thus, a favourable outcome usually requires a combination of neurosurgical evacuation of the abscess and prolonged high-dose antibiotic therapy to ensure eradication of bacteria within the abscess cavity. However, there are no randomised controlled trials on antibiotic treatment of brain abscess to support the standard regimen of 6-8 weeks intravenous treatment.
Reports of treatment failure, relapse and recurrence are very rare with current treatment recommendations. However, the long duration of IV treatment is often strenuous for patients to endure with associated discomfort of long-term admission, risks of hospital-acquired infections, and line complications (infection, bleeding, venous thrombosis, and need for line replacement due to malfunction). In addition, costs associated with such prolonged admissions are significant.
A shortened IV treatment for bacterial brain abscess has been reported to be successful in retrospective observational studies. However, properly controlled trials are needed to examine this treatment strategy in bacterial brain abscess patients.

Study objective

This study has been transitioned to CTIS with ID 2023-505483-11-00 check the CTIS register for the current data.

To investigate if early transition to oral treatment after two weeks or longer of IV antibiotic therapy is non-inferior to standard six weeks or longer of IV antibiotic treatment for bacterial brain abscess.

Study design

This is an investigator initiated, open-label, interventional (1:1 allocation), international, multicentre, parallel group, randomised, controlled, non-inferiority trial comparing two treatment strategies.

Intervention

One group will continue with intraveneus treatment, the other group will switch to oral antibiotics.

Study burden and risks

Participation in the study does include a few extra outpatient visits that may not be part of routine treatment. Patients assigned to early switch to oral therapy may have a theoretical increased risk of treatment failure, which could lead to complications and prolonged duration of treatment.The oral antibiotics used in this study are all approved and well-known for treatment of numerous infectious diseases in every day clinical care. There are no increased risks

for patients randomised to standard treatment.

Patients randomised to oral therapy may be candidates for early discharge and thereby spend considerably less time at hospital. As such, risks associated with long-term hospital admission (hospital-acquired infections, loss of daily life functions) and extended IV treatment (bleeding, infection, venous thrombosis, need for catheter replacement, development of bacterial resistance in the hospital environment) are decreased. For patients assigned to standard treatment there will be no changes to usual care.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adults >=18 years of age with bacterial brain abscess defined as:

1. A clinical presentation (e.g. headache, neurological deficit or fever) and cranial imaging (CT or MRI) consistent with brain abscess according to the hospital radiologist AND
2. The physician responsible for the patient decides to treat the patient for bacterial brain abscess

Further requirements for inclusion are:
3. Ability to absorb oral medications (including by nasogastric tube)
4. To have received guideline recommended empiric or targeted (according to in vitro susceptibility) IV antibiotic therapy for bacterial brain abscess for 14 consecutive days or longer before randomisation and no additional aspiration or excision of brain abscess planned
5. Expected to be treated with antibiotic therapy for at least another 14 days after time of randomisation
6. No progression in neurological deficits or occurrence of new-onset neurological symptoms (excluding seizures) within five days before time of randomisation

Exclusion criteria

1. Hypersensitivity to an antibiotic intended for use in the patient and no alternative drugs available.
2. Expected substantially reduced compliance with treatment
3. Pregnancy/ lactating women.
4. Concomitant treatment for proven or suspected CNS infection caused by mycobacteria, Nocardia spp., Pseudomonas spp., fungi, toxoplasmosis or other CNS parasites
5. Device related brain abscesses (e.g. deep brain stimulators, ventriculo-peritoneal shunts)
6. Severe immuno-compromise defined as ongoing need for biological- or chemotherapy, prednisolone >20 mg/day for >=14 days, uncontrolled HIV/AIDS (see Glossary), haematological malignancies (see Glossary), and organ transplant recipients
7. Concomitant or unrelated infections necessitating IV antibiotics beyond seven days of duration after time of randomisation
8. Brain abscesses caused by Staphylococcus Aureus
9. Previous enrolment into this trial

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-05-2023
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	30-11-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-505483-11-00
ClinicalTrials.gov	NCT04140903
CCMO	NL76390.018.22