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Study on the initial treatment of Whipple's disease

Submission date	Recruitment status	[_] Prospectively registered
30/05/2004	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
21/07/2004	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
02/02/2011	Digestive System	

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
N/A

Study information

Scientific Title

Acronym
SIMW

Study objectives
Whipples Disease (WD) is a rare, infectious disorder (a member of the Orphanet group). Based on pathology records, its incidence in Germany is estimated to be about 0.4 per million. On this basis, it has been stated that clinical studies cannot be done because there are not enough individuals affected by Whipples disease.

Consequently, no prospective controlled trials are available. One retrospective analysis came to the conclusion that co-trimoxazole was more efficient than tetracycline in inducing and in maintaining remission of WD. However, cerebral involvement became evident during continuous treatment with co-trimoxazole in one patient. WD leads to death unless treated with antibiotics. As also in vitro antimicrobial susceptibility data are not yet available for the causative actinomycete Tropheryma Whipplei (TW), antibiotic therapy is empirical. There is no standard treatment for WD based on hard scientific evidence. Since a major problem of WD is cerebral involvement, it has been proposed that treatment should be initiated with high doses of intravenously applied antimicrobials known to penetrate into the central nervous system.

In a pilot study, antibiotic susceptibility of phylogenetically related bacteria to TW was tested in vitro; 95% of them were susceptible to meropenem and 70% were susceptible to ceftriaxion (unpublished, Maiwald et. al). A randomised comparison of meropenem and ceftriaxon in the treatment of bacterial meningitis showed no significant difference in efficacy.

In SIMW, therefore, these two antibiotics, both licensed for the treatment of severe infections and both known to penetrate into the central nervous system are compared in randomised order: ceftriaxon versus meropenem or imipenem.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The SIMW trial was accepted by the Ethics Committee of the Landesärztekammer Mainz before the start of the trial.

Study design
Open label, parallel group, randomised controlled trial.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Not Specified

Participant information sheet

Health condition(s) or problem(s) studied
Whipple's Disease

Interventions
Amended on 17/08/2007:

Intravenous ceftriaxon versus intravenous meropenem/imipenem, followed by 12 months of oral co-trimoxazole. Enrolment for these two arms was completed in December 2003.

A non-randomised third arm to SIMW (with additional 20 patients) was started in July 2004. The participants in the third arm receive intravenous ceftriaxone (as in the first arm of SIMW), followed by oral co-trimoxazole for three months (instead of 12 months). Otherwise the protocols are identical to the other two arms. The third arm, therefore, examines whether short-term oral treatment with co-trimoxazole is noninferior to 12 months oral treatment. This third arm without an own control group will be compared with the two arms of SIMW. The third arm was introduced in order to facilitate participant recruitment as Whipple's disease is very rare.

Dosages:
Ceftriaxone 2 g daily intravenously for 14 days (in the first arm of SIMW and in the third arm)
Meropenem 3 x 1 g daily intravenously for 14 days (in the second arm of SIMW)(In this intent to treat trial imipenem can be used instead of meropenem).

Co-trimoxazole contains 800 mg sulphamethoxazole plus 160 mg trimethoprim, and is administered twice daily perorally in all three arms (In both arms of SIMW for a year, in the third arm for three months).

Interventions provided at time of registration:

Randomized antibiotic treatment: ceftriaxon versus meropenem / imipenem.

In both arms this initial treatment is followed by 12 months of oral co-trimoxazole. Enrolment complete in December 2003. A non-randomised third arm to SIMW was started in July 2004. In this arm we will admit a maximum of 20 new patients until December 2006. This trial SIMW is organised under the premise that WD is a rare disease.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
ceftriaxon versus meropenem/imipenem

Primary outcome measure
Remission maintained for three years

Secondary outcome measures

Prospective collection of clinical, immunological, and pathological data concerning diagnosis and course of Whipple's disease.

Overall study start date
01/01/1999

Completion date
31/12/2006

Eligibility

Key inclusion criteria
Patients with Whipple-typical macrophages in the duodenal mucosa or elsewhere confirmed by the reference pathologist

Participant type(s)
Patient

Age group
Not Specified

Sex
Both

Target number of participants
42 for the first and second arms. As of 17/08/2007: Additional 20 participants for the third arm (total of 62).

Key exclusion criteria
1. Current antimicrobial therapy for more than 1 month
2. Previous and unsuccessful antimicrobial therapy for Whipple's Disease
3. Recurrence of Whipple's Disease
4. Human Immunodeficiency Virus (HIV) infection, pregnancy, manifest tumor disease (except lymphoma)

Date of first enrolment
01/01/1999

Date of final enrolment
31/12/2006

Locations

Countries of recruitment
Austria

France

Germany

Switzerland

Study participating centre
DRK-Krankenhaus Neuwied
Neuwied
Germany
56564

Sponsor information

Organisation
German Red Cross Hospital Neuwied (DRK Krankenhaus Neuwied)

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
http://www.drk-kh-neuwied.de.drktg.de/

ROR
https://ror.org/02y3dtg29

Funder(s)

Funder type
Other

Funder Name
German Red Cross Hospital Neuwied (DRK Krankenhaus Neuwied)

Funder Name
The European Commission (ref: QLG1-CT-2002-01049)

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	07/12/2010		Yes	No