

# Study on the initial treatment of Whipple's disease

<b>Submission date</b> 30/05/2004	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 21/07/2004	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 02/02/2011	<b>Condition category</b> Digestive System	<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

**Protocol serial number**  
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bacteria to TW was tested in vitro; 95% of them were susceptible to meropenem and 70% were susceptible to ceftriaxion (unpublished, Maiwald et.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

## **Study type(s)**

Not Specified

## **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(s)**

Remission maintained for three years

#### **Key secondary outcome(s)**

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

#### **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

**Healthy volunteers allowed**

No

**Age group**

Not Specified

**Sex**

All

**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)

**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

**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?
<a href="#">Results article</a>	results	07/12/2010		Yes	No