PLEASE NOTE: *This trial has been registered retrospectively.*

Trial Description

Title

Three-armed study for therapy of primary and secondary syphilis in HIV infection

Trial Acronym

[---]*

URL of the trial

[---]*

Brief Summary in Lay Language

The best therapy for syphilis (a sexually transmitted bacterial disease) in HIV infected patients is yet unknown. Treatment guidelines are different in the US and in Germany. Different antibiotic regimens are tested in this study. HIV-positive patients with early syphilis (stage I or II) can participate. They will be treated with ceftriaxon 1g i.v./10d (intravenous drip), benzathine penicillin 2x 1,2 Mio i.U. i.m. (intramuscular) day 1 or benzathine penicillin 2x1,2 Mio i.U. i.m. day 1, 8, 15. Tolerability and efficacy is examined after 3, 6 and 12 months. No differences between the treatment forms are expected.

Brief Summary in Scientific Language

Background:
Since 2001 the incidence of syphilis in Germany is rising. In 2003 2932 new syphilis cases were registered, 500 (20%) more than 2002. The incidence rate of syphilis in 2003 was 3,6 cases per 100000 inhabitants. Mostly effected were men who have sex with men (76%) [1]. Ca. 15% of syphilis patients also have a HIV-infection, up to 80% of HIV-infected patients have syphilis antibodies.
Diagnostic Methods:
Basis diagnostic methods in syphilis/HIV-coinfected patients do not differ from HIV negative patients. For screening TPHA, VDRL or RPR are used. For confirmation VDRL-titration or IgG-FTA-ABS can be used. To evaluate treatment indication IgM-FTA-ABS and 19S-IgM-FTA-ABS can be helpful. Patients with positive 19S- IgM-FTA-abs or VDRL > 1:8 or titers rising more than 2 steps should be treated. [2]. Most HIV/syphilis coinfected patients show typical clinical symptoms and a normal serum reaction. Up to 40% of HIV patients with primary or secondary syphilis have upnormal cerebrospinal fluid findings. Cerebrospinal fluid puncture should be considered in all HIV/syphilis coinfected patients [3]. Serologic testing can be unreliable. False negative Results are seen in patients with inadequate antibody production.. The VDRL-test is not specific and can be false positive. Titers can stay high in spite of optimal treatment. FTA abs IgM and des VDRL should normalize within 6-24 months, TPHA can persist life long [2].
Clinical stages:
Clinical stages of syphilis do not differ in HIV-positive or HIV-negative patients.

There are more atypical or severe courses in HIV-coinfection. Cases of early progression to tertiary or neurosyphilis have been described. Symptoms of several stages can be seen at the some time. Reactivation of an old syphilis is possible.

Therapy:

Penicillin is the standard treatment of all syphilis stages. Bactericidal effect is seen in peripheral serum concentration of > 0,03IU/ml, intrathecal of > 0,078IU/ml. Generation time of treponema pallidum is ca. 30 hours. Bactericidal concentrations should be achieved for at least.8 days.

According to the German guidelines first line treatment for early syphilis (Stadium I or II up to one year after time of infection) in coinfected patients is benzathine penicillin 2,4 Mio i.U. (e.g. Pendysin? 1,2 Mio) i.m. in weekly intervals for 3 weeks [4]. The CDC recommends single shot treatment with benzathine penicillin 2,4 Mio i.E. i.U.. This is discussed because of case reports of neurological complications and treatment failure [4, 5, 6]. Rolfs et al examined 541 patients with early syphilis, including 101 HIV-positive patients, that were treated with single shot benzathine penicillin. 18% were classified as treatment failure after 6 months. Failure rate was higher in HIV-patients [7]. In another trial asymptomatic HIV/syphilis coinfected patients were treated i.m. with ceftriaxone or benzylpenicillin procain. No significant difference was seen with response rates around 70% [8]. Dowell et al. saw response rates to intramusculär ceftriaxone in HIV-infected patients with latent syphilis or neurosyphilis of 65%, 9 patients were classified as treatment failure, one patient showed progressive neurological symptoms [9]. Marra showed response rates of 80% to intraveneous ceftriaxone in HIV patients with neurosyphilis [10] In this study HIV-positive patients with early syphilis (stage I or II) will be treated with ceftriaxone 1g i.v./10d, benzathine penicillin 2x 1,2 Mio i.U. i.m. day 1 or benzathine penicillin 2x1,2 Mio i.U. i.m. day 1, 8, 15. Tolerability and efficacy are examined after 3, 6 and 12 months.

References:

10. Marra CM Boutin P, McArthur JC, Hurwitz S, Simpson PA, Haslett JA, van der Horst C, Nevin T, Hook EW (2000) A pilot study evaluating ceftriaxone and penicillin G as treatment agents for neurosyphilis in human immunodeficiency virus-infected individuals. Clin Infect Dis 30:540-544

Organizational Data

- DRKS-ID: **DRKS00000389**
- Date of Registration in DRKS: **2010/05/25**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2326 , Ethik-Kommission der Medizinischen Fakultät der Ruhr-Universität Bochum**

Secondary IDs

- Universal Trial Number (UTN): **U1111-1114-6421**

Health condition or Problem studied

- ICD10: **A53.9 - Syphilis, unspecified**

Interventions/Observational Groups

- Arm 1: **ceftriaxone 1g i.v. for 10 days**
- Arm 2: **Bezathine penicillin 2x1,2 Mio i.E. i.m. once**
- Arm 3: **benzathine penicillin 2x 1,2 Mio i.E. i.m. day 1, 8, 15**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **Open (masking not used)**
- Who is blinded: **[---]***
- Control: **Active control**
- Purpose: **Treatment**
- Assignment: **Parallel**

Study Type: **Interventional**

Study Type Non-Interventional: **[---]***

Allocation: **Randomized controlled trial**

Blinding: **Open (masking not used)**

Who is blinded: **[---]***

Control: **Active control**

Purpose: **Treatment**

Assignment: **Parallel**

- Phase: **IV**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

treatment failure defined as:
-retreatment or
-treatment with any antibiotic active against treponema pallidum or
-no reduction by 2 titer levels in VDRL or FTAabs19S IgM after 48 weeks

Secondary Outcome

none

Countries of recruitment

- DE **Germany**

Locations of Recruitment

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2004/08/03**
- Target Sample Size: **150**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

-HIV positive Patients with serologically proven early syphilis

Exclusion criteria

-known sensibilization agaist ß-lactam antibiotics
-patients that were treated within the last 48h with an agent that is active against treponema pallidum
-pregnant or lactating women
-patients with late syphilis (latent syphilis of unknown duration, tertiary syphilis or neuro syphilis

Addresses

- **Primary Sponsor**

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Contact for Public Queries

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Sources of Monetary or Material Support

- **Institutional budget , no external funding (budget of sponsor/PI)**

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URL: **[---]***

Status

- Recruitment Status: **Recruiting complete, follow-up complete**
- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

** This entry means the parameter is not applicable or has not been set.*
**** This entry means that data is not displayed due to insufficient data privacy clearing.*