A multicentre, prospective, randomized open-label pilot study to assess the feasibility and preliminary efficacy of interferon gamma in combination with Anidulafungin for the treatment of candidemia

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To evaluate the preliminary efficacy and feasibility of interferon gamma as adjunctive treatment in combination with the standard regimen, for the treatment of patients with candidemia using the following parametersSecondary objective: to evaluate...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON35641

Source
ToetsingOnline

Brief title
Efficacy of interferon in the treatment of candidemia

Condition

- Immunodeficiency syndromes
- Fungal infectious disorders

Synonym
candidemia, fungal bloodstream infection

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,BioMerieux

Intervention

Keyword: Anidulafungin, Candidemia, Interferon-gamma

Outcome measures

Primary outcome

The primary endpoint is the time to negative blood cultures.

Secondary outcome

Secondary endpoints are

• The overall survival

• Mortality at week 2 and week 8 after end of treatment (all causes)

• Time to death

• Outcome of fungal infection:

o Resolution of infection at week 2 and 8 after end of treatment

o Evaluation of patient status (succes, failure, death) at end of interferon

gamma (and at time of stopping antifungal treatment)

o Microbiological evaluation

• Duration of antifungal treatment

• Duration of hospitalization

• Immunological parameters

• Evaluation of host respons markers that can be used to identify patients with

immunoparalysis that will benefit from immunotherapy

• Monitoring the immunological respons to interferon-gamma

Study description

Background summary

Over the past decade, systemic infections caused by fungal pathogens, and particularly by Candida species, have become a prominent cause of disease, especially in severely ill immunocompetent and immunocompromised patients. Advances in health care technology and life support systems have increased the risk of nosocomial Candida infection.
The mortality rate associated with candidemia, independent of death from the underlying disease, is high at around 40%, and tends to increase in patients with unremitting underlying disease. The extent of the alteration of the host defense rather than pathogenic properties of the fungus appear to be the most important determinants of the severity of disease. *Most likely, sepsis-induced immunoparalysis in patients admitted to an intensive care unit (ICU) is an important factor leading to weakened host defenses and increased susceptibility to invasive candidiasis.

The host response to C. albicans infection is a complex interplay between cellular and humoral immunity and usually provides a sufficient defense against the microorganism in the healthy host. Interferon(IFN)-gamma is a key cytokine for innate as well as acquired resistance to candidiasis. Thus, in view of the relative deficiency of IFN-gamma in candidemic patients - especially those with sepsis-induced immunoparalysis - and the beneficial effects of IFN-gamma on anti-Candida host defense mechanisms, suppletion of rIFN-gamma is rational as adjunctive therapy in patients with severe invasive candidasis or candidemia, in addition to treatment with conventional antifungal drugs.

Study objective

To evaluate the preliminary efficacy and feasibility of interferon gamma as adjunctive treatment in combination with the standard regimen, for the treatment of patients with candidemia using the following parameters
Secondary objective: to evaluate host response markers that could be used to identify the patients who will benefit from immunotherapy according to their immunological status, and to monitor the patient*s immunological response to IFN-gamma.

Study design

Multicentre randomized open label study

Intervention

The intervention study group will receive 100 mcg of Interferon gamma through subcutaneous injection, thrice weekly during two weeks. The control group will receive no Interferon gamma.

Study burden and risks

Patients with candidemia are already admitted to a hospital. Therefore patients will not have to invest extra time in for the sake of study visits during their treatment. Daily sampling of blood for clinical purposes is standard care. Bloodsampling for this study will be combined with already planned venipunctures. Bloddcultures and biochemistry are performed as standard care in candidemic patients. Furthermore an extra amount of 22.5 ml of blood will be drawn 5 times during the first week, one time in the second week and at 2 and 8 weeks after the end of therapy.
Study treatment consists of in total 6 subcutaneous injections that will be given thrice weekly during 2 weeks. Besides local pain at the site of injection, interferon can cause (mild) flu-like reactions

De interventie bestaat uit 6 subcutane injecties die gedurende 2 weken, drie maal per week worden toegediend. Naast locale pijn op de injectieplaats kan interferon-gamma leiden tot (milde) griepachtige verschijselen, die in het algemeen met eventueel paracetamol goed verdragen worden.
Candidemie is een ernstige infectie met een zeer hoge mortaliteit. De bijwerkingen zijn in het algemeen zodanig mild dat deze niet opwegen tegen de potentiele voordelen van een verbetering van de immuunrespons tegen deze infectie. Het middel is dan ook reeds geregistreerd in selecte patientenpopulaties (verlagen van de frequentie van ernstige infecties zoals Candida bij chronisch granulomateuze ziekte en maligne osteopetrosis)

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

• Males or non-pregnant females (who must agree to use barrier methods of contraception during the study therapy period, women of childbearing age must have a negative urine pregnancy or serum test at baseline).
• Subjects who are 18 years of age or older
• Subjects with at least one positive blood culture isolation of Candida species from a specimen drawn within 96 hours prior to study entry.
• Subjects who have clinical evidence of infection AT SOME TIME WITHIN 96 HOURS PRIOR TO ENROLLMENT, including AT LEAST ONE of the following:
-Temperature >37.8 *C on 2 occasions at least 4 hours apart or one measurement > 38.2 *C
-Systolic blood pressure <90 or a >30 mmHg decrease in systolic BP from the subject*s normal baseline.
-Signs of inflammation (swelling, heat, erythema, purulent drainage) from a site infected with Candida (eg, joint, skin, eye, bone, esophagus)
-Radiologic findings of invasive canidiasis
•Subject or their legal representative must sign a written informed consent form.

Exclusion criteria

• Subjects with a history of allergy or intolerance to echinocandins or Interferon gamma
• Subjects with an absolute neutrophil count of less than 500/mm3 at study entry
• Women who are pregnant or lactating
• Subjects who are unlikely to survive more than 24 hours
• Subjects who have failed previous systemic antifungal therapy for the Candida spp. infection which is being studied.

• Subjects who have received more than 48 hours of systemic antifungal therapy for the current episode, within 96 hours prior to study entry.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2011
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Immukine
Generic name:	Interferon gamma
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	03-06-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	10-08-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2009-014600-66-NL
CCMO	NL28823.091.10
Other	volgt