A Randomized, Placebo-Controlled, Phase 2 Study of HB-101, a Bivalent Cytomegalovirus (CMV) Vaccine, in CMV-Seronegative Recipient (R-) Patients Awaiting Kidney Transplantation from Living CMV-Seropositive Donors (D+)

Published: 08-10-2018
Last updated: 10-01-2025

To assess the safety and reactogenicity of HB-101.To assess the immunogenicity of HB-101.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON48943

Source
ToetsingOnline

Brief title
Hookipa

Condition

- Viral infectious disorders

Synonym
Cytomegalovirus, infection

Research involving
Human

Sponsors and support

Primary sponsor: Hookipa Biotech AG
Source(s) of monetary or material Support: Hookipa Biotech

Intervention

Keyword: Cytomegalovirus (CMV), Kidney transplantation, Vaccine

Outcome measures

Primary outcome

Safety and reactogenicity of HB-101 will be assessed by treatment group (for

Groups 1 and 2 and open-label HB-101 for Group 3) and by number

of vaccinations:

(HB-101 versus placebo) and number of vaccinations:

1.Incidence and severity of AEs, SAEs, and changes in laboratory values

2.Incidence and severity of localized or generalized injection site reactions

The immunogenicity of HB-101 will be assessed using descriptive central

statistics presented by treatment group (for Groups 1 and 2 and open label

HB-101 for Group 3) and by post-transplant CMV management strategy (prevention

or preemption) for the following immunogenicity parameters:

3.CMV neut

4.CMV ELISPOT pp65

5.CMV ELISPOT gB

Secondary outcome

1.Incidence and time to clinically significant CMV infection, CMV disease, and

CMV syndrome

2.Incidence and time to CMV viremia requiring anti viral therapy

3.Incidence and duration (in days) of anti-CMV therapy courses (at therapeutic doses) required

4.Incidence and time to quantifiable CMV DNAemia, peak CMV DNAemia level, and duration of CMV DNAemia above the limit of quantitation

5.Incidence and time to graft failure and organ rejection

Additional immunogenicity parameters of HB-101 will be assessed using descriptive central statistics presented by treatment group for Group 1 and 2 and open-label HB-101 for Group 3 and by post-transplant CMV management strategy (prevention or preemption) for the following immunogenicity parameters:

6.LCMV neutralizing antibody

7.CMV ICS pp65

8.CMV ICS gB

9.LCMV ELISPOT NP

Study description

Background summary

An effective CMV vaccine administered prior to transplantation would overcome the limitations of both the prophylactic and preemptive approaches. Hookipa Biotech completed a Phase 1 healthy volunteer study (Study H-100-001) of the predecessor HB-101 (encoding pp65 and a truncated gB of HCMV).
In brief, Hookipa Biotech observed:
- Neutralizing antibodies formed against the antigen after 2 or 3 vaccinations.
- A favorable safety profile.
- CMV-neutralizing antibodies after 3 vaccinations on par with previously studied vaccines.
- gB- and pp65-specific T-cell immunogenicity previously shown to correlate with protection
(in adoptive T-cell transfer studies).
Based on this, Hookipa Biotech anticipates that the vaccine should be more effective than previous vaccines tested in the solid organ transplantation

(SOT) setting.

Study objective

To assess the safety and reactogenicity of HB-101.
To assess the immunogenicity of HB-101.

Study design

This is a randomized, placebo-controlled, Phase 2 study of HB-101, a bivalent CMV vaccine, in CMV-seronegative recipient (R-) patients awaiting kidney transplantation from living CMV-seropositive donors (D+).

Intervention

There will be 2 groups stratified by treatment intent (as per the investigator and institutional standards) regarding the use of anti-CMV anti-virals post-transplantation. Each group will be randomized into 2 arms:

- Group 1: Patients to be followed preemptively post-transplant:
Arm 1a: CMV seronegative (-) patients awaiting kidney transplant from a CMV seropositive (+) living donor randomized to receive HB-101 before transplant, and
monitoring after transplant.
Arm 1b: CMV seronegative (-) patients awaiting kidney transplant from a CMV seropositive (+) living donor randomized to receive placebo before transplant, and
monitoring after transplant.

- Group 2: Patients to be treated prophylactically post-transplant:
Arm 2a: CMV seronegative (-) patients awaiting kidney transplant from a CMV seropositive (+) living donor to receive HB-101 and anti-viral prophylaxis before
transplant, and monitoring after transplant.
Arm 2b: CMV seronegative (-) patients awaiting transplant from a CMV seropositive (+)
living donor to receive placebo and anti-viral prophylaxis, before transplant, and
monitoring after transplant.

Study burden and risks

Risks associated with the administration of study medication.
Higher frequency of study visits for Group 1 during the post-transplant period.

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

English
1. Male or female patients 18 years of age or older.
2. Patients willing and able to give written informed consent for participation in the study.
3. Patients must be eligible to undergo kidney transplantation from a living donor as per institutional standards.
4. For Group 1 and 2, patients must be CMV immunoglobulin G (IgG) seronegative (-) and will be
receiving kidney for transplantation from donors who are CMV IgG seropositive (+). (If CMV IgG serology is indeterminate, repeat testing is recommended. If the serology for the donor is indeterminate upon repeat testing, it should be considered positive; if the serology for the

recipient is indeterminate upon repeat testing, it should be considered negative).
5. For Group 3, patients must be CMV IgG seropositive (+) and will be receiving a kidney for transplantation from donors who are CMV IgG seropositive (+) or CMV IgG seronegative (-). Group 3 patients must have documentation of a planned transplant that is scheduled to occur between 2 and 4 months after the first study drug injection.
6. Post-transplant CMV management will follow either preemptive treatment strategy (Group 1) or prophylactic anti-viral medication(s) (e.g., valganciclovir) per institutional standard of practice (Group 2).
7.Female patients of childbearing potential can participate in the study if they agree to use highly effective contraception. This applies from the time period between signing of the informed consent form and up to 12 months after the last study drug (HB-101 or placebo) injection or up to completion of the study, whichever is longer. Highly effective contraception methods include:
• Total abstinence.
• Male or female sterilization.
• Combination of any 2 of the following categories (Categories 1+2, 1+3, or 2+3):
o Category 1: Use of oral, injected, or implanted hormonal methods of contraception.
o Category 2: Placement of an intrauterine device or intrauterine system.
o Category 3: Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/vaginal suppository.
8. Female patients must have a negative serum human chorionic gonadotropin pregnancy test prior to each dose of study drug (HB-101 or placebo) unless the pregnancy test is deemed a false positive and clinical evidence is negative for pregnancy after discussion between the
sponsor and investigator on a case-by-case basis; or be surgically or biologically sterile or menopausal.
Post-menopausal females are defined as:
• Age >50 years with amenorrhea for at least 12 months.
• Age <=50 years with 6 months of spontaneous amenorrhea and follicle-stimulating hormone level within post-menopausal range (>40 mIU/mL).
• Permanently sterilized women (hysterectomy or bilateral oophorectomy).
9. Male patients with sexual partners of childbearing potential can participate in the study if they agree to use barrier contraception from the time period between signing of the informed consent form and through 3 months after the last dose of study drug.
10. Male patients must agree to refrain from sperm donation from the time period between signing of the informed consent form and through 3 months after the last dose of study drug.
11. Patients who would comply with the requirements of this protocol (e.g., return for follow up visits), as judged by the investigator.

Exclusion criteria

English
1. Patients who are highly sensitized or who are likely to undergo desensitization at time of transplant (e.g., donor-specific antibody titers at the local laboratory >2000).
2. Patients planning to undergo multi-organ transplantation.
3. Patients participating in another interventional clinical study.
4. Previous vaccination with an investigational CMV vaccine.
5. Patients with known diagnosis of human immunodeficiency virus.
6. Patients who are pregnant, breastfeeding, or planning to become pregnant during the study.
7. Any Screening safety laboratory value of alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >5 X upper limit of normal (ULN), total bilirubin >2 X ULN, absolute neutrophil count <500 cells/µL, or lymphocyte count <200 cells/µL.
8. Any confirmed or suspected immunodeficiency disorder (based on medical history and physical examination) that could interfere with the immune response or that presents a risk for the patient to receive a vaccine candidate in development.
9. Treatment with any chronic immunosuppressive medication or other immuno modifying drugs within 6 months prior to study entry (unless agreed otherwise between the sponsor and investigator on a case-by-case basis). However, inhaled and topical steroids and low-dose oral corticosteroids (<=10 mg milligrams a day of prednisone or equivalent) are allowed.
10. For Groups 1 and 2 only, patients with prior history of CMV disease or CMV infection requiring anti-viral therapy.
11. For Group 3 only, patients with active CMV infection requiring antiviral therapy within 30 days prior to the first injection of study drug.
12. Patients with a history of severe allergic reactions and/or anaphylaxis that could interfere with the immune response (including an allergy or hypersensitivity to any ingredient found in the study drug [HB101 or placebo]) or that presents a risk for the patient to receive a vaccine candidate in development.
13. Patients with a severe coagulation abnormality that would preclude intramuscular injection.
14. Patients with a rash, dermatological condition, or tattoo in the area of the injection site(s) that could interfere with administration site reaction rating. (Note: The injection site(s) can be the non-dominant arm [most preferred injection site], dominant arm, or either thigh [least preferred injection site], as judged by the investigator).
15. History or current evidence of medical disorders or conditions that could prevent the successful completion of the study, as judged by the investigator.
16. It is anticipated that the patient will be unavailable to complete study follow-up.
17. Fever (>= 38°C) occurs within 7 days prior to first dose (unless agreed

otherwise between the sponsor and investigator on a case-by-case basis).
18. For patients in the post-transplant CMV prophylactic therapy management group only, patients who will be receiving Cytogam® in their post-transplant CMV prophylaxis regimen.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	22
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	HB-101

Ethics review

Approved WMO

Date:	08-10-2018
Application type:	First submission

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-05-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-08-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-10-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-11-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-12-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-02-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO	

Date:	31-08-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-09-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	20-11-2020
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-01-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-01-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-02-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

Haag)

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	EUCTR2017-005047-32-NL
CCMO	NL66352.000.18

Study results

Results posted: 27-06-2023

Summary results
Trial never started

First publication
06-06-2023