A CMV vaccine based on non-replicating lymphocytic choriomeningitis virus vectors expressing gB and pp65 is safe and immunogenic in humans

Michael Schwendinger¹, Georges Thiry¹, Beatrice De Vos², Fien De Boever², Geert Leroux-Roels², Anders Lilja¹

¹Hookipa Biotech GmbH, Vienna, Austria. ²BEJAMAD, Brussels, Belgium. ³Ghent University Hospital, Center for Vaccinology, Gent, Belgium. ⁴Ghent University and University Hospital, Center for Vaccinology, Gent, Belgium

Background

Cytomegalovirus infection is most common after transplantation and has major impact on clinical outcome. CMV infection is primarily a disease of immunosuppression playing a role in organ/bone marrow transplant, some biologic therapies and HIV treatment. Due to the fact that the infection is not curable and that the current antiviral therapies are limited, a vaccine to prevent clinically is a unmet medical need.

Hookipa Pharma’s bivalent CMV vaccine HB-101 expresses pp65 and a truncated isoform of gB on the proprietary Vaxwave® platform. gB is clinically validated antigen for development of specific neutralizing antibodies and pp65 is a strong inducer of cytotoxic T-cells eliciting a specific effect on CMV replication. To support further evaluation of HB-101 for the prevention and treatment of CMV based diseases, a Phase 1, first-in-human study was conducted to assess the safety, tolerability and immunogenicity of HB-101.

Study design, aims and endpoints

The HB-100-001 (no. NCT027398692) study was a first-in-human randomized, placebo-controlled, double-blind, Phase 1 dose-escalating trial.

- 54 healthy volunteers enrolled in study
- Primary objective: Evaluate the safety, tolerability and immunogenicity of the HB-101 CMV vaccine in 3 different dose levels and to identify the optimal dose level(s) of the HB-101 CMV vaccine in CMV-seronegative healthy subjects
- Secondary objective: Assess antibody and T cell persistence after vaccination with HB-101 CMV vaccine following 3 different vaccination schedules (1, 2 or 3 vaccinations).
- Inclusion criteria: 54 healthy, CMV-negative male and female adults, 18 to 45 years of age
- Normal laboratory values
- Exclusion criteria: History of testing positive for HIV, HBsAb or HCV

Subjects were randomized in 3 groups

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose</th>
<th>Administrations</th>
<th>no. of subjects</th>
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<tbody>
<tr>
<td>1</td>
<td>2.6x10⁶ FFU or placebo</td>
<td>months 0, 1, 3</td>
<td>14 vaccine, 4 placebo</td>
</tr>
<tr>
<td>2</td>
<td>2.6x10⁷ FFU or placebo</td>
<td>months 0, 1, 3</td>
<td>14 vaccine, 4 placebo</td>
</tr>
<tr>
<td>3</td>
<td>2.6x10⁸ FFU or placebo</td>
<td>months 0, 1, 3</td>
<td>14 vaccine, 4 placebo</td>
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Administration of study drug

- HB-101 was administered intramuscularly

Follow up, samples for ELISPOT, intracellular staining, ADAs (Nabs, Babs)

- Subjects were monitored for 24 hours and followed up to 12 months
- ELISPOT sampling: LCMV: days0, 14, 28, 42, 84, 98, months 4, 6, 12; HCMV: days0, 14, 28, 42, 84, 98, months 4, 6, 12
- Samples for intracellular staining: LCMV: days0, 14, month 1, day42, month3, day98, months4, 6, 12; HCMV: days0, 14, month 1, day42, month3, day98, months4, 6, 12
- ADA sampling: Nabs LCMV: days0, 28, 84, months 4, 12; Nabs HCMV: days0, 28, 84, months 4, 12, 6, 12

Safety results

- Subcutaneous Local Symptoms
- Subcutaneous General Symptoms
- Solicited Local Symptoms
- Solicited General Symptoms
- Moderate Related AEs
- Severe Related AEs

Conclusions

HB-101 is safe and potently immunogenic from doses 2.6x10⁶ to 2.6x10⁸ FFU

- All subjects in cohort 3 have HCMV-neutralizing antibodies after two vaccinations, 10 subjects after 12 months
- All cohorts have robust HCMV-specific cellular immunity at month 12
- HB-101 elicited a high proportion of polyfunctional HCMV- specific CD4+ and CD8+ T-cells (IFNγ, IL-2+, TNFα+ CD8+ T-cells is a reported predictor of protection in solid organ transplant recipients)
- Vaxwave® vectors do not efficiently elicit neutralizing antibodies

The HB-101 safety and immunogenicity data warrant further evaluation of the vaccine in a phase 2 trial in solid organ transplant recipients

References


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Contact

Camille Nelson Kotton, MD, FIDSA, FAST
Clinical Director, Transplant and Immunocompromised Host Infectious Diseases Group, Infectious Diseases Division
Massachusetts General Hospital
Associate Prof., Havard Medical School
55 Fruit Street, Boston, MA 02114-2696
CKOTTON@mgh.harvard.edu