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Impact of bepirovirsen on immune response in chronic hepatitis B patients

Submission date 30/10/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 30/10/2025	**Overall study status** Ongoing	
Last Edited 30/10/2025	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims
This study is looking at how the immune system reacts to a potential new treatment for chronic hepatitis B called Bepirovirsen. Researchers want to understand why some people respond better to the treatment than others, especially those who continue to have lower levels of the virus after treatment. To do this, they'll study stored blood samples from people who took part in an earlier clinical trial called B-Well.

Who can participate?
No new participants are needed for this study. It will only use samples from people who already took part in the previous trial and gave permission for their samples to be used in future research.

What does the study involve?
There is no involvement required from participants. The study will use previously collected and anonymised blood samples, so no one will be contacted or asked to do anything new.

What are the possible benefits and risks of participating?
Since no new participation is required, there are no direct risks or benefits for individuals. However, the research could help improve future treatments for hepatitis B by helping scientists understand how the immune system responds to Bepirovirsen.

Where is the study run from?
Chang Gung Memorial Hospital in Taiwan.

When is the study starting and how long is it expected to run for?
October 2025 ti October 2027.

Who is funding the study?
GlaxoSmithKline Research & Development Ltd.

Who is the main contact?
Professor Wen-Juei (Rachel) Jeng, rachel.jeng@gmail.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Study information

Scientific Title
The impact of bepirovirsen on host HBV-specific immune response in relation to HBsAg decline and its durability

Study objectives
To explore the changes in HBV-specific T-cell phenotype during Bepirovirsen administration and their association with HBsAg decline and durability.
Secondary objectives include investigating (1) changes in innate-like CD8 T cells and their relationship with ALT elevation, (2) phenotype alterations in monocytes, and (3) plasma cytokine patterns (IL-12, IL-15, IL-18) during treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 17/07/2025, Chang Gung Medical Foundation Institutional Review Board (199, Tung Hwa North Road, Taipei, 10507, Taiwan; +886-3-3196200; irb@cgmh.org.tw), ref: 202500942B0

Study design
Observational single-centre retrospective cohort sub-study

Primary study design
Observational

Study type(s)
Efficacy, Other

Health condition(s) or problem(s) studied
Chronic Hepatitis B (CHB) infection; functional cure; HBsAg seroclearance; immune reconstitution after Bepirovirsen.

Interventions
Drug (interventional parent trial with Bepirovirsen); this sub-study is observational using biological samples.

Brief methodology of the parent trial:
The parent trial is a Phase 2b randomized controlled study (B-Well) evaluating Bepirovirsen, an antisense oligonucleotide (ASO) targeting all HBV mRNAs.
-Design: 1:3 randomization (Bepirovirsen 300 mg vs placebo).
-Dose and duration: Participants receive weekly subcutaneous injections of 300 mg Bepirovirsen for 24 weeks, followed by a 24-week off-treatment observation period.
-Comparator: Placebo administered on the same schedule.
-Population: Chronic hepatitis B (CHB) patients with long-term nucleos(t)ide analogue (Nuc) suppression.
-Sub-study (current project): Retrospective observational analysis of immunologic changes in 20 participants (10 cross-sectional and 10 longitudinal) from the B-Well cohort to evaluate Bepirovirsen's impact on HBV-specific and innate-like T-cell responses and cytokine signatures.

Intervention Type
Other

Primary outcome(s)
HBV-specific CD8 T-cell phenotype measured using multicolor flow cytometry (Symphony) and single-cell RNA sequencing of PBMC samples at baseline (before IP/placebo), Week 7–10, Week 21–23 (end of IP treatment), and Week 40–46 (24 weeks post-treatment follow-up)

Key secondary outcome(s))
1. Innate-like CD8 T-cell frequency and activation status (CD38HLA-DR CD8 T cells) measured by flow cytometry and scRNA-seq at baseline, Week 7–10, Week 21–23 and Week 40–46.
2. Innate immunity status measured by flow cytometry and scRNA-seq at baseline, Week 7–10,

Week 21–23 and Week 40–46.
3. Plasma cytokines (IL-12, IL-15, IL-18) measured by BD Cytometric Bead Array at baseline, Week 7–10, Week 21–23 and Week 40–46.

Completion date
29/10/2027

Eligibility

Key inclusion criteria
1. Adults with chronic hepatitis B enrolled in the Bepirovirsen-based B-Well trial
2. Provided informed consent for optional immunologic sub-study
3. Available peripheral blood mononuclear cell (PBMC) and plasma samples collected at predefined time points

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
20

Key exclusion criteria
1. Hemoglobin < 10 g/dL
2. Withdrawal of consent for B-Well sub-study
3. Insufficient sample quality or quantity for immune analysis

Date of first enrolment
31/10/2025

Date of final enrolment
11/10/2027

Locations

Countries of recruitment
Taiwan

Study participating centre
Chang Gung Memorial Hospital LinkouChang Gung Memorial Hospital, Linkou Medical Center
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Sponsor information

Organisation
Chang Gung Memorial Hospital

ROR
https://ror.org/02verss31

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline Research & Development Ltd

Results and Publications

Individual participant data (IPD) sharing plan
De-identified data will be shared in aggregated form with GlaxoSmithKline Research & Development Ltd and may be made available to qualified researchers upon reasonable request, following institutional and IRB approval. No individual-level identifiers will be released publicly.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	07/07/2025	30/10/2025	No	No