THERAPEUTIC HBV *NEWSLETTER*

204852
TH HBV VV-001

Edition December 2023

WELCOME

Dear Investigators and Study Coordinators,

Welcome to the 26th edition of the Therapeutic HBV Vaccines newsletter! In this edition we cover the following information:

Current Focus

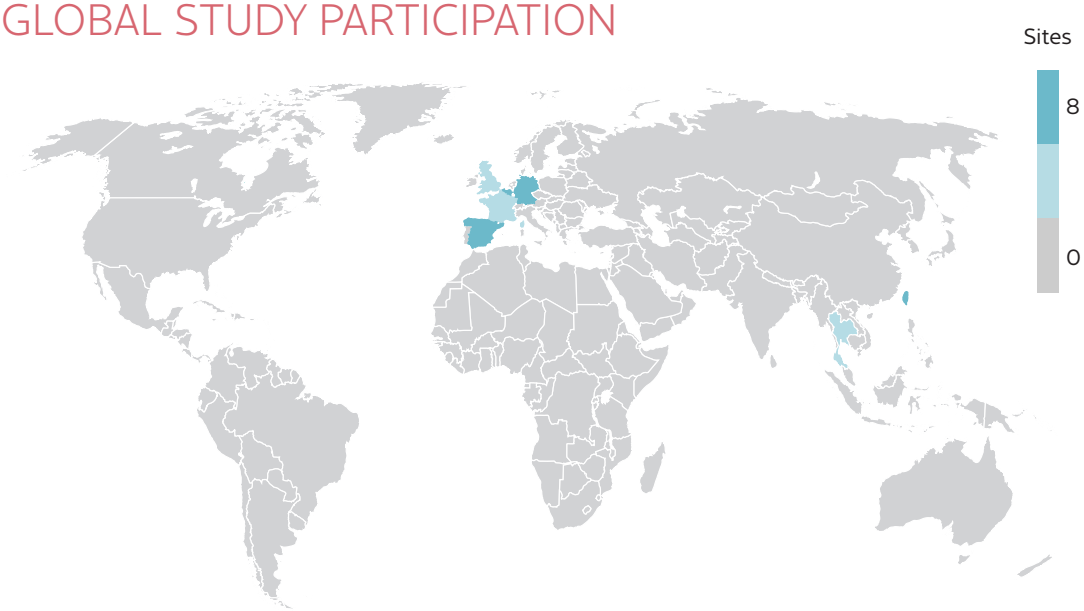
- Recruitment closed – final status by country
- Steps B and C ongoing oversight
- Interesting Reads
- Highlights
- Tips & Reminders

We want to *thank you and your site staff for all your efforts* for conducting this study in your clinic! Best wishes for Christmas from the TH HBV VV-001 Team.

Regards,

GSK Central Study Team

GLOBAL STUDY PARTICIPATION



In this Edition...

1. RECRUITMENT COMPLETION

Country	Screened	Screen failures	Patients randomized	Patient not yet dosed due to study on hold	Patients dosed
Belgium	8	4	4	0	4
France	2	2	0	0	0
Germany	5	2	3	0	3
Hong Kong	10	4	6	0	6
Poland	11	6	5	5	0
Spain	19	9	10	2	8
Taiwan	13	2	11	0	11
Thailand	13	4	9	0	9
United Kingdom	8	4	4	0	4
Total	**89**	**37**	**52**	**7**	**45**

- Step A: Achieved
- Step B: Last patient last visit planned for 3 June 2024
- Step C: Enrollment status

Country	Screened	Screen failures	Patients randomized	Patient Dosed	Patient Withdrawn	Patients Completed the treatment	Patients to Complete Dose 4
Belgium	9	5	4	4	0	4	0
France	2	2	0	0	0	0	0
Germany	5	2	3	3	0	3	0
Hong Kong	10	4	6	6	0	6	0
Poland	7	7	0	0	0	0	0
Spain	13	7	6	6	0	5	1
Taiwan	14	3	11	11	0	11	0
Thailand	13	4	9	9	0	6	2
United Kingdom	7	3	4	4	2	2	0
Total	**80**	**37**	**43**	**43**	**2**	**37**	**3**

- Step C status (enrolled 45, targeted 57), recruitment closed and last *V22 planned for 26 May 2024 - max 6 July 2024* *(preferably min intervals to be used)*
  - 17 patients completed treatment before study hold
  - 8 patients still to receive last dose (Visit 14) from November to December 2023
  - 16 patients received last dose as planned
  - 2 patients lost
  - 2 patients removed from treatment for other reasons

2. SUBMISSION AND APPROVAL STATUS

The Therapeutic HBV IB (TH HBV IB Edition 7) and the iSRC charter are currently being updated. Update of TH HBV IB is classified as CTA substantial amendment. Submissions to regulatory authorities are planned for 8 December 2023.

3. INTERESTING READS

A role for immune modulation in achieving functional cure for chronic hepatitis B among current changes in the landscape of new treatments, Expert Review of Gastroenterology & Hepatology, https://doi.org/10.1080/17474124.2023.2268503

4. HIGHLIGHTS

A new Edition 7 of the Investigator's Brochure (IB) is in preparation and will be released shortly. Section 3 includes timings of regulatory submissions. We are planning to organize a new Scientific Engagement meeting in the first quarter of 2024 (Q1 2024) to provide more details on the content of the new IB Edition. We will provide more information soon on the timing and format of this Scientific Engagement meeting.

- We have already communicated that the current MVA-HBV lot will expire on **31 December 2023.** The **MVA-HBV cannot be administered to (arm C1 or arm C2) study participants beyond 31 December 2023.** Therefore, we remind you to adhere to the per protocol planned visit intervals between study visits as much as possible. Apply an interval of a minimum of 53 days to a **maximum of 63 days between subsequent treatment visits** to secure the MVA-HBV administration to ongoing study participants before 31 December 2023.
- Upcoming **Interim Efficacy/Immunogenicity Analysis for Step C** is planned for the second quarter 2024 (Q2 2024). In order to meet this timing, we are asking you to schedule the 6-months post-dose 4 visit (Visit 22, Day 337) for your patients well in advance and preferably within the shortest interval (i.e., 147 days after Dose 4/V14) in accordance with the table below.

Interval	Optimal length of interval a	Allowed interval c
Visit 14 (Day 169) → Visit 22 (Day 337)	168 days	147 - 188 days

  - We want to remind you that the collection of biological samples at Visit 22 is critical for the evaluation of efficacy and immunogenicity endpoints in the study. Please ensure samples are collected at this visit **and shipped appropriately.**
  - An Internal Safety Review Committee (iSRC) meeting to review the safety data of all ongoing patients in Step B and Step C took place on 3 October 2023 (Data Lock Point: 15 September 2023). No safety concerns were raised, and the decision of the iSRC was that the study can continue as planned. **The next iSRC meeting would be planned for the end of March 2024.**

5. TIPS & REMINDERS

- HBV DNA samples: 11.23% of samples have been deemed Quantity Not Sufficient (QNS) samples. QNS samples lead firstly to delays in releasing results (almost 1 week). These delays can be potentially harmful to patients in the event of HBV DNA breakthroughs. Secondarily, QNS samples increase the logistics burden for providing a back-up sample. As you may recall, the back-up sample is normally dedicated for tertiary endpoints. Should the back-up sample also be QNS, both samples are pooled together for a third test attempt. In the worst-case scenario, the third test attempt could be a failure. Consequences of this include the potential impact on patient safety, three weeks lost, and two samples lost. Please remind your staff to carefully follow lab manual instructions for the collection and processing of HBV DNA samples.
- Sites need to complete overdue CRFs, including those that are mandatory for screen-failed subjects as well, and respond to open queries that have been unanswered for more than 50 days. DM is sending out YNTL and query reports on a regular basis. This would assist DM in thoroughly cleaning the data in preparation for the upcoming iSRC/IA5 milestones.
- PI signatures are required on forms associated with screening conclusions.