**Supplementary Methods**

**Sample size calculation**

For HBeAg-positive participants, assuming a treatment response rate of 45% for TMF and 20% for blank control, with a one-sided test, an α of 0.025, and a β of 0.18, a total of 104 participants was required. For HBeAg-negative participants, assuming response rates of 80% and 40% for two groups, respectively, a total of 40 participants was required. To account for a dropout rate of at least 25%, the final sample size was determined to be 200 participants.

**Statistical analysis**

Missing values, except at baseline, were imputed using the Last Observation Carried Forward (LOCF) method. Continuous variables with normal distribution were compared between two groups using the independent-samples t-test. For non-normally distributed variables, the Wilcoxon rank-sum test was employed. Categorical variables were analyzed using Analysis of Covariance or Fisher’s exact test for comparisons between groups. Subgroup analyses were conducted based on sex, age, HBV-DNA level, and HBeAg status.