

Supplemental Table 1. Characteristics of participants experiencing HBeAg seroreversion after treatment withdrawal.

| ID | Study Arm | HBeAg at baseline | HBeAg at week 192 | HBV Genotype | Time of HBeAg seroreversion since withdrawal (weeks) | ALT Elevation | Time of ALT elevation since withdrawal (weeks) | Grade 3+ (5x ULN) ALT elevation | Restart treatment after withdrawal | Time of treatment restart since withdrawal (weeks) |
|----|------------|-------------------|-------------------|--------------|--|---------------|--|---------------------------------|------------------------------------|--|
| 1 | TDF | Pos | Neg | C1 | 37 | No | --- | No | No | --- |
| 2 | TDF | Pos | Neg | A2 | 11 | Yes | 11 | Yes | Yes | 13.6 |
| 3 | TDF | Pos | Neg | A2 | 11 | Yes | 11 | No | No | --- |
| 4 | TDF+PegIFN | Pos | Neg | A1 | 15.6 | Yes | 18.4 | Yes | No | --- |
| 5 | TDF+PegIFN | Pos | Neg | C1 | 9.1 | Yes | 9 | Yes | Yes | 9.1 |
| 6 | TDF | Pos | Neg | B4 | 9 | Yes | 9 | Yes | Yes | 10 |

--- Not applicable

Supplemental Table 2. Association of ALT elevations with qHBsAg decline between TDF withdrawal (Week 192) and one year after withdrawal (Week 240)

| | qHBsAg (log 10 IU/ml) change from withdrawal (week 192) to week 240 (negative values indicate decline) | | |
|--|--|-----------|-----------|
| ALT elevation status | Least Square Mean | 95% Lower | 95% Upper |
| 1 None | -0.23 | -0.45 | -0.01 |
| 2 ALT elevation but < 5 X ULN | -0.38 | -0.61 | -0.14 |
| 3 ALT flare | -0.17 | -0.39 | 0.04 |
| Pair-wise comparison of p-value | | | |
| 1 vs 2 | 0.38 | | |
| 1 vs 3 | 0.72 | | |
| 2 vs 3 | 0.22 | | |

Supplemental Table 3. Factors associated with treatment restart (univariable analysis)

| Variable | Hazard Ratio and 95% CI | P |
|---|-------------------------|------|
| Tenofovir vs. Tenofovir+ peg-interferon | 1.41 (0.47,4.19) | 0.54 |
| Female vs. Male | 1.22 (0.40,3.74) | 0.73 |
| Others vs. Asian | 0.35 (0.05,2.67) | 0.31 |
| Age at week 192 (per year) | 1.03 (0.99,1.08) | 0.18 |
| At study entry (pre-treatment) | | |
| HBeAg at baseline (Positive vs. Negative) | 3.60 (1.21,10.72) | 0.02 |
| ALT at baseline (per ULN) | 0.99 (0.92,1.08) | 0.87 |
| HBV DNA Baseline (per log 10) | 1.52 (1.04,2.24) | 0.03 |
| qHBsAg Baseline (per log 10) | 1.17 (0.55,2.52) | 0.68 |
| At Treatment Withdrawal | | |
| ALT at 192 (per ULN) | 0.60 (0.18,1.98) | 0.40 |
| HBV DNA 192 (per log 10) | 1.06 (0.37,3.01) | 0.91 |
| qHBsAg 192 (per log 10) | 1.10 (0.60,2.05) | 0.76 |
| qHBsAg decline from baseline to week 192 (per log 10) | 0.99 (0.45,2.18) | 0.98 |

Supplemental Table 4. Association of pre-withdrawal factors with safe TDF withdrawal (no ALT flare, no treatment restart, and no transition to immune active phase one year after withdrawal)

| Variable | Odds Ratio (95% CI) | P-value |
|--|----------------------------|----------------|
| Tenofovir+ peg-interferon vs. Tenofovir* | 1.56 (0.65, 3.76) | 0.32 |
| Age at study entry (per year) | 0.94 (0.90, 0.98) | 0.01 |
| HBeAg Baseline (Positive vs. Negative) | 0.77 (0.27, 2.18) | 0.62 |
| ALT Baseline (X ULN) | 0.98 (0.92, 1.04) | 0.50 |
| qHBsAg at week 192 (log ₁₀ IU/mL) | | 0.049 |
| Within Tenofovir | 1.39 (0.63, 3.06) | 0.42 |
| Within Tenofovir+ peg-interferon | 0.49 (0.23, 1.00) | 0.051 |

*At the median value 2.91 log₁₀ IU/mL of qHBsAg at week 192