Supplementary Table 1. Additional HBeAg seroconversion during long-term follow-up

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Entry | Follow-up | 12M | 24M | 36M | 48M | 60M |
| n=196 | HBeAg SC (+), n | 40 | 29 | 18 | 13 | 4 |
|  | HBeAg SC (−), n | 156 | 127 | 83 | 49 | 31 |
|  | Censored, n | 0 | 26 | 21 | 14 | 11 |
|  | (Additional) SC rate | 14% | 18.6% | 17.8% | 21% | 11.4% |

SC, seroclearance

\* Patients were censored at retreatment or the last follow-up.

Supplementary Table 2. HBeAg seroclearance in different nucleos(t)ide analogues with and without hepatic steatosis (HS)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | HBeAg seroclearance | | | | | | | | | |
| Overall, | LAM, n=75 | | ETV, n=61 | | LdT, n=46 | | ADV, n=2 | TDF, n=12 | | p value |
| n=196 | 29 (38.7)a,b,c | | 44 (72.1)a | | 29 (63)b | | 0 (0) | 8 (66.7)c | | 0.001 |
|  | HS (−), 40 | HS (+), 35 | HS (−), 25 | HS (+), 36 | HS (−), 23 | HS (+), 23 | − | HS (−), 5 | HS (+), 7 |  |
|  | 18 (45) | 11 (31.4) | 18 (72) | 26 (72.2) | 14 (60.9) | 15 (65.2) | − | 4 (80) | 4 (57.1) |  |
| p value | 0.334 | | 1.000 | | 1.000 | |  | 0.576 | |  |
| Age/gender- | LAM, n=46 | | ETV, n=32 | | LdT, n=27 | | ADV, n=2 | TDF, n=5 | | p value |
| matched, | 14 (30.4)d,e | | 26 (81.3)d | | 16 (59.3)e | | 0 (0) | 2 (40) | | <0.001 |
| n=112 | HS (−), 24 | HS (+), 22 | HS (−), 16 | HS (+), 16 | HS (−), 12 | HS (+), 15 | − | HS (−), 3 | HS (+), 2 |  |
|  | 10 (41.7) | 4 (18.2) | 12 (75) | 14 (87.5) | 6 (50) | 10 (66.7) | − | 2 (66.7) | 0 (0) |  |
| p value | 0.159 | | 0.654 | | 0.452 | |  | 0.400 | |  |

Presented with number (%)

LAM, lamivudine; ADV, adefovir dipivoxil; LdT, Telbivudine; ETV, entecavir; TDF, tenofovir disoproxil fumarate; HS: hepatic steatosis

a, p<0.001; b, p=0.016; c, p=0.132; d, p<0.001; e, p=0.030

Supplementary Table 3. Comparison of baseline characteristics and treatment response among patients with different degrees of histological steatosis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Steatosis\* | Mild | Moderate | Severe | p |
| No | 64 | 25 | 13 |  |
| Age at treatment, year | 43.7±10.6 | 41.4±12.0 | 40.5±9.5 | 0.608 |
| Male | 48 (75) | 23 (92) | 10 (77) | 0.198 |
| BMI, kg/m2 | 24.3±2.8 | 26.2±3.0 | 27.9±3.1 | 0.191 |
| Genotype  B  C | 29 (49.2)  30 (50.8) | 6 (25)  18 (75) | 5 (45.5)  6 (54.5) | 0.128 |
| Treatment-naïve | 50 (78.1) | 20 (80) | 12 (92.3) | 0.501 |
| Cirrhosis | 23 (35.9) | 12 (48) | 5 (38.5) | 0.577 |
| AST, U/L | 66 (47-87) | 49 (34-81) | 47 (36-71) | 0.070 |
| ALT, U/L | 125 (68-163) | 92 (56-142) | 81 (37-122) | 0.106 |
| Total bilirubin, mg/dL | 0.8 (0.6-1.0) | 0.8 (0.7-0.9) | 0.9 (0.7-1.1) | 0.607 |
| Platelet, 109/L | 177 (152-217) | 192 (150-220) | 195 (162-229) | 0.620 |
| qHBsAg, log IU/mL | 3.7±0.9 | 3.7±0.6 | 3.5±0.5 | 0.757 |
| HBV DNA, log IU/mL | 7.6±1.2 | 7.1±1.3 | 6.6±1.0 | 0.433 |
| Treatment duration, m | 24.4 (12.3-48.6) | 24.3 (13.1-64.1) | 24.2 (12.1-36.3) | 0.565 |
| **Treatment response** | | | | |
| HBeAg seroclearance | 37 (57.8) | 14 (56) | 5 (38.5) | 0.438 |
| Virological response | 40 (62.5) | 17 (68) | 8 (61.5) | 0.875 |
| Age at e seroclearance | 47.3±10.8 | 42.6±11.8 | 40.8±8.8 | 0.419 |
| Time to seroclearance, m | 17.7 (9.8-41.6) | 15.2 (6-38.6) | 16 (11.2-32.9) | 0.898 |

Data were presented as mean ± S.D. or median (interquartile range) and number (%)

BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; qHBsAg, quantitative HBsAg

\*Steatosis: mild, 5-33%; moderate, 33-66%; severe, >66%

Supplementary table 4. Baseline clinical characteristics among patients with lamivudine (LAM) and entecavir (ETV) treatment\*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | LAM | ETV | LdT | p |
| No | 75 | 61 | 46 |  |
| Age, year | 35 (28-42) | 44 (37-53) | 36 (29-43) | <0.001 |
| Male | 58 (77.3) | 43 (70.5) | 60 (65.2) | 0.337 |
| BMI, kg/m2 | 23.7 (22.0-27.0) | 23.9 (22.3-26.6) | 22.9 (20.1-25.4) | 0.107 |
| Genotype  B  C | 39 (52.7)  35 (47.3) | 23 (40.4)  34 (59.6) | 32 (71.1)  13 (28.9) | 0.008 |
| Treatment-naïve | 55 (73.3) | 51 (83.6) | 44 (95.7) | 0.007 |
| Cirrhosis | 17 (22.7) | 31 (50.8) | 1 (2.2) | <0.001 |
| AST, U/L | 61 (42-83) | 70 (40-112) | 60 (44-86) | 0.504 |
| ALT, U/L | 103 (77-155) | 106 (54-195) | 121 (68-176) | 0.871 |
| <2x ULN  2-5x ULN  >5x ULN | 14 (18.7)  48 (64)  13 (17.3) | 23 (37.8)  19 (31.1)  19 (31.1) | 12 (26.1)  23 (50)  11 (23.9) | 0.006 |
| Total bilirubin, mg/dL | 0.9 (0.8-1.2) | 0.7 (0.6-0.9) | 0.8 (0.6-0.9) | <0.001 |
| Platelet, 109/L | 210 (164-237) | 181 (149-214) | 193 (172-218) | 0.064 |
| qHBsAg, log IU/mL | 3.9 (3.5-4.3) | 3.7 (3.3-4.1) | 4.1 (3.6-4.4) | 0.149 |
| HBV DNA, log IU/mL | 7.5 (6.8-8.0) | 7.4 (6.4-8.0) | 8.0 (7.6-8.6) | <0.001 |

Presented with median (interquartile range) or number (%)

\*2 adefovir dipivoxil (ADV) and 12 tenofovir disoproxil fumarate (TDF) were not included