Abstract 388

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Loss of HBsAg in Nucleoside-Naïve HBeAg(+) Chronic Hepatitis B Patients Following Treatment with Entecavir or Lamivudine: Evaluation of HBV Genotypes

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Background

- Spontaneous HBsAg seroclearance has been estimated to occur at a rate of 0.5% to 1.7% per year[1-4]
- Rate of HBsAg seroclearance varies among different patient populations[1-5]
- In the phase III study ETV-022, 5.1% of nucleoside-naïve HBeAg(+) chronic hepatitis B (CHB) patients treated with entecavir (ETV) had confirmed HBsAg loss by week 120[6]
- In this analysis we evaluated the distribution of HBsAg loss according to the HBV genotypes in patients treated with ETV or lamivudine (LVD) in Study ETV-022

Objective

- To describe characteristics of patients who achieved a confirmed HBsAg loss treated with entecavir (ETV) or lamivudine (LVD) in study ETV-022

Methods

- HBeAg(+) nucleoside-naïve adults with chronic hepatitis B (CHB), elevated serum alanine aminotransferase (ALT), and compensated liver disease were randomized to double-blind treatment for up to 96 weeks with ETV 0.5 mg/day or LVD 100 mg/day, with up to 24 weeks of off-treatment follow-up
- HBsAg was measured at regular intervals during on- and off-treatment follow-up using Abbott AxSYM microparticle enzyme immunoassay
- For this analysis, confirmed HBsAg loss was defined as HBsAg loss documented on two consecutive measurements or at last observation, regardless of treatment period

Results

Table 1. Baseline Demographic and Disease Characteristics of Patients With and Without Confirmed HBsAg Loss at 120 Weeks

Characteristics	Patients With Confirmed HBsAg Loss N=28	Patients Without Confirmed HBsAg Loss N=681
Male (%)	23 (82)	512 (75)
Asian (%)	4 (14)	402 (59)
Caucasian (%)	22 (79)	259 (38)
Mean viral load (log_{10} copies/ml)	9.8	9.6
Knodell necroinflammatory score (mean)	9.1	7.7
Serum ALT (U/L) (median)	163	101

Genotype, %

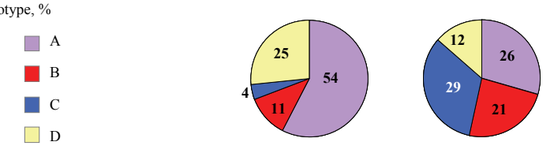


Table 2. Baseline Demographic and Disease Characteristics in All Treated Subjects: Proportions of HBV Genotypes among Different Regions, n (%)

HBV Genotypes	Asia N=339	Europe N=172	North America N=102	South America N=96
A	36(11)	79 (46)	35 (34)	46(48)
B	121(36)	5 (3)	19(19)	0
C	157(46)	11(6)	29 (28)	4(4)
D	2(<1)	65 (38)	7(7)	12(13)
F	0	3 (2)	0	29(30)
Others*	23(7)	9 (5)	12(12)	5(5)

* Others include genotype E, mixed genotypes, indeterminate and subjects with missing genotype information

- Among all treated subjects with either ETV or LVD, proportions of HBV genotypes vary among different regions
  - Majority of Asians had genotype B and C (82%)
  - Majority of Europeans had genotype A and D (84%)
  - North Americans mainly had a mix of genotype A, B, and C (81%)
  - South Americans mainly had genotype A and F (78%)

Table 3. Baseline Characteristics in Patients With or Without Confirmed HBsAg Loss by Week 120

	With confirmed HBsAg loss ETV N=18	With confirmed HBsAg loss LVD N=10	Without confirmed HBsAg loss N=681
Male (%)	14/18 (78)	9/10 (90)	512 (75)
Mean age, years	40	36	34.8
Asian (%)	3/18 (17)	1/10 (10)	402 (59)
Caucasian (%)	14/18 (78)	8/10 (80)	259 (38)
Mean viral load (log_{10} copies/mL)	9.6	10.2	9.6
Median ALT (U/L)	159.5	178	101
Knodell necroinflammatory score	9.1	9.0	7.7

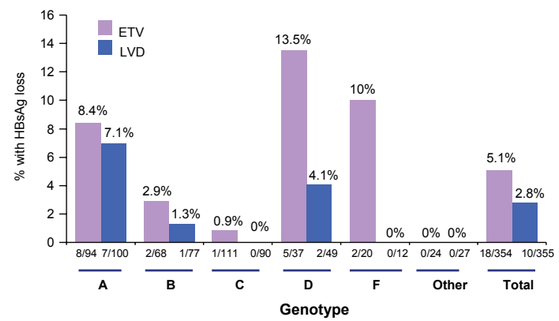
- More Caucasians had HBsAg loss compared to Asians
- In all the patients treated with ETV or LVD, at the time of confirmed HBsAg loss:
  - all had HBV DNA $<10^4$ copies/mL
  - 89% had HBV DNA <300 copies/mL
  - 93% had ALT normalization
  - 86% had HBeAg loss
- With continued follow-up during the maximum observation period of 120 weeks on and off treatment:
  - 96% achieved HBV DNA <300 copies/mL
  - 96% and 86% achieved confirmed HBeAg loss and HBe seroconversion, respectively

Table 4. Demographics and Genotypes in Patients With Confirmed HBsAg Loss by Week 120

Genotypes	# Patients ETV N=18	# Patients LVD N=10
A	8	7
Caucasian	7/8	6/7
African American	1/8	1/7
B	2	1
Asian	2/2	1/1
C	1	0
Asian	1/1	0/0
D	5	2
Caucasian	5/5	2/2
F	2	0
Caucasian	2/2	0/0

- The majority of patients with genotype A or D HBV are Caucasians
- All 4 patients with genotype B or C HBV are Asians
- Two Caucasians with genotype F HBV are from South America

Figure 1. Proportion of Patients With HBsAg Loss among Each Genotype by Week 120



- Among 18 patients treated with ETV with confirmed HBsAg loss, proportions of patients with HBsAg loss were 8.4% and 13.5% for genotype A and D, respectively, compared to 2.9% and 0.9% for genotype B and C,
- Combining genotypes A and D, 9.8% (13/132) patients treated with ETV had confirmed HBsAg loss compared to 6%(9/150) of those treated with LVD

Summary

- Among all treated subjects with either ETV or LVD, proportions of HBV genotypes vary among different regions
  - Majority of Asians had genotype B and C
  - Majority of Europeans had genotype A and D
  - North Americans had a mix of genotype A, B, and C
  - South American mainly had genotype A and F
- Among patients with confirmed HBsAg loss:
  - The majority of the patients with HBV genotype A or D were Caucasians
  - All 4 patients with HBV genotype B or C were Asians
  - Two Caucasians with HBV genotype F HBV were from South America
  - Most achieved HBV DNA <300 copies/mL, ALT normalization and HBeAg loss during the observation period
- Among all patients treated with ETV or LVD in study ETV-022:
  - Combining genotypes A and D, 9.8% (13/132) patients treated with ETV had confirmed HBsAg loss compared to 6% (9/150) of those treated with LVD

Conclusions

- About 5% of entecavir-treated patients experienced HBsAg loss during a maximum observation period of 120 weeks on and off treatment
  - Most achieved HBV DNA <300 copies/mL, ALT normalization and HBeAg loss
- HBsAg loss was mostly associated with Caucasian patients with HBV genotype A or D infection

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Disclosures

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