

Lack Of Influence Of Baseline Genotype On Antiviral Response In Subjects With Chronic Hepatitis B Infection

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Introduction

- Hepatitis B Virus (HBV) is a heterogeneous virus that is classified into eight viral genotypes (A-H) based on DNA sequence divergence
- The severity of liver disease as well as the response to antiviral treatment may be influenced by the HBV viral genotype¹

Methods

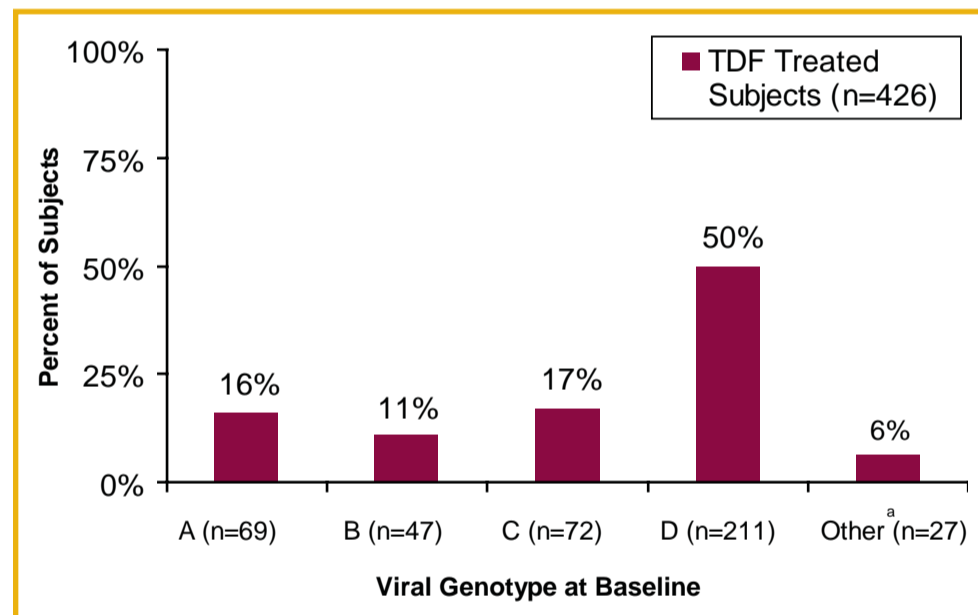
- Subjects were enrolled in one of two double-blind, randomized studies of tenofovir DF [GS-US-174-0102 (HBeAg-) or GS-US-174-0103 (HBeAg+)]
- At Week 48, subjects were evaluated for biochemical, virological, serological and histological response
- Viremia was assessed using the Roche COBAS TaqMan assay, with a lower limit of quantification (LLOQ) of 169 copies/mL [29 IU/mL]
- Viral genotypes were determined by phylogenetic mapping of the HBsAg nucleotide sequence
- Pairwise Fisher's exact tests were used to compare response between viral genotypes using a significance level of 0.05

Objective

- To evaluate the influence of baseline viral genotype (A-H) on antiviral response among HBeAg+ and HBeAg- subjects with chronic hepatitis B (CHB) virus receiving tenofovir DF (TDF) 300 mg QD

Results

Figure 1. Distribution of Viral Genotypes at Baseline Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103



a. Includes viral genotypes E-H and missing data

Figure 2. Distribution of Viral Genotypes at Baseline by Geographic Region Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103

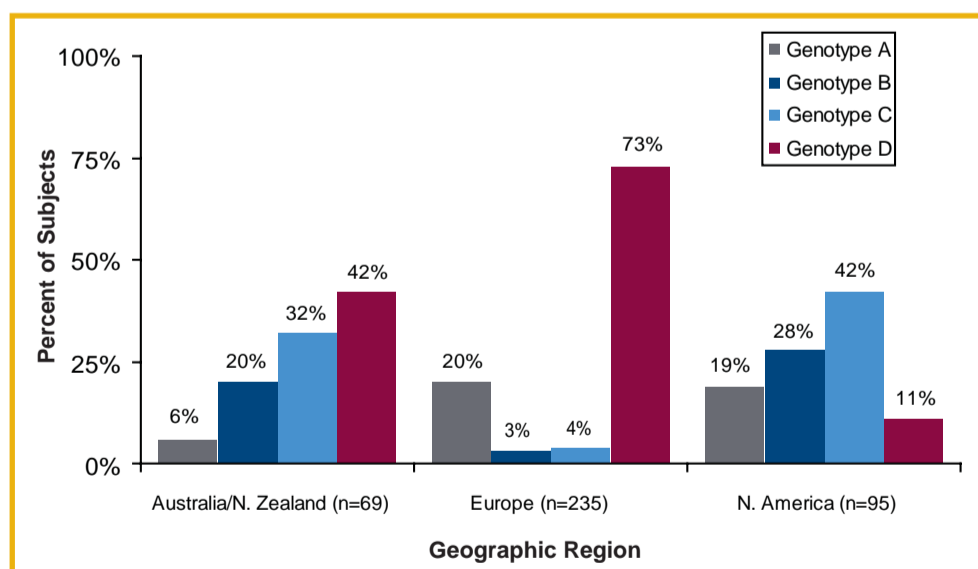
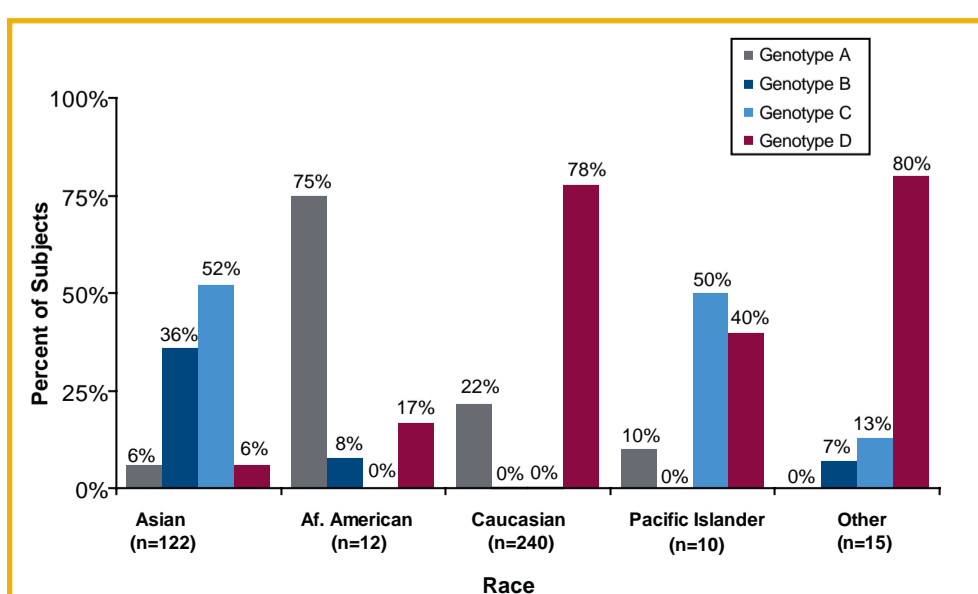


Figure 3. Distribution of Viral Genotypes at Baseline by Race Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103



Results (cont'd)

Figure 4. HBV DNA Log₁₀ Viral Load by Study Week Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103 by Baseline Viral Genotype

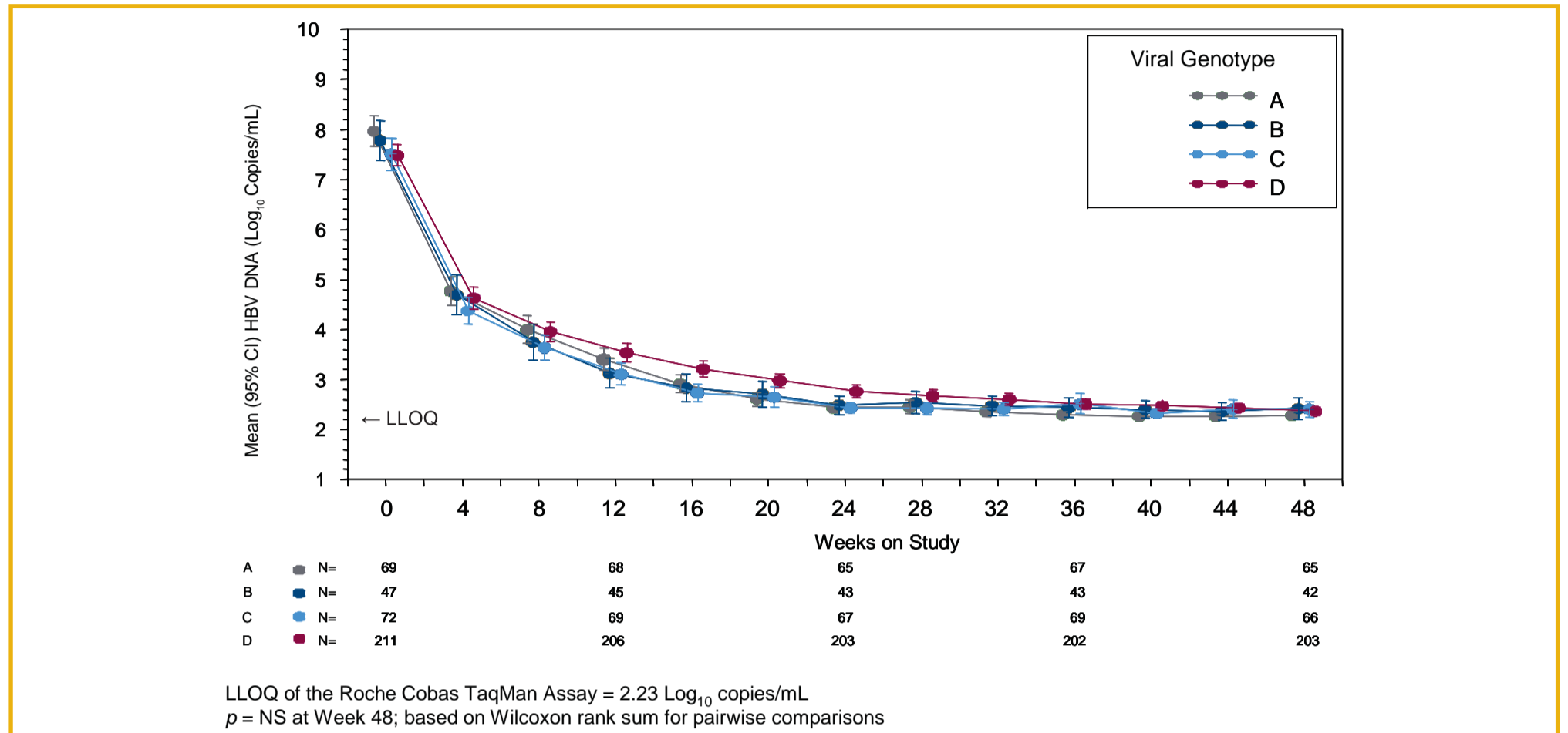


Figure 5. Percentage of Subjects with HBV DNA < 400 copies/mL Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103 by Baseline Viral Genotype

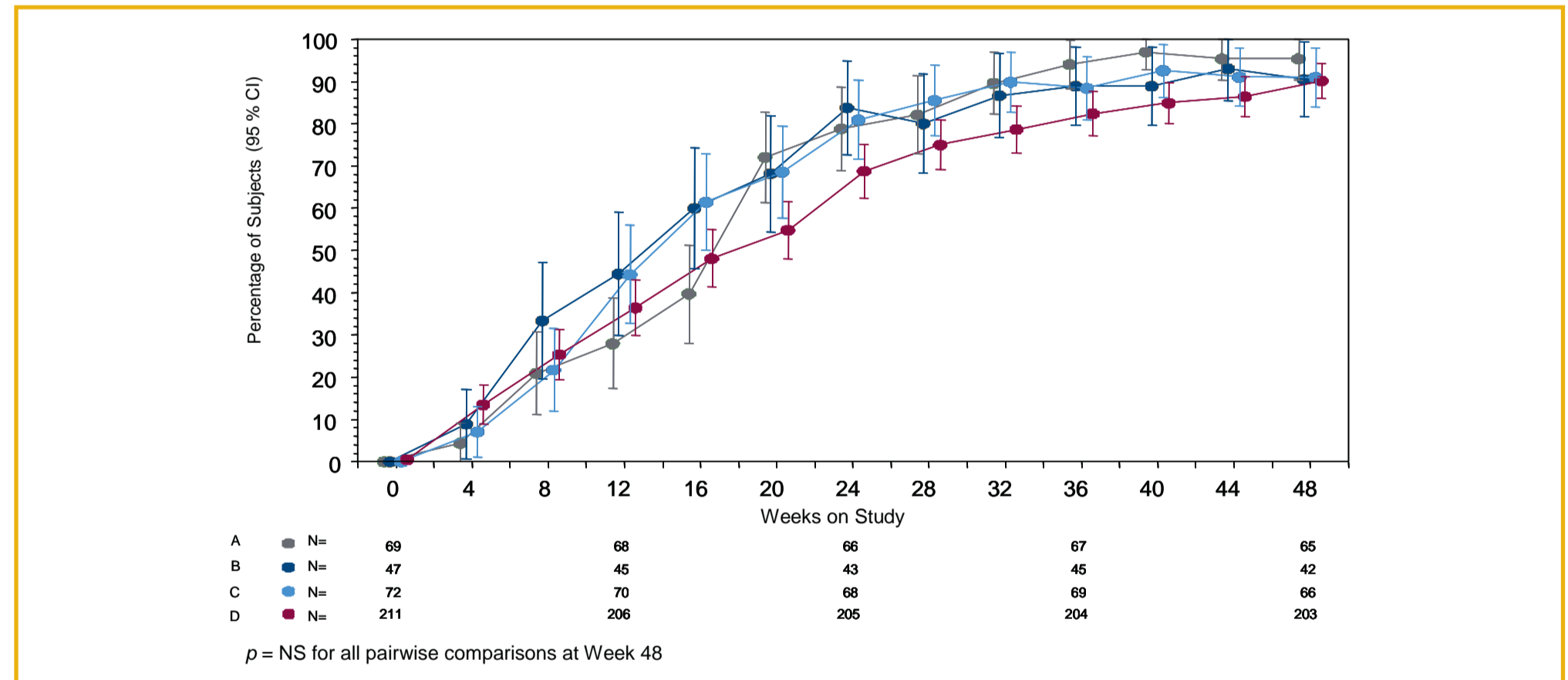


Figure 6. Biochemical Response^a and Histological Improvement^b at Week 48 Among TDF-Treated Subjects in Studies GS-US-174-0102 and GS-US-174-0103 by Baseline Viral Genotype

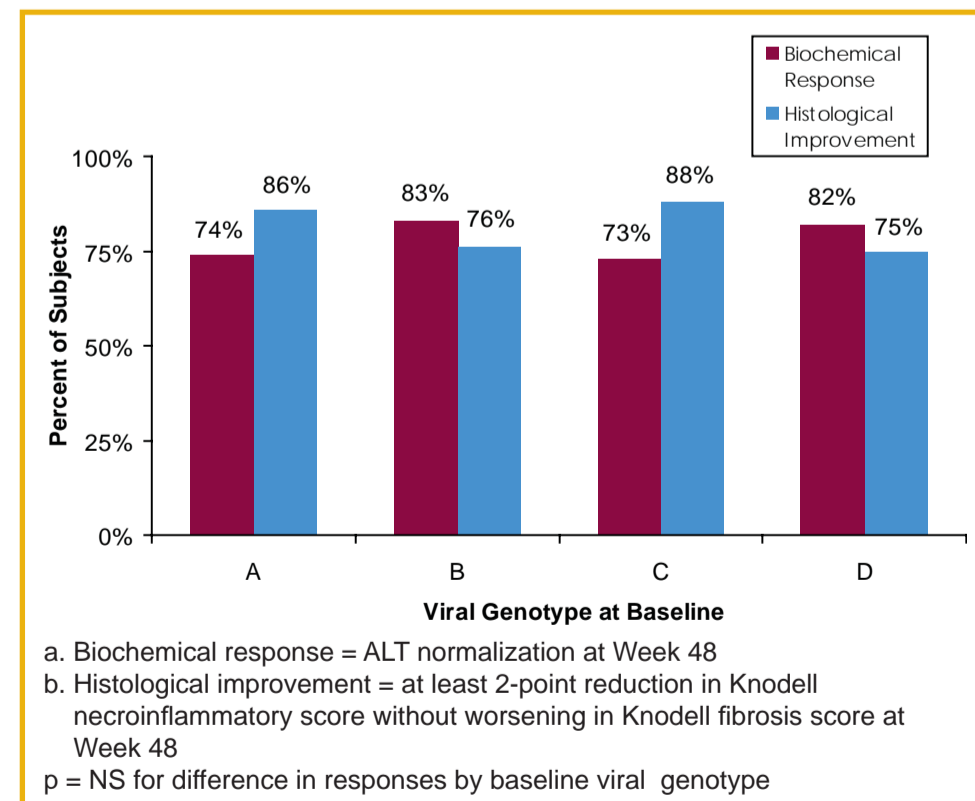


Table 1. Proportion of TDF-Treated Subjects in GS-US-174-0103 Experiencing HBeAg Seroconversion by Baseline Viral Genotype

| Baseline Viral Genotype | HBeAg Seroconversion |
|-------------------------|----------------------|
| A | 11/36 (31%) |
| B | 2/22 (9%) |
| C | 6/35 (17%) |
| D | 10/49 (20%) |

There were no significant differences between any two viral genotypes for the parameter of HBeAg seroconversion

Table 2. Summary of Treatment Naïve TDF-Treated Subjects who Achieved HBsAg Loss at Week 48^a

| Subject Number | Baseline HBV DNA ^b | Baseline Viral Genotype | Week 48 HBV DNA ^c | Week 48 HBV DNA Change from BL ^b |
|-------------------|-------------------------------|-------------------------|------------------------------|---------------------------------------------|
| 1876 ^d | 8.8 | D | < LLOQ | -6.6 |
| 7602 ^d | 9.6 | A | < LLOQ | -7.4 |
| 5253 | 9.1 | D | < LLOQ | -6.9 |
| 6601 | 9.6 | D | < LLOQ | -7.4 |
| 7651 | 9.2 | A | < LLOQ | -7.0 |

- All 5 subjects were enrolled in the GS-US-174-0103 study and were HBeAg+ at BL
- HBV DNA values are presented in log₁₀ copies/mL
- LLOQ of the Roche Cobas TaqMan Assay = 2.23 Log₁₀ copies/mL
- These subjects seroconverted for HBsAg

Conclusions

Across baseline viral genotypes A, B, C and D, 48 weeks of treatment with TDF 300 mg QD produced

- Potent virological response
- Serological response
- Biochemical response
- HBsAg seroconversion
- Histological improvement

References