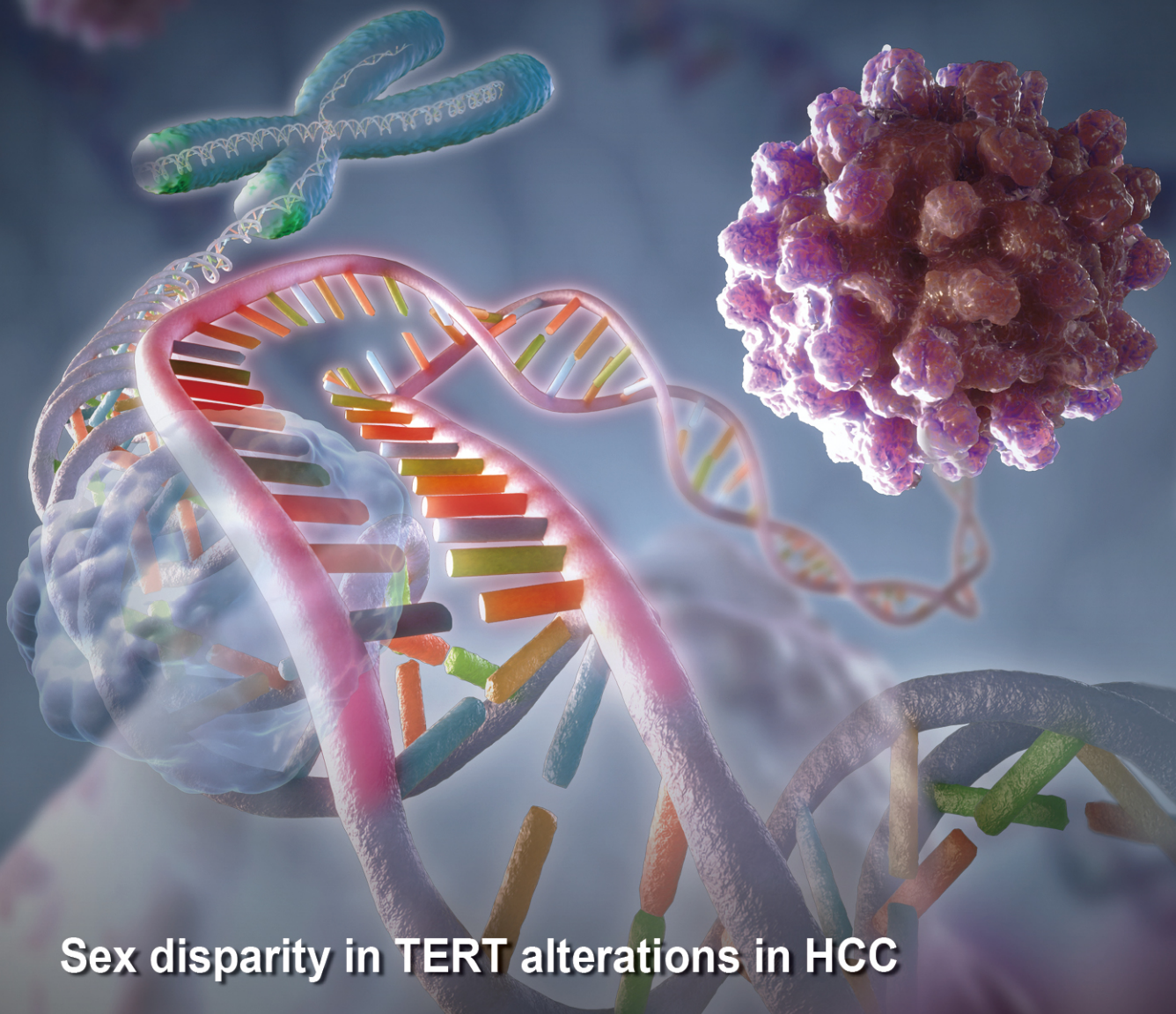
VOLUME 31 NUMBER 2 April 2025
pISSN 2287-2728
eISSN 2387-285X

CLINICAL and MOLECULAR HEPATOLOGY

The forum for latest knowledge of hepatobiliary diseases



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pISSN 2287-2728
eISSN 2287-285X

CLINICAL and MOLECULAR HEPATOLOGY

https://doi.org/10.3350/cmh.2024.0960
Clinical and Molecular Hepatology 2025;31:e140-e142

Letter to the Editor

Treatment response to nucleos(t)ide analogs in chronic hepatitis B with mildly elevated alanine aminotransferase: Letter to the editor on "Antiviral therapy for chronic hepatitis B with mildly elevated aminotransferase: A rollover study from the TORCH-B trial"

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Keywords: Nucleos(t)ide analogs; Chronic hepatitis B; Alanine aminotransferase

Dear Editor,

We read with interest the study by Hsu et al.[1], who evaluated the treatment response in chronic hepatitis B (CHB) patients with mild alanine aminotransferase (ALT) elevation. Favorable histopathological, virological, and biochemical response was achieved in these patients after three years of tenofovir disoproxil fumarate therapy.[1] This study suggested that patients with mild ALT elevation might benefit from antiviral therapy, providing important evidence for the expansion of treatment indications for these patients. However, there is no comparative group of patients with ALT >2 × upper limit of normal (ULN). Moreover, only few patients were hepatitis B e antigen (HBeAg)-positive (18.5%).[1] Thus, the virological response to nucleos(t)ide analogs (NAs) in patients with mild ALT elevation needs further investigation. We conducted a real-world, multicenter cohort study to validate the treatment response to first-line NAs in CHB patients with mild ALT elevation (1–2×ULN), and compare with patients with ALT >2×ULN.

A total of 724 treatment-naïve non-cirrhosis CHB patients with ALT >1×ULN (40 U/L) and hepatitis B virus (HBV) DNA >2,000 IU/mL were retrospectively included from three hospitals. All patients received antiviral treatment with first-line NAs. Patients were followed up longitudinally at intervals of 6 months or less during antiviral therapy. Virological response was defined as undetectable HBV DNA level (<20 IU/mL), and HBeAg clearance was defined as HBeAg loss regardless of antibody against HBeAg status.

Overall, the median age of patients was 34.0 years and

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Editor: Gi-Ae Kim, Kyung Hee University, Korea

Received : Oct. 29, 2024 / **Revised:** Nov. 2, 2024 / **Accepted:** Nov. 29, 2024

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72.9% of patients were male. The median levels of ALT, HBV DNA, and hepatitis B surface antigen (HBsAg) were 126.3 U/L, 7.0 $\log_{10}$ IU/mL, and 3.8 $\log_{10}$ IU/mL, respectively. 75.1% of patients were HBeAg-positive. The proportion of patients with 1–2×ULN of ALT and ALT >2×ULN were 31.4% and 68.6%, respectively. At baseline, patients with ALT >2×ULN had slightly higher HBV DNA (7.2 $\log_{10}$ IU/mL vs. 6.3 $\log_{10}$ IU/mL, *P*<0.001) and HBsAg (3.9 $\log_{10}$ IU/mL vs. 3.6 $\log_{10}$ IU/mL, *P*<0.001) levels, as well as higher proportion of HBeAg positivity (82.1% vs. 59.9%, *P*<0.001) while were younger (34.0 years vs. 36.0 years, *P*=0.039) than patients with ALT 1–2×ULN (Supplementary Table 1). The 2-year cumulative incidence of ALT normalization (94.1% vs. 96.0%, *P*=0.090, Fig. 1A) and virological response (69.7% vs. 67.8%, *P*=0.357, Fig. 1C) were comparable between ALT 1–2×ULN and ALT >2×ULN groups. Similar results were found in both HBeAg-positive and HBeAg-negative subgroups (Fig. 1D–1G). However, the 2-year cumulative rate of HBeAg clearance was significantly lower in patients with ALT of 1–2×ULN compared to patients with ALT >2×ULN (16.5% vs. 32.9%, *P*=0.001, Fig. 1B).

The indication for antiviral therapy in CHB patients with mild ALT elevation remains in debate.[2-5] Consistent with the results by Hsu et al.[1], our results confirmed that CHB patients with ALT of 1–2×ULN could achieve similar virological response and biochemical response compared to patients with ALT >2×ULN. However, patients with ALT of 1–2×ULN had lower rate of HBeAg clearance compared to patients with ALT >2×ULN. The long-term treatment response and benefit of antiviral therapy for CHB patients with mild ALT elevation deserves further investigation.

Authors' contributions

Author Contributions: Dr. Rui Huang had full access to all

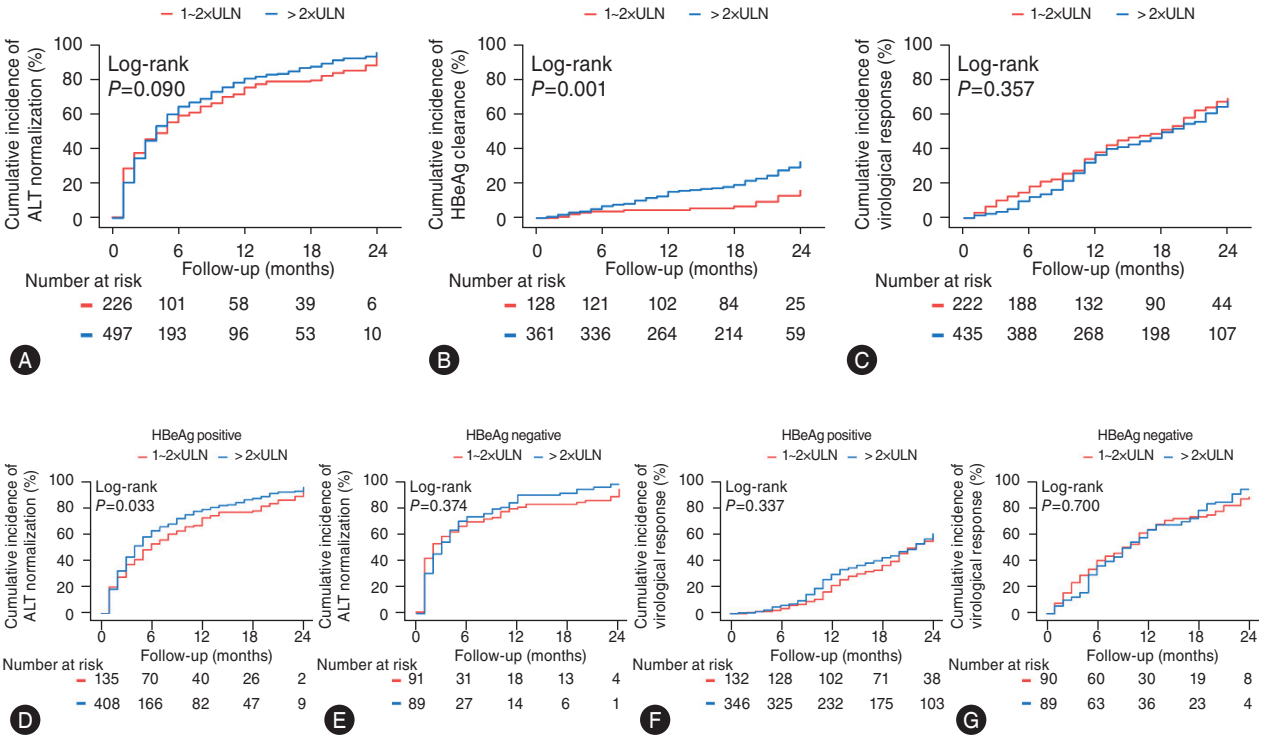

Figure 1. Cumulative incidence of ALT normalization, HBeAg clearance, and virological response between patients with ALT 1–2×ULN and ALT >2×ULN. ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; ULN, upper limit of normal.

Abbreviations:

ALT, alanine aminotransferase; CHB, chronic hepatitis B; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; NAs, nucleos(t)ide analogs; ULN, upper limit of normal

of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Rui Huang, Jian Wang, Chao Wu. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Jian Wang, Rui Huang. Critical review of the manuscript for important intellectual content: Rui Huang. Statistical analysis: Jian Wang, Fei Cao. Administrative, technical, or material support: Jian Wang, Fei Cao, Chuanwu Zhu. Supervision: Rui Huang.

Acknowledgements

This work was supported by grants of Clinical Trials from the Affiliated Drum Tower Hospital, Medical School of Nanjing University (No. 2022-LCYJ-MS-07 and 2021-LCYJ-PY-43).

Conflicts of Interest

The authors have no conflicts to disclose.

SUPPLEMENTARY MATERIAL

Supplementary material is available at Clinical and Molecular Hepatology website (http://www.e-cmh.org).

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