

Long-Term Safety of Fetal Exposure to Tenofovir in Infants from Hepatitis B Mothers

Prof. Calvin Q. Pan¹, Zhongping Duan², Dr. Er Hei Dai³, Dr. Guo-Rong Han⁴, Dr. Shu Qing Zhang⁵, Dr. Yuming Wang⁶, Dr. Huai Hong Zhang⁷, Dr. Bao Shen Zhu⁸, Dr. Suwen Li⁸, Dr. Hong-Xiu Jiang⁴, Dr. Yi Ding⁴, Dr. Wen Jing Zhao⁹, Shi Lian Li¹⁰, Xiao Hu Zhang⁷ and Dr. Huai Bin Zou², (1)Division of Gastroenterology and Hepatology, New York University Langone Health, (2)Artificial Liver Center, Beijing Youan Hospital, (3)The Fifth Hospital of Shijiazhuang, (4)Department of Gynecology and Obstetrics, The Second Affiliated Hospital of the Southeast University, (5)Department of Artificial Liver, Hepatobiliary Disease Hospital of Ji Lin Province, (6)Institute for Infectious Diseases, Southwest Hospital, Army Medical University, (7)Department of Medicine, Nanyang Center Hospital, (8)Department of Gynecology and Obstetrics, The Fifth Hospital of Shijiazhuang, (9)Central Laboratory, Hepatobiliary Disease Hospital of Ji Lin Province, (10)Institute for Infectious Diseases, Southwest Hospital

Abstract Text

Background:

Randomized-trial data on the long-term effects on infants' physical growth and neurodevelopment of the use of tenofovir disoproxil fumarate (TDF) in chronic hepatitis B (CHB) mothers are lacking.

Methods:

All 180 infants who completed the IN-US174-0174 study were offered participation in a long-term follow-up (LTFU) study.¹ They were from CHB mothers who were randomly assigned (1:1 ratio) to receive usual care without antiviral therapy or to receive TDF from 30 to 32 weeks of gestation until postpartum week 4. For the LTFU study, infants were assessed at the ages of 72, 120 and 192 weeks for growth and neurodevelopment with Bayley-III measurement. Their bone mineral density (BMD) was measured at week 192. The neurodevelopmental delay was defined by cognitive and language composite scores <85 (1 SD below the mean of 100).² These parameters were compared between the TDF-exposed and TDF-unexposed groups.

Results:

Among 180 infants completed in the initial study, 176 (98%) participated in the LTFU study and 144 (82%) completed the LTFU. In the TDF-exposed group, the mean (\pm SD) duration of fetal exposure to TDF was 8.57 ± 0.53 weeks. The gestational age, delivery mode, weight, height, and Apgar score at birth were similar in the two groups. At week 192, there was no significant difference in the pre-specified outcomes between groups including head circumference, height, BMD, cognitive, social-emotional, and adaptive behavior measurements between groups. There was no neurodevelopmental delay in the cohort. In the TDF-exposed group, children had significantly higher motor-composite scores (146.46 ± 6.39 vs 142.88 ± 9.54 ; $p=0.009$) and boys had significantly lower mean body weight (18.48 ± 2.35 kg vs 19.84 ± 3.46 kg; $p=0.029$). However, the boys' mean body weight in the TDF-exposed group was significantly higher than that of the national Chinese reference value of 4-year-old boys (18.48 ± 2.35 kg vs 16.64 ± 1.89 ; $p=0.010$).³

Conclusion:

Among infants with fetal exposure to TDF, the physical growth, BMD, and neurodevelopment were similar to those without the exposure and within the normal range of Chinese reference values during 192-week follow-up. Our data support the safety of using TDF during the third trimester in mothers with CHB.

Acknowledgment:

(Funded by Gilead Sciences; ClinicalTrials.gov number, NCT01488526.)

References:

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Table 1. Infants' Growth, BMD, and Bayley III Measurements at Week 192

| Variables Mean ± SD, or specified | Entire Cohort (n=145) | TDF-exposed infants (n=70) | TDF unexposed infants (n=75) | P-value |
|--------------------------------------|--------------------------|-------------------------------|---------------------------------|---------|
| Male - n (%) | 90 (62%) | 41 (59%) | 50 (67%) | |
| Weight, kg | | | | |
| - Boys, kg | 19.22 ± 3.06 | 18.48 ± 2.35 | 19.84 ± 3.46 | 0.029 |
| - Girls, kg | 17.36 ± 2.39 | 17.02 ± 2.59 | 17.75 ± 2.12 | 0.260 |
| Height, cm | | | | |
| - Boys, cm | 107.17 ± 4.63 | 106.56 ± 4.11 | 107.67 ± 5.00 | 0.249 |
| - Girls, cm | 105.09 ± 5.22 | 104.79 ± 6.34 | 105.30 ± 3.62 | 0.716 |
| Head circumference, cm | | | | |
| - Boys, cm | 50.61 ± 1.38 | 50.66 ± 1.25 | 50.56 ± 1.48 | 0.765 |
| - Girls, cm | 50.00 ± 1.20 | 50.11 ± 1.40 | 49.88 ± 0.98 | 0.523 |
| BMD z-scores | 1.36 ± 2.57 | 1.37 ± 2.59 | 1.36 ± 2.58 | 0.968 |
| Cognitive-composite | 142.86±6.31 | 143.50±4.29 | 142.27±7.72 | 0.233 |
| Language-composite | 130.72±8.89 | 131.97±7.51 | 129.55±9.91 | 0.098 |
| - Receptive subscale | 17.30±1.77 | 17.57±1.52 | 17.05±1.95 | 0.076 |
| - Expressive subscale | 13.19±1.61 | 13.36±1.40 | 13.03±1.77 | 0.214 |
| Motor-composite | 144.61±8.34 | 146.46±6.39 | 142.88±9.54 | 0.009 |
| - Fine motor-subscale | 17.66±1.66 | 18.01±1.54 | 17.33±1.70 | 0.012 |
| - Gross motor-subscale | 17.14±2.01 | 17.31±1.85 | 16.99±2.14 | 0.325 |
| Social-emotional composite | 126.99±8.76 | 127.57±8.92 | 126.45±8.64 | 0.445 |
| General adaptive composite | 130.79±8.64 | 132.21±8.13 | 129.45±8.94 | 0.053 |

TDF: tenofovir disoproxil fumarate; BMD: bone mineral density.

Disclosures

Calvin Q. Pan – Gilead: Consulting; Gilead: Grant/Research Support; Gilead: Speaking and Teaching; Abbvie: Speaking and Teaching; Intercept: Speaking and Teaching; Bayer: Consulting

The following people have nothing to disclose: Zhongping Duan, Guo-Rong Han

Disclosure information not available at the time of publication: Er Hei Dai, Shu Qing Zhang, Yuming Wang, Huai Hong Zhang, Bao Shen Zhu, Suwen Li, Hong-Xiu Jiang, Yi Ding, Wen Jing Zhao, Shi Lian Li, Xiao Hu Zhang, Huai Bin Zou