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Kenneth E. Sherman, MD, PhD
University of Cincinnati
College of Medicine
231 Albert Sabin Way
Cincinnati, Ohio 45267-0595
Kenneth.sherman@uc.edu

#1248
Relationship Between ALT and New HBV Biomarkers in HBV/HIV Coinfected Persons Started on Antiviral Therapy

KE Sherman[1], SD Rouster[1], JT Blackard[1], PS Horn[2], MG Peters[3], M Anderson[4], M Stec[4], GA Cloherty[4]

[1]University of Cincinnati College of Medicine, Cincinnati, OH; [2]Department of Pediatrics, Cincinnati Children's Medical Center, Cincinnati, OH;
[3]Department of Medicine, University of California San Francisco, San Francisco, CA; [4]Abbott Diagnostics, Abbott Park, IL

Background

- While HBV DNA has served as a primary biomarker of HBV infection, newer biomarkers including pre-genomic HBV RNA (pgRNA) and quantitative HBV surface antigen (qHBsAg) may prognosticate treatment responses better.
- We analyzed the changes in these biomarkers over time following initiation of antiviral therapy in persons living with HIV (PLWH) to determine the relationship to ALT, a key marker of liver injury.
- HBV pre-genomic RNA (pgRNA) represents active transcription from the cccDNA minichromosome within infected hepatocytes.
- Despite recent interest in HBV pgRNA as a prognostic and therapeutic biomarker, there are few studies describing its kinetics in persons living with HIV (PLWH) who are HBV coinfected.

Methods - Subjects

- NIH AIDS Clinical Trials Group Study 5127 enrolled HBV/HIV coinfected PLWH into a Phase 2 treatment trial.
- Subjects were randomized to receive 48 weeks of either tenofovir (TDF) or adefovir (ADV).
- Participants were followed for 48 weeks after treatment initiation.
- Serum samples were collected and stored at each study visit.
- ALT and HBV DNA clinical lab values were available as measures of treatment response.

Methods - Lab assays

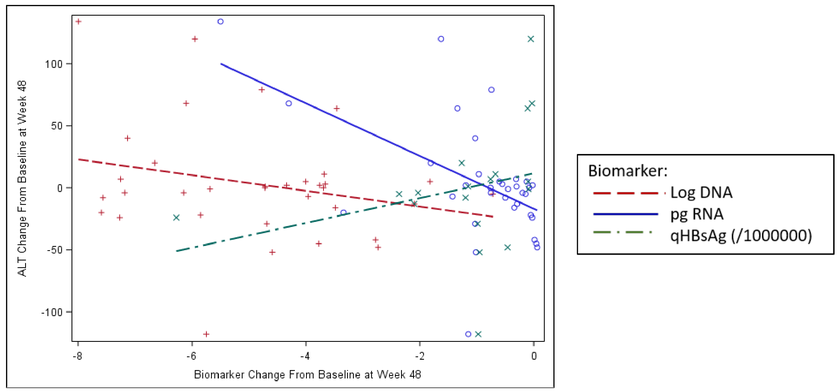
- Stored samples were tested for HBV pgRNA and qHBsAg at baseline, 4, 12, 24, 36, and 48 weeks.
- HBV pgRNA was isolated using RNA-selective extraction chemistry followed by a multiplex RT-qPCR that targets the HBV X and core proteins on the m2000 system (Abbott Molecular, Des Plaines, Illinois).
- A sensitive second-generation HBV pgRNA assay with a lower limit of quantification (LLOQ) of 10 copies/mL was utilized.
- Quantitative HBsAg was determined by Abbott ARCHITECT (List# 6C36) with a LLOQ of 0.05 IU/mL.
- Data were analyzed using SAS® version 9.4.

Results

SUBJECTS, n	47
GENDER	
Male, %	93.6
Female, %	6.4
RACE	
White, non-Hispanic, %	55.3
Black, non-Hispanic, %	34.0
Hispanic (regardless of race), %	8.5
American Indian, Alaskan Native, %	2.1
Baseline ALT, U/L, mean	64.9
Baseline HBV DNA, copies/mL, mean	9.1
Baseline HBV pgRNA, log U/mL, mean	7.0
Baseline qHBsAg, IU/mL, mean	195,574.0
Baseline positive HBeAg, %	79

Results

- 47 study participants had sufficient samples for biomarker testing.
- Groups were evenly randomized to receive either TDF (n=23) or ADV (n=24).
- Over the course of treatment, pgRNA changes from baseline were significantly correlated with the change in serum ALT levels (r=0.48; p=0.004) but not with HBV DNA (r=0.21; p=0.226). (Figure)
- Change in ALT from baseline was negatively correlated with qHBsAg change (r=-0.52; p=0.023).
- pgRNA change from baseline was also highly negatively correlated with change in qHBsAg (r=-0.491; p=0.034) but not with change in HBV DNA (r=0.132; p=0.591).



Conclusions

- HBV pgRNA is a better predictor of ALT change – a key measure of hepatocyte injury – than HBV DNA in PLWH who are initiated on nucleotide/nucleoside therapy.
- Quantitative HBsAg is inversely associated with ALT levels, supporting the hypothesis that HBsAg inhibits immune mediated injury to hepatocytes.

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Disclosures

All authors have no relevant disclosures.

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