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Abstract 805

Serum HBV DNA, Pregenomic RNA, HBsAg, HBcrAg, and ALT kinetic characterization during 24-week tenofovir disoproxil fumarate monotherapy

Leeor Hershkovich[1*], Louis Shekhtman[1,2*], Michel Bazinet[3], Mark Anderson[4], Jeff Gersch[4], Vera Holzmayer[4], Mary Kuhns[4], Gavin Cloherty[4], Scott J. Cotler[1], Andrew Vaillant[3], Harel Dahari[1]

[1]Program for Experimental & Theoretical Modeling, Division of Hepatology, Department of Medicine, Stritch School of Medicine, Loyola University Chicago, Maywood, IL, USA; [2]Network Science Institute, Northeastern, University, Boston, MA, USA; [3]Replicor Inc., 6100 Royalmount Ave., Montreal, Quebec, H4P 2R2, Canada; [4]Abbott Diagnostics, Abbot Park, IL, USA. *Equally contributed,

INTRODUCTION

- Serum HBV pregenomic RNA (pgRNA), and HBV core-related antigen (HBcrAg) were suggested markers of cccDNA activity[1,2].
- Little is known about the relationship among serum HBV DNA (sDNA), pgRNA, HBcrAg, and alanine aminotransferase (ALT) during tenofovir disoproxil fumarate (TDF) therapy.
- The aim of this analysis was to characterize sDNA, pgRNA, HBcrAg, and ALT during 24-week TDF monotherapy in the REP 401 study[2].

METHODS

- 40 participants with HBeAg negative chronic HBV in the REP 401 study [2] received 24 weeks of TDF monotherapy.
- Serum Samples were analyzed for sDNA (Abbott Realtime, LLoQ 10 IU/mL) at baseline and 10, 18, and 24 weeks after start of treatment.
- Abbot RUO assay for pgRNA (LLoQ 1.65 log10 copies/mL) and Fujirebio HBcrAg (LLoQ 3 log10 U/mL) were used at baseline and at the end of TDF monotherapy.

sDNA kinetic patterns

- Distinctions between kinetic phases in sDNA were defined as a 2-fold change in slope.
- A monophasic response was defined as a single-phase decline.
- A flat partial response (FPR) was defined as a 1st phase of decline followed by a plateau.
- A biphasic response was defined as a rapid 1st phase decline followed by a 2nd slower phase of decline.
- Two patients who had undetectable sDNA at week 10 were excluded from analysis.

RESULTS

- Six participants had monophasic sDNA declines.
- Twenty participants had biphasic sDNA declines.
- Twelve participants had a FPR.
- The mean rapid 1st phase of sDNA decline slope across all 38 patients was 0.345 ± 0.082 log IU/wk and was not correlated with baseline ALT (R=0.06, p =0.76).
- In the biphasic group, the mean 2nd phase sDNA decline slope was 0.90 ± 0.085 log IU/wk and was positively correlated with baseline ALT levels (**Figure 1**).
- At the end of TDF monotherapy, 6 of the 40 patients reached undetectable values of HBV DNA.
- Overall declines in pgRNA (R=0.62, p=1e-5) and HBcrAg (R=0.71, p=1e-7) were significantly correlated with baseline ALT (**Figure 2**).
- HBcrAg had a significantly (p=0.03) higher decline in the biphasic group compared to the FPR group (Figure 3).
- No significant differences were observed in overall declines in HBcrAg and pgRNA between monophasic and biphasic groups (**Figure 3**).

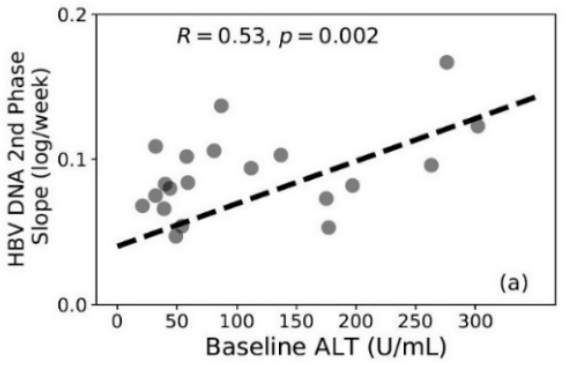

Figure 1: Correlation between 2nd phase sDNA decline and baseline ALT level for participants experiencing a biphasic sDNA decline.

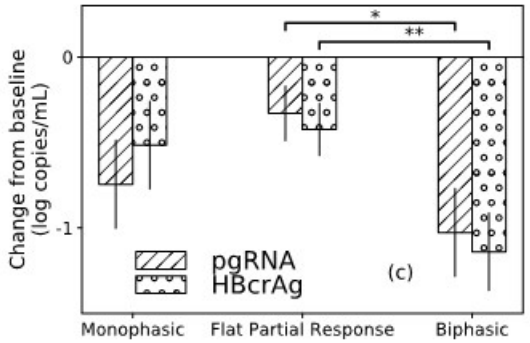

Figure 2: Correlation between baseline ALT level and pgRNA and HBcrAg decline after 24 weeks of TDF monotherapy.

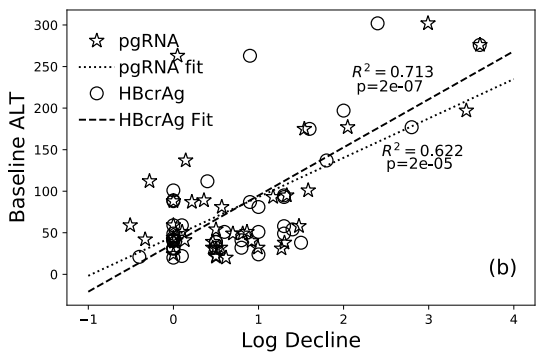

Figure 3: Change from baseline levels in pgRNA and HBcrAg after 24 weeks of TDF monotherapy, grouped by sDNA response pattern. Error bars represent standard error. *,p=0.06, **,p=0.03.

CONCLUSIONS

- **Rate of turnover of infected hepatocytes, as indicated by baseline ALT, is associated with a decline in markers of cccDNA activity during TDF monotherapy.**
- **More detailed kinetic studies are needed to examine the HBV-host dynamics during TDF monotherapy.**

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CONTACT

Harel Dahari: hdahari@luc.edu
Andrew Vaillant: availlant@replicor.com