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Abstract 840

Rapid monophasic HBsAg decline during NAP-based therapy predicts functional cure

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INTRODUCTION

- Combination therapies using nucleic acid polymers (NAPs) show promise in treating HBV[1].
- To better understand these treatments and their mode of action, we explore the interplay among HBsAg, anti-HBs, and ALT during combination therapy with REP 2139-Mg or REP 2165-Mg, pegylated interferon alpha-2a (pegIFN) and tenofovir disoproxil fumarate (TDF) in the REP 401 study[2].

METHODS

- Participants with HBeAg negative chronic HBV infections in the REP 401 study [2] received 48 weeks of triple combination therapy with NAPs, pegIFN and TDF.
- In the experimental group (n=20), triple therapy followed 24 weeks of TDF monotherapy (Figure 1)
- In the control group (n=20), introduction of triple therapy was delayed until completion 24 weeks of TDF monotherapy and 24 weeks of TDF + pegIFN dual therapy (**Fig. 1**)
- Outcomes at end of therapy were based on 48 weeks of follow-up.
- Serum HBsAg (Abbot Architect) and anti-HBs (Abbot Architect were measured every two weeks, and serum ALT was measured weekly.

Analysis Methodology

- HBV DNA kinetics were not analyzed since it was <2.1 log IU/mL in 39/40 participants after TDF monotherapy and remained low/undetectable throughout triple therapy.
- Distinctions between kinetic phases in HBsAg were defined as a 2-fold change in slope
- Participants with HBsAg reduction < 1 log IU/mL from baseline at end of treatment (EOT) were defined as non-responders (NR).

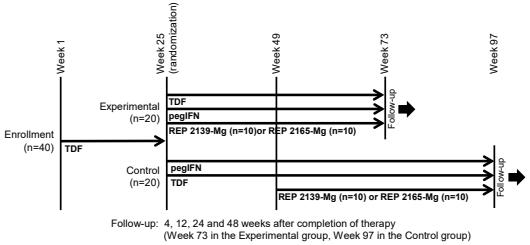

Figure 1: Design of the REP 401 study[2].

RESULTS

Three HBsAg kinetic patterns were identified in both immediate and delayed groups (Fig. 2)

- non-responders (n=4 and n=3),
- monophasic (n=12, n=12), and
- biphasic decline (n=4, n=5), ~~respectively~~

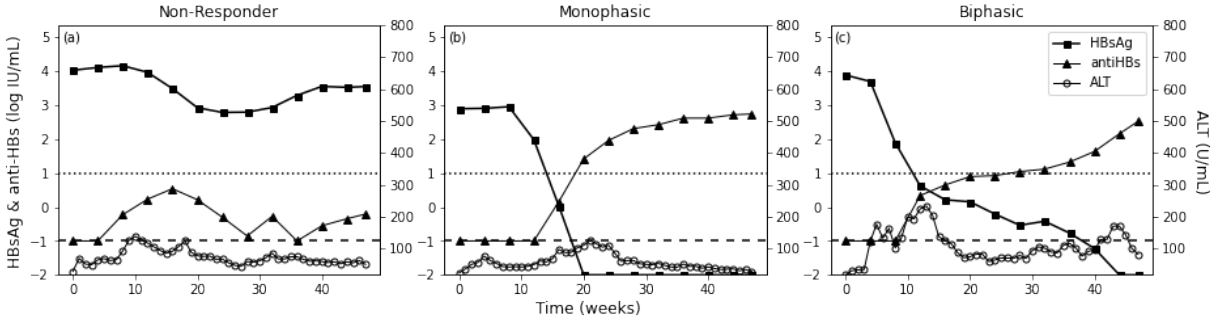

Figure 2: Representative figures for the three identified HBsAg kinetic patterns. Dotted line represents anti-HBs seroconversion. Dashed line represents HBsAg lower limit of quantification.

Outcome of NAP-based therapy (Fig. 3)

- Fourteen (35%) participants achieved functional cure, FC (HBV DNA target not detected, HBsAg < LLoQ, normal ALT)
- Fifteen (38%) participants achieved partial cure (HBV DNA < 2000 IU/mL, normal ALT)
- Eleven (28%) participants experienced a viral rebound (VR)

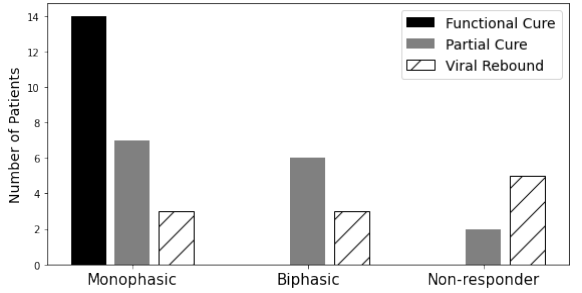

Figure 3: The distribution of therapy outcomes for each HBsAg kinetic pattern.

Monophasic HBsAg kinetic pattern was associated with FC (Fig. 4)

- Monophasic kinetic pattern had a 67% positive predictive value of FC.
- 100% of participants with FC had a monophasic kinetic pattern (negative predictive value, NPV).
- Monophasic participants with FC had shorter (p=0.007) mean time to HBsAg LLoQ (18±7 wk) compared to monophasic non-FC (30±11 wk)

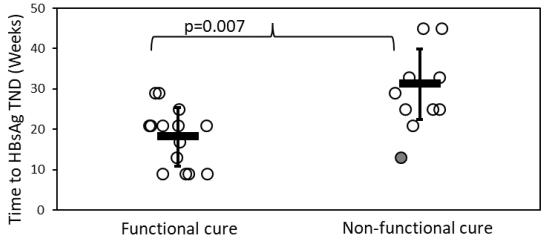

Figure 4: Time to HBsAg TND for FC and non-FC participants with monophasic HBsAg decline. The shaded circle represents a participant who did not complete triple therapy.

CONCLUSIONS

- **Rapid monophasic HBsAg decline may predict functional cure with NAP-based therapy.**
- **Non-monophasic HBsAg kinetic pattern was associated with 100% NPV for achieving functional cure.**

REFERENCES

1. Vaillant, ACS Inf Dis. 2019; 5: 675-687
2. Bazinet et al., Gastro 2020; 158:2180-94

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