OCTOBER 11-12, 2024 MILAN, ITALY
DeltaCure 3rd International Meeting
P18
Poster for you

HDV RNA assay sensitivity is critical for determining a correct outcome during Bulevirtide antiviral therapy

Carey I, Anderson M, Cargill Z, Shah S, Lok J, Cloherty G, Dusheiko G & Agarwal K

Introduction

- Sensitive and pan-genotypic assays are critical for diagnosis and monitoring of response to antiviral therapy in patients with chronic hepatitis delta (HDV).
- Bulevirtide (BLV) mimics a pre-S1 HBsAg protein and blocks viral entry to hepatocytes.
- NICE (National Institute for Health and Clinical Excellence) recommends that therapy with BLV should be continued for as long it is associated with a clinical benefit (1). Currently there are no futility stopping rules written into HDV EASL guidelines, but accurate determination of on-treatment response would guide the field (2).
- Variability in RNA extraction methods, different primer/probe design for nucleic acid tests, lack of standardization across testing laboratories contribute to substantial variability in performance characteristics of research-based and commercial HDV RNA assays.

Study Design/ Aims

We aimed to compare the performance of our in-house real-time PCR assay (LLoQ 640 copies/ml = 677 IU/ml) (3) and a research use only assay – HDV RNA test mRealTime by Abbott Diagnostics (LLoQ 5 IU/ml) (4) in a cohort of patients receiving bulevirtide to determine their virological response.

Materials & Methods

- Blood samples were collected from 10 HBV/HDV co-infected patients treated with BLV (all HDV RNA positive at baseline, median age 48 years, males n=6, 90% compensated cirrhosis; 90% genotype 1 & 10% genotype 5).
- Plasma was collected at baseline, week 12 and week 24, and HDV RNA was measured by two methods: HDV RNA (Abbott Diagnostics research use only mRealTime assay (LLoQ =5 IU/ml) and in-house real-time PCR (LLoQ=640 copies/ml = 677 IU/ml).

The response to BLV was categorised as:

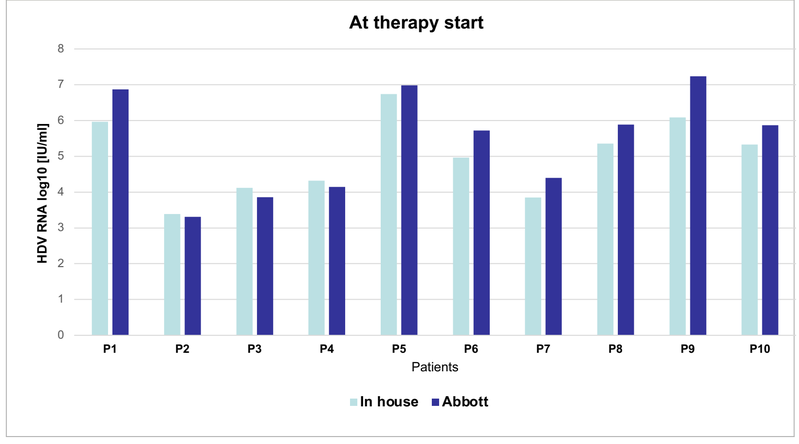
- **Responder (R)**: decline >2 log_{10}IU/ml,
- **Partial responder (PR)**: drop 1-2 log_{10}IU/ml
  Non-responder (NR): decline < 1 log_{10} IU/ml

  at week 12 and week 24 when compared to start of therapy

Results baseline

HDV RNA levels by the Abbott assay were slightly higher than the in-house assay (median: 5.43 log_{10} IU/ml vs. 4.72 log_{10} IU/ml, p=0.76) (**Figure 1**)

Figure 1 **Baseline HDV RNA levels by both assays**



Results therapy start vs. week12

HDV RNA declined significantly (p=0.025), but HDV RNA levels were higher in the Abbott assay (4.36 log_{10} IU/ml vs. 3.73 log_{10} IU/ml, p=0.86). (**Figure 2 & 3**)

Figure 2 **Week 12 HDV RNA levels by both assays**

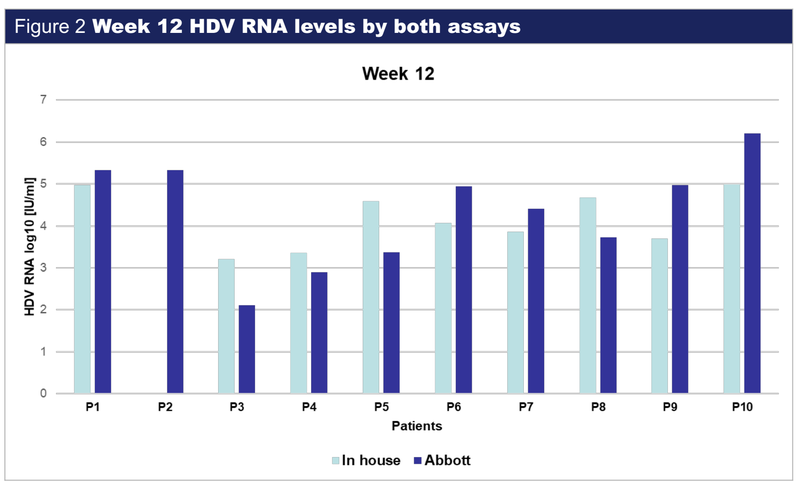
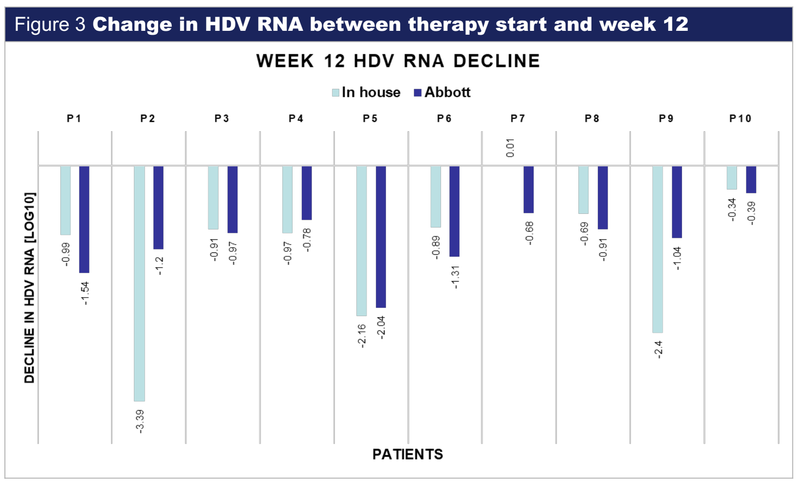


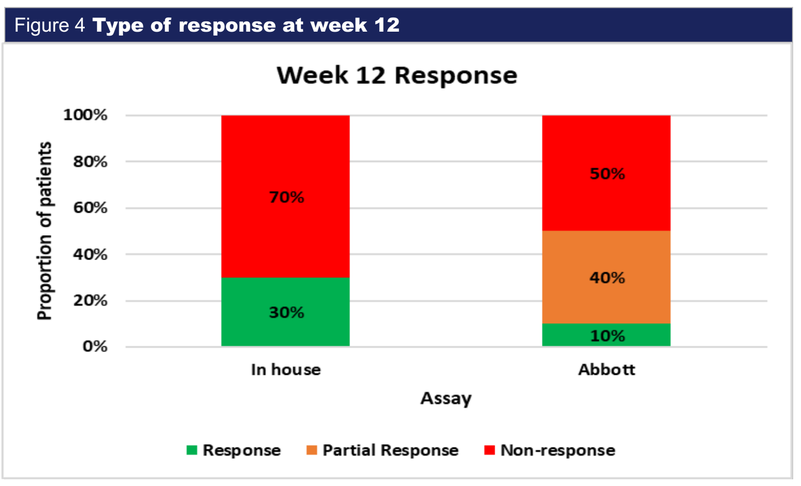
Figure 3 **Change in HDV RNA between therapy start and week 12**



Response at week 12

The categorisation of response varied between assays: while only 1 patient (10%) achieved a HDV RNA decline >2 log_{10} vs. 4 patients (40%) with PR (1-2 log_{10} decline) and 5 patients (50%) with a HDV RNA decline <1 log_{10} by the Abbott assay there were 3 (30%) responders and 7 (70%) non-responders by in-house assay (**Figure 4**)

Figure 4 **Type of response at week 12**



Results therapy start vs. Week 24

HDV RNA declined significantly (p=0.001) in both assays and again HDV RNA levels were higher in Abbott assay (3.6 log_{10} IU/ml vs. 3.29 log_{10} copies/ml, p=0.89) (**Figure 5 & 6**).

Figure 5 **Week 24 HDV RNA levels by both assays**

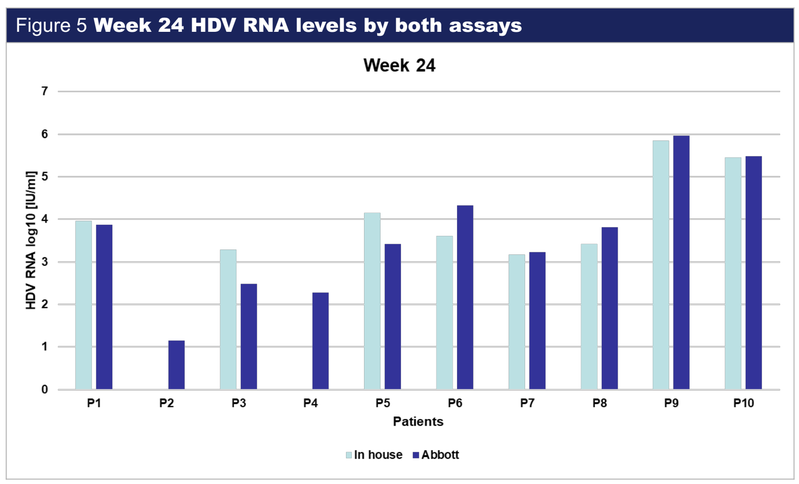
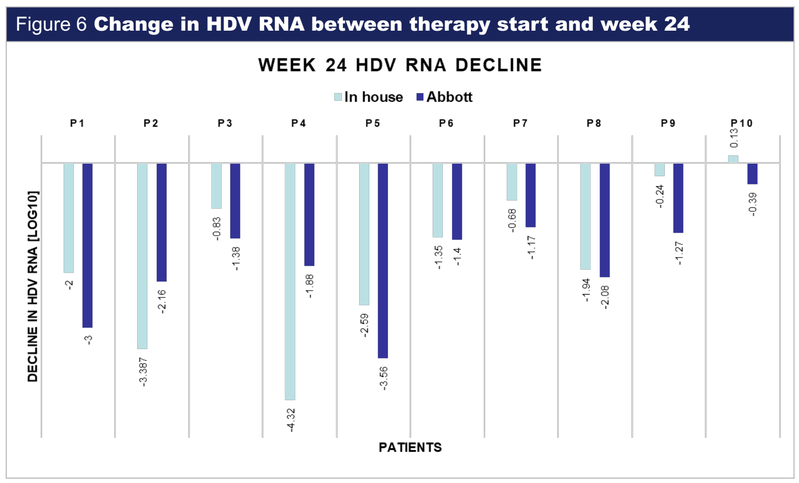


Figure 6 **Change in HDV RNA between therapy start and week 24**

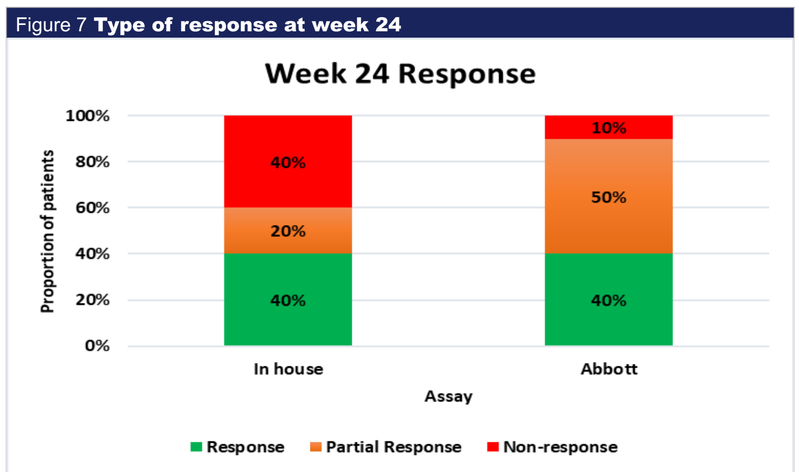


Response at week 24

The number of patients categorised as responders (>2 log_{10}) were similar by both assays – 4 (40%) responders by Abbott assay and in-house assay. In the Abbott assay there were 5 (50%) PR and 1 NR vs only 2 (20%) partial responders and 4 (40%) non-responders determined by in-house assay (**Figure 7**)

Two patients had undetectable HDV RNA by in-house assay, but were detected by Abbott assay.

Figure 7 **Type of response at week 24**



Conclusion

HDV RNA assays with high sensitivity and accuracy are critical for determining a correct outcome and management during Bulevirtide antiviral therapy.

Reference

1. NICE Guidance: Bulevirtide for treating chronic hepatitis D. www.nice.org.uk/guidance/TA896
2. EASL Clinical Practice Guidelines on hepatitis delta virus. J Hepatol 2023
3. Shah D et al J of Virological Methods 2012
4. Coller KE et al Scientific Reports 2018