

# Investigation into the clinical utility of HBsAg quantitation.



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## Introduction

Viral Hepatitis B (HBV) is a major health issue which can cause acute and chronic infection.

Chronic (CHB) status is gained if Hepatitis B surface antigen (HBsAg) is detectable for longer than six months following acute infection.

Four phases of CHB are widely recognised (Vasamakias, 2007), these include: Immune tolerance, Immune active, Immune control, Immune clearance. Patients can either be e antigen positive (HbeAg+) or e antigen negative (HbeAg-) which is a marker of infectability.

Two groups of antiviral interventions are offered to help control CHB, these include:

- Nucleoside analogues (NAs) - Entecavir (ETV), Tenofovir alafenamide (TAF) and Tenofovir disoproxil fumarate (TDF)
- Pegylated interferon alfa (PegFN)

HBV Viral load is a marker of viral replication which is often used to help identify the phase of infection, patients who would benefit from antiviral intervention, monitoring and when these should be stopped.

Quantitation of HBsAg is often analysed alongside HBV VL and has been proposed to be used as a surrogate marker to HBV VL, however, this remains unclear (Yang *et al.* 2018).

Suppression of HBV VL is possible in those taking PegFN therefore HBsAg may be the only viable quantitative marker available to assess carrier status, disease progression and treatment response.

## Aims

Currently, QHBsAg testing is offered externally with an TATT of 8 days. The aims of this study were to verify the Murex HBsAg Quant assay on the Liaison XL for diagnostic use, using the Liaison XL analyser and to assess the utility of QHBsAg.

## Methods: Verification

Multiple characteristics were measured to ensure the assay was fit for purpose and produced reliable results.

- WHO working standard for HBsAg (0.2IU/mL) was ran in triplicate on multiple days to assess precision (%CV)
- 3 specimens of known value, one of high medium and low value were analysed multiple times, on the same runs with the Replicates analysed on different days.
- to assess Repeatability and analytical accuracy (%CV)
- A set of dilutions (Neat- 1:10000) of WHO 3<sup>rd</sup> international standard (47.5IU/mL) was ran in triplicate on multiple days to assess analytical sensitivity and linearity.
- Controls containing other serological targets were ran to assess Analytical specificity.
- 35 previously tested QHBsAg positive patients and 32 HBsAg negative patients were analysed to assess the diagnostic sensitivity and specificity (%)

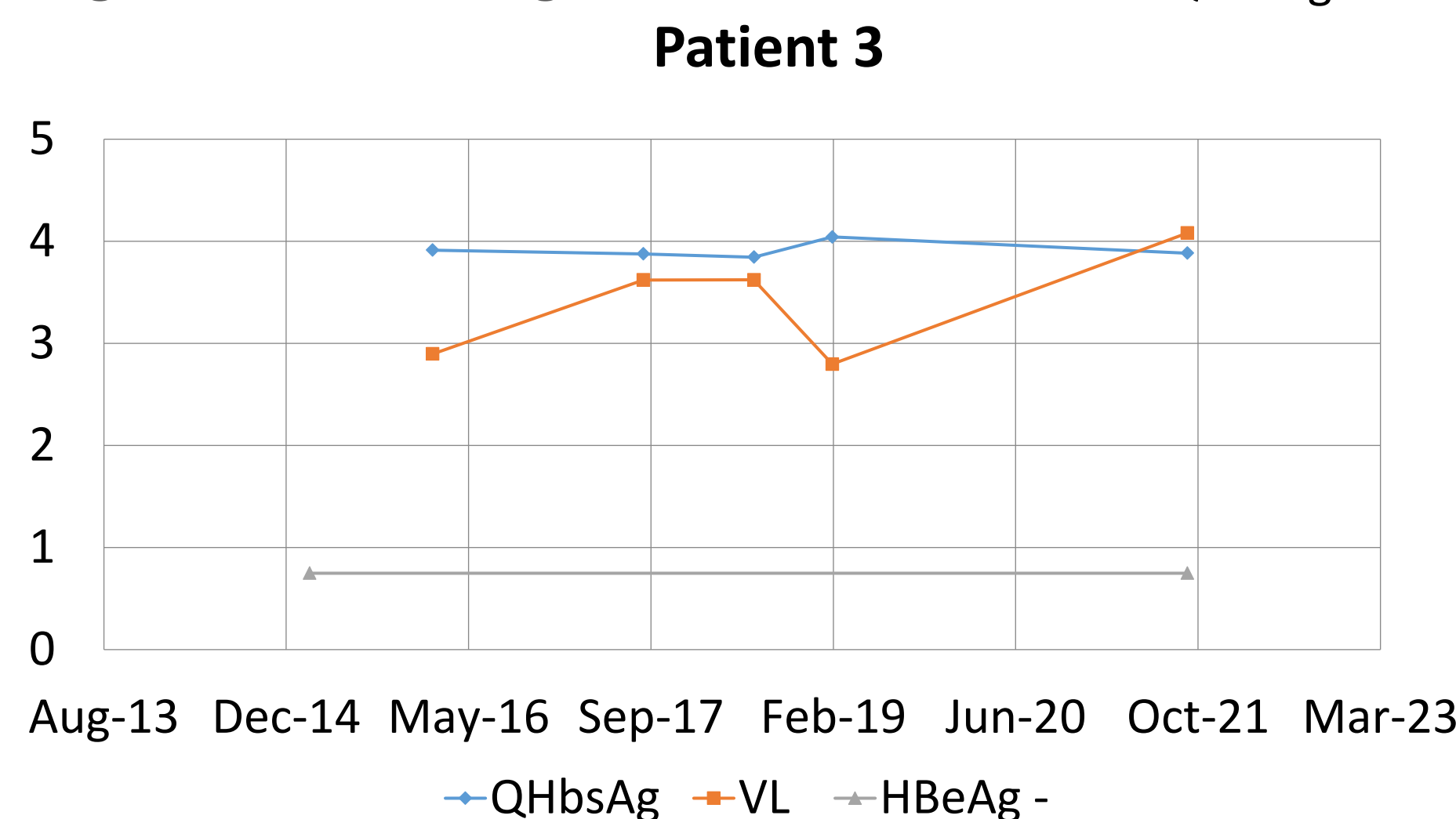
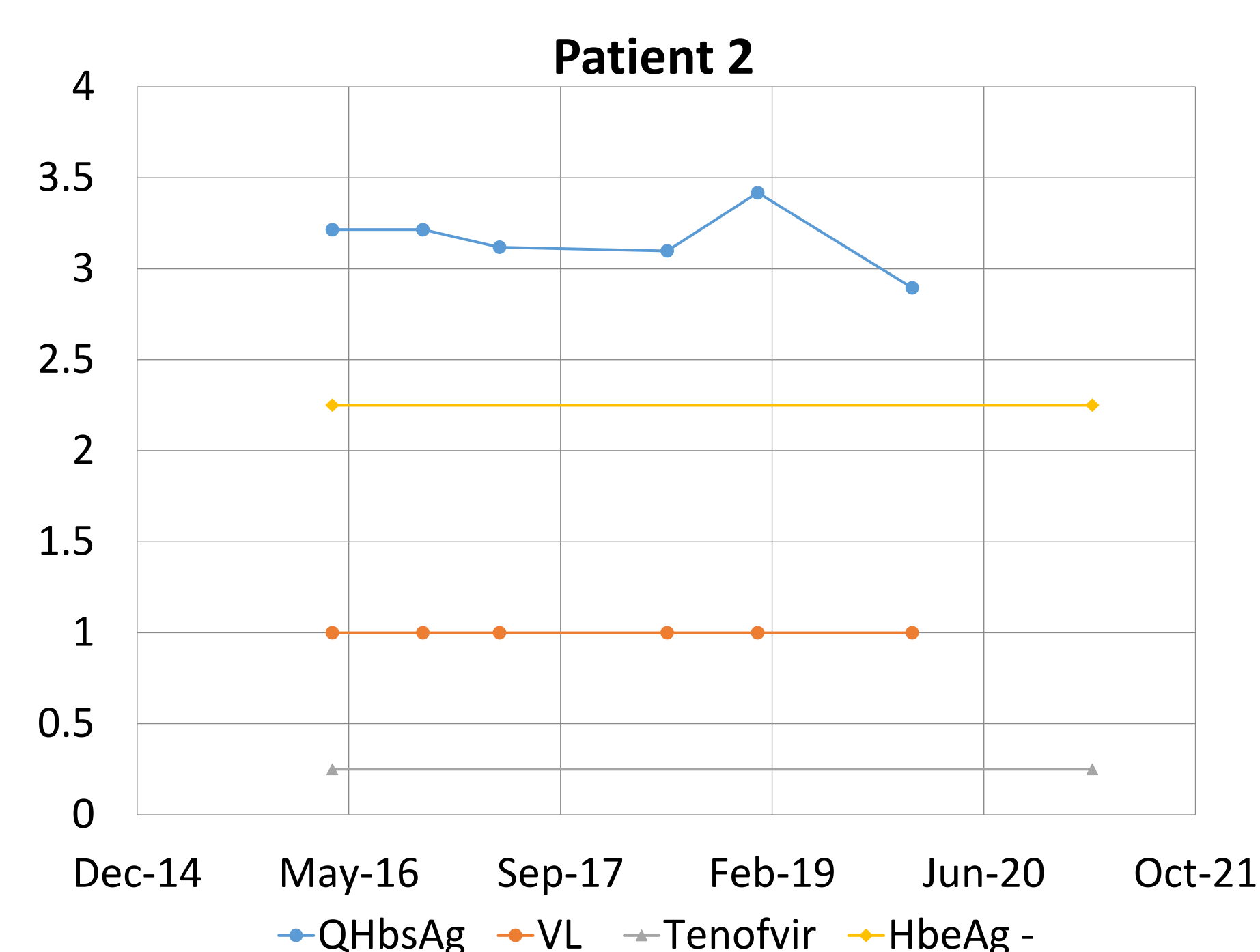
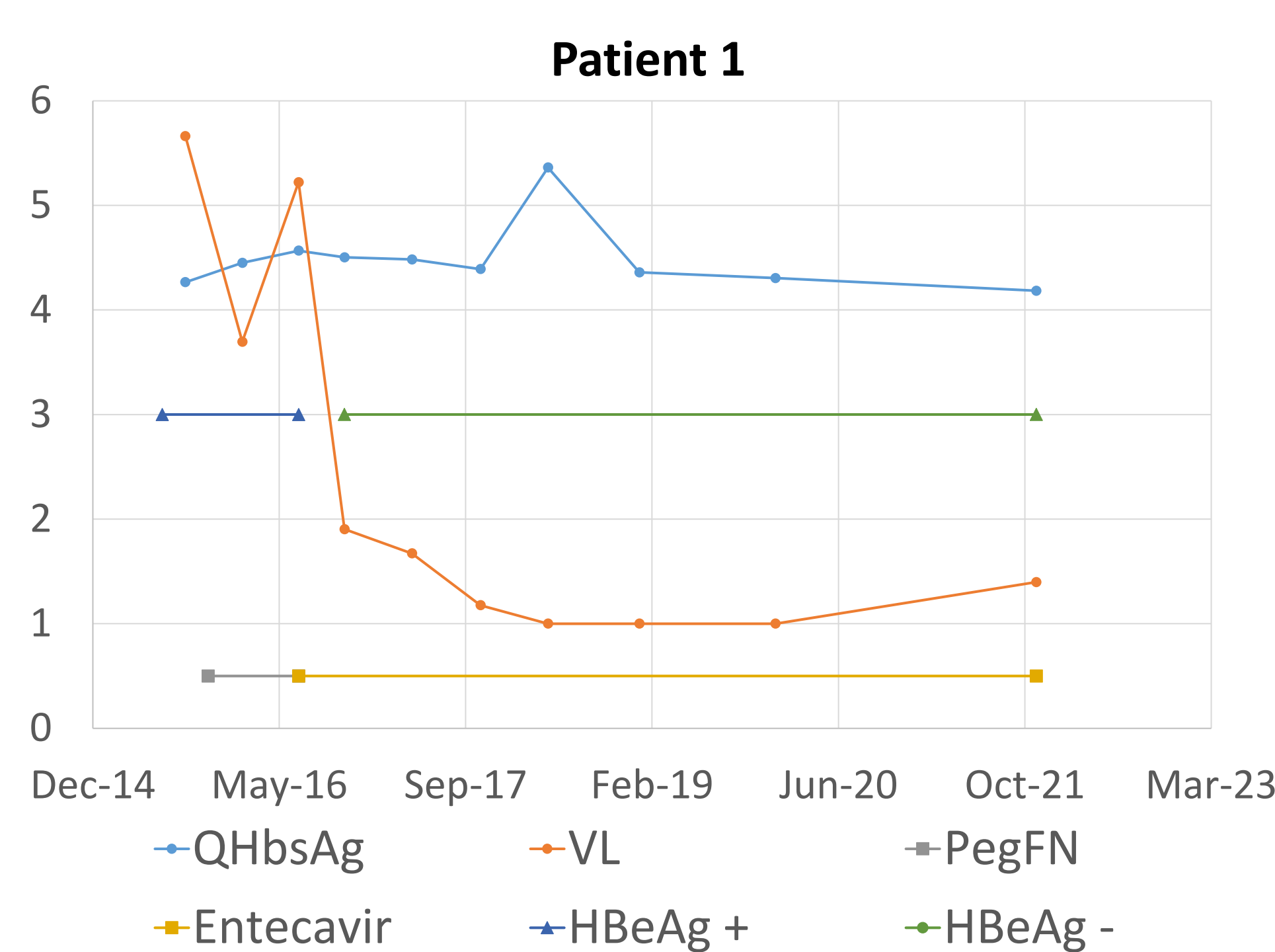
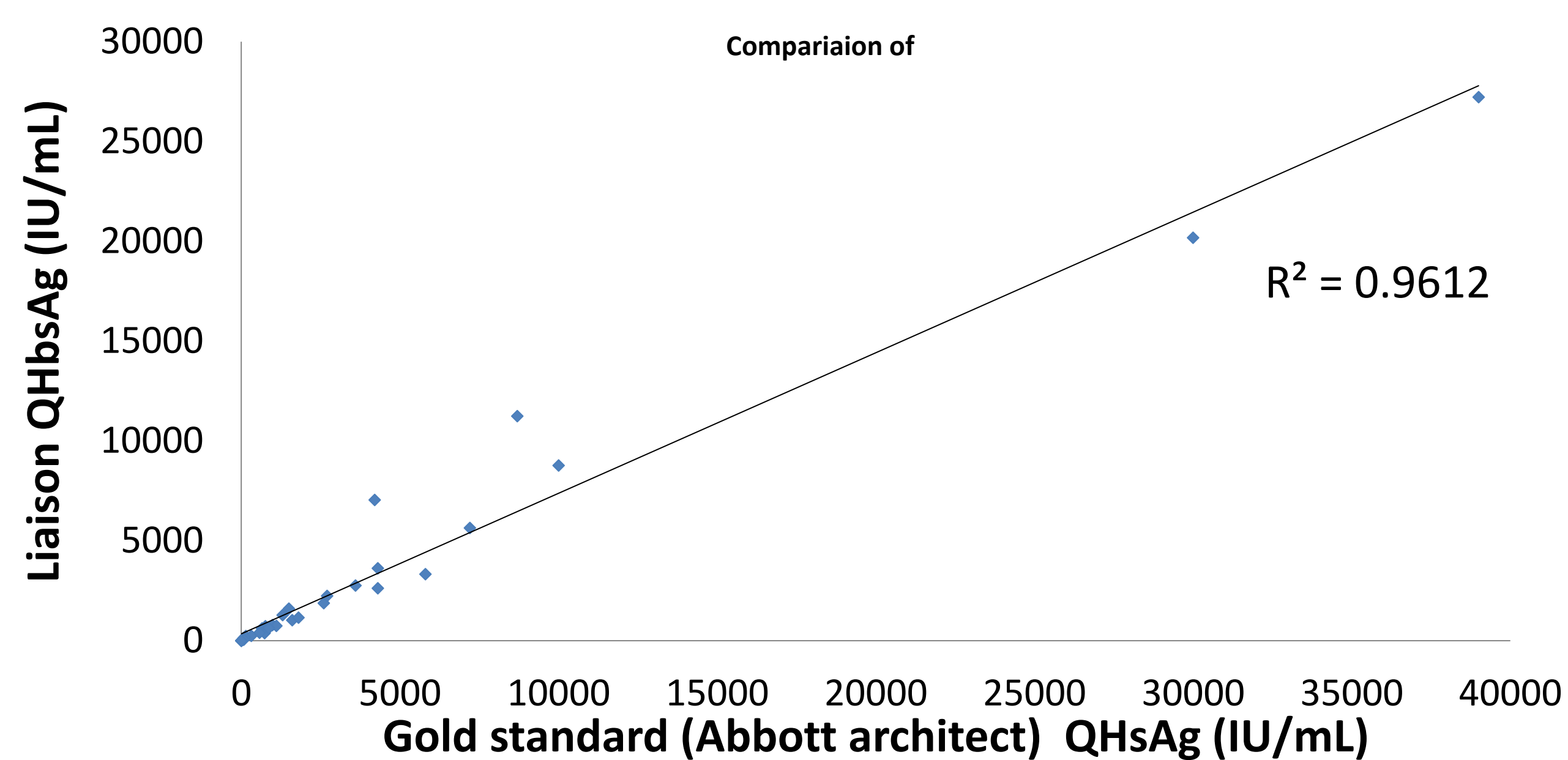
## Method: Clinical utility

3 patients who had received multiple QHBsAg and viral load results were used assess clinical utility. 2 patients are receiving antiviral treatment, whilst 1 is not on treatment.

VL is tested in house with the analytical sensitivity of 10IU/mL therefore levels that are below this threshold are deemed undetectable

## Results

Characteristic	Result
Precision	7(%CV)
Repeatability/accuracy	Very good
Analytical sensitivity	<0.03IU/mL
Analytical specificity	100%
Diagnostic sensitivity and specificity	100%
Measurement range	<0.03-150IU/mL



## Discussion

The Liaison XL demonstrates a sensitivity and specificity of 100% respectively and shows good levels of repeatability and precision. The measurement range is < 0.03 – 150IU/mL, a figure reported by the assay manufacturer.(Diasorin, 2018)

A high level of correlation and agreement has been demonstrated between the Liaison XL and Abbott Architect (R2 = 0.96). Therefore, it can be concluded that the assay is fit for purpose. Though insignificant, this study demonstrates a higher HBsAg level is obtained by the Liaison XL, an opposite observation was made by Wilkinson *et al.* (2016)

Patient 1 and 2 illustrated a slow decline in QHBsAg levels. Both patients are on classes of NA's which aim to suppress the replication of HBV but does not have a direct effect on cccDNA, which QHBsAg is a measurement of therefore a slow decline is expected.

Readings obtained for patient 3 suggests the patient is a candidate for antiviral therapy.. Biochemical markers are also utilised to help with clinical decisions, with treatments not routinely offered to those who do not have clinical evidence of cirrhosis or has an aspartate aminotransferase to platelet ratio index score <2 (Terrault *et al.* 2018) which could explain why patient 3 was not offered treatment.

## Conclusion

The QHBsAg assay on the liaison XL can be offered for diagnostic use. QHBsAg levels can be influenced by treatment and are present, even when the VL are undetectable therefore be used as an additional marker to assess treatment durability though other markers also considered to aide clinical decisions.

## References

- Diasorin. (2018). LIAISON® XL HBsAg Quant ([REF] 310250) package insert. [HBsAg Quant version 6 2018-05.pdf](#). (Last accessed 05.05.22)
- Valsamakias A. (2007). Molecular testing in the diagnosis and management of chronic hepatitis B. *Clinical microbiology reviews*, 20(3), 426–439.
- Terrault, NA. *et al.* (2018). Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* (Baltimore, Md.), 67(4), 1560–1599.
- Wilkinson, DE. *et al.* (2016). International collaborative study on the 3<sup>rd</sup> WHO International Standard for hepatitis B surface antigen. *Journal of clinical virology: the official publication of the Pan American Society for Clinical Virology*, 82, 173–180.



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