Extended follow-up in the REP 301 and REP 401 studies demonstrates durable clinical benefit from NAP therapy

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Disclosures

Employee and shareholder, Replicor Inc.

Nucleic Acid Polymers (NAPs)

Target HBV SVP assembly from cccDNA or integrated HBV DNA
also target the envelopment of HDV RNP

Direct interaction with HDAg likely drives observed upstream antiviral activity against HDV

Current studies have demonstrated durable clinical outcomes in HBV and HDV:

REP 401 study in HBV mono-infection (1 year after therapy)

78% with immune control and normal liver function
39% HBV functional cure

REP 301 study in HBV / HDV coinfection (3.5 years after therapy)

64% (7/11) HDV RNA undetectable with normal liver function
4 with HBV functional cure, 3 with HBV partial cure

Shamur et al., Hepatol. 2017; 66: 504A
Bazinet et al., Lancet Gastroenterol Hepatol 2017; 2: 877-889
Bazinet et al., Hepatology Comm. 2020 5: 189-202
Bazinet et al., Gastroenterol. 2020; 158: 2180-2194
Boulon et al., Hepatol. 2021; 74: 512A
Bazinet et al., J Viral Hep 2021; 28: 817-825
Bazinet et al., Hepatol Comm 2021; 28: 817-825

Extended follow-up in the REP 301 and REP 401 studies

Patients from these studies still residing in the Republic of Moldova were recently reassessed to examine safety and clinical outcomes

Patients were assessed at the original trial sites (Toma Ciorbă Infectious Diseases Hospital, Chișinău, Republic of Moldova) between December 2022 – January 2023

For REP 401 study, visit dates constituted a mean of 5.3 (4.5-5.7) years of follow-up
For REP 301 study, visit dates constituted a mean of 7.4 (7.2-7.6) years of follow-up

Patient visits included general assessment, liver function tests, fibroscan, liver ultrasound and harvesting of frozen serum.

Frozen serum was assessed at the Institute of Virology, University Hospital Essen (Essen, Germany)

- **qHBsAg (Abbott Architect©)**
- **anti-HBs (Abbott Architect©)**
- **HBV DNA (Abbott *Realtime*©)**
- **HDV RNA (Robogene 2.0 using Instant Virus RNA/DNA extraction kit)**

REP 301 study patient availability

10/11 patients who completed therapy were available

1 patient (001-01) is working abroad in Italy

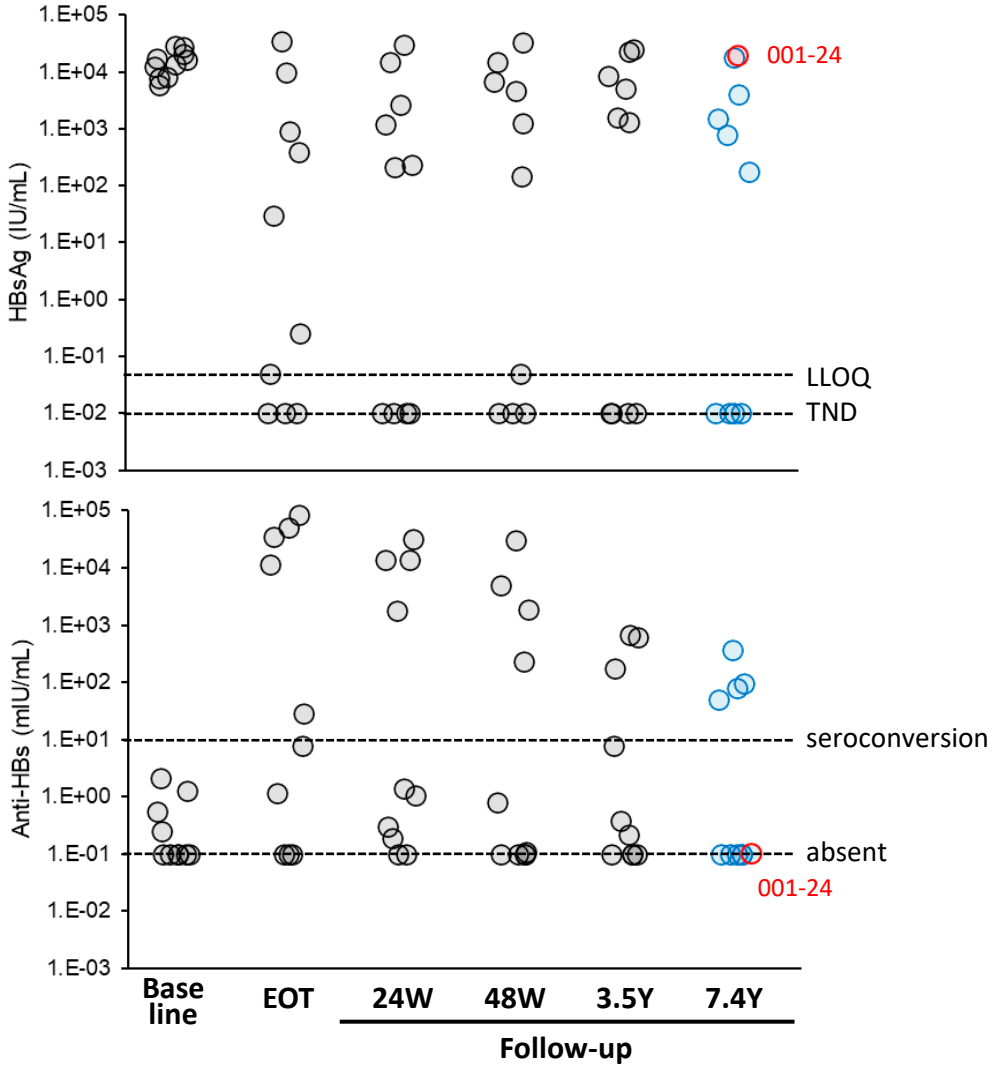
Functional cure of HDV (undetectable HDV RNA) and HBV at 3.5 years follow-up

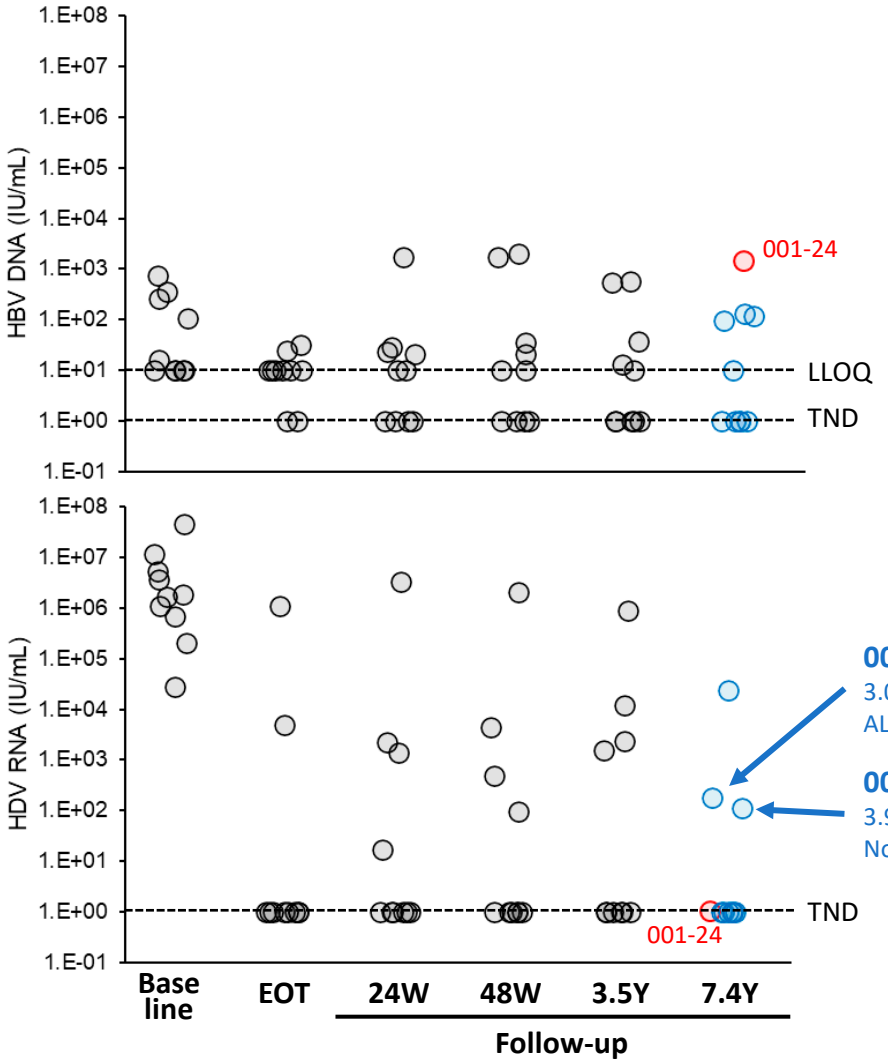
1 patient (001-24) rebounded during pegIFN monotherapy in REP 301 study

Subsequently enrolled in MYR 204 study after 3.5 year follow-up and completed treatment and follow-up 6 months before the current visit (data during BLV therapy not available)

REP 301 extended follow-up virology

(10/11 patients who completed therapy)



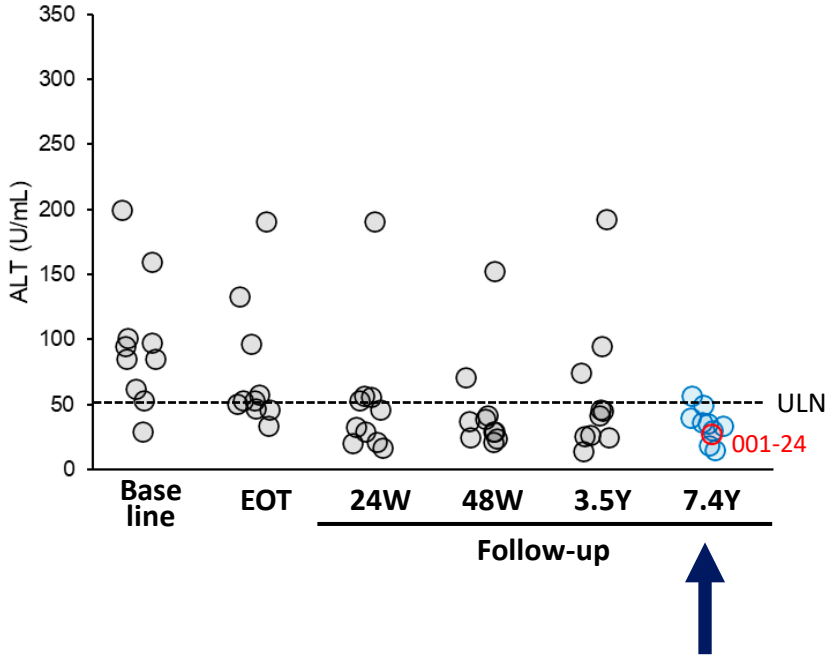


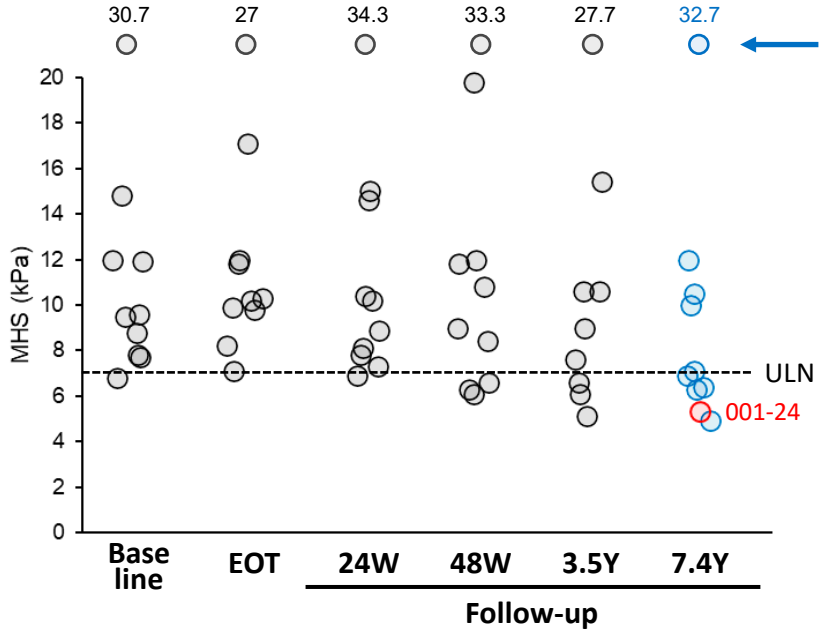
001-09
3.07 log_{10} decline from baseline
ALT 56.9 (ULN 50)

001-22
3.98 log_{10} decline from baseline
Normal ALT

REP 301 extended follow-up liver function

(10/11 patients who completed therapy)





Patient 001-26
Persistent functional cure of HBV and HDV

AST, GGT, total bilirubin, albumin and INR all normal

Liver ultrasound in all patients:
No changes from baseline
No detectable HCC

REP 301 7.4-year follow-up summary

HDV RNA remains TND in all 6 available patients with HDV RNA TND at 3.5 years

- Liver function is normal in all 6
- Median hepatic stiffness is normal in 5/6

- HBV functional cure present at 3.5 years persists in all patients (4/6)
- HBV partial cure present at 3.5 years persists in all patients (2/6)

2 additional patients established persistent clinical benefit in the absence of therapy
(>2 $\log_{10}$ IU/mL decline in HDV RNA from baseline with normal ALT)

No evidence of hepatotoxicity or HCC in all 10 patients evaluated

REP 401 study patient availability

21/37 patients who completed therapy were available

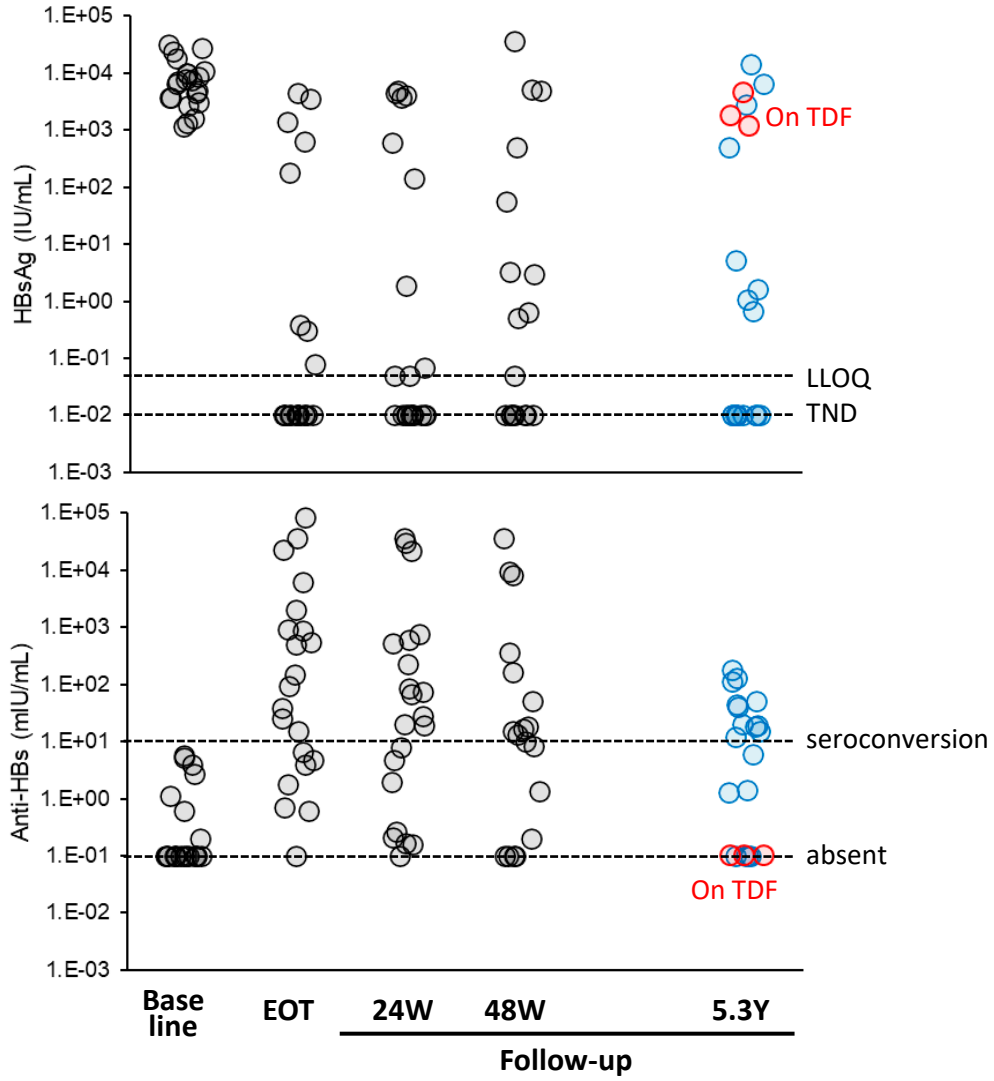
Unavailable patients

Patient	Reason not available	Outcome at 48 weeks
01-004	left the clinical study before the end of follow-up (rebound)	Rebound
01-007	out of the country	Partial cure
01-008	out of the country	Partial cure
01-010	unrelated death during study by polytrauma	Rebound
01-019	no resposne to inquiries	Rebound
01-046	emigrated to USA	Partial cure
01-074	working in Italy	Rebound
01-082	working in Italy	Functional cure
01-075	working in England	Rebound
02-024	working in UK	Functional cure
02-019	moved to Romania	Functional cure
02-058	working in the UK	Functional cure
02-001	working in UK	Functional cure
02-011	working in Russia	Partial cure
02-036	working in UK	Functional cure
03-023	no access to personal contact information at site 3	Partial cure

Three available rebound patients were placed on TDF after 48 weeks follow-up (01-017, 02-003 and 02-018)

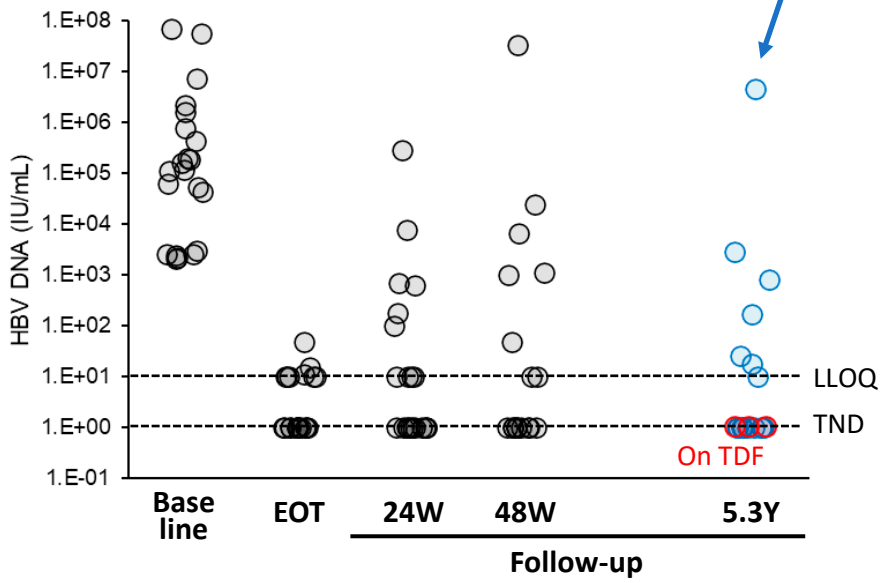
REP 401 extended follow-up virology

(21/37 patients who completed therapy)



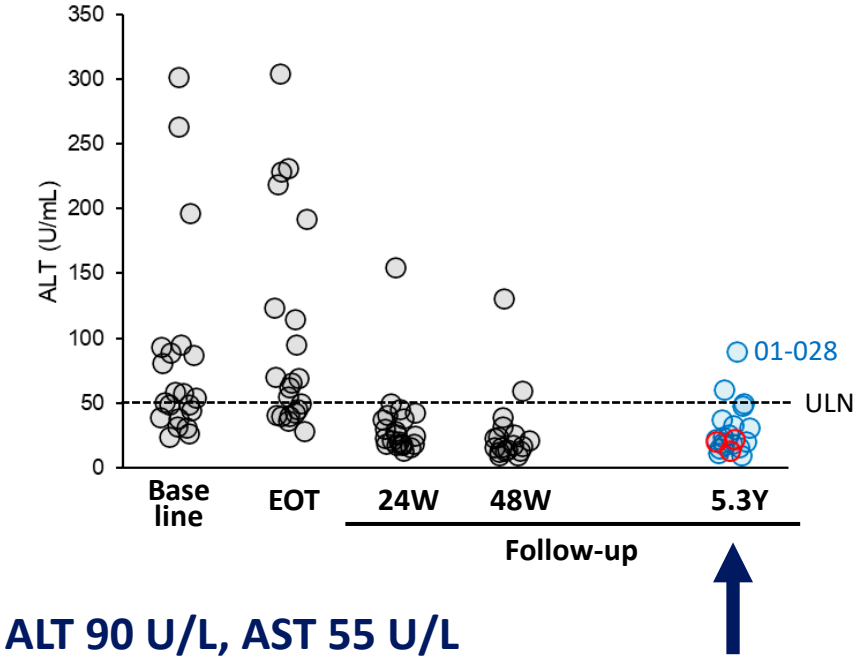
Patient 01-028

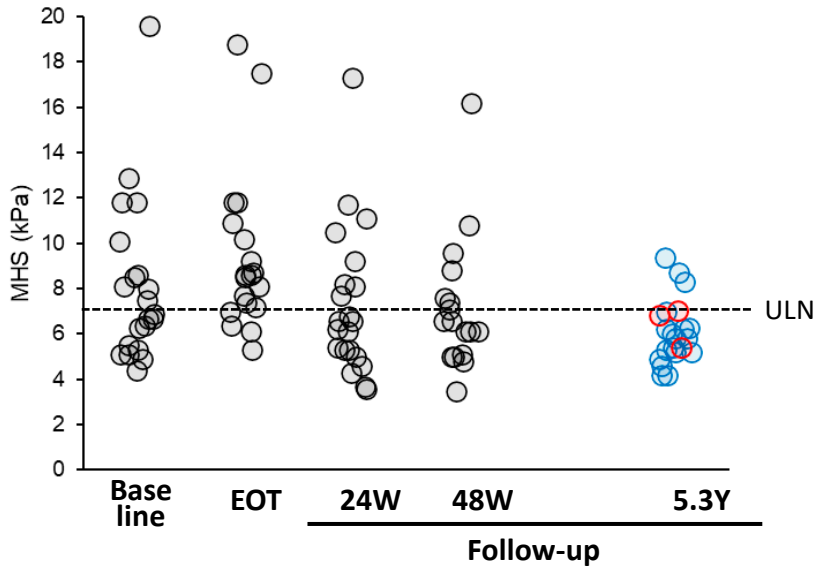
- Mild rebound with normal ALT during initial follow-up
- Started on TDF following this assessment (ALT 90 U/L)



REP 401 extended follow-up liver function

(21/37 patients who completed therapy)





01-028: ALT 90 U/L, AST 55 U/L

Otherwise AST, GGT, total bilirubin, albumin and INR all normal

Liver ultrasound in all patients:

No changes from baseline

No detectable HCC

REP 401 5.3-year follow-up summary

8 participants with functional cure at 48 week follow-up

6 preserved at 5.3 years follow-up

2 transitioned to “borderline” functional cure

02-050: HBsAg 0.68 IU/mL, HBV DNA < LLOQ, normal ALT

02-057: HBsAg 1.07 IU/mL, HBV DNA 18 IU/mL, normal ALT

9 participants with partial cure at 48 week follow-up

4 preserved at 5.3 years follow-up

4 transitioned to functional cure

1 transitioned to rebound

01-003: HBsAg 506 IU/mL, HBV DNA 2825 IU/mL, normal ALT

Continued decline or normalization of median hepatic stiffness in most patients

No evidence of hepatotoxicity or HCC in all 21 patients evaluated

Summary

Establishment of immune control of HBV or control of HDV with NAP-based combination therapy is very durable

- **REP 301 study (HBV /HDV) at least 7.4 years**
- **REP 401 study (HBV) at least 5.3 years**

Control includes preservation of undetectable HDV RNA, HBV functional cure or HBV partial cure

Continued decline or normalization of median hepatic stiffness continues in most patients

No detectable liver toxicity or development of HCC following NAP-based therapy

Based on available data, immune control following therapy in the REP 401 study demonstrates a net improvement over time, suggesting functional cure rates as high as 56%