Ongoing analysis of off-therapy control of HBV and HDV infection following REP 2139-Ca and pegIFN therapy in the REP 301-LTF study: 3.5 year follow-up results

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replicor

Antiviral effects of REP 2139

1 Inhibition of HBV SVP assembly / secretion and HDV envelopment

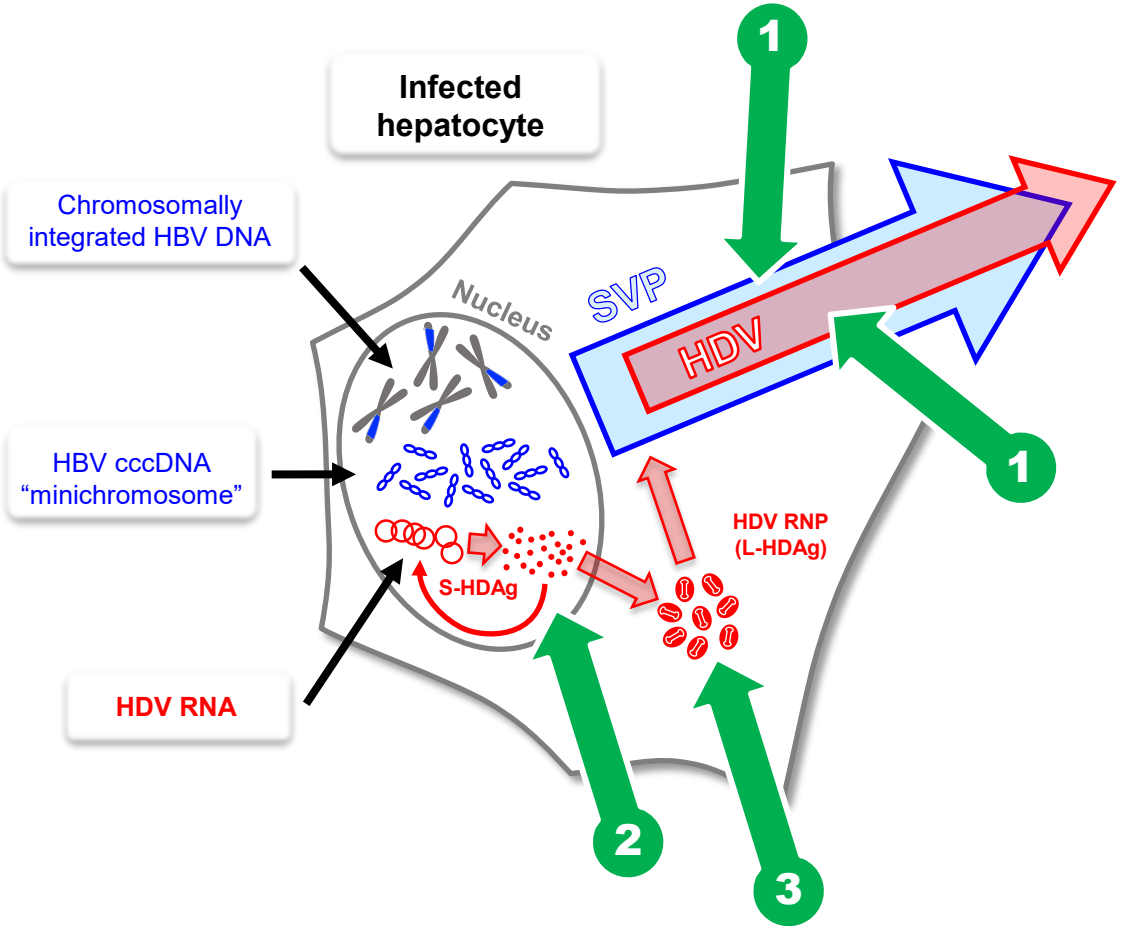
- Allows host mediated clearance of HBsAg / HDV
- Blocks release of HDV

2 Interaction with S-HDAg

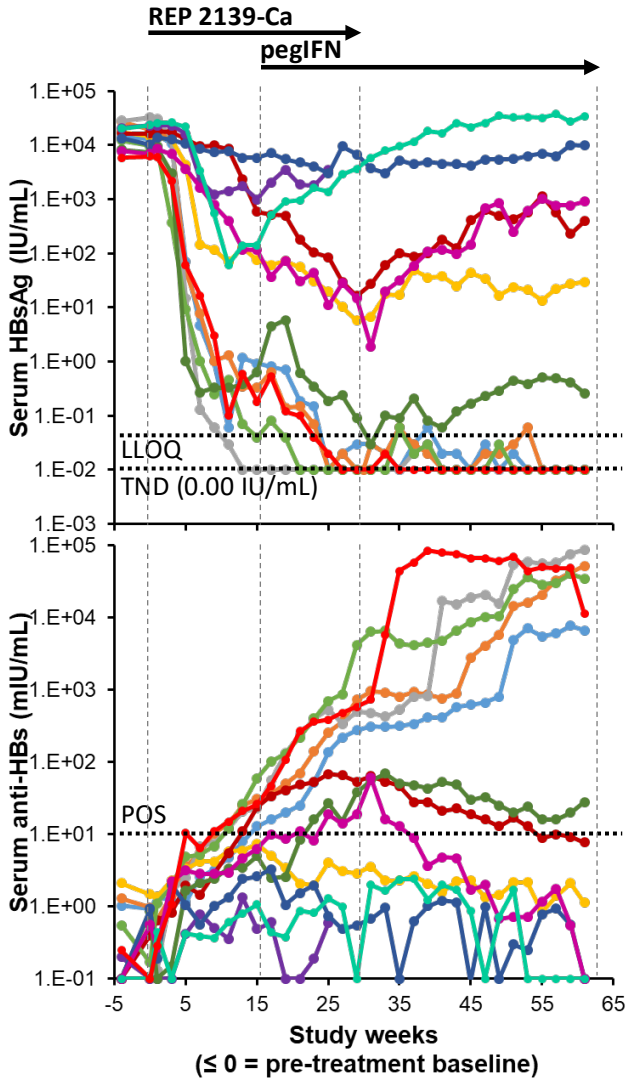
- Potential upstream inhibition of HDV RNA synthesis

3 Interaction with L-HDAg

- Potential upstream inhibition of HDV RNP assembly



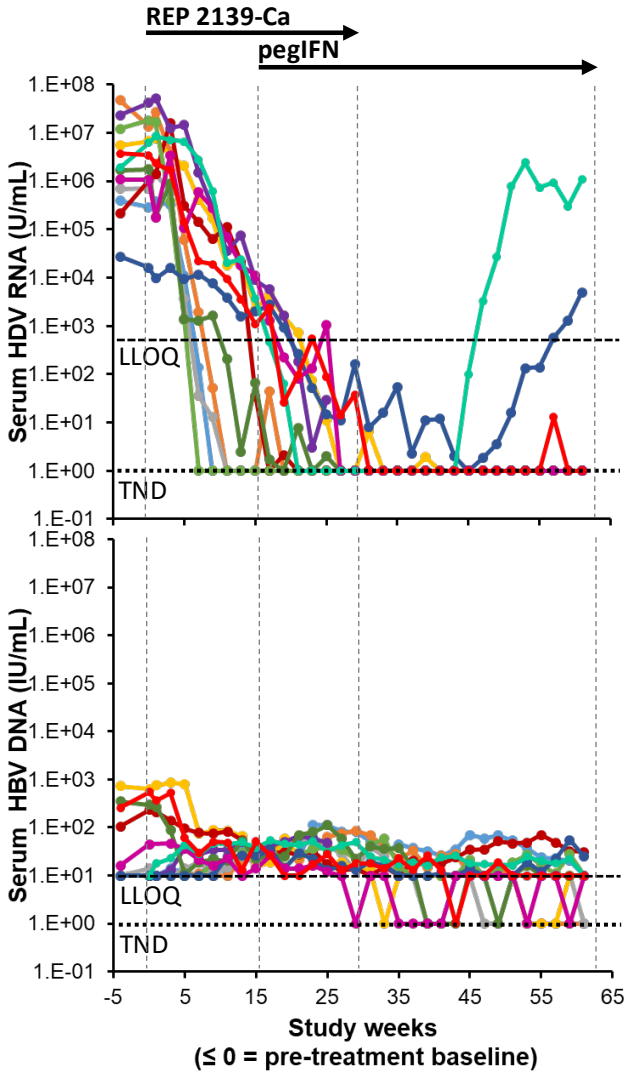
Antiviral effects during REP 2139-Ca / pegIFN in REP 301



Rapid HBsAg clearance prior to pegIFN

Rapid and dramatic increase in anti-HBs with pegIFN

Only with HBsAg < 1 IU/mL prior to pegIFN



Universal and rapid HBV RNA response

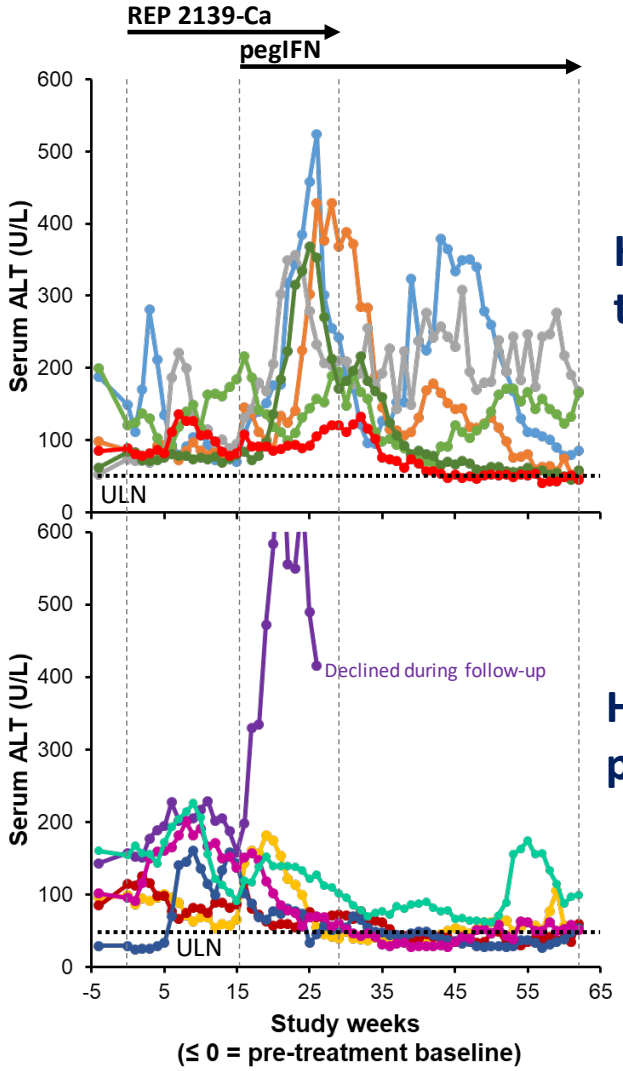
Target not detected in all participants during therapy

Even in participants with moderate HBsAg response

Likely due to upstream direct effects against HDV replication

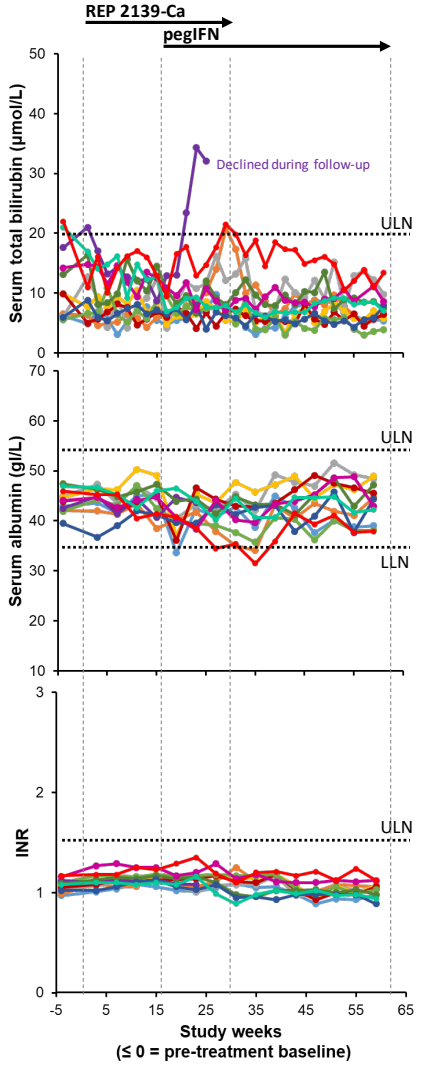
HBV DNA remains well controlled in absence of NUCs

Therapeutic transaminase flares



HBsAg < 1 IU/mL prior to pegFN

HBsAg > 1 IU/mL prior to pegIFN



Liver function unaffected

(except one case of pegIFN induced DILI)

REP 301-LTF

All participants completing therapy in the REP 301 (11/12) were enrolled.

Treatment free follow-up in the REP 301 study (24 weeks) was extended for an additional 3 years

(3.5 years total follow-up)

All participants have now formally completed follow-up (3.5 year data available in 10/11).

Persistent clinical, HBsAg and HDV RNA responses in REP 301-LTF

Completed treatment and 3-3.5 years of follow-up		**11**
Clinical response	Normal ALT	8/11 (73%)
	Normal / declining liver median stiffness	7/11 (64%)
HBsAg response	< 1 IU/ml	6/11 (55%)
	≤ LLOQ (0.05 IU/mL)	5/11 (42%)
	Seroconversion	4/11 (36%)
HDV RNA response	**> 2 log_{10} reduction from baseline**	**9/11 (82%)***
	TND	**7/11 (64%)**

***2 participants maintaining 2.67 and 2.12 log_{10} HDV RNA reduction from baseline at 3.5 years follow-up did not maintain normal liver function during follow-up.**

HBV outcomes in participants with persistent HDV RNA negativity

Functional cure of HDV at 3-3.5 years of follow-up (HDV RNA TND, ALT normal)		**7**
HBV DNA response	≤ 2000 IU/mL	7/7 (100%)
	Target not detected (TND)	5/7 (71%)
HBV virologic response	Virologic control HBV (HBV DNA ≤ 2000 IU/mL, normal ALT)	3/7 (43%)
	Functional cure HBV (HBsAg < LLOQ, HBV DNA TND, normal ALT)	4/7 (57%)
	HBV clinical benefit, no therapy required (Low risk of progression, reduced risk of HCC)	**7/7 (100%)**
On-therapy flare	**Asymptomatic transaminase flare while HBsAg ≤ 1IU/mL**	**7/7 (100%)**

Summary

REP 2139-Ca and pegIFN achieve high rates of HBsAg loss, HBsAg seroconversion and HDV RNA loss during therapy

- likely driven by blocking SVP assembly and interfering with upstream HDV replication

Strong pegIFN-mediated transaminase flares universal when HBsAg < 1 IU/mL

Functional cure of HDV (HDV RNA target not detected, normal ALT) persists in 64% participants after 3-3.5 years of treatment-free follow-up.

All with virologic control or functional cure of HBV
All had asymptomatic transaminase flares with HBsAg ≤ 1 IU/mL during therapy

Response rates are expected to improve with 48 weeks of TDF + pegIFN + REP 2139-Mg as used in the REP 401 study.

A collaborative effort !

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