

# REP 2139 monotherapy and combination therapy with pegylated interferon: Safety and potent reduction of HBsAg and HDV RNA in Caucasian Patients with chronic HBV / HDV co-infection

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Presentation O-09

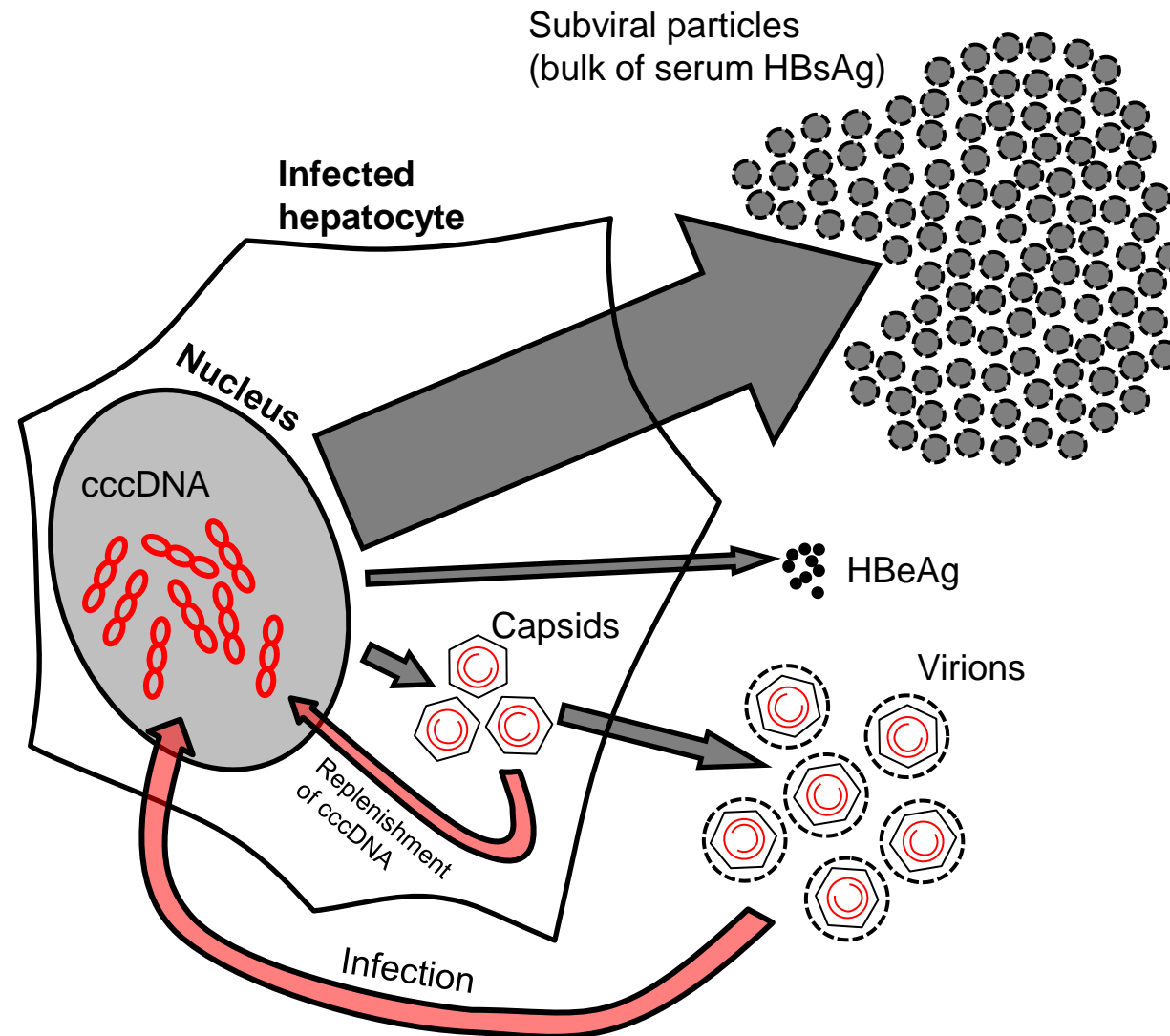
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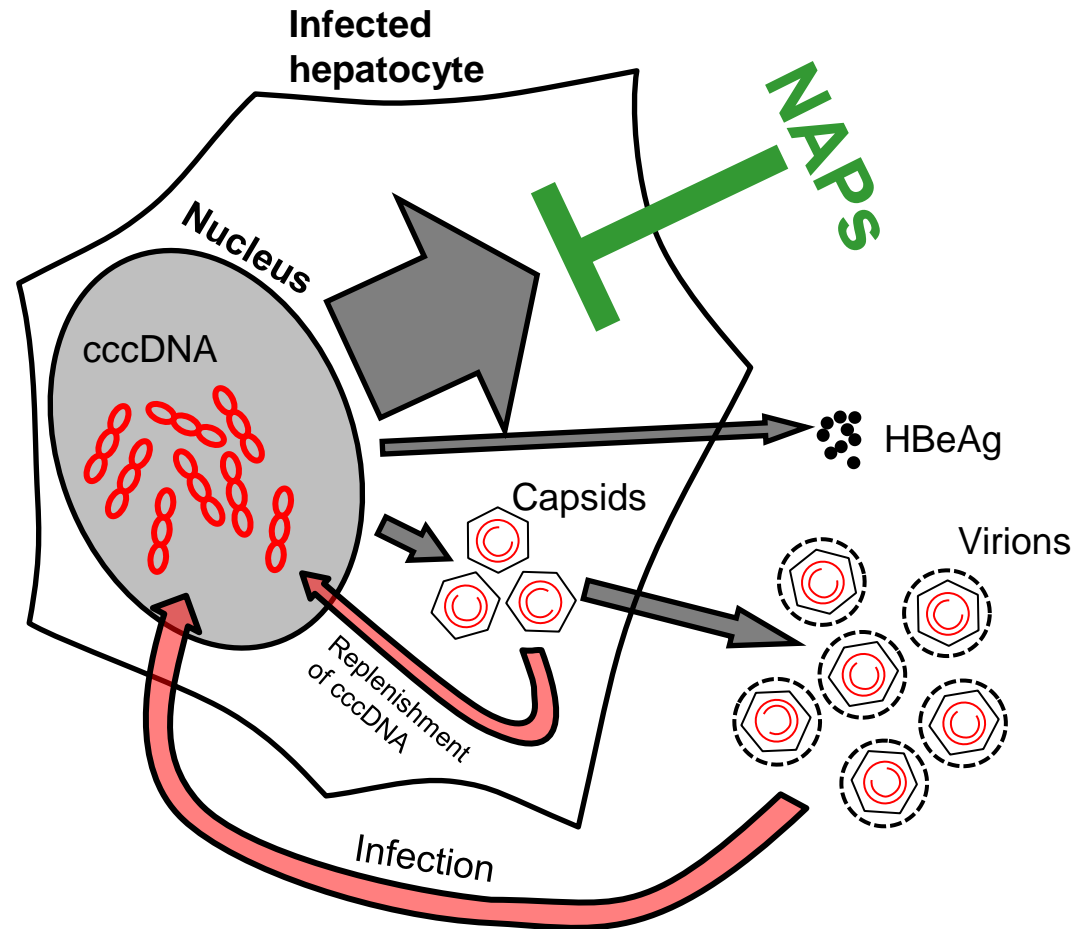
# Nucleic Acid Polymers (NAPs)

- Synthetic, amphipathic polymers (oligonucleotides)  
NOT antisense (think heparin sulfate....) -> block viral entry
- Post-entry effects appear critical for antiviral effect in vivo
- Naturally taken up by hepatocytes with parenteral administration
- Interfere with apolipoprotein / HBsAg interactions required for HBV subviral particle (SVP) assembly
- Target the host apolipoprotein H (no resistance)
- Effect is selective for SVPs (virions not directly targeted)

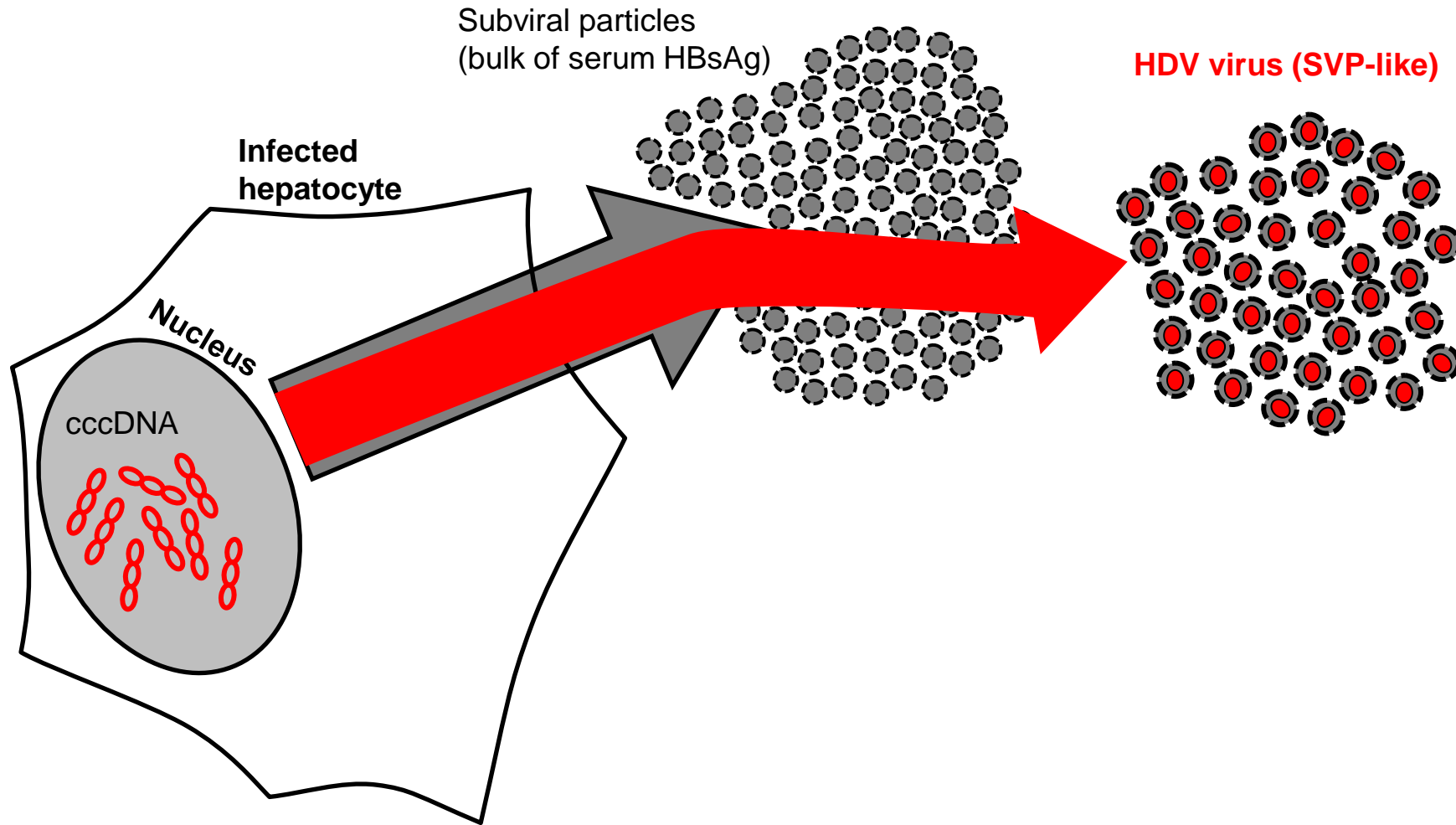
# Particle production in HBV infection



# The NAP effect in HBV infection



# Potential NAP effect in HDV



Bonino et al., 1986 J. Virol. 58: 945-950

# REP 2139-Ca + Pegasys® in HBV / HDV co-infection (REP 301)

Caucasian patients treated in Chisinau, Moldova  
CRO monitored trial compliant with EU GCP  
Clinicaltrials # NCT02233075

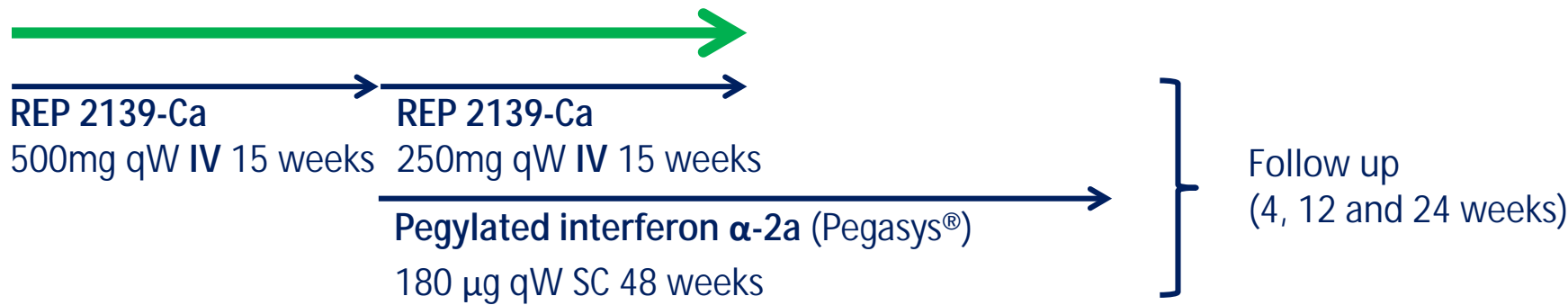
12 patients enrolled with HBV / HDV co-infection at the start of treatment:

- Anti-HDAg+
- Serum HBsAg > 1000 U / ml
- HBeAg-
- compensated liver disease
- mild to moderate fibrosis, non cirrhotic.

Viremia monitored at University of Duisburg-Essen, Germany:

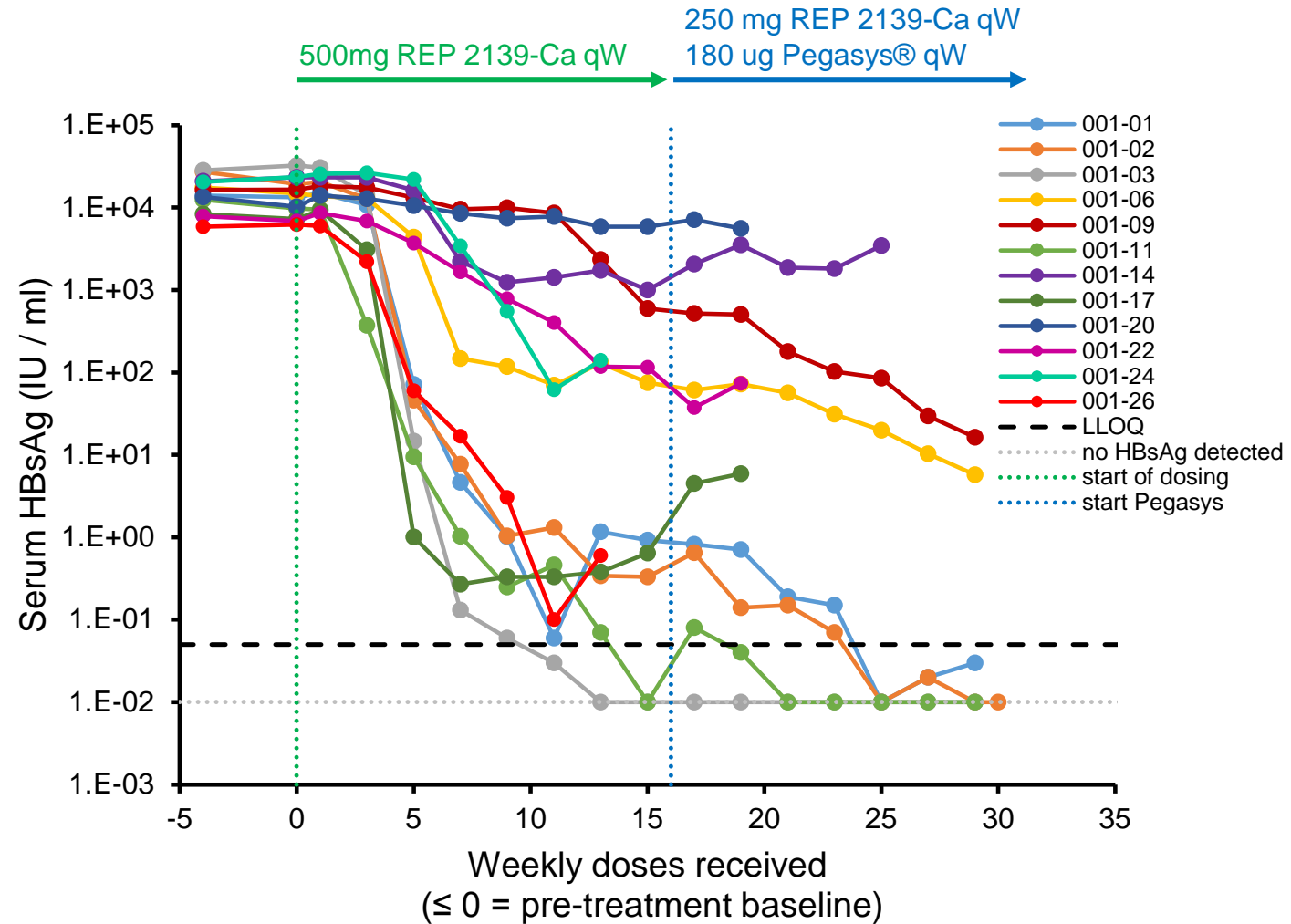
- Abbott PCR (HBV DNA)
- Abbott Architect (HBsAg and anti-HBs)
- Robogene RT-PCR (HDV RNA)
- Diasorin (anti-HDAg)

# REP 301 Trial Design



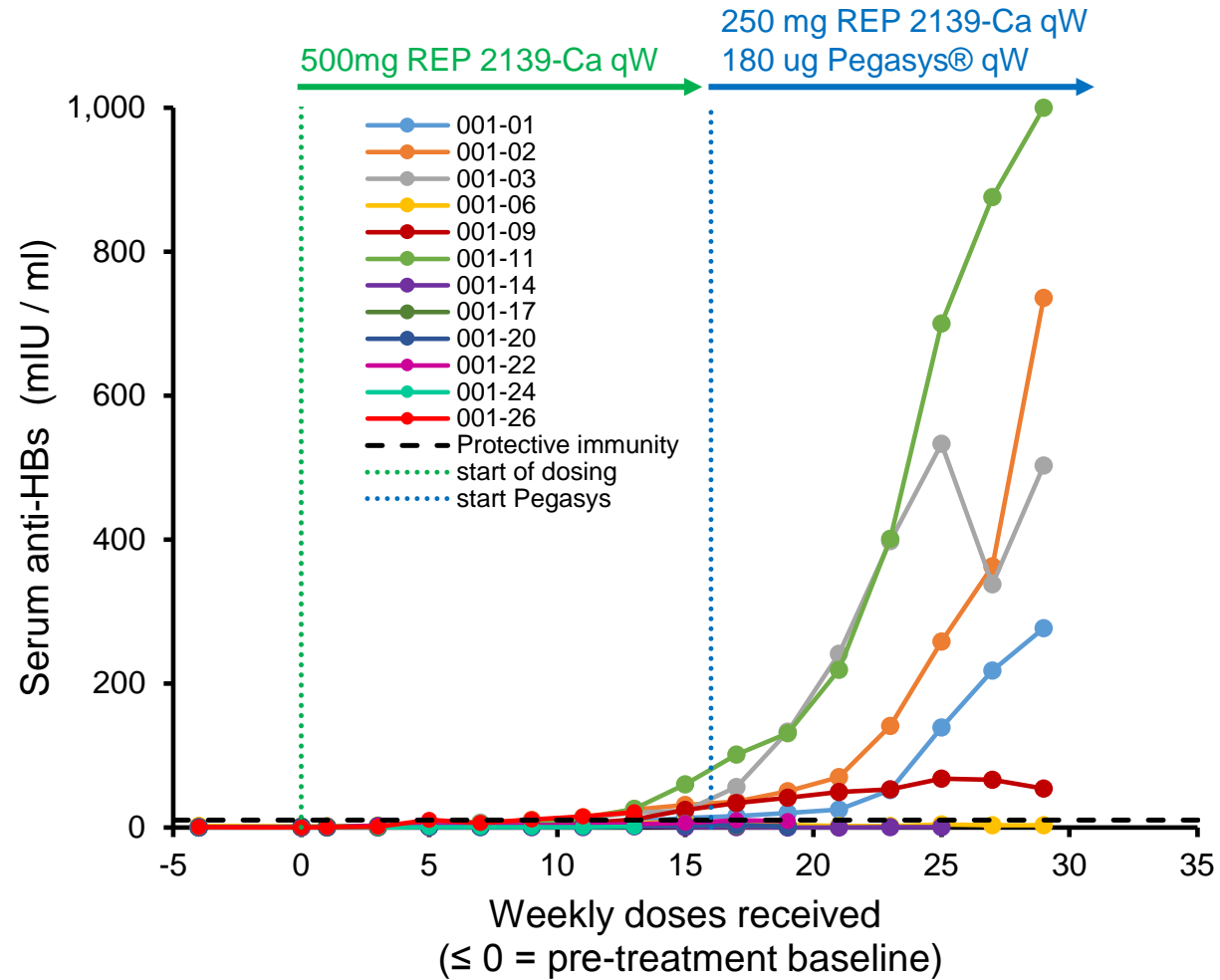
REP 2139-Ca qW regimen is well established for this drug class (PS-ONs)

# Interim REP 301 Efficacy Data (serum HBsAg)

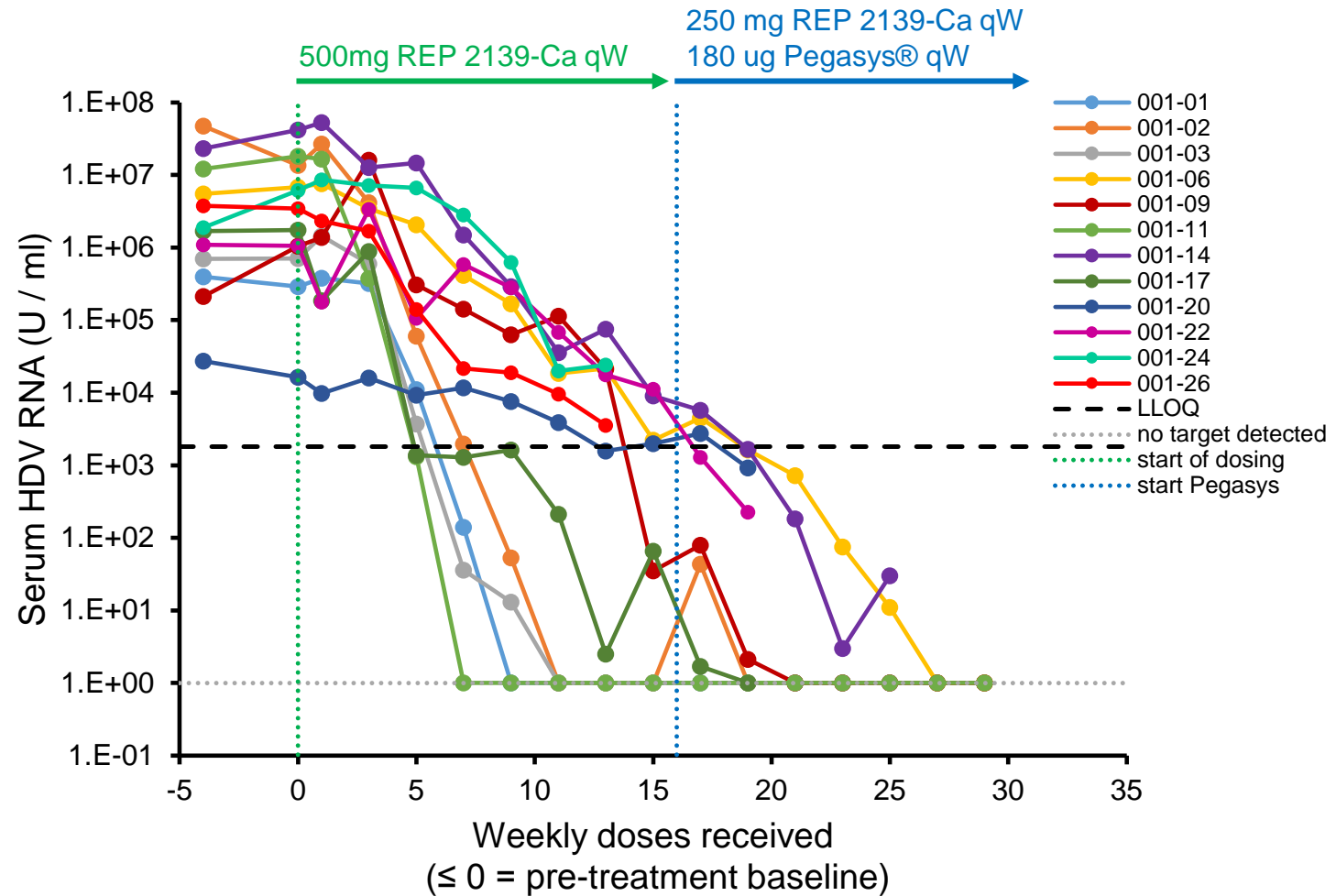




# Interim REP 301 Efficacy Data (serum anti-HBs)

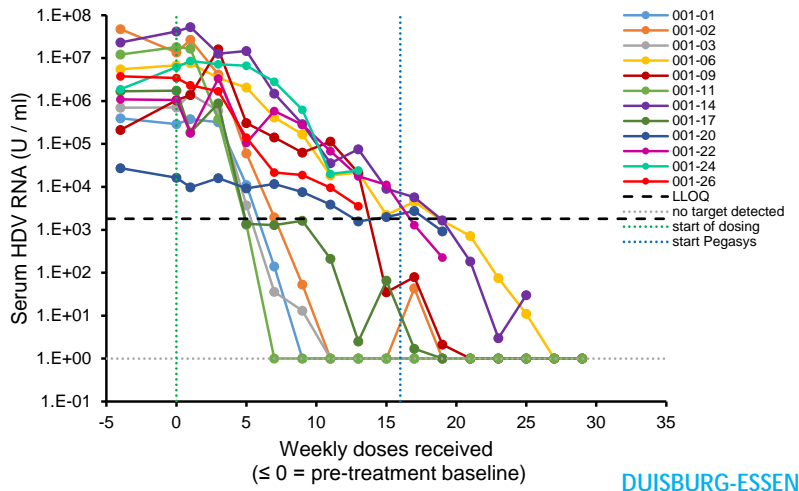


# Interim REP 301 Efficacy Data (serum HDV RNA)

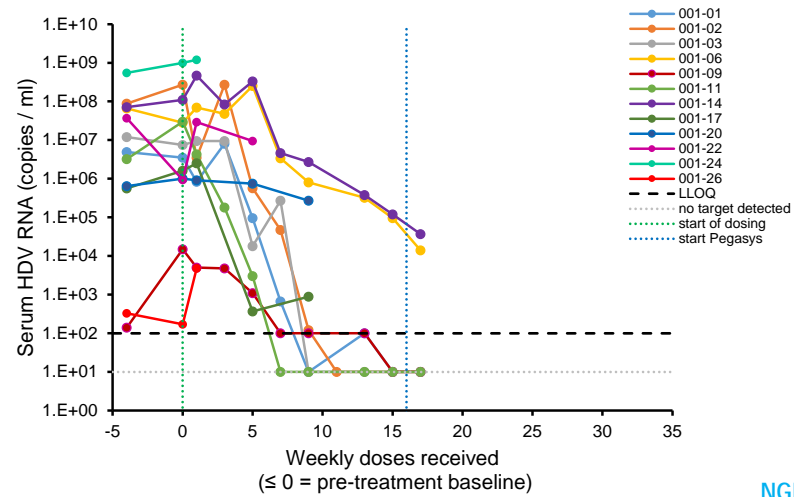


# Validation of REP 301 HDV RNA

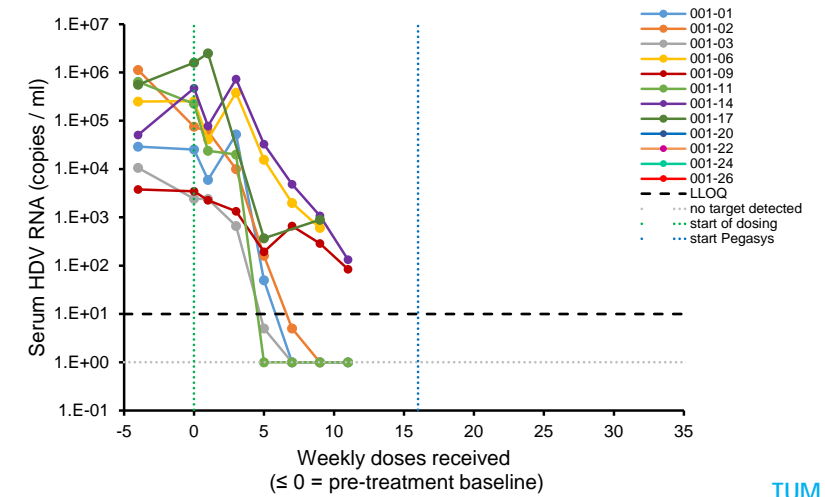
Study site



Validation site #1



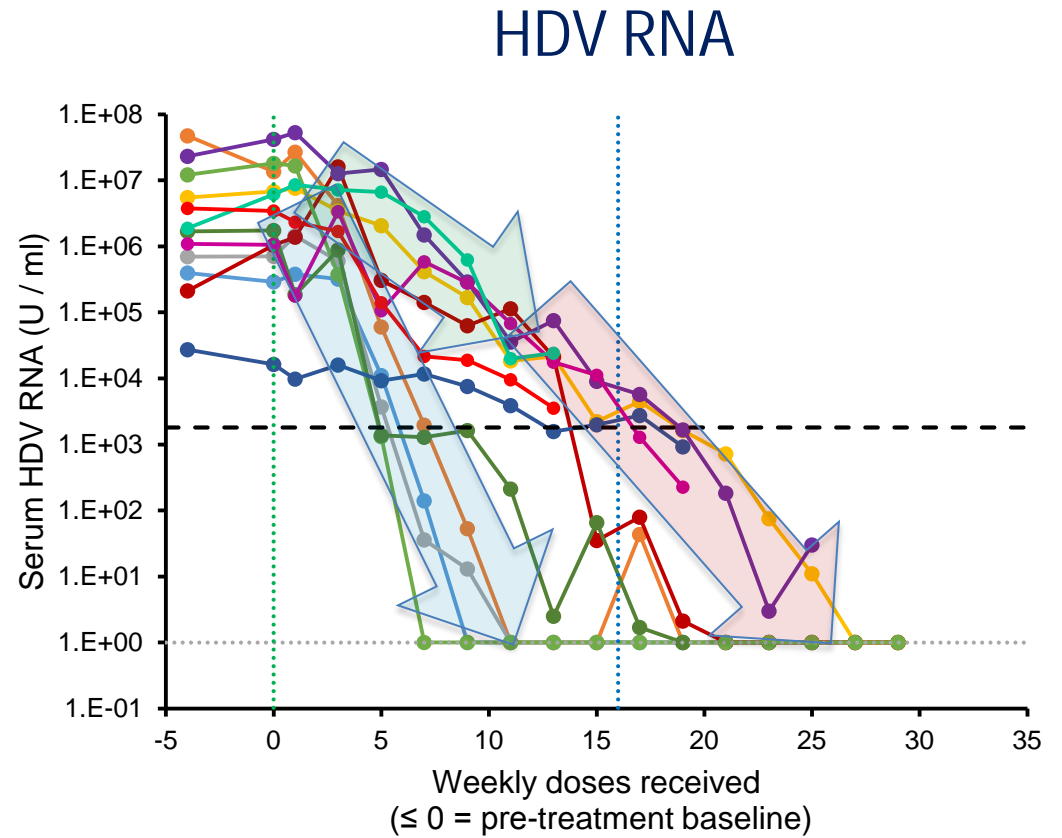
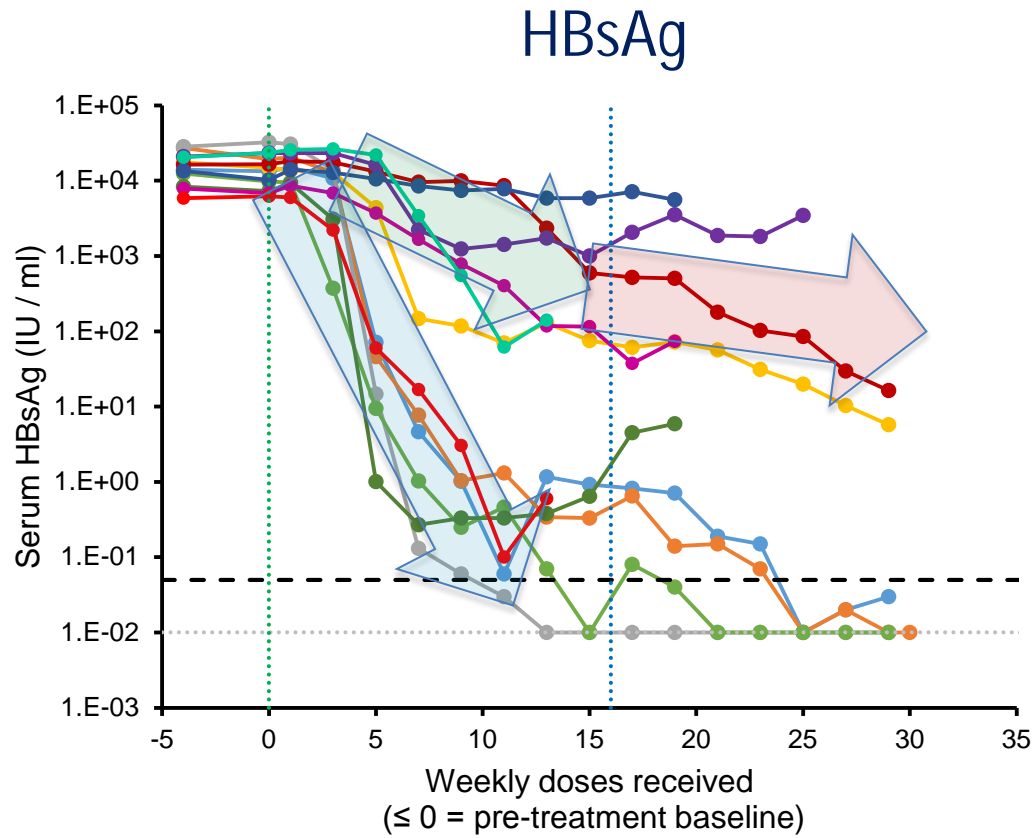
Validation site #2



GT1 primer set on separate serum samples

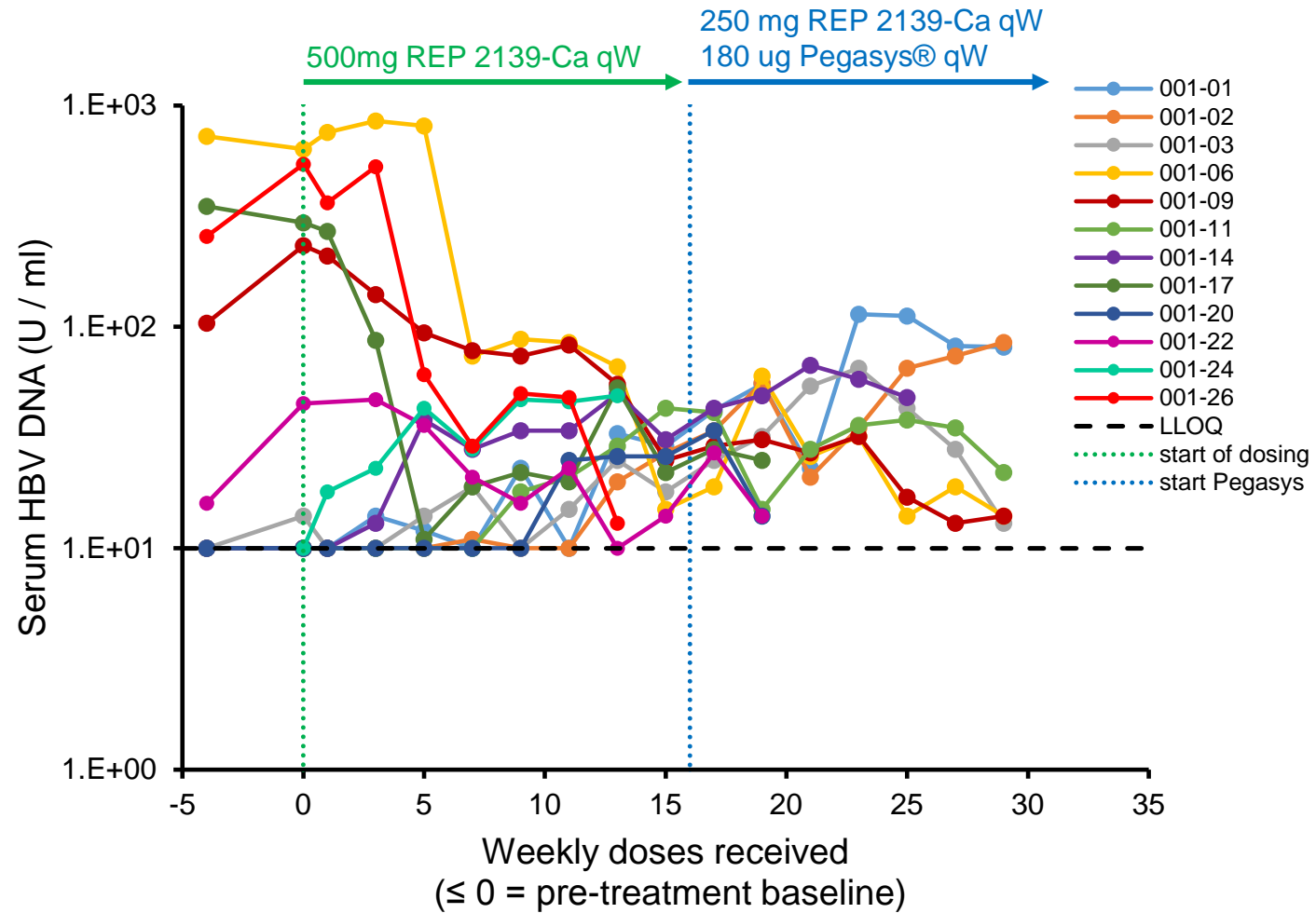
Independent primer set on RNA from study site

# HBsAg versus HDV RNA response



Multiple antiviral effects may be present

# Interim REP 301 Efficacy Data (serum HBV DNA)



# REP 2139-Ca safety profile in the REP 301 protocol (interim analysis)

- All AEs are grade 1-2 (fever, redness or headache) and are associated with IV infusion:
  - typically become less frequent as dosing regimen progresses
  - self-resolve after completion of IV infusion (infrequently requiring supportive treatment)
  - attributed to the presence of phthalate plasticisers in IV tubing
- Clinical serology monitored weekly with no clinically significant findings
- One patient removed from dosing after 10 weeks of Pegasys<sup>®</sup> exposure due to Pegasys<sup>®</sup>-related DILI.

# Summary

Serum HBsAg clearance previously observed with NAPs in Asian patients is replicated in Caucasian patients.

REP 2139-Ca can simultaneously reduce HBsAg and HDV RNA

- multiple antiviral mechanisms
- de-repression of serum HBV DNA – NUC therapy may be required

REP 2139-Ca is well tolerated and does not alter tolerability of Pegasys®.

- may provide an additional productive antiviral response.

NAP-based antiviral therapy may become an important new treatment option for patients with HBV / HDV co-infection.

# Acknowledgements

Validation of HDV RNA test results were performed at:

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Dr. Peter Schmid

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