Sustained off therapy control of HBV and HDV infection following removal of NAP-based therapy in cirrhotic HBV / HDV co-infection

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Introduction

Nucleic acid polymers (NAPs) inhibit HDV RNA replication and HDV RNP formation via HDAg interaction and HDV envelopment and release by blocking the assembly of HBV subviral particles. Compassionate use of the NAP REP 2165-Mg was initiated in a cirrhotic patient with chronic HBV / HDV co-infection.

Methods

The subject (male, 59 years of age) had HBV / HDV co-infection with decompensated cirrhosis and portal hypertension with limited previous exposure to ETV prior to compassionate use therapy. Therapy was started with daily TDF (300mg) and once weekly IV REP 2165-Mg (250mg). Following HBsAg loss, sequential add-on immunotherapeutic approaches included vaccination with Prehevbrio (5 double dose inoculations), thymosin α1 (Tα1, 2x 1.6 mg qW) and pegylated interferon α2a (pegIFN, 45µg qW). Local safety assessments were accompanied by confirmation of antiviral response to therapy using standard assays: HBV DNA (Abbott Realtime), HDV RNA (Robogene MKII) and quantitative HBsAg and anti-HBs (Abbott Architect).

Results

REP 2165-Mg administration was asymptomatic. Unrelated viral pneumonia at week 9 and burst esophageal varices at week 15 resolved on treatment with supportive therapy. A self-resolving transaminase flare (weeks 3 – 15, with ALT_{max} of 213 U/L) was otherwise asymptomatic.

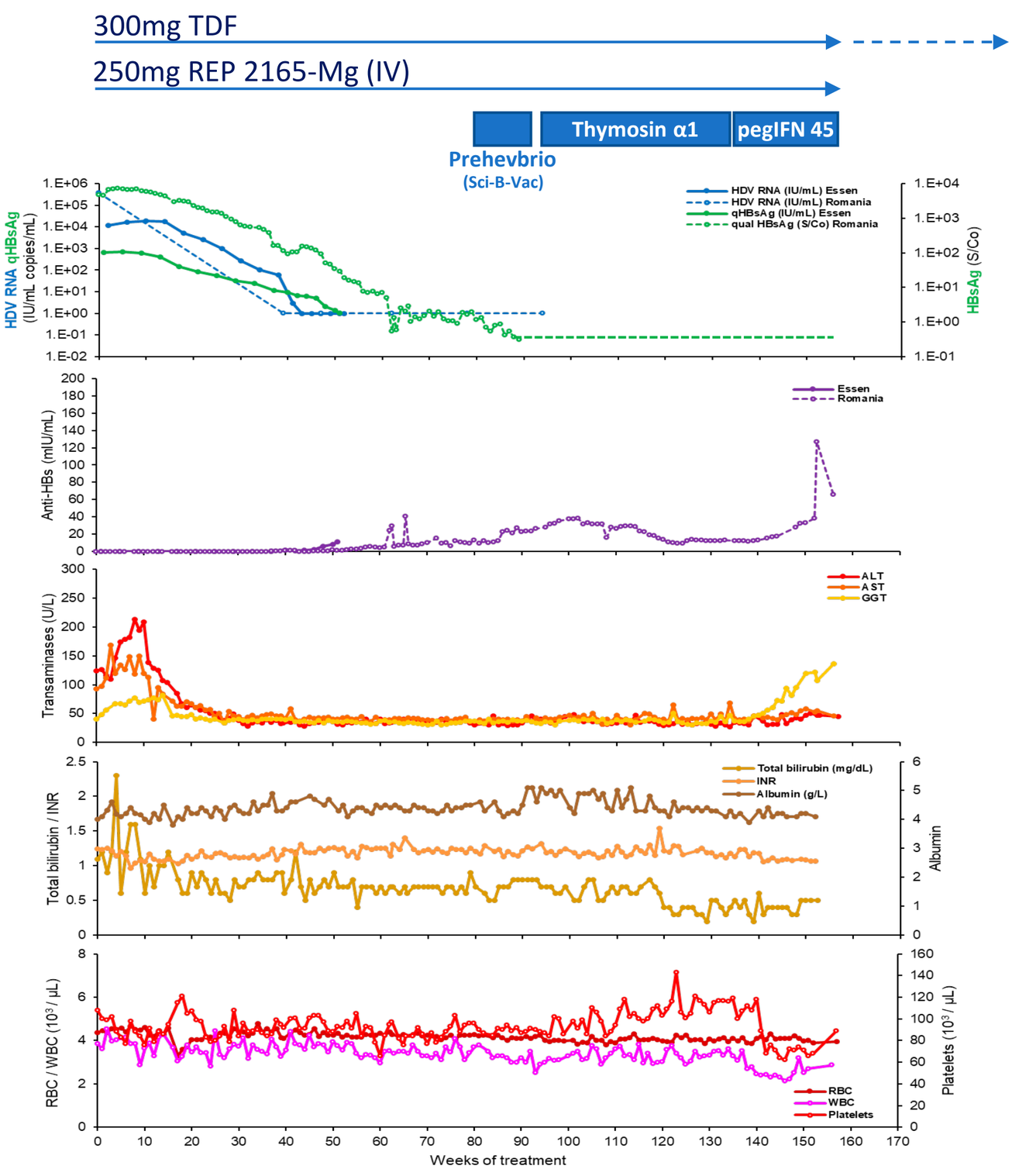
HDV RNA and HBsAg declines accompanied the transaminase flare. HBsAg loss occurred at week 63 and HDV RNA became undetectable at week 47. HBsAg seroconversion was observed prior to vaccination with Prehevbrio. Anti-HBs flares were observed during Tα1 (38.7 mIU/mL) and pegIFN (126.92 mIU/mL)/.

Three months following cessation of REP 2165-Mg and pegIFN, HBsAg loss, HBsAg seroconversion and undetectable HDV RNA persist with normal liver function. TDF therapy has now been withdrawn.

Conclusion:

REP 2165-Mg and the accompanying transaminase flare were well tolerated in this cirrhotic subject and achieved durable control of HBV and HDV infection in the absence of therapy.

Antiviral / safety evaluations during therapy



Follow-up after removal of therapy

Off therapy follow up:
REP 2165-Mg + pegIFN 45: 7 months
Removal of TDF: 2 months

HDV RNA target not detected
HBV DNA target not detected
HBsAg negative (qualitative)

ALT 23 IU/mL
AST 28 IU/mL
GGT 64 IU/mL