Poster Abstract P11

Response guided long-term treatment of chronic hepatitis D patients with bulevirtide - results of a "real world" study

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Background
Bulevirtide (BLV) blocks the uptake of the hepatitis D Virus (HDV) into hepatocytes via the sodium/bile acid cotransporter NTCP. BLV was conditionally approved by EMA but real-life data on BLV efficacy are limited.

Methods
BLV was provided by MyrPharma (Leipzig/Germany) in a compassionate use program until 8/2020, and thereafter was prescribed. HDV-RNA was determined by PCR (according le Gal et.al,J.Clin Microbiol 2005; LLQ:100 copies/mL). BLV dosing and treatment duration was at the discretion of the investigator. Patient were classified as responder (≥2log drop of HDV-RNA within 24 weeks followed by further decline), partial responder (≥2log drop within 24 weeks and no further decline), non-responder (<2log drop of HDV-RNA within 24 weeks).

Results
17 patients (m/f:6/11; mean age: 50.2 years (range; 29-68; 11 with cirrhosis; ALT:98±20 IU/mL; median HDV-RNA: 950000 [range:100-59000000] copies/mL) received BLV (2mg/d in n=15; 10 mg/day in n=2). In 15 patients (84.6%), BLV was combined with NUCs (n=3 ETV, n=10 TDF, n=2 TAF), n=13 patients had a previous nonresponse to PEGIFN.Four patients were classified as responders: BLV treatment was terminated in 2 patients with undetectable HDV-RNA for >6 months after a total of 63 and 130 weeks, respectively, with one patients remaining HDV-RNA negative also 20 weeks after cessation of BLV therapy, and with the other patient (compensated cirrhosis) becoming HDV-RNA positive again 4 weeks after cessation of BLV therapy (BLV treatment was resumed in the latter patient). 2 responders are still on BLV treatment.
In 4 non-responders treatment with peginterferon-alfa2a (PEGIFN) was added – leading to a rapid decline of HDV-RNA in all (log drop within 12 weeks: 0,97; 1.19; 1,23; 1.54). 6 partial responders are still on BLV monotherapy. Two patients dropped out due to noncompliance after 8 and 24 weeks, and one patient underwent liver transplantation at week 25 of BLV, respectively.
ALT levels normalized in 11 (84.6%) patients. During BLV therapy HBsAg changes levels did not change and bile acid levels increased without pruritus.

Conclusions
Long-term BLV is safe and effectively decreaseg HDV-RNA and ALT. Optimal treatment duration to achieve sustained HDV suppression has not been established - but likely requires >1 year. Our data indicate the need for an individualized approach when using BLV for HDV treatment (see proposed BLV treatment algorithm, Figure-1).