Eurasian Journal of Clinical Sciences
an Uptodate In Medicine's open access journal

Safety, effectiveness and t-cell activation profiles of long-term myrcludex-B treatment in two patients with hdv related compensated cirrhosis

APASL Single Topic Conference Delta Hepatitis
June 27-28, 2019 Baku, Azerbaijan

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Background and Aim. Mycludex B (MYR) is a new promising anti-HDV therapy, but the effectiveness and safety of long-term administration in compensated cirrhotics treated in a real-life setting are presently unknown. Aim of this study was therefore to describe the effectiveness, safety and impact on HDV/HBV-specific T cell profiles in the first two European patients treated with MYR outside clinical trials. Methods. A 69-year-old female and 51-year-old male Caucasian HBeAg-negative patients with HDV related compensated cirrhosis on long-term term TDF treatment, started MYR 10 mg/day on January and May 2018 in a compassionate use program. Liver function tests, bile acids and virological markers were monitored every 4 weeks. HDV RNA was tested by RoboGene®. HDV and HBV specific T cell quantity were analyzed monthly in blood by direct ex-vivo IFN-y ELISPOT methods using overlapping peptides covering the HDV and HBV proteome. Results. Both patients had active compensated HDV related cirrhosis at baseline: ALT 150 and 250 U/L, GGT 23 and 250 U/L, platelets 95 and 74 x109/L, bilirubin 0.7 and 0.4 mg/dL, total bile acids 7 and 15 µmol/L, AFP 7 and 21 ng/mL, albumin 4.3 and 3.6 g/dL, HDV RNA 23,600 and 392,000 IU/mL, HBsAg 9 and 11,111 IU/mL, undetectable HBV DNA. Liver stiffness were 17 and 18 kPa, spleen length 12 and 14 cm, small esophageal varices were present in the second patient. During 48 and 36 weeks of MYR treatment, ALT levels rapidly normalized (16 and 8 weeks), as well as AFP levels (to 3 ng/mL in 28 weeks and 24 weeks); platelets progressively increased up to 154 and 112 x109/L, as well as albumin (4.5 and 4.4 g/dL). HDV RNA levels progressively declined in both patients to became undetectable after 36 weeks and 28 weeks, respectively. Liver stiffness at week 24 were 17 and 14 kPa; last HBsAg levels were 26 and 7,995 IU/mL. These clinical and virological improvements were not associated with changes of circulating HDV/HBV-specific T cells that remained at a very low frequency during the first 6 months of the study. As far as safety is concerned, total bile acids rapidly increased up to 53 and 124 µmol/L, but this was not associated to any symptom, neither to bilirubin nor GGT alteration. Conclusions. Myrcludex-B 10 mg/day, in combination with TDF, is a safe and effective treatment option for HDV compensated cirrhotics, yet without any recovery of T cell function.