1 Background and Aims
Hepatitis B/D coinfection is associated with rapid progression to severe liver disease and hepatocellular carcinoma (1) and poses a relevant public health challenge in numerous countries (2). Effective drug therapy options for chronic hepatitis D (CHD) are still needed. Until 2020 interferon alpha was the only treatment option for HDV infection. With serious side effects and a limited efficacy of about thirty percent, it remains an ineffective option for a majority of patients (6-9).

In July 2020, bel vaporide (2mg/day) was approved in the European Union for the treatment of CHD. The drug blocks the bile salt transporter NTCP, which is also the entry receptor for Hepatitis B and D viruses (10, 11). In Germany it received market approval in September 2020. An early access programme allowed for a therapy start with bel vaporide (BLV) around six weeks before market approval. Here we describe the first sixteen weeks of therapy with bel vaporide in hepatitis delta patients who were included in an early access programme in the hepatology outpatient clinic of Charité University Medicine Berlin, Germany.

2 Method
We included patients with active hepatitis B/D coinfection who were eligible for the early access programme. The main exclusion criteria were liver cancer, Child-Pugh Score B or C, bronchiectasia below 50%, hepatocellular carcinoma or planned pregnancy. All included patients were newly diagnosed, had detailed information and training for drug administration. We used a mixed effects model to control for interindividual variation and applied log transformation to address skewed data.

3 Conclusions
These are the first real-life data on bel vaporide therapy in Germany. Overall, we observed a favorable safety profile as well as a marked biochemical and virological response in the majority of our patients. However, many questions remain open regarding the treatment of CHD with bel vaporide. The optimal duration of treatment is not known and there is no clear recommendation concerning this issue, which is particularly relevant when considering the relatively high costs of treatment (currently around 13,000 Euro per month in Germany). We currently have no data on the long-term effect of bel vaporide on the development of cirrhosis and hepatocellular carcinoma. Middle- and long-term data are needed to evaluate the impact of bel vaporide treatment on clinical endpoints in hepatitis delta patients.

4 References
(1) Petersen, K.; Blank, A. et al. “First real-life experiences with bel vaporide for the treatment of hepatitis delta – data from a tertiary reference centre in Germany.” 1 Charité - University Medicine Berlin, Department of Hepatology & Gastroenterology, Campus Virchow Klinikum and Charité Campus Mitte

5 Figures
Figure 1: Baseline demographics.
Figure 2: Evolution of the aminotransferase levels during treatment with BLV.

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Table 1: Baseline characteristics of all patients during treatment with BLV

Table 2: Mean ALT values before and during bel vaporide (BLV) treatment

Table 3: Week 12 bile virus RNA levels (log10 copies/mL)

Table 4: Table showing the HDV RNA levels before and during BLV therapy

Results
Patient characteristics are summarized in table 1. The majority of patients were male (88%) and mean age was 49 years (+/- 7 SD). Three patients were cirrhotic. One patient dropped out shortly after inclusion because of a newly diagnosed hepatocellular carcinoma (HCC), and seven patients completed at least 16 weeks of therapy. All patients were under concomitant therapy with nucleoside/nucleotide analogues. None had a concomitant interferon therapy, mostly due to patients’ reluctance or contraindications. A majority of patients had already completed at least one course of interferon therapy in the past.

ALT declined in a majority of patients during treatment with BLV. Mean ALT values before treatment (baseline) were 78 U/l (+/- 53 SD) and declined to 39 U/l (+/- 21 SD) after 16 weeks of therapy. The coefficient of fixed effects was 0.09 according to our model, indicating an estimated reduction in ALT of 7% between each consultation. During therapy, HDV-RNA dropped quickly in all patients except one. Mean HDV RNA was 10,241,700 copies/cell (+/- 79,036) at week 16 (+/- 9,253,452 SD). The coefficient of fixed effects was -0.55 according to our model, indicating an estimated reduction in HDV-RNA value of 55% between each consultation (+/-0.05). One patient showed no significant biochemical or viral response and was discontinued at week 16 (Patient 3). Evolution of ALT and HDV-RNA levels during treatment with bel vaporide are shown in tables 3 and 4, as well as figures 1 and 2, respectively.

There were no patient-reported adverse events. We observed no relevant lab abnormalities during treatment besides an asymptomatic elevation of bile acids (table 2).