Poster Abstract P6

Therapeutic vaccination with the pre-S based vaccine VVX001 - interim analysis

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Background
VVX001 is an HBV vaccine candidate based on a preS polypeptide fused to grass pollen allergen peptides. It is studied if vaccination with VVX001 can induce an immune reaction in vaccine-naïve adults, non- or low responders, in chronic hepatitis B patients and in patients infected with chronic hepatitis B virus (HBV).

Methods
Four cohorts are studied in a prospective double-blind, placebo-controlled clinical trial (NCT03625934). Cohort 1: vaccine naive subjects; cohort 2: subjects having failed to seroconvert upon vaccination with a licensed HBV vaccine (non- or low responders); cohort 3: chronic hepatitis B patients classified as inactive carriers; cohort 4: patients with chronic HBeAg negative hepatitis B who are on long-term treatment with nucleo(t)side analogues (NUCs). Participants received 5 injections (s.c.) of either VVX001 or placebo in 4-week intervals (randomized 3:1) at visits 2, 3, 4, 5, 6, respectively. Inclusion criteria for cohort 3 and cohort 4a, respectively, are: HBV DNA <2000 IU/ml (cohort 3), not detectable (cohort 4a); HBsAg <3000 IU/ml (cohort 3), <2000 IU/ml (cohort 4a). In the still ongoing cohort 4a, NUCs were stopped after three vaccinations (visit 4). After treatment phase completion, patients were followed until week 52 (visit 9). IgG and CD4+/CD8+ responses specific for recombinant preS were studied by ELISA and FACS-based CFSE dilution assay (cohort 3). Respective results for cohort 4a are pending. 17 of the 20 included cohort 4a patients completed treatment and follow-up at this point.

Results
All 9 actively treated subjects of cohort 3 and all 6 actively treated subjects of cohort 1, who completed vaccination, developed robust preS-specific antibody responses peaking one month after the last injection and declining at month 12. A modest CD4+ and CD8+ preS-specific T cell response was observed in naïve subjects.
Except local injection site-reactions, VVX001 was well tolerated in all participants and no SAEs were reported.
In cohort 4a, HBV DNA became again quantifiable in 5 patients during follow up, in 2 of them associated with a marked increase in alanine aminotransferase (ALT). In these 2 patients, NUC therapy was restarted. In the remaining 3 patients HBV-DNA decreased again below or to <20 IU/ml. 12 patients (70.6%) remained HBV-DNA negative with normal ALT, and a total of 15 required no NUC treatment (88%).

Conclusions
VVX001 is safe and well tolerated and induces a preS-specific immune response in vaccine naïve subjects and in patients with chronic hepatitis B infection. Whether VVX001 induces this preS-specific immune response also in patients with chronic HBeAg-neg hepatitis B (cohorts 4a and 4b) who discontinue NUC therapy is currently studied. In 88% of patients in cohort 4a of this ongoing study, after stopping NUCs, no repeated treatment with NUCs was necessary. The precise mechanism how this was achieved is still under investigation.