Interim results of HBV001, a phase 1 study evaluating the safety and tolerability of therapeutic vaccination with ChAdOx1-HBV in healthy volunteers and patients with chronic Hepatitis B infection

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INTRODUCTION

Candidate therapeutic vaccine ChAdOx1-HBV encodes genotype C Hepatitis B (HBV) core, polymerase and surface antigens in a non-replicative chimpanzee adenoviral vector.

It has been show to generate high magnitude, polyfunctional T cell responses in healthy mice,[1] but has not been assessed in humans.

AIM

To evaluate the safety, tolerability, and immunogenicity of ChAdOx1-HBV in humans.

MATERIAL & METHODS

HBV001 is an open-label, non-randomised, Phase I clinical trial (NCT042979.17) of ChAdOx1-HBV in healthy controls (HC) and patients with chronic HBV (CHB) with supressed HBV DNA on nucleos(t)ide therapy.

Participants received low dose (2.5 x10^9 viral particles (vp)) or high dose (2.5 x10^{10} vp) intramuscular ChAdOx1-HBV.

Participants were followed for 168 days for adverse events and HBV serology. HBV-specific T cell responses were assessed by interferon-gamma (IFNγ) ELISpot assays using overlapping peptides,15 amino acids in length, corresponding to the vaccine immunogen.

RESULTS

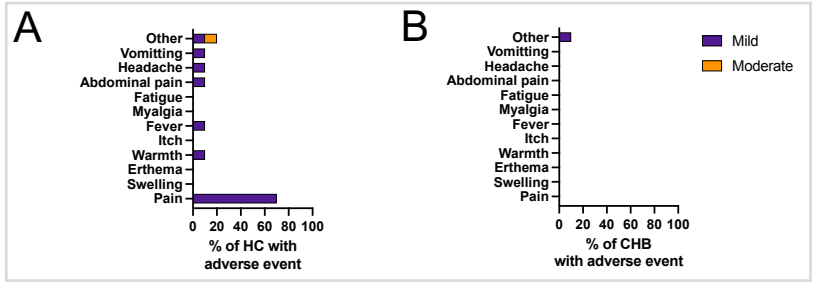
A total of 19 participants were enrolled and received ChAdOx1-HBV at low dose (n=5 HC, n=6 CHB) or high dose (n= 5 HC, n=3 CHB).

Vaccination was well tolerated with no serious adverse events reported. In HC, injection site pain was the most frequently occurring local adverse event (n=7, 70%) and all cases were mild in severity (Figure A). In patients with CHB, the only adverse event was an elective laparoscopic procedure, not related to vaccination (Figure B).

Total T cell responses to the HBV immunogen peaked at day 28 post vaccination in both HC (Figure C) and CHB (Figure D). The magnitude of peak T cell responses was significantly higher in HC than in CHB (mean 1284 vs.189 spot forming units (SFU) per million peripheral blood mononuclear cells (PBMCs), p<0.0001).

The highest magnitude of vaccine induced T cell responses in HC were specific for HBV polymerase (pol) and HBV surface, whereas in CHB the highest responses were specific for HBV pol and HBV core (Figure E).

Cross-reactive HBV-specific T cell responses generated by vaccination were reactive to both genotype C and genotype D peptides (Figure F).



CONCLUSION

Vaccination with ChAdOx1-HBV is safe and well tolerated in humans.

The magnitude of HBV-specific T cell responses induced by vaccination are higher in HC than CHB.

A Phase Ib/IIa trial of ChAdOx1-HBV with MVA-HBV and an anti-PD1 agent is currently underway (HBV002, NCT04778904).

REFERENCES

1. Design and Development of a Multi-HBV Antigen Encoded in Chimpanzee Adenoviral and Modified Vaccinia Ankara Viral Vectors; A Novel Therapeutic Vaccine Strategy against HBV. Vaccines. 2020 Apr 14;8(2).

DISCLOSURES

SKC and EB are named inventors and TNC is a contributor on a patent application describing ChAdOx1-HBV vaccine (International Application No. PCT/GB2018/050948). BK, RM, SS, LB, EEV, HH, HS and TE are employees of Vaccitech, who have licensed the Intellectual Property from Oxford University and financially supported the trial.

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