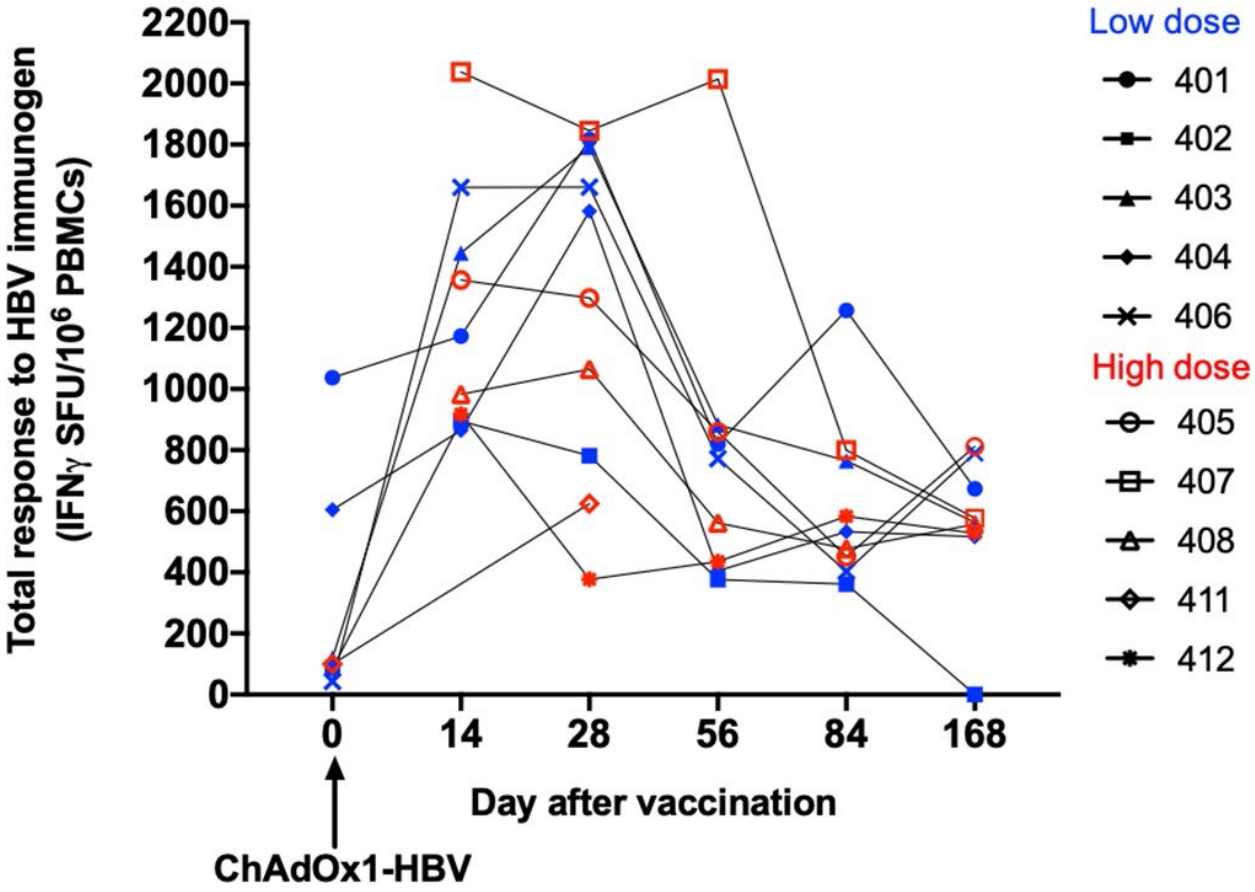
833

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 *Tamsin Cargill1, Paola Cicconi2, Anthony Brown1, Benaka Karanth3, Senthil Chinnakannan1, Sarah Sebastian3, Louise Bussey3, Elizabeth Eagling-Vose3, Henrik Sorensen3, Tom Evans3 and Eleanor Barnes1,4, (1)Peter Medawar Building for Pathogen Research, University of Oxford, (2)Jenner Vaccine Trials Centre for Clinical Vaccinology and Tropical Medicine, University of Oxford, (3)Clinical Operations, Vaccitech, (4) National Institute for Health Research, Biomedical Research Centre, University of Oxford*

Background: Chronic infection with Hepatitis B virus (HBV) is a major global health threat. Therapeutic vaccination aims to restore the HBV specific adaptive immune response and induce functional HBV cure. Candidate therapeutic vaccine ChAdOx1-HBV encodes HBV core, polymerase and surface antigens and molecular adjuvant shark-invariant chain in a nonreplicative chimpanzee adenoviral vector. HBV001 evaluated the safety, tolerability, and immunogenicity of ChAdOx1-HBV in healthy volunteers and patients with chronic HBV.

Methods: HBV001 is an open label, non-randomised, dose escalation phase I clinical trial (NCT04297917) of ChAdOx1-HBV in healthy volunteers and patients with chronic HBV with suppressed HBV DNA on nucleos(t)ide therapy. Five healthy volunteers and 6 patients with chronic HBV received low dose (2.5 x109 viral particles (vp)) and 5 healthy volunteers and 1 patient with chronic HBV received high dose (2.5x1010 vp) intramuscular ChAdOx1-HBV. Participants were assessed prospectively for 168 weeks after vaccination for adverse events, serum alanine-aminotransferase (ALT) and quantitative Hepatitis B surface antigen (HBsAg). HBV specific T cell responses were detected by incubating peripheral blood mononuclear cells (PBMC) with overlapping HBV peptides corresponding to the entire HBV immunogen in interferongamma (IFNg) ELISpot assays. **Results:** Ten healthy volunteers and 7 patients with chronic HBV were enrolled (n=7 male, median age 40 (range 30-48 years)). Vaccination was tolerated well with no significant adverse events. Pain at the injection site was the most frequently reported adverse event, occurring in 7 participants (41%). ChAdOx1-HBV induced T cell responses specific for HBV core, polymerase and surface antigens and the summation of these responses (total response in IFNg spot forming units (SFU)) peaked at day 28 after vaccination. Peak responses were higher in healthy volunteers (median 1440, mean 1284 SFU per million PBMC, Figure 1) compared with patients with chronic HBV (median 88, mean 224 SFU per million PBMC, p=0.002). In patients with chronic HBV, ALT levels did not increase more than 2-fold and HBsAg levels did not significantly decrease during follow up. **Conclusion:** Vaccination with ChAdOx1-HBV is well tolerated and induces T cell responses in healthy volunteers and patients with chronic HBV. A phase II study of ChAdOx1-HBV in combination with MVA-HBV and the anti-PD1 agent Nivolumab in patients with chronic HBV is ongoing (HBV002, NCT04778904).

Figure 1: Longitudinal T cell responses after ChAdOx1-HBV vaccination in healthy volunteers



Disclosures:
Louise Bussey – Vaccitech Ltd: Employment
Elizabeth Eagling-Vose – Vaccitech Ltd: Employment
The following people have nothing to disclose: Tamsin Cargill, Anthony Brown, Eleanor Barnes
Disclosure information not available at the time of publication: Paola Cicconi, Benaka Karanth, Senthil Chinnakannan, Sarah Sebastian, Henrik Sorensen, Tom Evans