Phase 1b/2a study of heterologous ChAdOx1-HBV/MVA-HBV therapeutic vaccination (VTP-300) combined with low-dose nivolumab in virally-suppressed CHB patients

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INTRODUCTION

Induction of a CD8+ T cell response to HBV is considered to be a needed mechanism to achieve a functional cure of chronic hepatitis B (CHB). The highest magnitude CD8+ T cell responses achieved to date in man have used replication incompetent adenoviral vectors followed by attenuated poxvirus vector boosts.

AIM

The goal of this study is to assess the immunogenicity and activity on cccDNA of VTP-300, when combined with low-dose checkpoint inhibition, in virally suppressed, chronic hepatitis B patients.

MATERIAL & METHODS

Vaccitech has developed a therapeutic HBV vaccine using a chimpanzee adenoviral vector (ChAdOx1-HBV) and a heterologous Modified vaccinia virus Ankara boost (MVA-HBV), both encoding the inactivated polymerase, core, and the entire S region from a consensus genotype C virus1 (VTP-300). A Phase 1b/2a trial is enrolling 64 patients (16 per group in 4 Groups) with virally suppressed CHB patients. Each group in 4 Groups) with HBV DNA <40 copies/ml and HBsAg <4,000 IU) in Taiwan, South Korea, and the UK: Group 1, MVA-HBV (1 x 10^7 pfu) followed at d28 by homologous MVA HBV; Group 2, ChAdOx1-HBV (2.5 x 10^10 viral particles) followed at d28 by MVA-HBV; Group 3, same as Group 2 but low dose (LD) nivolumab (0.3 mg/kg IV) at d28; Group 4 same as Group 2 with LD nivolumab at d0 and d28 (HBV002, NCT04778904).

Enrollment criteria

- On effective antiviral treatment for one year
- HBV DNA <40 copies/ml
- SAg <4,000 IU

As of September 2021, 30 patients had been enrolled, and no concerning safety signals or Serious Adverse Reactions have been reported. We report on the first six patients in Groups 1 and 2, all from Taiwan sites, who had reached a day 30 time point for immunogenicity assessment in September. Initial results use a qualified Gamma Interferon ELISpot assay. Flow cytometry results are forthcoming.

RESULTS

VTP-300 induces antigen specific T cell responses to all antigens, with robust responses to core and polymerase, as compared to healthy controls, who exhibit a greater response to surface antigen (see accompanying poster on HBV001, NCT04297917).

The local reactogenicity was as expected, and no vaccine-associated SAEs are reported. One transaminase flare has occurred in one patient in each of Groups 1 (1/7) and 4 (1/6).

The data show that responses were optimal following the heterologous prime-boost. There is good cross-reactivity to O-specific peptides, and robust T cell responses to core were seen in the majority of the CHB patients.

CONCLUSION

VTP-300 induces antigen specific T cell responses to all antigens, with robust responses to core and polymerase, as compared to healthy controls, who exhibit a greater response to surface antigen (see accompanying poster on HBV001, NCT04297917).

REFERENCES

1. Design and Development of a Multi-HBV Antigen Encoded in a Chimpanzee Adenoviral and Modified Vaccinia Ankara Viral Vectors; A Novel Thymic Vaccine Strategy against HBV. Vaccines. 2020 Apr 12;8.

DISCLOSURES

TE, LB, EE-V, KA, AV are employees of Vaccitech (UK) Limited. EB is an inventor on the vaccine and receives consultancy income from Vaccitech (UK) Limited.

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