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PHASE 1b/2a STUDY OF HETEROLOGOUS ChAdOx1/MVA THERAPEUTIC VACCINATION COMBINED WITH LOW-DOSE NIVOLUMAB (LDN) IN WELL-CONTROLLED CHB

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Background: Induction of a CD8+ T cell response to HBV is considered to be a needed mechanism in the search of a functional cure of chronic hepatitis B. The highest magnitude CD8+ T cell responses achieved to date in man have used replication incompetent adenoviral vectors followed by attenuated poxvirus boosts. **Methods**: Vaccitech has developed a therapeutic HBV vaccine using a chimpanzee adenoviral vector (ChAdOx1-HBV) and a heterologous Modified vaccine Ankara boost (MVA-HBV), both encoding the inactivated polymerase, core, and the entire S region from a consensus genotype C virus. The vaccines also include a partial shark invariant chain as a molecular adjuvant. A Phase 1b/2a trial is enrolling 64 patients (16 patients each in 4 groups) with virally-suppressed CHB (on antivirals for a minimum of one year with VL undetectable and HBsAg < 4,000 IU) in Taiwan, South Korea and the UK: Group 1, MVA-HBV (1x 10*8 pfu) followed at d28 by homologous MVA-HBV; Group 2, ChAdOx1-HBV (2 x 10*10 viral particles) followed at d28 by MVA; Group 3, same as group 2 with LDN (0.3 mg/kg IV) at d28; Group 4 same as Group 2 with LDN at day 0 and day 28. **Results:** As of June 16, 24 patients had been enrolled, and no concerning safety signal or Serious Adverse Reaction has been reported. The 3-month HBsAg reduction, pgRNA, core-related antigen, and immune responses measured by ELISpot and multi-parameter flow cytometry will be reported for all patients enrolled by the end of June. **Conclusion:** Induction of CD8+ T cells may be critical to eventual functional cure, and we present our progress to that goal.

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