APOLLO Trial: ChAdOx1 and MVA Heterologous Prime-boost (VTP-200) Immunotherapeutic in Low-grade HPV-related Cervical Lesions

K Hellner[1], P Simon[2], KL Vahula[3], G Hancock[1], A Sawdon[4], B Jones[4], R Kennerley[4], KT Rutkowski[4], V Wheeler[4], T Evans[4], K Anderson[4], A Vardeu[4], J Kopycinski[4], C Davis[4], A Trickett[4], A Bridges-Webb[4], S O'Brien[4], MA Marshall[4]

(1) Nuffield Department of Women's & Reproductive Health, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom

(2) OB: GYN Department, Hôpital Érasme, University Libre de Bruxelles (ULB), Belgium (3) Pärnu Hospital Women's and Children's Clinic, Pärnu, Estonia

(4) Vaccitech plc, Didcot, United Kingdom

Background

Immunotherapeutic candidates are a promising approach to establish the T cell immunity that appears central in clearance of persistent high-risk HPV infections. VTP-200 is a heterologous ChAdOx1-HPV prime and MVA-HPV boost regimen of 2 viral vectors that contain 59 conserved regions from all early proteins of 5 common high-risk HPV genotypes. The APOLLO trial (also known as HPV001) is evaluating the safety, immunogenicity and efficacy of VTP-200 in participants with persistent cervical high-risk HPV (hrHPV) infection and coexisting low-grade (CIN1) cervical lesions, or HPV-related change only (LSIL/ASCUS).

Method

The primary objective is to evaluate the safety and tolerability of VTP-200. The trial will also determine the effect on the hrHPV infection and lesion(s), as well as select the appropriate dose for further development. Enrolment of the safety lead-in groups (N=9) and main phase groups (N=99; active:placebo 2:1) has completed. The main phase is a blinded, randomised, placebo-controlled trial investigating 3 dose levels of ChAdOx1-HPV (Day 0) and 2 dose levels of MVA-HPV (Day 28), with a 12-month follow-up period. The main-phase visit schedule and assessments are shown in figure 2. An interim analysis has taken place on 58 participants who have reached their 6-month timepoint. Immunogenicity results are available from a subset of these participants who entered into the immunogenicity sub-study and have sample results available (N=45).

Figure 1: APOLLO Trial Design

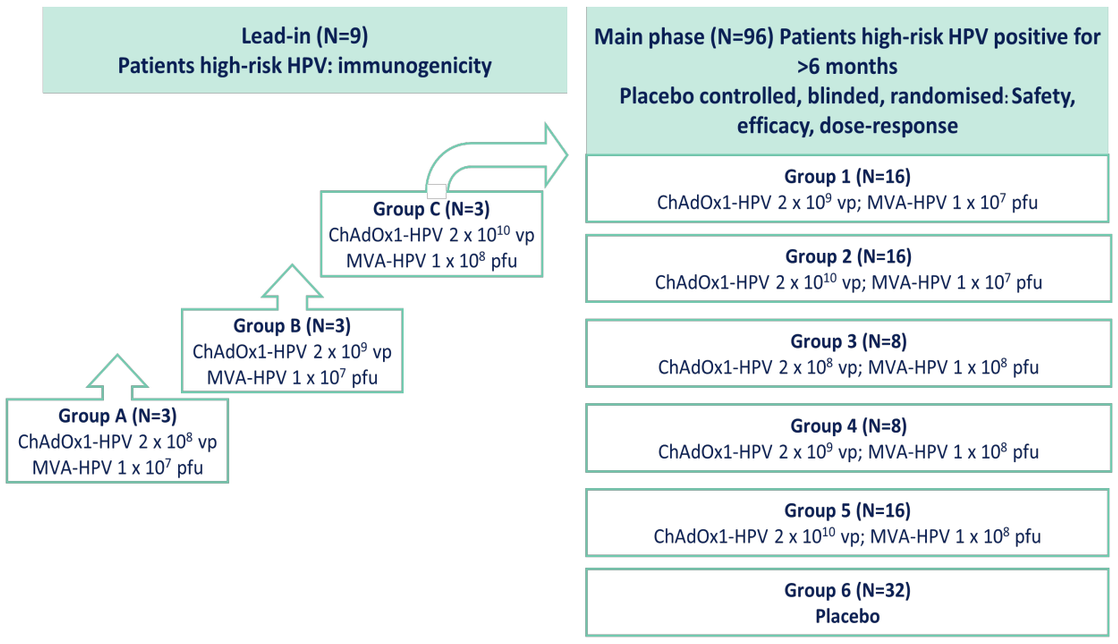
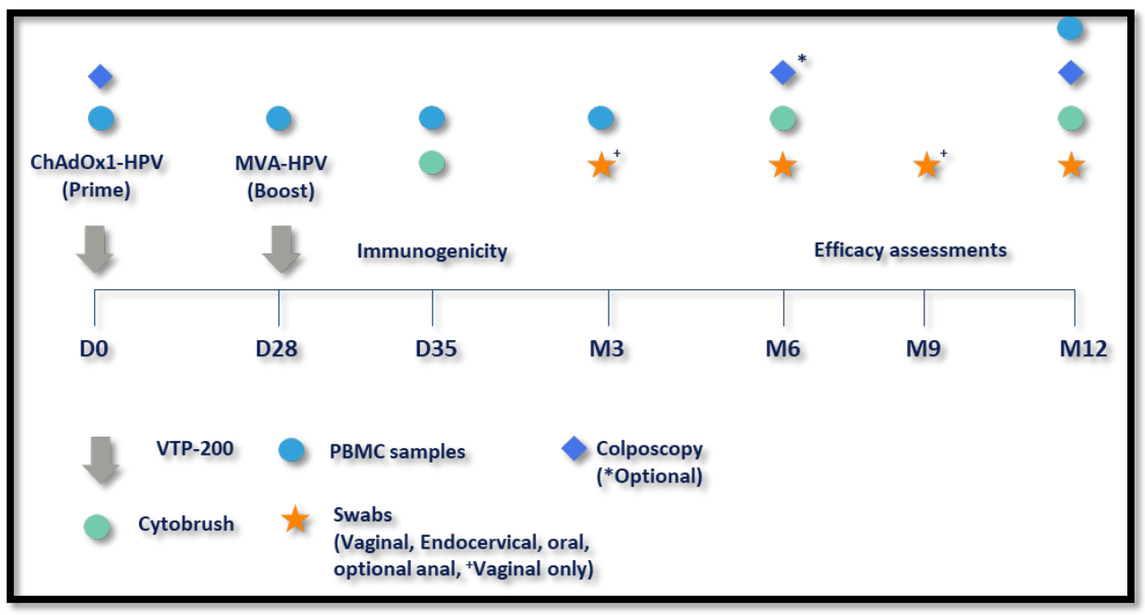


Figure 2: Main Phase Visit Schedule and Assessments



Results

Evaluation of Safety: Of the 108 participants treated:

- No related serious or related Grade ≥3 adverse events were reported.
- 7 participants reported 1 or more severe reactions in their eDiaries. The most common severe reactions were tiredness (5 participants), muscle pain (4 participants) and headache (3 participants).

Immunogenicity: Results antigen-specific ELISpot to the six antigens [E1, E2, E4, E5, E6, E7] and flow cytometry [ICS]) are presented below.

Table 1: hrHPV Genotypes at Baseline

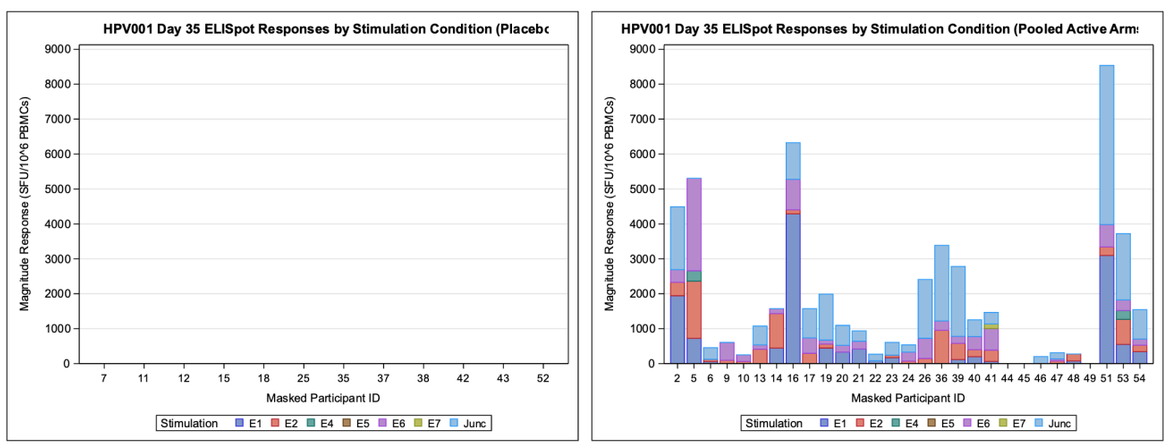
As determined by AnyPlex™ assay

Genotype	N (%)
HPV 16	26 (24%)
HPV 18	12 (11%)

# of hrHPV Genotypes	N (%)
1 hrHPV genotype	28 (26%)
2 hrHPV genotypes	20 (19%)
≥3 hrHPV genotypes	60 (56%)

Figure 3: Gamma Interferon Positive ELISpot Responses

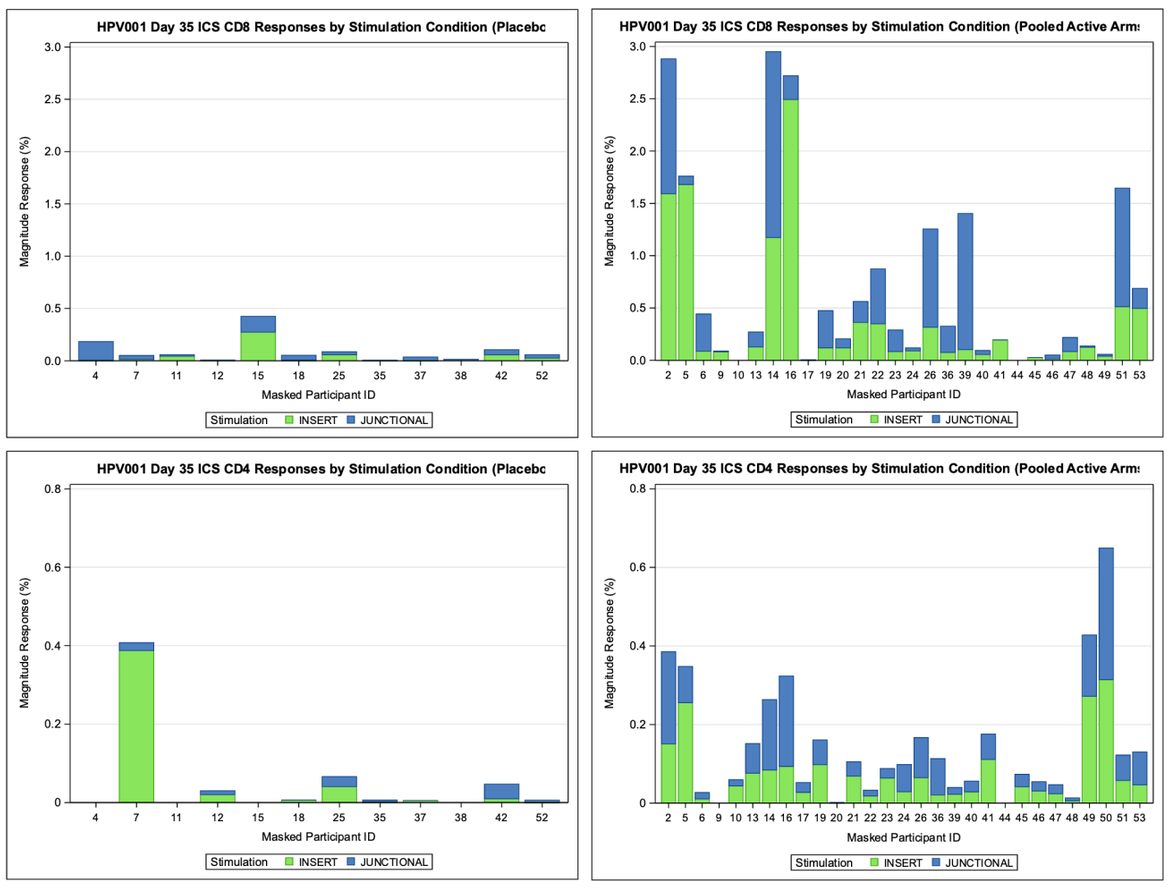
Results are shown for day 35 (peak response) in the immunogenicity sub-study participants with available immunogenicity results at the time of the interim analysis. Baseline ELISpot responses were essentially negative.



Placebo Arm | Active Arms (Pooled)

Figure 4: CD8+ and CD4+ T cell Responses by ICS

Day 35 T cell responses as measured by intracellular cytokine staining (IFNg, IL-2, TNFa) in a multiparametric flow cytometry assay. The graphs show CD8+ (top row) and CD4+ (bottom row) T cells that are positive for at least one of the three cytokines. Robust CD8+ T cell responses make up the majority of the ELISpot responses shown above (note scale difference for CD8+ versus CD4+). Baseline responses were essentially negative.



Placebo Arm | Active Arms (Pooled)

Conclusions

- The APOLLO trial is fully enrolled with minimal loss to follow-up to date.
- VTP-200 was generally well-tolerated with no product-related serious adverse events (SAEs).
- Interim data showed encouraging initial immunogenicity results, particularly in relation to the E1, E2 and E6 antigens used in VTP-200.
- The APOLLO trial will continue as planned to the 12-month primary endpoint.

APOLLO

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