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## Safety, efficacy, immunogenicity of arenavirus-based vectors HB-201 and HB-202 in patients with HPV16+ cancers

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### Background

Human papillomavirus 16 positive (HPV16+) cancers are caused by stable expression of HPV16-specific E7 and E6 oncoproteins, also a source of immunogenic neoantigens. Replicating arenavirus vectors HB-201 (LCMV) and HB-202 (Pichinde virus), expressing the same non-oncogenic HPV16 E7E6 fusion protein, induce tumour-specific T-cell responses.

### Methods

A phase I first-in-human study assessed HB-201 monotherapy and HB-201 & HB-202 alternating 2-vector therapy (HB-201/HB-202) intravenously (IV) with or without 1 intratumoral dose (IT/IV) in HPV16+ cancers. Safety, tolerability, and preliminary anti-tumour activity by Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 or immune RECIST were evaluated, as well as immunogenicity and pharmacodynamic biomarkers in blood and tumour tissue samples.

### Results

The study treated 38 patients (29 with  $\geq 1$  efficacy scan) with confirmed HPV16+ cancers with a median (range) of 3 (1–10) prior anticancer therapies. The most common primary cancer site was oropharynx (76%), followed by cervical (7.9%). Eighteen patients received HB-201 monotherapy IV and 9 IT/IV; 11 patients received HB-201/HB-202 alternating therapy. Treatment was generally well tolerated. Twenty patients (53%) reported treatment-related adverse events (all Grade  $\leq 2$ ). Two of 11 evaluable patients treated with HB-201 IV every 3 weeks had partial response (including 1 unconfirmed immune complete response of target lesion) and 6 had stable disease (SD) lasting 1.2–5.9 months. All 6 evaluable patients that received HB-201/HB-202 had SD. HPV16-specific T-cells in peripheral blood were detected at several time points post-administration through direct *ex vivo* stimulation. Different schedules, regimens, modes of administration, and doses will be presented with corresponding immunogenicity data. The proposed pathway to the recommended phase II regimen will be discussed.

### Conclusions

Arenavirus-based vectors HB-201 and HB-201/HB-202 appeared well tolerated and showed preliminary anti-tumour activity as single agents in this heavily pretreated population of patients with HPV16+ cancers. Induction of circulating E7E6-specific activated CD8+ T-cells was observed.

### Clinical trial identification

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## Legal entity responsible for the study

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