

PREDICTIVE VALUE OF CIRCULATING TUMOR DNA IN PATIENTS WITH ADVANCED HPV16-POSITIVE CERVICAL CANCER TREATED WITH VB10.16 IN COMBINATION WITH ATEZOLIZUMAB

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Background Use of circulating tumor DNA (ctDNA) has potential value as a minimally invasive approach for the diagnosis, monitoring, and management of cancer patients. Here, we investigated the potential of using HPV16 ctDNA levels as a predictive biomarker of clinical response to the therapeutic HPV16-specific cancer vaccine VB10.16, designed using a unique modular vaccine technology based on linking antigens to a CCL3L1 targeting module and developed to treat HPV16-associated premalignant and malignant lesions, in combination with atezolizumab in patients with advanced cervical cancer.

Methods Patients with recurrent or metastatic HPV16-positive cervical cancer were enrolled and received up to 11 doses of 3 mg VB10.16 intramuscularly in combination with intravenous atezolizumab 1200 mg for up to 48 weeks or until disease progression or unacceptable toxicity. Anti-tumor activity was evaluated using RECIST 1.1 criteria. Blood samples were collected at baseline and every 9 weeks to quantify HPV16 ctDNA in plasma by digital PCR (dPCR). The study was approved by the national regulatory authorities and Independent Ethic Committees (NCT04405349).

Results Of the 47 patients included in the efficacy population, the objective response rate was 19% in the overall population and 29% in PD-L1+ patients (cutoff date Dec 22, 2022). 25 of these patients had detectable baseline levels of HPV16 ctDNA and available post-baseline samples. All patients with clinical response also demonstrated molecular response (>50% decrease in HPV16 ctDNA level). Early on-treatment decreases of HPV16 ctDNA levels (week 9–11 post-baseline) were significantly correlated with disease control (11/16 patients with disease control vs 1/9 patients with progressive disease, $p = 0.011$). In contrast, increase in on-treatment levels of HPV16 ctDNA was observed in the majority of patients with progressive disease, indicating that early changes in HPV16 ctDNA levels may predict clinical outcome.

Conclusions The data suggest that molecular response and early changes in HPV16 ctDNA are promising predictive biomarkers in patients with HPV16-positive recurrent or metastatic cervical cancer treated with VB10.16 in combination with atezolizumab.

Trial Registration NCT04405349

Ethics Approval The study was approved by the national regulatory authorities and Independent Ethic Committees (NCT04405349).

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