# Use of HPV16 circulating tumor DNA detected in liquid biopsies to predict response in patients with advanced HPV16-positive cervical cancer

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## BACKGROUND

Circulating tumor DNA (ctDNA) can provide a valuable tumor-specific and non-invasive biomarker for longitudinal monitoring of a patient responses to therapy. We aimed to quantify HPV16 ctDNA in patients with advanced cervical cancer and explore the potential use of ctDNA to predict clinical outcome on treatment with VB10.16 in combination with atezolizumab.

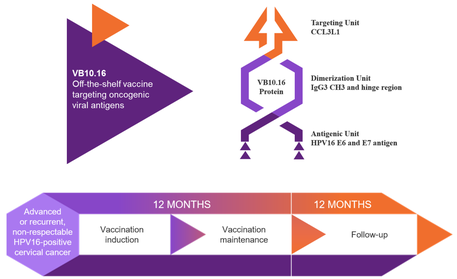
## STUDY

| Baseline characteristics | N (%) |
|---|---|
| Age (mean) | 48.9 yrs |
| Ethnicity (white) | 39 (100%) |
| Prior systemic treatment lines | |
| 1 | 12 (31%) |
| 2 | 15 (39%) |
| ≥3 | 12 (31%) |
| Prior surgery | |
| Y | 19 (49%) |
| N | 20 (51%) |
| Prior radiotherapy | |
| Y | 31 (80%) |
| N | 8 (20%) |
| Prior chemotherapy | |
| Y | 39 (100%) |
| N | 0 (0%) |
| ECOG | |
| 0 | 22 (56%) |
| 1 | 17 (44%) |
| ctDNA detected | |
| Y | 21 (54%) |
| N | 18 (46%) |
| PD-L1 status at baseline | |
| TIC 0 (<5%) | 12 (31%) |
| TIC 1 (5-10%) | 3 (8%) |
| TIC 2 (>10%) | 19 (49%) |
| Missing | 5 (13%) |
| Histology | |
| Squamous cell | 28 (72%) |
| Adenocarcinoma | 8 (21%) |
| Missing/unknown | 3 (7%) |
| Metastases* | |
| Liver | 7 (18%) |
| Lung | 17 (44%) |
| Other | 19 (49%) |
| Extra-pelvic metastases present | |
| Y | 35 (90%) |
| N | 4 (10%) |

*Sum >100% as 4 patients had both liver and lung metastases

## STUDY

This open-label, single-arm, Phase 2a trial was conducted in patients with HPV16-positive recurrent or metastatic cervical cancer. Patients received multiple doses of the therapeutic DNA vaccine VB10.16 in combination with atezolizumab.

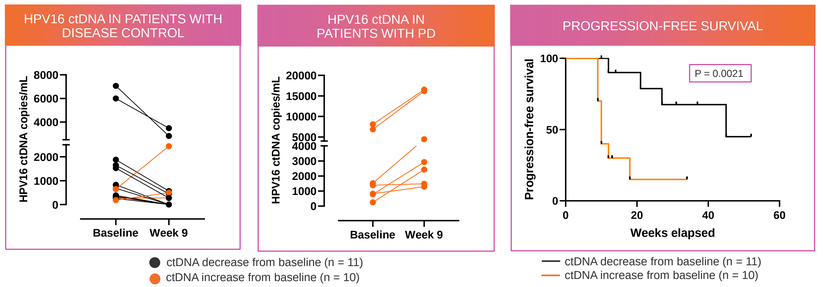



At the cut-off date of 14 February 2022 for this interim analysis, 39 patients were included in the efficacy analysis. Blood specimens were collected at baseline and every 9 weeks during treatment to quantitatively determine the HPV16 E7 viral DNA in plasma by validated duplex digital PCR (dPCR).
Primary endpoint: Objective response rate assessed by an independent central review using RECIST version 1.1 criteria.
HPV16 ctDNA was correlated with the defined clinical response as an exploratory endpoint. The study was approved by the national regulatory authorities and Independent Ethic Committees (NCT04405349).

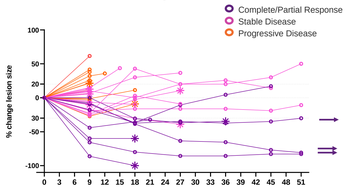
## RESULTS

### Reduced HPV16 ctDNA correlated with clinical response and longer time to progression

Analysis of liquid biopsies in patients with HPV16-positive recurrent or metastatic cervical cancer, treated with VB10.16 in combination with atezolizumab indicate that monitoring HPV16 ctDNA may predict clinical outcome and duration of response in an HPV16-specific therapy setting.




### VB10.16 in combination with atezolizumab showed promising efficacy with durable responses



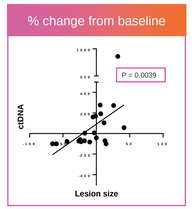

N=38
1=NE; not evaluable
Treatment period week 0-48

The cohort had
- ORR 21%
- DCR 64%
- PFS 4.2 months

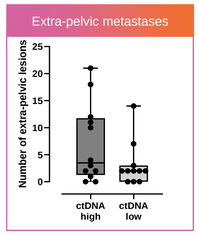
✱ *Subjects with ongoing study treatment at cut off date (n=12)*
→ *3 responders who completed study treatment showed ongoing response on last available scan (Week 51)*

### ctDNA correlates with post-baseline lesion size

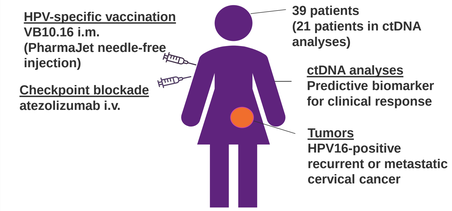
In all patients (n = 21), the percent change from baseline in post-treatment analyses (week 9) of ctDNA and lesion size were correlated.




### Trend towards higher baseline ctDNA levels in patients with extra-pelvic metastases




## SUMMARY




- VB10.16 in combination with atezolizumab showed promising efficacy in patients with advanced HPV16+ cervical cancer
- VB10.16 in combination with Atezolizumab showed durable responses with a high DCR in advanced cervical cancer patients
- Reduced HPV16 ctDNA levels were significantly correlated with clinical outcomes indicating that HPV16 ctDNA may be an early marker of response to treatment
- VB10.16 in combination with atezolizumab has a favorable safety profile

**Acknowledgement**
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