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vaccibody

An Exploratory Safety and Immunogenicity Study of Human Papillomavirus (HPV16+) Immunotherapy VB10.16 in Women with High Grade Cervical Intraepithelial Neoplasia (HSIL; CIN 2/3)

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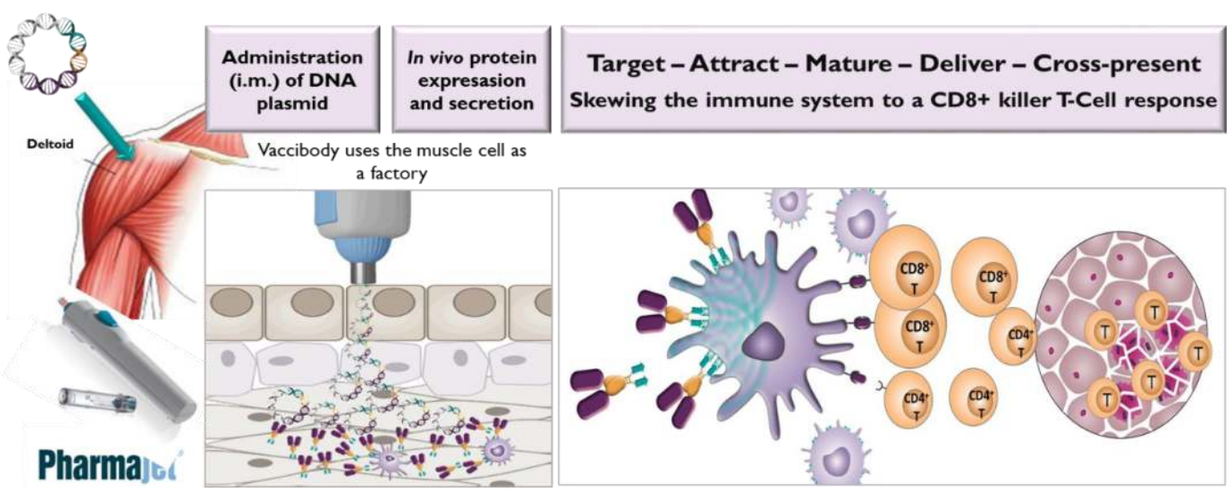
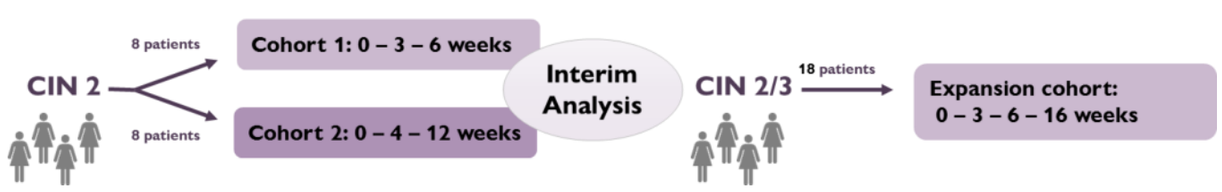
BACKGROUND

Persistent HPV infection can lead to high-grade squamous intraepithelial lesions (HSIL) in cervical cells; current treatments are exclusively ablative which can lead to long-term reproductive morbidity.

VB10.16, an investigational immunotherapy designed to treat precancers and cancers induced by HPV16, is a potent DNA plasmid vaccine with intrinsic adjuvant effect designed for efficient delivery of antigens E6 and E7 from HPV16 to elicit strong immune responses.



STUDY DESIGN



VB C-01 is a first-in-human dose, open-label, multicenter phase 1/2a study of VB10.16 immunotherapy for the treatment of high grade Cervical Intraepithelial Neoplasia (CIN 2/3) caused by HPV16. Patients were followed for 12 months after first vaccination.

The **primary objective** of the study was to evaluate the safety and tolerability of VB10.16. The **secondary objectives** were to assess peripheral T cell immunogenicity and to evaluate early signs of efficacy by means of CIN regression and HPV clearance.

DEMOGRAPHICS & TREATMENT

Demographic Characteristics	Cohort 1	Cohort 2	Expansion	Overall
Number of Patients	8	8	18	34
Age (years)				
Mean	31.4	27.4	29.1	29.2
Min - Max	25-46	25-30	24-41	24-46
Categorization of CIN				
CIN2	8 (100.0%)	8 (100.0%)	8 (44.4%)	24 (70.6%)
CIN3	0	0	10 (55.6%)	10 (29.4%)
Number of vaccinations				
Two	0	0	1 (5.6%)	1 (2.9%)
Three	8 (100.0%)	8 (100.0%)	0	16 (47.1%)
Four	0	0	17 (94.4%)	17 (50.0%)

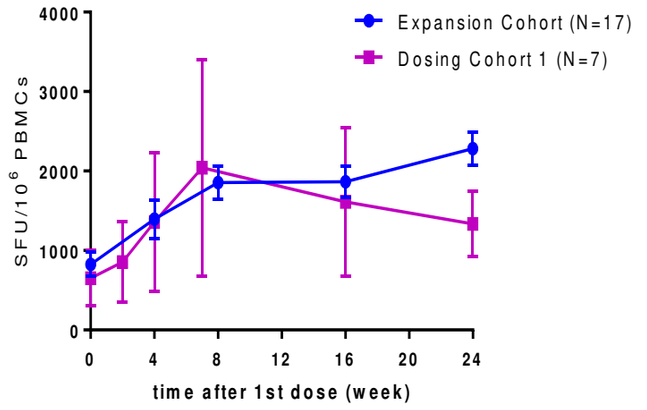
The phase 2a study enrolled 18 CIN2/CIN3 patients, 1 patient was not HPV16 positive and thus 17 patients received four doses of 3 mg VB10.16 at week 0, 3, 6 and 16. LPLV 17Jan2019.

SAFETY

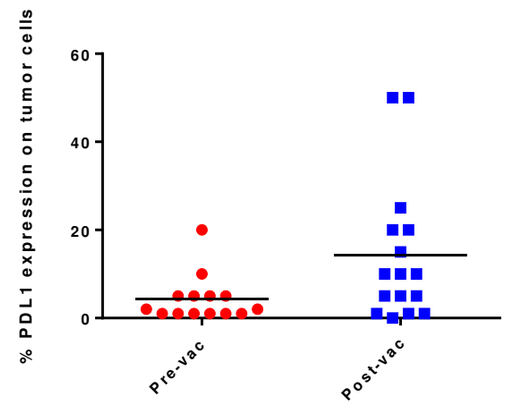
Treatment with VB10.16 was well tolerated, and mild to moderate injection site reactions were reported as the most frequent related adverse events. No patients experienced SAEs or discontinued the study vaccine due to an AE. The highest grade of AEs were Grade 3 in 3 patients (one of the patients reported two injection site Grade 3 related AEs).

IMMUNOGENICITY

VB10.16 induced strong, long-lasting HPV16 specific immune responses



PD-L1 up-regulated in patients after vaccination

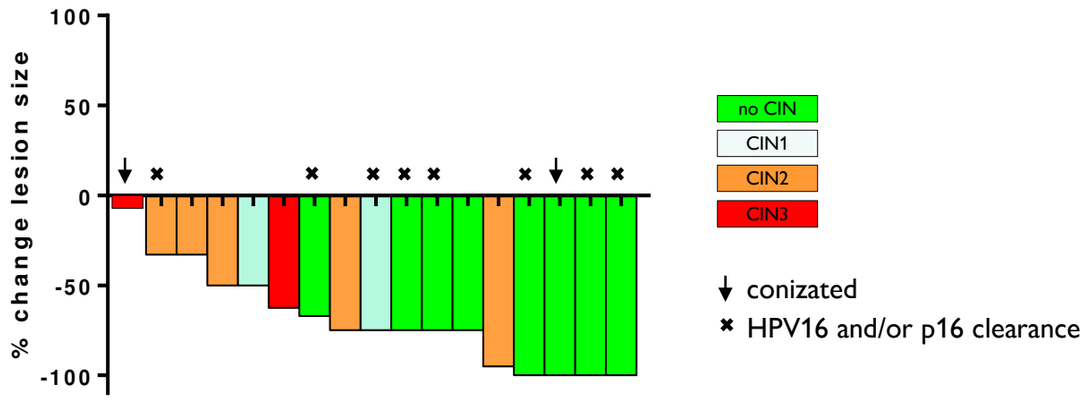


Immunological analyses of the peripheral T cell responses demonstrated a strong HPV16-specific T cell immune response in 94% of the patients. Adding a booster dose at week 16 in the Expansion cohort leads to stronger and longer-lasting T cell responses to HPV16 E6 and E7 proteins as measured in IFN-γ ELISpot (left).

PD-L1 was up-regulated in patients after vaccination, which is in line with the vaccine VB10.16 inducing strong local IFN-γ T cell responses (right).

CLINICAL EFFICACY

VB10.16 shows promising clinical efficacy in expansion cohort



Of the 17 patients evaluated in the phase 2a expansion cohort, 16 patients showed a reduction in the lesion size as best overall response. Of these, 12 had more than a 50% reduction. HPV16 and/or p16 clearance was observed in 8 patients.

Histopathological regression to low grade neoplasia (CIN1) or no disease was seen in 10 patients as best response.

Of the 6 patients that have not regressed to CIN1 or less at 12 months, 6 patients showed upregulation of PD-L1 in the lesions which may delay or inhibit elimination of all affected cells.

Two patients had conization prior to 12 months follow-up. One patient withdrew consent.

CONCLUSIONS

- Strongly encouraging phase 2a safety, tolerability, immunogenicity and signs of clinical efficacy results for a therapeutic HPV16 DNA plasmid vaccine VB10.16 in women with HSIL are reported.
- VB10.16 is capable of eliciting HPV16-specific CD4+ and CD8+ T cells contributing to elimination of HPV16 infected and transformed cells, leading to reduction in lesion size and CIN grading.
- Up-regulation of PD-L1 post vaccination provides a rationale for investigating the combination of checkpoint inhibitors with VB10.16 in HPV16 associated cancers.
- A phase 2 clinical trial in HPV16 positive cervical cancer in combination with atezolizumab (Tecentriq®) is planned to start early 2020.

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