Efficacy and safety of VB10.16, a therapeutic DNA vaccine specifically targeting antigen presenting cells, in combination with atezolizumab in patients with advanced HPV16-positive cervical cancer: results from a pre-planned interim analysis

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BACKGROUND

VB10.16 is a novel therapeutic antigen-presenting cell targeting DNA vaccine developed to treat HPV16-positive cancers.

We aimed to investigate whether VB10.16 is safe and efficacious when administered to patients with advanced cervical cancer in combination with atezolizumab.

METHODS

In this open-label, single-arm, phase 2a trial, patients with recurrent or metastatic HPV16-positive cervical cancer were recruited at 13 hospitals across Europe.

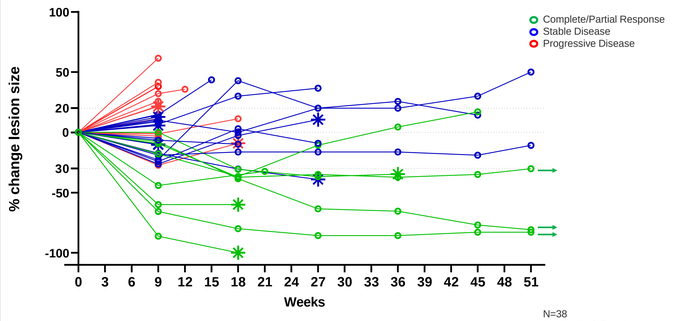
Patients received up to 11 intramuscular 3 mg VB10.16 vaccinations in combination with 3-weekly 1200 mg atezolizumab for up to 48 weeks, or until disease progression or unacceptable toxicity.

Anti-tumor activity was assessed by central independent review using RECIST v1.1 criteria.

RESULTS

At the cut-off date of 14 February 2022 for this interim analysis, 39 patients had at least one post-baseline scan available and were included in the efficacy analysis. 69% of patients had received 2 or more prior systemic treatment lines.
Overall Response Rate (ORR) was 21%, with 2 Complete Responses (CR) and 6 Partial Responses (PR). Responses were observed in both PD-L1 positive and negative patients (ORR 27% and 17%, respectively). Disease Control Rate (DCR) was 64% (77% in PD-L1 positive and 58% in PD-L1 negative patients).
50 patients had received ≥1 dose of VB10.16 and atezolizumab and were included in the interim safety analysis. 5 patients (10%) experienced treatment-related adverse events (TRAEs) of grade 3, including 1 patient (2%) who experienced a grade 3 TRAE related to VB10.16. No grade 4-5 TRAEs were reported.

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

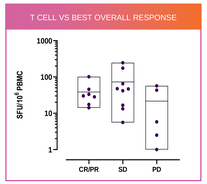


✱ *Subjects with ongoing study treatment at cut off date (n=12)*
→ *3 responders who completed study treatment showed ongoing response on last available scan (Week 51)*

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

System Organ Class Preferred Term	Any Grade N=50 (%)	Grade 3 N=50 (%)	Grade 4-5 N=50 (%)
All TRAEs related to VB10.16	15 (30)	1 (2)	-
General disorders and adm. site conditions.	8 (16)	-	-
Administration site pain	2 (4)	-	-
Fatigue	1 (2)	-	-
Injection site bruising	2 (4)	-	-
Injection site discomfort	2 (4)	-	-
Injection site haematoma	1 (2)	-	-
Injection site pain	1 (2)	-	-
Injury, poisoning and procedural complications	1 (2)	-	-
Infusion related reaction	1 (2)	-	-
Metabolism and nutrition disorders	1 (2)	-	-
Decreased appetite	1 (2)	-	-
Musculoskeletal and connective tissue disorders	3 (6)	1 (2)	-
Arthralgia	1 (2)	1 (2)	-
Myalgia	1 (2)	-	-
Pain in extremity	1 (2)	-	-
Skin and subcutaneous tissue disorders	4 (8)	-	-
Erythema	1 (2)	-	-
Pruritus	2 (4)	-	-
Rash	2 (4)	-	-

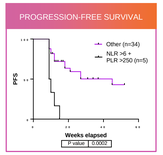
HPV16-specific T cell responses observed in majority of patients with clinical response



- *IFN-g T cell responses were evaluated in 21 subjects*
- *T cell responses were evaluated in ex vivo ELISpot detecting HPV16 E6 and E7 antigens separately*

Blood based biomarkers as prognostic and predictive factors

Patients with elevated neutrophile-lymphocyte ratio (NLR) and platelet-lymphocyte ration (PLR) values (>6 and >250) had worse clinical outcomes



NLR > 6 + PLR ≥ 250	Total (n = 39)	CR/PR (n = 8)	SD (n = 17)	PD (n = 13)	NE (n = 1)	ORR	DCR
Yes	5 (13%)	0 (0%)	2 (12%)	3 (23%)		0%	33%
No	34 (87%)	8 (100%)	15 (88%)	10 (77%)	1 (100%)	**23%**	**68%**

CONCLUSIONS

- VB10.16 combined with atezolizumab had a favorable safety profile in heavily pre-treated patients.
- The combination treatment showed clinically relevant HPV16-specific T cell responses and promising and durable clinical activity with a high DCR of 64% and 8 patients achieving CR or PR.
- Anti-tumor efficacy was observed in both PD-L1 positive and negative patients, with 27% overall response rate (ORR) and 77% DCR in PD-L1 positive patients, and 17% ORR and DCR 58% in PD-L1 negative patients.
- Elevated NLR and PLR values appeared to be applicable prognostic and predictive factors, indicating that baseline levels of these readily accessible inflammation markers could aid in patient selection.

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