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Phase 2 study of AI-designed personalized neoantigen cancer vaccine, EVX-01, in combination with pembrolizumab in advanced melanoma

EVAXION AI-Immunology™ Powered Vaccines

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Introduction

Despite the recent progress in checkpoint inhibitor therapy, there remains an unmet need to further improve the outcomes of patients with advanced melanoma. Here, we report one-year data from a phase 2 study, assessing safety, efficacy and immunogenicity of the personalized neoantigen (neoAg) peptide vaccine, EVX-01, combined with pembrolizumab in advanced melanoma (NCT05309421). In this study, we identified and selected tumor-specific neoAgs based on tumor DNA- and RNA-sequencing data using the proprietary vaccine target discovery platform, AI-Immunology™.

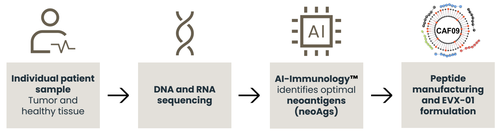
The top-ranked neoAgs for each patient were manufactured as synthetic long peptides (max. 10 neoAgs) and formulated with a liposomal adjuvant, creating the personalized cancer vaccine, EVX-01, tailored to each patient's individual tumor and immune system characteristics.

Conclusions

- The combination of EVX-01 and anti-PD-1 therapy led to an encouraging observed response rate, ORR, of 11/16 (68.8%) in the overall cohort
- Further improvements in clinical responses were observed following the introduction of EVX-01 at week 12; PR to CR: 2/9 (22.2%) and SD to PR/CR: 2/5 (40.0%)
- 3/16 (18.8%) patients achieved complete remission of tumor target lesions
- A decrease in target lesion size was observed in 15 out of the 16 patients
- The AI-Immunology™ platform predicted immunogenic neoAgs with a high success rate of 78.6%
- A positive correlation was observed between AI-Immunology™ predictions and neoAg immune response (p=0.00013)
- Our results indicate that EVX-01 holds promise as a safe and effective therapeutic approach when used in combination with anti-PD-1 therapy

1. Clinical Study Design & Demographics

a)



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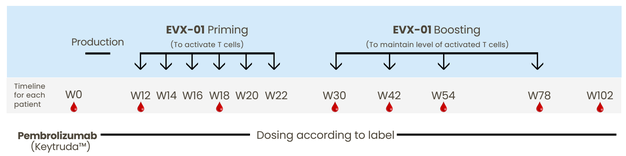
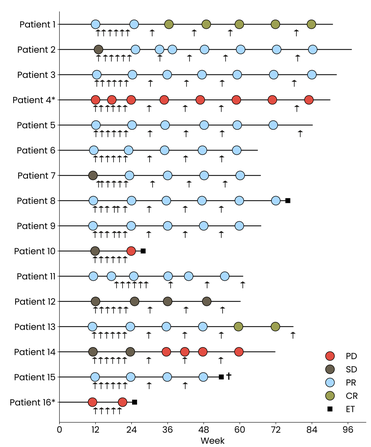


Figure 1.
a) Manufacturing process of EVX-01 personalized vaccine. Production process from tumor biopsy, prediction and selection of neoAgs, manufacturing and establishing the final EVX-01 product consisting of peptides and CAF09b® liposomal adjuvant.
b) Clinical study design and blood sampling. The combination treatment consisted of **Pembrolizumab** (400mg IX Q6W) and **EVX-01** (2mg IM). EVX-01 was administered Q2W during priming vaccination followed by four booster vaccinations given at W30, W42, W54 and W78.
c) Tumor PD-L1 expression was analyzed in a four-plex fluorescence assay using the PD-L1 specific antibody clone 28-8. PD-L1 positivity was defined as 5/100 cells (immune & tumor cells) showing significant membrane staining (>5%).

c)

Patient demographics and disease characteristics at study baseline	
Sex, n (%)	
Male	11 (69)
Female	5 (31)
Age, n (%)	
<65	7 (44)
≥65	9 (56)
Ethnicity, n (%)	
Caucasian	16 (100)
ECOG performance-status score, n (%)	
0	15 (94)
1	1 (6)
Disease stage, n (%)	
Unresectable Stage IIIB	2 (12.5)
Unresectable Stage IV	14 (87.5)
Number of lesions, mean [interval]	
Target	2.1 [1-5]
Non-target	1.1 [0-4]
PD-L1 expression, n (%)	
<5%	4 (25)
>5%	8 (50)
Unknown	4 (25)
BRAF mutation status, n (%)	
Positive	8 (50)
Negative	6 (38)
Unknown	2 (13)
Lactate dehydrogenase, n (%)	
Normal	10 (63)
Elevated	2 (13)
Unknown	4 (25)

2. Clinical Event Timeline and Safety



Overview of clinical responses at week 12 compared to best overall response

Clinical response per RECIST 1.1.	Week 12 response, n	Best overall response, n
Complete response	0 (0.0%)	2 (12.5%)
Partial response	9 (56.3%)	9 (56.3%)
Stable disease	5 (31.3%)	3 (18.8%)
Progressive disease	2 (12.5%)	2 (12.5%)
No assessment, not included	1	1

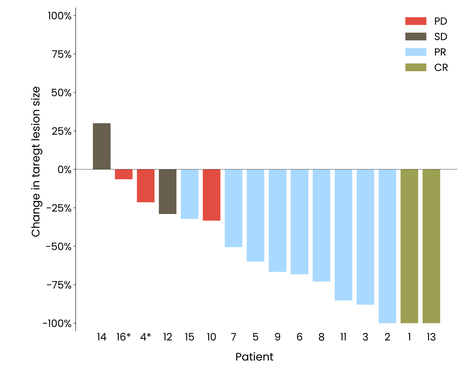
EVX-01 Safety (n=16)

For the 16 patients dosed with EVX-01, 159 treatment emergent adverse events (AEs) were reported which were primarily Grade 1/2. Reported AEs included 8 injection site reactions (5.0%), 5 diarrhea (3.1%), 2 fatigue (1.3%) and 3 rash (1.9%). For the treatment combination of EVX-01 and Pembrolizumab the following AEs were reported; 1 immune related type 1 diabetes (G3), initially reported as secondary diabetic ketoacidosis. 1 immune related type 1 diabetes (G4), initially reported as pancreatitis. 2 SAEs; 1 being fatigue and 1 anorexia. At the time of publication, the G4 event was still ongoing. 1 death was reported with no relation to study treatment. Data cut-off: 27-Jul-2024.

Figure 2. Clinical Event Timeline
Overview of clinical response assessments and EVX-01 dosing. Week 0 is defined as the date of first Pembrolizumab treatment. Circles indicate the day of each clinical response assessment and are colored according to the assessment per RECIST 1.1. The arrows indicate the day of each EVX-01 administration. Early termination (ET) is indicated with a black square and a cross indicates early termination due to death. The primary analysis includes patients with SD or PR after 12 weeks of pembrolizumab treatment and evaluates if additional treatment with EVX-01 improves the clinical responses of these patients to PR or CR. *Patients not included in the primary analysis. Patient 4 had PD at week 12 but experienced tumor reduction later (see Fig. 3b).

3. Clinical Response

a)



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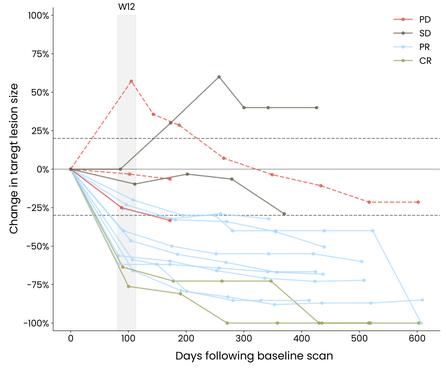


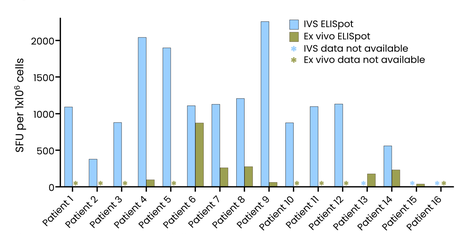
c)

Best Overall Response	
Improvement from SD to PR/CR	2/5 (40.0%)
Improvement from PR to CR	2/9 (22.2%)
ORR	11/16 (68.8%)
Median Follow up (months)	14.8
Median OS	NR
Median PFS	NR

Figure 3. Best Clinical Response
a) Largest reduction in target lesion size for each patient compared to baseline. Bars are colored according to each patient's best overall response at the data cut-off date as assessed by RECIST 1.1. *Patients not included in the primary analysis as they were not SD or PR at week 12.
b) Change in target lesion size over time. Day 0 is defined as the day of the baseline scan. Lines are colored according to each patient's best overall response at the data cut-off date as assessed by RECIST 1.1. Dashed lines indicate patients that are not included in the primary analysis.
c) Best response as evaluated by investigators. Data cut-off: 21-Aug-2024. For the observed response rate (ORR), 95% 2-sided CI: [41.3%, 89.0%] (Clopper-Pearson).

4. Immunogenicity

a)



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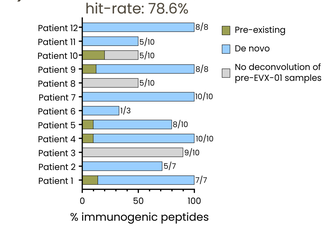

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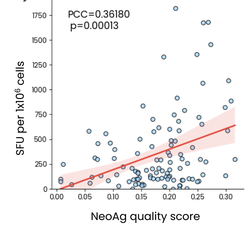

Figure 4. Immunogenicity
a) Best observed immune response against EVX-01 peptide pool measured by IFNγ ELISpot directly ex vivo or after in vitro stimulation (IVS). **b)** Immunogenicity of individual neoAgs after six or more EVX-01 vaccinations. In total 103 peptides were analyzed, of which 81 were immunogenic (78.6%). **c)** Linear regression and Pearson correlation analysis of predicted neoAg quality score and best observed immune response in IFNγ ELISpot. Background signals are subtracted from all ELISpot data. PCC: Pearsson correlation coefficient.

Acknowledgement and Contact

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