Real-World Comparator Study to MVX-ONCO-1, a cell-based immunotherapy currently in Phase II, shows prolonged OS and PFS for patients with Recurrent/Metastatic Head & Neck Squamous Cell Carcinoma (R/M HNSCC)

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BACKGROUND

- MVX-ONCO is a unique, innovative personalized cell-based cancer vaccine.
- MVX-ONCO is the combination of irradiated autologous tumor cells and local delivery at the subcutaneous vaccination of sustained, stable, standardized GM-CSF for 7 days. Thus using the widest and most specific tumor associated antigens and one of the most potent adjuvant methods.
- GM-CSF is one of the most potent immunostimulatory cytokines when delivered locally at the site of immunization, at low dose and in a sustained manner over days. In many murine models, local, stable release of GM-CSF over days at the immunization site by genetically modified irradiated tumor cells is among the strongest adjuvants. It induces potent, long-lasting, specific anti-tumor immunity in all cancer type tested. Cell Encapsulation Technology developed by MaxiVAX provides a clinical grade immunization platform recapitulating the murine scheme.
- All therapeutic products are processed in GMP conditions.
- After the successful completion of the Phase I, MaxiVAX is currently running the multicenter Phase IIa in patients with R/M HNSCC failing at least one line of systemic therapy.
- In order to better characterize the clinical data in R/M HNSCC treated with MVX-ONCO we performed a real world external comparator study, comparing all R/M HNSCC treated with MVX-ONCO with a matched control from two clinical sites from IQVIA's Oncology Evidence Network: University Hospital Frankfurt (Frankfurt) , Germany and Portuguese Oncology Institute of Porto (IPO-Porto), Portugal.

MVX-ONCO THERAPY

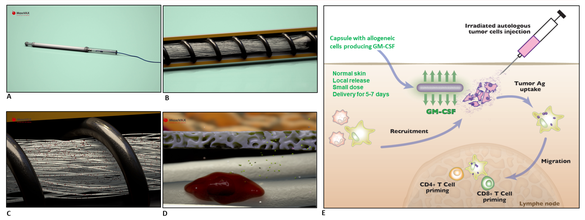
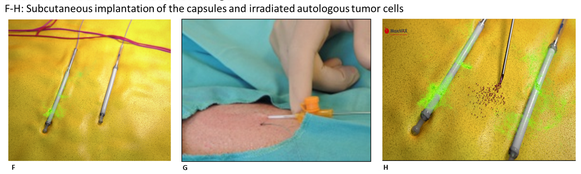
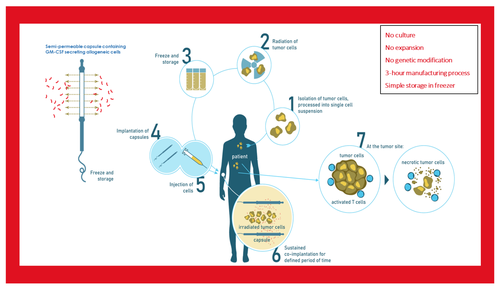


Fig 1 Encapsulation Cell Technology
A-D: Clinical Grade Capsule illustration
E: Scheme of the Cancer Vaccine at the Priming Site
F-H: Subcutaneous implantation of the capsules and irradiated autologous tumor cells



TREATMENT SCHEME



Treatment dose

Each treatment dose consists of two capsules containing $8x10^5$ MVX-1 cells and a single injection containing $4x10^6$ lethally irradiated autologous tumour cells. Capsules are removed after 1 week.

Treatment regimen

6 vaccinations over 9 weeks
No maintenance therapy

STUDY DESIGN

Patient cohorts

	SAKK 11/16 Trial Cohort	Real World Comparator Cohort
Total number of patients	16	62
Total number of eligible lines of therapy	16	105

A comparator patient can have more than one eligible line of therapy for matching providing the I/E criteria are met at the start of each line

Primary Objectives

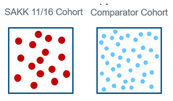
The primary objective of this study will be to evaluate the **effectiveness of anticancer therapy approaches in real-world practice in European matched cohort control, Versus the SAKK11/16 trial population.** The effectiveness of anticancer therapies will be evaluated in terms of the **endpoints:**

- **Overall Survival (OS)**
- **OS at 26 weeks**
- **Time to Subsequent Therapy (TTST)**
- **Progression-Free Survival (PFS)**

The cohorts were balanced to improve their comparability

- All patients in the trial and comparator cohorts have met the inclusion/exclusion criteria (with the necessary adaptations required for the comparator) – the two cohorts therefore contain the same type of patients
- In addition to this, balancing (matching and weighting) is conducted to ensure the trial and comparator cohorts are similar:
  - Matching involves comparing similar patients on a patient level, whilst weighting applies a value (0-1) to each patient (eligible LoT) based on its likeleness to patricipate in the trial
  - While direct 1:1 matching requires that completely identical patients in both cohorts exist, balancing adjusts the distributions of variables that may affect a patient's prognosis between the SAKK 11/16 and comparator cohort.
  - In this study, the cohorts were balanced for line of therapy number, age, sex, year of R/M HNSCC diagnosis, time from HNSCC to R/M HNSCC diagnosis, tumor site, WHO score, HPV status and having previously received radio-chemotherapy or immunotherapy for R/M HNSCC

SAKK 11/16 Cohort Comparator Cohort



Before balancing

Select prognostic variables	SAKK 11/16 Cohort	Comparator Cohort
Average age	61.0	59.2
Average time from HNSCC to R/M HNSCC	22.3	6.7
% WHO Score 0	37.5	7.56

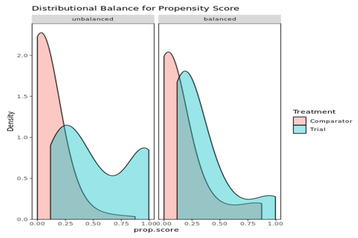
After balancing

SAKK 11/16 Cohort	Comparator Cohort
59.9	59.5
13.6	7.2
27.7	15.1

Matching identifies comparator patients (blue balls) that are similar to the trial patients (red balls) across a range of prognostic variables. Weighting applies weights to each patient (red and blue balls) with the goal of balancing distributions of prognostic variables. This will result in two cohorts that are more similar at the cohort level, and thus the outcome at a cohort level can be assessed as would be the case in a two-armed RCT

The propensity score density plot also reveals that the comparator and trial cohorts are more comparable after balancing

The greater the overlap between the two cohorts, the more comparable they are



While efforts were made to design a robust study, it is important to keep in mind that there were some unavoidable limitations

Limitations	Mitigatiuons
The trial cohort has a small sample size (N016)	A weighting approach was used as a main analysis retaining more patients in the analysis than a matching approach
Patients from the comparator sites (IPO-Porto and Frankfurt) may not be representable and generalisable to all R/M HNSCC patients	The same inclusion/exclusion criteria (with the necessary adapations required fot the comparator) were applied to both the trial and comparator cohorts
IPO-Porto, Frankfurt and MaxiVAX may have interpreted LoT grouping differently	Guidelines were provided in the Statistical Analysis Plan (SAP) and any uncertain ,case were discussed and agreed collaboratively
IPO-Porto, Frankfurt and MaxiVAX may have interpreted variable definitions differently	All parties used the same common data model
PFS is more rigorously captured for the trial patients than for real-world comparator patients	Follow-up data from IPO-Porto and Frankfurt are generally of high quality, yet still being real-world data. No further mitigation could be applied

ANALYSIS

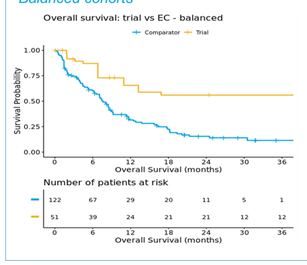
Balanced cohort characteristics

		SAKK 11/16 Trial Cohort N	SAKK 11/16 Trial Cohort %	Real World Comparator Cohort N	Real World Comparator Cohort %
Cohort Size [sum of weights]	N	50.9	100%	121.7	100%
Demographics					
Age at index (years)	Mean (SD)	59.9 (7.8)		59.5 (7.8)	
	Median (Q1-Q3)	57.0 (53.5-66.3)		58.8 (53.9-64.1)	
	Min-Max	42 - 76		41 - 78	
Sex	Male	49.6	97.5%	108.4	89.1%
	Female	1.3	2.6%	13.3	10.9%
Clinical characteristics					
Year of aHNSCC diagnosis	2013	2.7	5.3%	0	0%
	2015	10	19.7%	9.1	7.5%
	2016	0	0%	15.1	12.4%
	2017	4.6	9%	21.1	17.3%
	2018	6.4	12.6%	39.7	32.6%
	2019	15.9	31.2%	25.6	21%
	2020	3.1	6.1%	11.1	9.1%
	2021	8.2	16.1%	0	0%
Time from HNSCC diagnosis to aHNSCC diagnosis (for early diagnosed) (months)	Mean (SD)	13.6 (19.7)		7.2 (7.6)	
	Median (Q1-Q3)	8.0 (4.2-13.8)		7.5 (0.03-10.6)	
	Min-Max	0.1 - 110.3		0.03 - 43.4	
Tumour site	Oral cavity	22.7	44.6%	41.5	34.1%
	Oropharynx	17.3	34%	32	26.3%
	Hypopharynx	8.2	16.1%	40.4	33.2%
	Larynx	2.7	5.3%	7.8	6.4%
WHO performance score at index	0	14.1	27.7%	18.4	15.1%
	1	31.4	61.7%	83.9	68.9%
	2	5.4	10.6%	16.4	13.5%
	Unknown	0	0%	3	2.5%
HPV at index	Positive	4.9	9.6%	5	4.1%
	Negative	5.6	11%	11.2	9.2%
	Unknown	40.4	79.4%	105.4	86.7%
P16 at index	Positive	18	35.4%	10.3	8.5%
	Negative	24.5	48.1%	34.9	28.7%
	Unknown	8.4	16.5%	76.5	62.9%
Previous radio-chemotherapy or immunotherapy	Yes	38.5	75.5%	54.9	45.1%
	No	12.5	24.5%	66.8	54.9%
Treatment Characteristics					
Year of index	2014	2.7	5.3%	0	0%
	2016	8.3	16.3%	14.5	11.9%
	2017	0	0%	6.4	5.3%
	2018	5.2	10.2%	18.4	15.1%
	2019	3.3	6.5%	26.5	21.8%
	2020	20.1	39.6%	47.2	38.8%
	2021	6.5	12.8%	8.6	7.1%
	2022	4.7	9.3%	0	0%
Index LoT (Line of Threapy)	1	0	0%	8	6.6%
	2	30	58.8%	68.2	56%
	3	13.7	26.9%	30.8	25.3%
	4	5.6	11%	12	9.9%
	5	1.7	3.3%	2.7	2.2%
Had subsequent therapy after index therapy	Yes	16.1	31.6%	76	62.5%
	No	34.8	68.4%	45.7	37.6%
Time from aHNSCC diagnosis to index (months)	Mean (SD)	14.3 (11.8)		14.4 (9.7)	
	Median (Q1-Q3)	9.9 (6.8-18.4)		12.1 (7.8-19.8)	
	Min-Max	2.1 - 60.3		0.2 - 48.7	
Index treatment	Cetuximab +- other IO	0	0%	12.9	10.6%
		0	0%	33.7	27.7%
	Non-platinum based chemo	0	0%	64.3	52.8%
	Platinum based chemo	0	0%	10.8	8.9%
	Trial treatment	50.9	100%	0	0%
Index LoT duration (days)	N	49.9	98%	120.7	99.2%
	Mean (SD)	52.6 (10.3)		129.4 (206.6)	
	Median (Q1-Q3)	55.3 (44.5,56.3)		70.4 (23-138.3)	
	Min-Max	29 - 71		1 - 1476	
	Missing/Unknown	1	2%	1	0.8%

Overall Survival (OS) & OS at 26 weeks

87.1% vs 60.2 %

Balanced cohorts



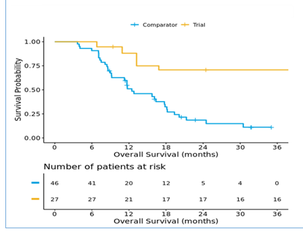
	SAKK 11/16 Trial Cohort	Real World Comparator Cohort
Patient Count [sum of weights]	50.9	121.7
OS – Survival time		
Number of censored observations (%)	32.3 (63.5)	28.2 (23.1)
Number of events (%)	18.6 (36.5)	93.5 (76.9)
25% quantile survival time in months [95% CI]	6.8 [4.5, NA]	2.8 [1.4, 5.3]
Median survival time in months [95% CI]	NA [6.8, NA]	7.6 [6.0, 9.2]
75% quantile survival time in months [95% CI]	NA [NA, NA]	16.4 [11.7, 24.5]
OS – Survival rate		
At 3 months, % [95% CI]	91.6 [80.2, 100.0]	74.3 [63.3, 87.3]
At 3 months, ARR, % [95% CI]	17.2 [0.2, 34.3]	
At 26 weeks, % [95% CI]	**87.1 [73.8, 100.0]**	**60.2 [49.5, 73.1]**
At 26 weeks, ARR, % [95% CI]	**26.9 [8.4, 45.4]**	
At 9 months, % [95% CI]	73.0 [49.9, 100.0]	39.8 [30.5, 52.0]
At 9 months, ARR, % [95% CI]	33.2 [3.5, 62.9]	
At 12 months, % [95% CI]	65.6 [41.0, 100.0]	31.6 [23.0, 43.2]
At 12 months, ARR, % [95% CI]	34.0 [1.6, 66.4]	

ARR = absolute risk reduction; CI = confidence interval Robust CI with bootstrapping in [1-2%, 48.6%

Overall Survival (OS) & OS at 26 weeks in pts with subsequent therapy

100% vs 90.8 %

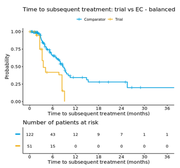
Balanced cohorts



	SAKK 11/16 Trial Cohort	Real World Comparator Cohort
Patient Count [sum of weights]	34.8	45.7
OS – Survival time		
Number of censored observations (%)	22.1 (63.6)	10.6 (23.2)
Number of events (%)	12.7 (36.4)	35.1 (76.8)
Median survival time in months [95% CI]	NA [10.9, NA]	12.8 [11.3, 18.2]
OS – Survival rate (at 26 weeks)		
At 26 weeks, % [95% CI]	100.0 [100.0, 100.0]	90.8 [82.5, 99.8]
At 26 weeks, ARR, % [95% CI]	9.2 [0.6, 17.8]	

Time to Subsequent Therapy (TTNT)

Balanced cohorts

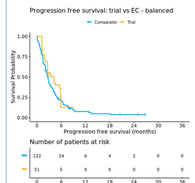


	SAKK 11/16 Trial Cohort	Real World Comparator Cohort
Patient Count [sum of weights]	50.9	121.7
TTNT – Time		
Number of censored observations (%)	16.1 (31.6)	76.0 (62.5)
Number of events (%)	34.8 (68.4)	45.7 (37.5)
Median survival time in months* [95% CI]	**4.1 [1.8, NA]**	**8.7 [7.3, 14.9]**
TTNT – Rate (at 26 weeks)		
At 26 weeks, % [95% CI]	41.8 [17.3, 100.0]	65.3 [55.1, 77.3]
At 26 weeks, ARR, % [95% CI]	-23.4 [-61.9, 15.1]	NA

- Median TTNT is 4.1 months in the trial cohort vs. 8.7 months in the comparator cohort
- Expected that trial patients are more likely to receive additional treatment due to being more closely monitored while on an interventional trial.

Progression Free Survival (PFS)

Balanced cohorts



	SAKK 11/16 Trial Cohort	Real World Comparator Cohort
Patient Count [sum of weights]	50.9	121.7
PFS – Time		
Number of censored observations (%)	14.1 (27.6)	9.7 (8)
Number of events (%)	36.8 (72.4)	112.0 (92)
Median survival time in months* [95% CI]	**4.1 [1.8, NA]**	**2.7 [2.1, 3.5]**
PFS – Rate (at 26 weeks)		
At 26 weeks, % [95% CI]	12.5 [2.0, 78.6]	21.0 [14.1, 31.2]
At 26 weeks, ARR, % [95% CI]	-8.5 [-32.9, 16.0]	NA

- Median PFS is 4.1 months in the trial cohort vs. 2.7 months in the comparator cohort

CONCLUSIONS

- MVX-ONCO is a novel personalized cancer vaccine using Encapsulating Cell Technology, currently in Phase IIa
- MVX-ONCO is very safe with no systemic therapy related adverse event reported in >50 treated patients
- Early analysis on all 16 heavily pretreated R/M HNSCC pts are intriguing with clear signs of immune stimulation, tumor control and prolonged survival
- This Real-World Comparator Study was conducted to have a better understanding of the potential therapeutic effect of MVX-ONCO on survival in pts with advanced R/M HNSCC, in progression after at least one prior line of systemic anticancer therapy
- These results clearly show a meaningful improvement in Median OS and an ARR of death of 26.9% at 26 weeks and 34.0% at 12 months
- The subgroup analysis of pts receiving subsequent therapies is also favorable to MVX-ONCO
- With strong signs of single agent activity, very good safety profile and biological evidence of synergy between cell-based vaccine and IO, combination therapy with anti-PD-1/PD-L-1 moAB should be tested in R/M HNSCC and other cancers such as NSCLC, melanoma, kidney, bladder and liver.