NOVEL PERSONALIZED IMMUNOTHERAPY WITH CELL-ENCAPSULATION TECHNOLOGY FOR ADVANCED REFRACTORY HEAD AND NECK SQUAMOUS CELL CARCINOMA

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ABSTRACT

Despite current cancer therapies, the vast majority of patients with advanced disease die within 5 years. Preclinical data show that sustained, local delivery of low doses of GM-CSF by irradiated, genetically engineered tumor cells at the immunization site leads to specific, long-lasting anti-tumor immunity in several tumor types. Excess of GM-CSF and/or systemic activity leads to tolerance, accentuating the critical delivery method for this adjuvant. Providing sustained levels of GM-CSF subcutaneously in a clinical setting remains challenging. Cell-Encapsulation Technology enables the sustained and controlled delivery of GM-CSF by allogeneic cells. Moreover, each tumor is distinct and no single Tumor Associated Antigen has proven its efficacy as single target.

MVX-ONCO is an active, personalized cancer immunotherapy combining irradiated autologous tumor cells as a specific source of Antigen and Encapsulated allogeneic human cells genetically engineered to secrete human GM-CSF as a strong adjuvant.

This strategy can be applied to any cancer types and in all settings (adjuvant, advanced 1st line, 2nd line).

MATERIALS AND METHODS

Source of Antigens: The patient's own cancer cells as source of Antigens

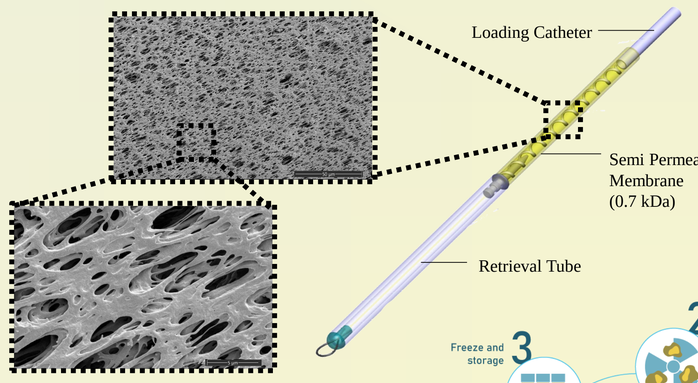
Wide, diverse and specific antigenic repertoire.

Adjuvant : GM-CSF

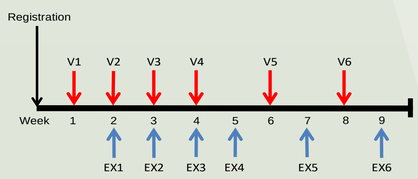
Mode of Delivery: CELL-ENCAPSULATION TECHNOLOGY

for Local delivery in a sustained manner of small dose of the adjuvant

Allogeneic human cells genetically engineered to secrete human GM-CSF, encapsulated into a macrocapsule constituted with semipermeable membrane.

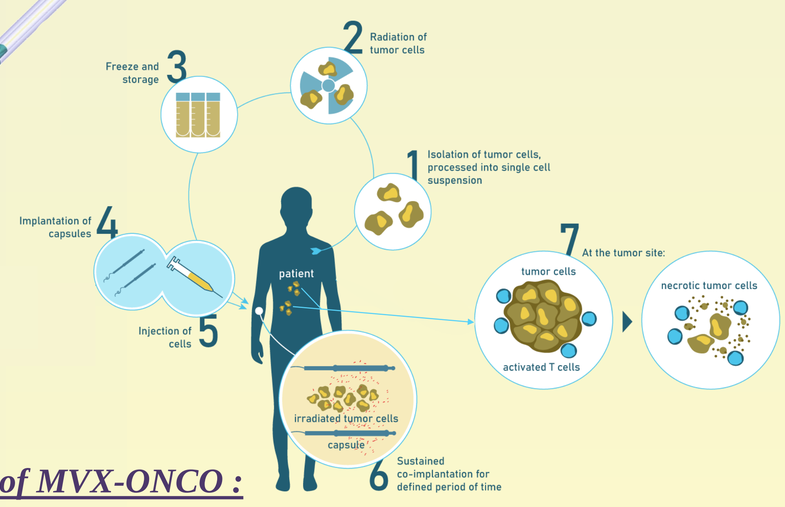


See in Video :
How "Capsules" are working



TREATMENT REGIMEN :

4 vaccinations 1 week apart, followed by 2 boosters 2 weeks apart = 6 vaccinations over 8 weeks.
Each dose consists of 2 capsules co-implanted subcutaneously with an injection of irradiated autologous tumor cells. Capsules are removed after 1 week.



RESULTS

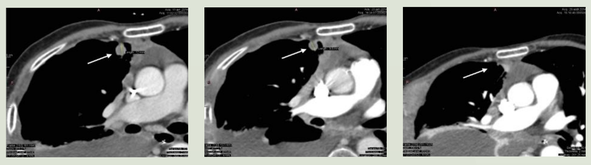
Phase I first in human trial completed:

34 patients were treated in a single-arm clinical trial (NCT02193503) evaluating the feasibility, safety and efficacy of MVX-ONCO :

No patients experienced any treatment-related systemic toxicities. Local hematoma at the implantation site was reported in a minority of patients.

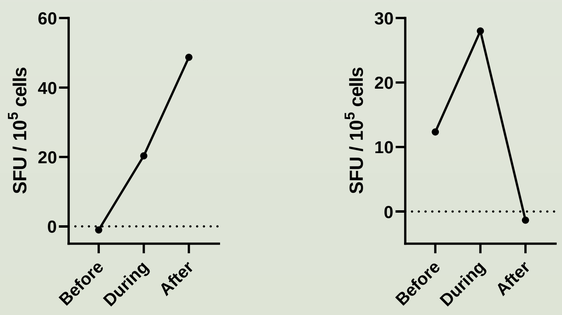
Some degree of disease control was observed in 20/34 patients: Prolonged survival in 2/2 R/M HNSCC patients correlated with **IFN-γ ELISpot** :

- Partial Clinical Response to MVX-ONCO :

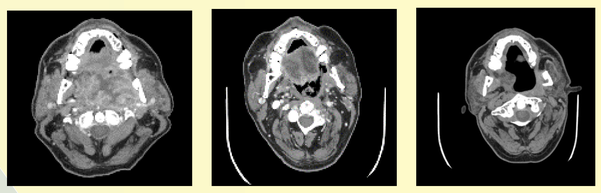


Baseline – Before MVX-ONCO | *Partial Response – After MVX-ONCO* | *Complete Response – 2 Months after MVX-ONCO*

IFN- γ secretion after stimulation with brachyury protein analyzed by ELISPOT



- Complete Clinical Response to MVX-ONCO + Subsequent Treatment :



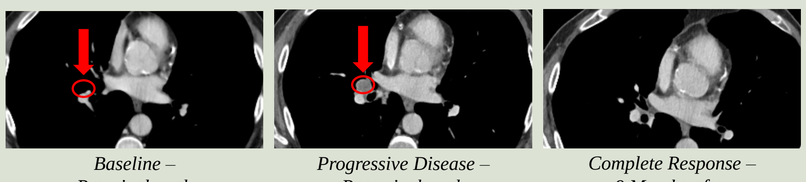
Baseline – Before MVX-ONCO | *Partial Response – 7 Months after MVX-ONCO* | *Complete Response – 5 Years after MVX-ONCO*

Phase II Head and Neck Carcinoma :

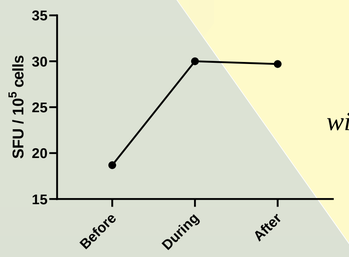
Ongoing, actually 15 patients were treated (NCT02999646) :

Metastatic Head & Neck carcinoma patients progressing after at least one line of systemic therapy.

- Complete Clinical Response to MVX-ONCO :



Baseline – Pre-nivolumab | *Progressive Disease – Post-nivolumab Before MVX-ONCO* | *Complete Response – 9 Months after MVX-ONCO*



IFN- γ secretion after stimulation with autologous irradiated tumor cells analyzed by ELISPOT

CONCLUSION

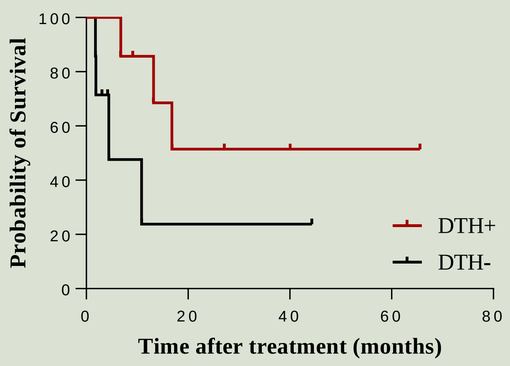
All Head and Neck Patients :

- **79% (11/14) failed prior immune checkpoint therapy**
- **71% (10/14) alive at 6 months**
- **55% (6/11) alive at 12 month**

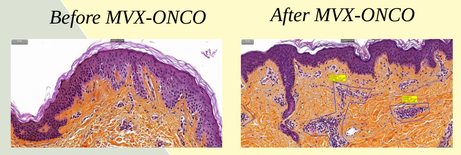
1 Complete Response obtained with MVX-ONCO alone
2 Complete Response achieved with subsequent therapy
1 Partial Response obtained with MVX-ONCO alone
2 Partial Response achieved with subsequent therapy
6 Stable Disease / 2 Progressive Disease

Circulating T cell reactivity (IFN-γ ELISpot) and DTH (Delayed Type Hypersensitivity) positivity correlates with >6 months survival

	6 Months SURVIVAL	DTH	IFN- γ ElISPOT
Patient 1 (Ph I)	YES	NEG	POS
Patient 2 (Ph I)	YES	POS	POS
Patient 3 (Ph II)	YES	NEG	NEG
Patient 4 (Ph II)	YES	POS	POS
Patient 5 (Ph II)	YES	POS	NEG
Patient 6 (Ph II)	NO	NEG	NA
Patient 7 (Ph II)	YES	POS	POS
Patient 8 (Ph II)	YES	POS	NEG
Patient 9 (Ph II)	NO	NEG	NA
Patient 10 (Ph II)	NO	NEG	NA
Patient 11 (Ph II)	YES	POS	POS
Patient 12 (Ph II)	YES	POS	POS
Patient 13 (Ph II)	YES	NEG	NEG
Patient 14 (Ph II)	NO	NEG	POS



Before MVX-ONCO | *After MVX-ONCO*



Skin Punch Biopsy of the Delayed Type Hypersensitivity site show perivascular immune cells recrutment during treatment

MVX-ONCO is feasible, safe, and well-tolerated. Preliminary efficacy data show immune stimulation, intriguing prolonged survival and tumor control including PR and CR as Best Overall Response.
Single-agent efficacy Phase II study is ongoing in this population.

SCAN ME

Concurrent use of anti-PD1 and MVX-ONCO should be tested in a subsequent clinical trial.

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