Personalized immunotherapy with cell-encapsulation technology for ≥2nd line R/M HNSCC: Safety and early efficacy data from all HNSCC patients treated with MVX-ONCO-1 in two clinical trials

Eugenio Fernandez [1], Remi Vernet [2], Emily Charrier [2], Markus Joerger [3], Veronika Nagy [3], Marie-Claude Belkouch [2], Muriel Urwyler [2], Olivier Von Rohr [2], Olivier Rubin [4], Jean Villard [4], Virginie Ancrenaz [1], Nicole Grandjean [1], Emmanuel Lavaliere [1], Elisabeth Lafferma [1], Julien Grogg [5] and Nicolas Mach [1]

1 Clinical Research Unit, Oncology Division, Geneva University Hospital, Switzerland, 2 Cell-based Immunotherapy lab, Onco-hematology Translational Research Center, Geneva Medical School, Geneva Switzerland, 3 St-Gallen Cancer Center, St-Gallen, Switzerland, 4 Clinical Cell Therapy Lab, Diagnostic Dpt, Geneva University Hospital, Geneva Switzerland, 5 MaxiVAX SA, Geneva, Switzerland

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BACKGROUND

→Potent anticancer immunization requires tumor-specific antigens (Ag) and strong adjuvant.
→ Despite decades of intense research, no defined Ag is approved for active immunotherapy of any solid tumor, including HNSCC. Irradiated autologous tumor cells provide a source of all potential Ag and can be processed easily.
→ GM-CSF is one of the most potent immunostimulatory cytokine 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.
→ Systemic delivery or high doses of GM-CSF is not a good adjuvant method as it recruits MSDC and does not boost cancer immunity.
→Using Cell Encapsulation Technology, we have developed a novel sc clinical grade immunization platform combining encapsulated, allogeneic cells genetically engineered to release GM-CSF and lethally irradiated autologous tumor cells.
→This novel cell-based immunotherapy combines sustained, stable, standardized, local release of GM-CSF and tumor specific antigens.

TECHNOLOGY

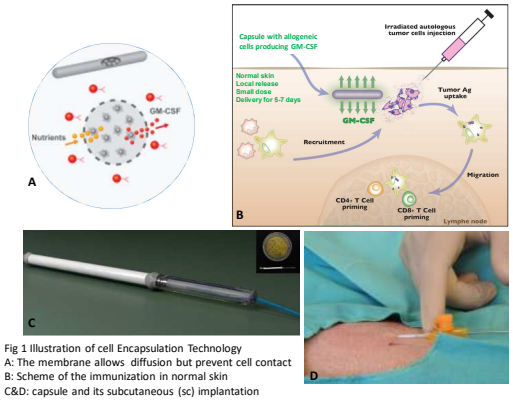

Fig 1 Illustration of cell Encapsulation Technology
A: The membrane allows diffusion but prevent cell contact
B: Scheme of the immunization in normal skin
C&D: capsule and its subcutaneous (sc) implantation

METHODS

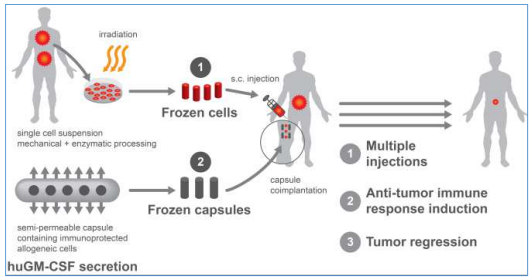

Fig 2 Illustration of the immunization process with 2 components
Component **1** is personalized as it is made of autologous irradiated tumor cells harvested from a tumor deposit ($1cm^3$)
Component 2 is similar for all pts. It is a biocompatible capsule loaded with $8x10^5$ MVX-1 cells.
MVX-1 is a certified, allogeneic cell line, engineered to secrete stable level of huGMCSF.
Boths components 1&2 are implanted sc next to each other in normal skin, distant from any tumor deposit
While irradiated tumor cells are not retrieved, capsules are removed after 1 week
Immunizations are repeated on distinct location for a maximum of 6 times over a 8 week period

CLINICAL DATA

2nd extension of Phase I trial is ongoing. > 30 pts, including 2 R/M HNSCCH pts have been treated (NCT02193503)
Phase II, single arm, multicentric, efficacy study is ongoing in 5 centers in Switzerland for R/M HNSCC pts progressing after at least one line of systemic therapy (NCT 02999646).
Primary endpoint is OS at 6 months, sample size is 41pts
Recruitment has decreased significantly over the last 15 months due to the pandemic but sites have restarted enroling pts.
We present here all 11 pts treated with MVX-ONCO-1. Doses and treatment schedules are similar in both studies. Data cut off is April 25th 2021
Except for one pt (1116013) all pts have more than 15 months follow-up

EXPERIMENTAL TREAMENT SCHEME

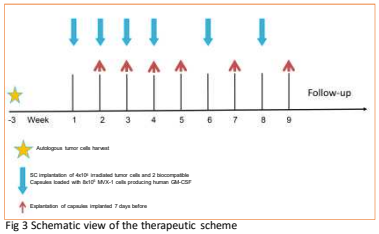

Fig 3 Schematic view of the therapeutic scheme

Patient Demographics	N=11
Age Range	42-77 yo
Sex Male/Female	10/1
Habits Smoker / Non Smoker	10/1
Site Oral Cavity/oro/hypo/larynx	5/5/0/1
HPV status +/- (only for Oropharyngeal SCC)	2/3
Extension at enrolment Locally advanced /Metastatic	2/9
PDL-1 status CPS <1 / >1	5/6
Previous lines (all included) 2 / 3 / 4 / 5	3/4/4/1
Previous exposure and progression on ICI (Pembrolizumab or Nivolumab)	8

FEASIBILITY / SAFETY	% (N=11)
Sucessfull IMP manufacturing	100
Enrolled in the treament Phase / treated	100
Tumor processed sucessfully	100
Sucessfull capsules manufacturing and implantation	100
Systemic adverse event related to the therapeutic product G1-5	0
Local reaction at the immunization site 0/G1/2/3/4	7/2/2/0/0

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Swiss Cancer League

CLINICAL DATA

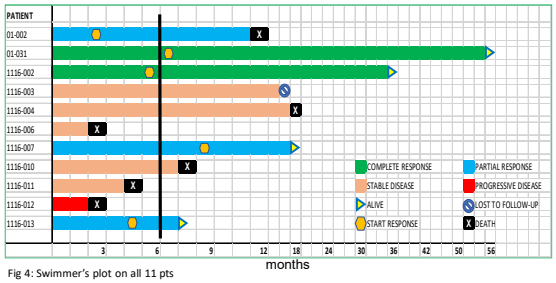


Fig 4: Swimmer's plot on all 11 pts

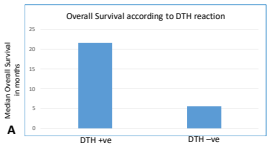
Overall survival	6 months	9 months	12 months	15 months
	8/11	6/10	5/10	5/10

Pt 1116013 is alive, in PR and has not yet reach the 9 months follow-up mark, therfore only 10 pts are censored for OS at 9,12 and 15 months

Best Overall Response	N=11	%
Complete Response	2	18.2
Partial Response	3	27.3
Stable Disease	5	45.5
Progressive Disease	1	9
Overall response Rate	5	45.5
Disease Control Rate	10	91

While 1 PR was observed on MVX-ONCO-1, 1PR and 1CR were observed on subsequent Nivolumab therapy (both CPS=0), and 1 CR and 2PR were observed after subsequent palliative chemotherapy.

IMMUNOMONITORING



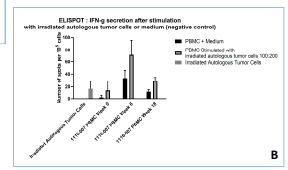


Fig 8
A:DTH with $5x10^5$ irradiated autologous tumor cells is performed at baseline, Week 6 and Week 12. All pts were negative at baseline. 10 pts are analyzed for this survival analysis as pt 1116013 follow-up is still short.
B: INF gamma Elispot for pt 1116007

Sofar seromic analysis and INF γ Elipsot were performed on blood samples from 6 pts at baseline, Week 6 and Week 18. By seromics upregulated potential antigens were observed in all pts, with some interesting targets shared by 4 out of 6 pts (data not presented) . INF γ Elispot using autologous tumor cells showed interesting results such as data observed in pt 11160007. Correlation between DTH, INF γ Elispot and seromic is ongoing

CONCLUSIONS

- MVX-ONCO-1 has a very good safety profile with no systemic AE.
- Early data on all 11 heavily pretreated R/MHNSCC pts are intriguing with clear signs of immune stimulation, tumor control and prolonged survival. DCR is observed in >90% of pts with both CRs and PRs
- Prolonged survival is observed in pts pretreated with immune-checkpoint inhibitors and in patients subsequently treated with palliative chemotherapy, raising questions on antigenic stimulation by MVX-ONCO-1 leading to subsequent tumor control
- A coordinated Immune education upon immunization with MVX-ONCO-1 is observed with both cellular (INF γ Elispot), humoral (seromic anylsis) and delayed type hypersensitivity responses (+ve DTH test to autologous tumor cells)
- Combining MVX-ONCO-1 with immune-checkpoint inhibitor should be tested in subsequent clinical studies

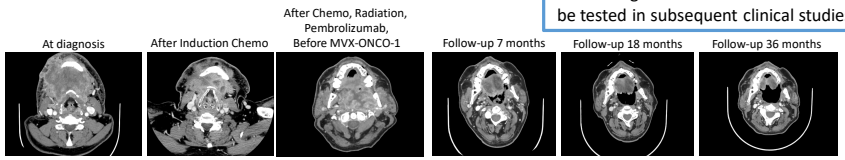


Fig 5: Illustration of radiological response of pt 001-002. This pt was treated with Pembrolizumab in Keynote040, progressed before enrolling in MVX-ONCO-1 trial

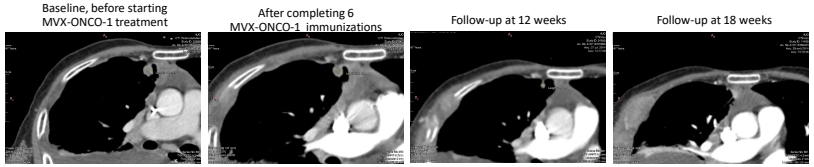


Fig 6: Illustration of radiological response of pt 001-001. The lung metastasis (12 mm) shows a complete response over several months during MVX-ONCO1 treatment

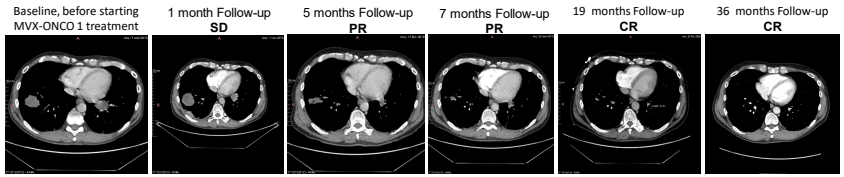


Fig 7: Illustration of radiological response of pt 1116002. Pt had PD after 3 cycles of Extreme regimen, has >5 lung mets, one removed to manufacture personalized immunotherapy . While in SD after >4 months follow-up, pt was started on Nivolumab despite CPS=0 and developped a sustained CR ongoing for > 2 years

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