

Immunologic correlates of ONCOS-102 therapy in patients with advanced solid tumors

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on behalf of ONCOS-102 investigators
November 6, 2015

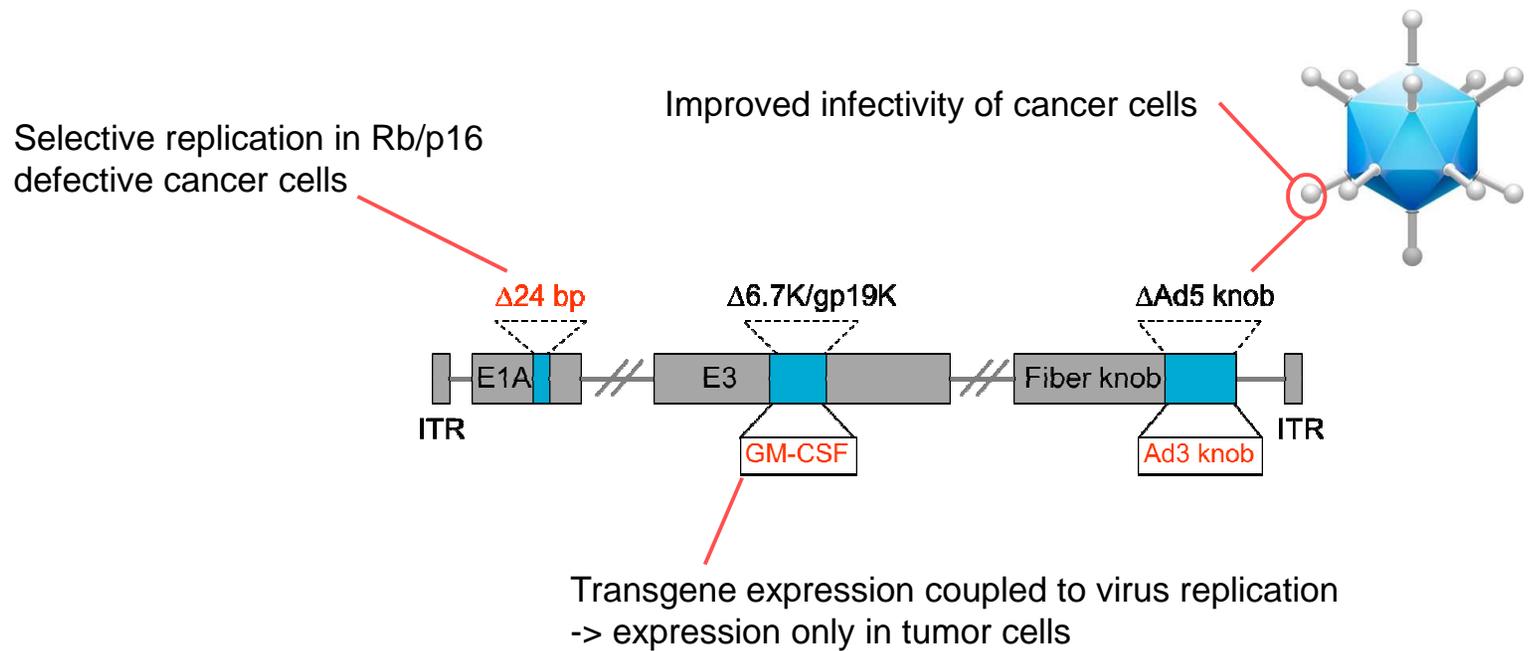
Presenter Disclosure Information

Dmitriy Zamarin MD PhD

The following relationships exist related to this presentation:

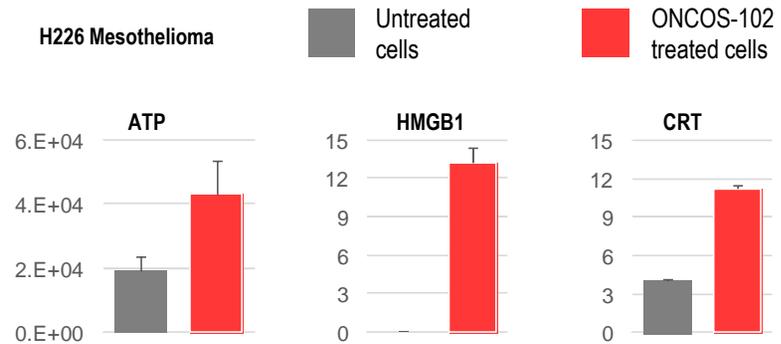
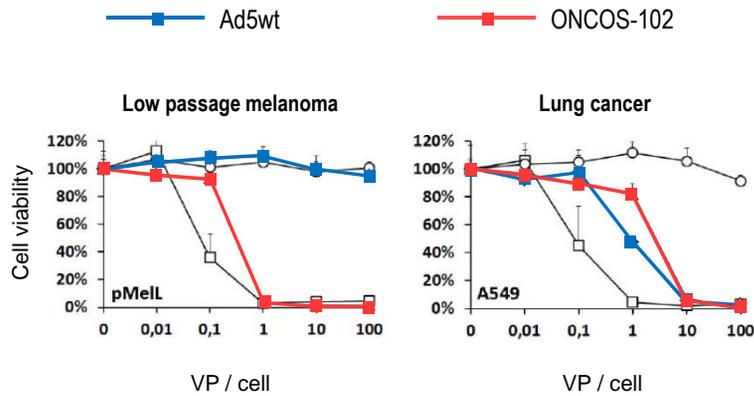
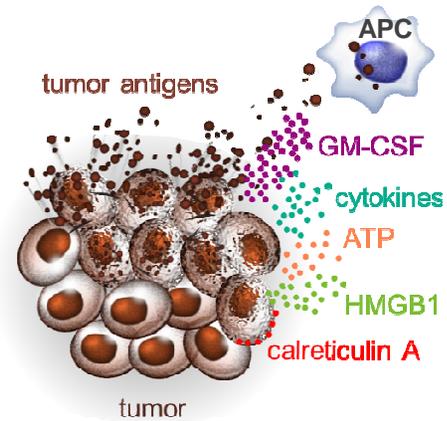
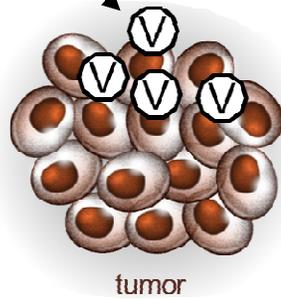
No relationships to disclose

ONCOS-102: genetically modified oncolytic adenovirus encoding GM-CSF



ONCOS-102 replicates in cancer cells and induces immunogenic cell death

Intratumoral administration

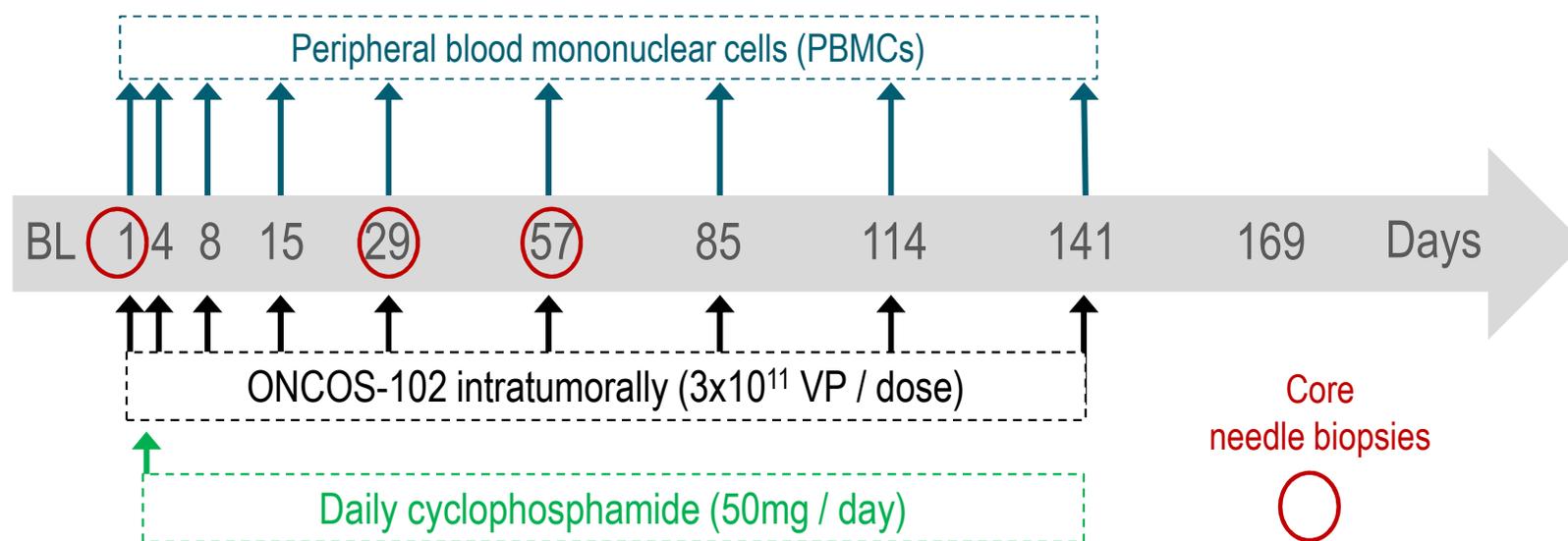


Phase I study of intratumoral ONCOS-102 with low dose cyclophosphamide in patients with advanced solid tumors

Dose	Patient number	WHO score	Age/ Sex	Cancer type	Number of previous lines of therapy
3x10 ¹⁰ VP	F11-01	1	64 / F	Ovarian	16
	F11-02	0	61 / M	Colon	3
	F11-04	0	55 / F	Colon	4
1x10 ¹¹ VP	F11-06	0	63 / M	Liver	2
	F11-08	1	63 / F	Lung	3
	F11-09	1	63 / M	Mesothelioma	2
3x10 ¹¹ VP	F11-13	0	53 / M	Rectum	4
	F11-14	1	68 / M	Mesothelioma	2
	F11-15	1	67 / F	Endometrial	5
	F11-17	1	64 / F	STS	6
	F11-18	1	51 / F	Breast	11
	F11-19	0	38 / F	Ovarian	7

- 115 cancer patients with solid refractory tumors were treated with ONCOS-102 in Advanced Therapy Access Program (ATAP) before the current Phase 1 study

ONCOS C1: a Phase I study of intratumoral ONCOS-102 with low dose cyclophosphamide in patients with advanced solid tumors



Safety:

- No DLT's were seen in any treatment groups
- Most AEs were grade 1-2, primarily pyrexia and flu-like symptoms.

Efficacy assessment

Patients

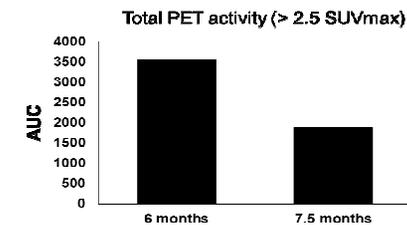
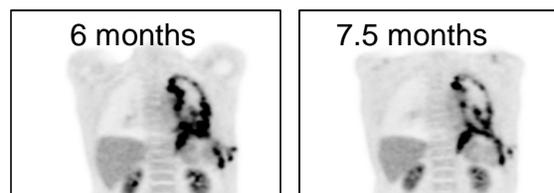
- 100% chemo refractory (up to 16 lines)
- 66% had prior surgery
- 50% had prior radiotherapy
- 2 pts died before 3 months

Patient	RECIST1.1 (3 months)
FI1-01 Ovarian	SD
FI1-02 Colon	SD
FI1-04 Colon	PD
FI1-06 Liver	PD
FI1-08 Lung	PD
FI1-09 Mesothelioma	PD
FI1-13 Rectum	PD
FI1-14 Mesothelioma	SD
FI1-17 STS	PD
FI1-19 Ovarian	SD

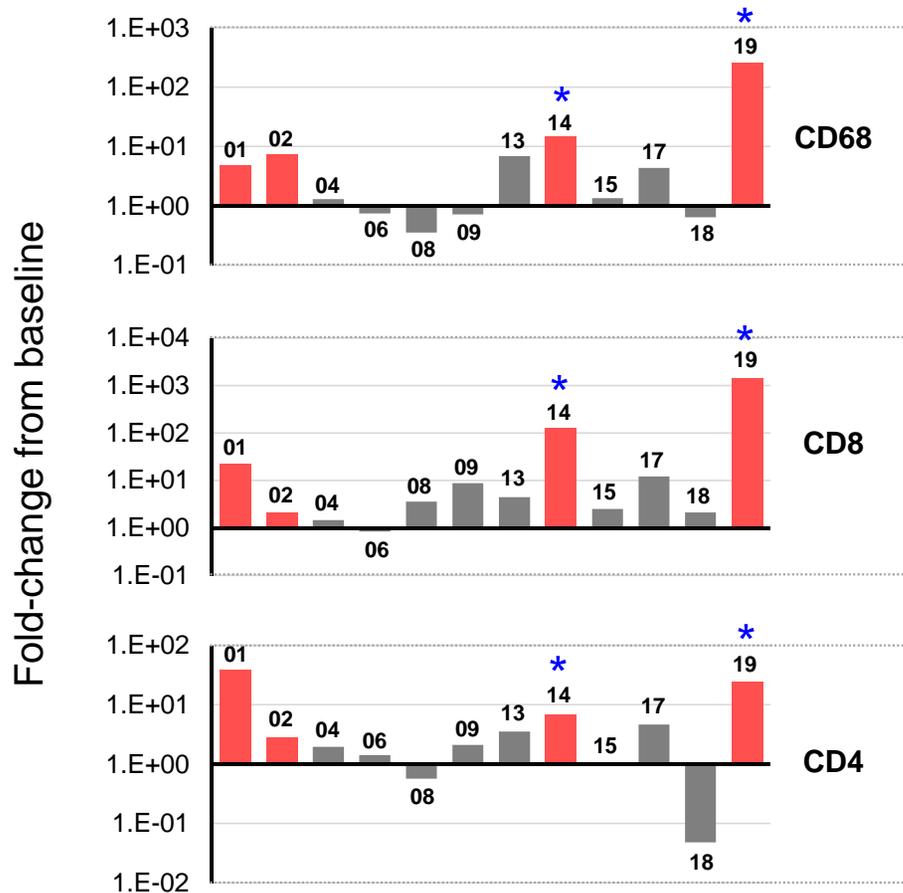
Alive with SD
>24 months

SD =Stable disease, PD =Progressive disease

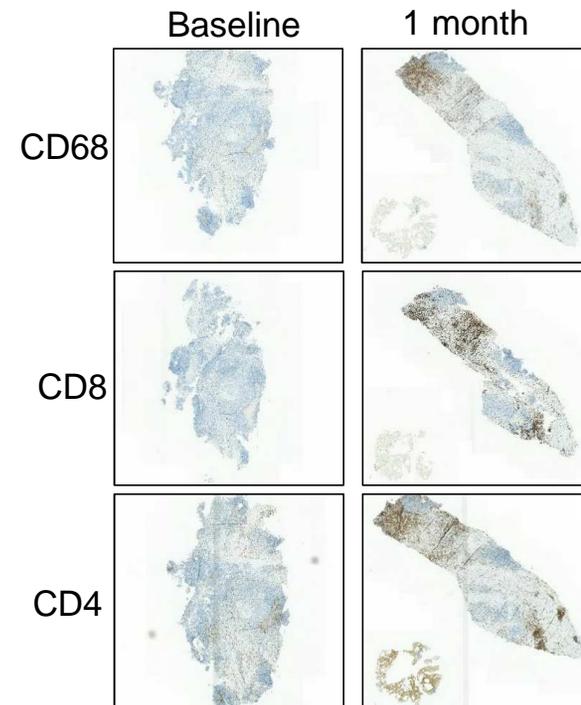
FI1-14 Mesothelioma



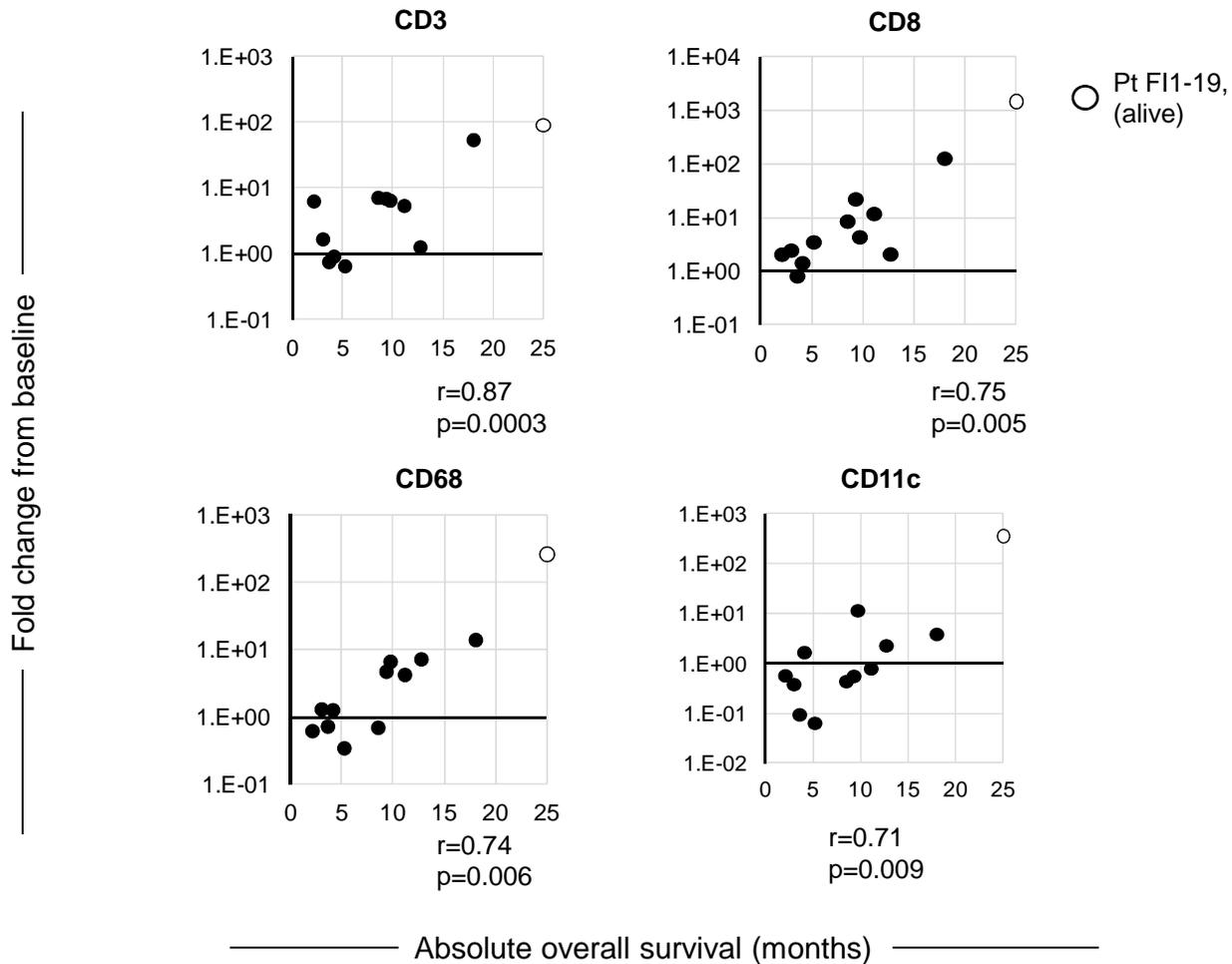
Several immune cell subsets were increased in tumors following ONCOS-102



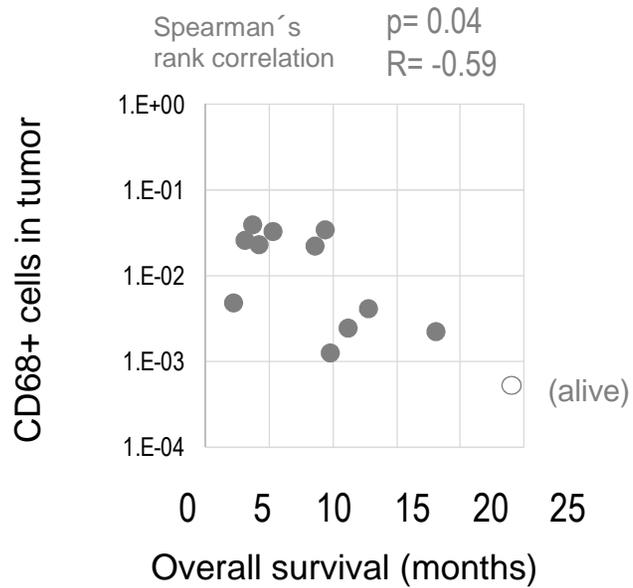
- SD at 3 months
- PD at 3 months
- * Tumor-specific CD8+ T cells in blood



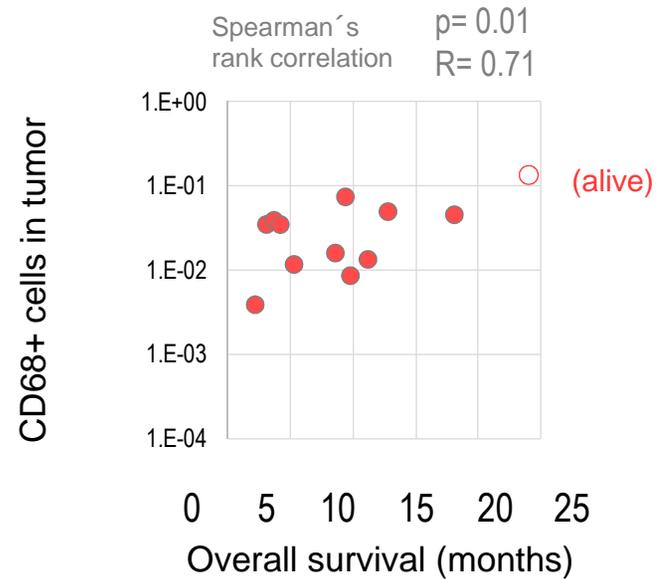
Increase in tumor-infiltrating immune cells following ONCOS-102 treatment is associated with increased survival



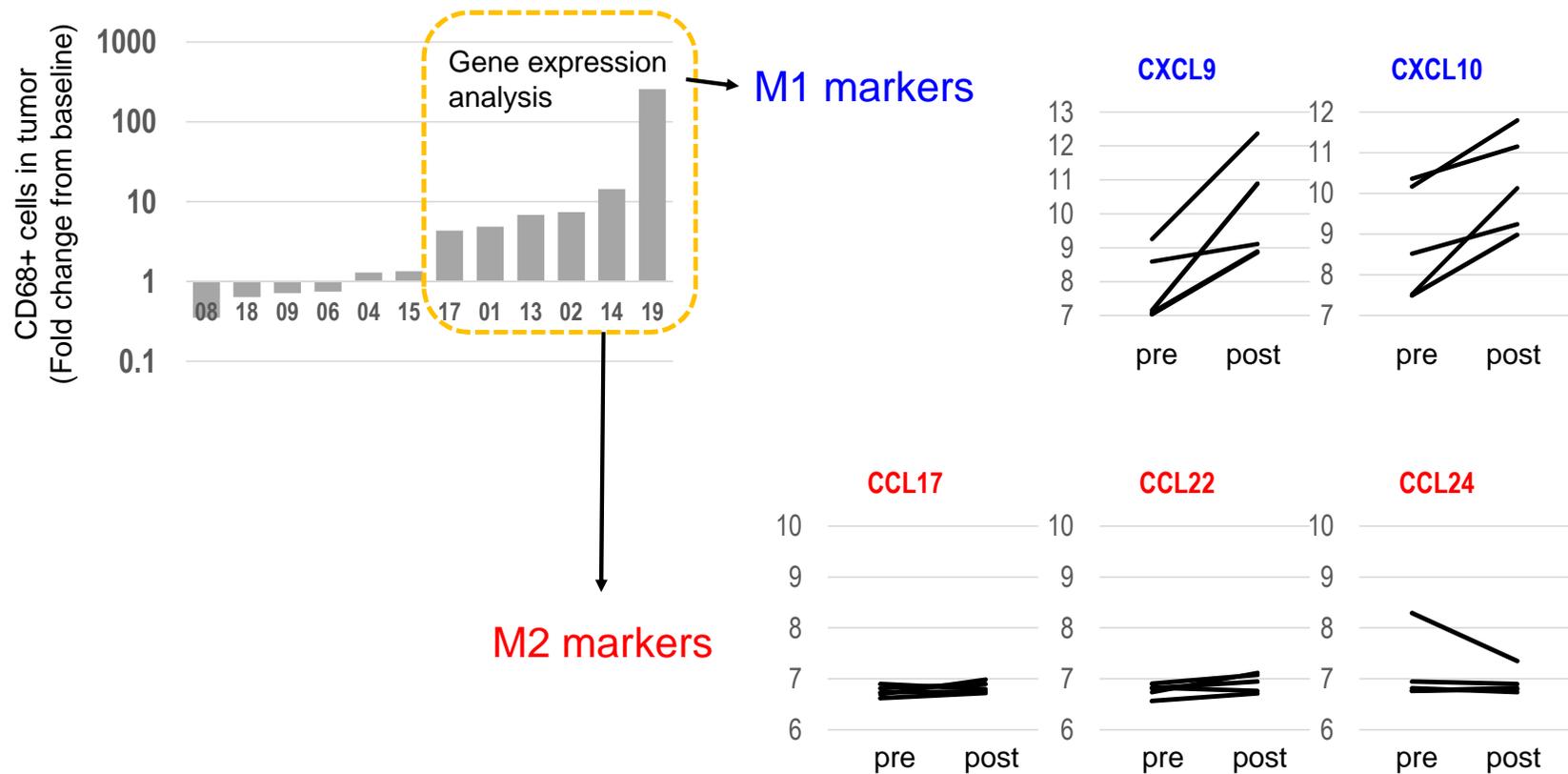
High number of CD68+ TAMs in baseline tumors was associated with short survival



High number of intratumoral CD68+ cells after ONCOS-102 therapy was associated with increased survival

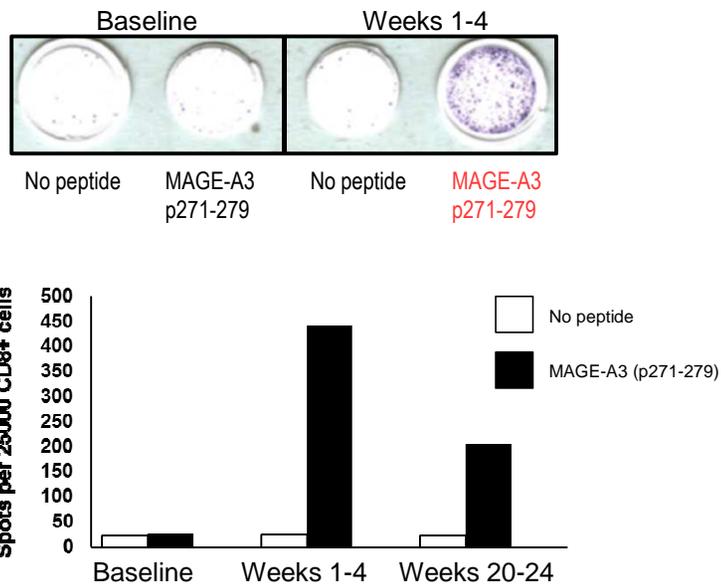


Tumors with increased CD68+ cells exhibit M1 macrophage transcriptional signature

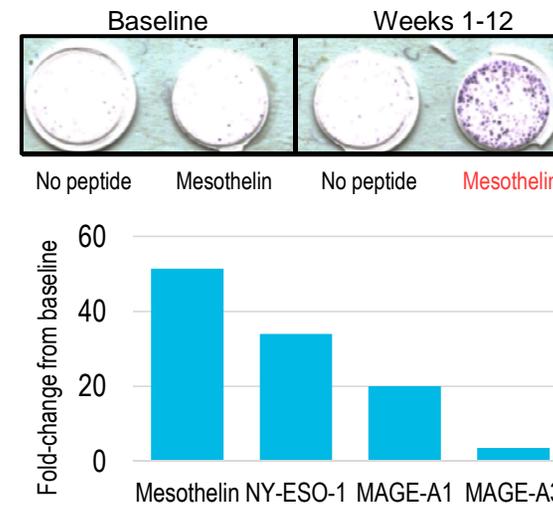


Local ONCOS-102 administration leads to induction of systemic tumor-specific CD8+ T cell response:

Mesothelioma pt FI1-14: induction of MAGE-A3 specific CD8+ T cells



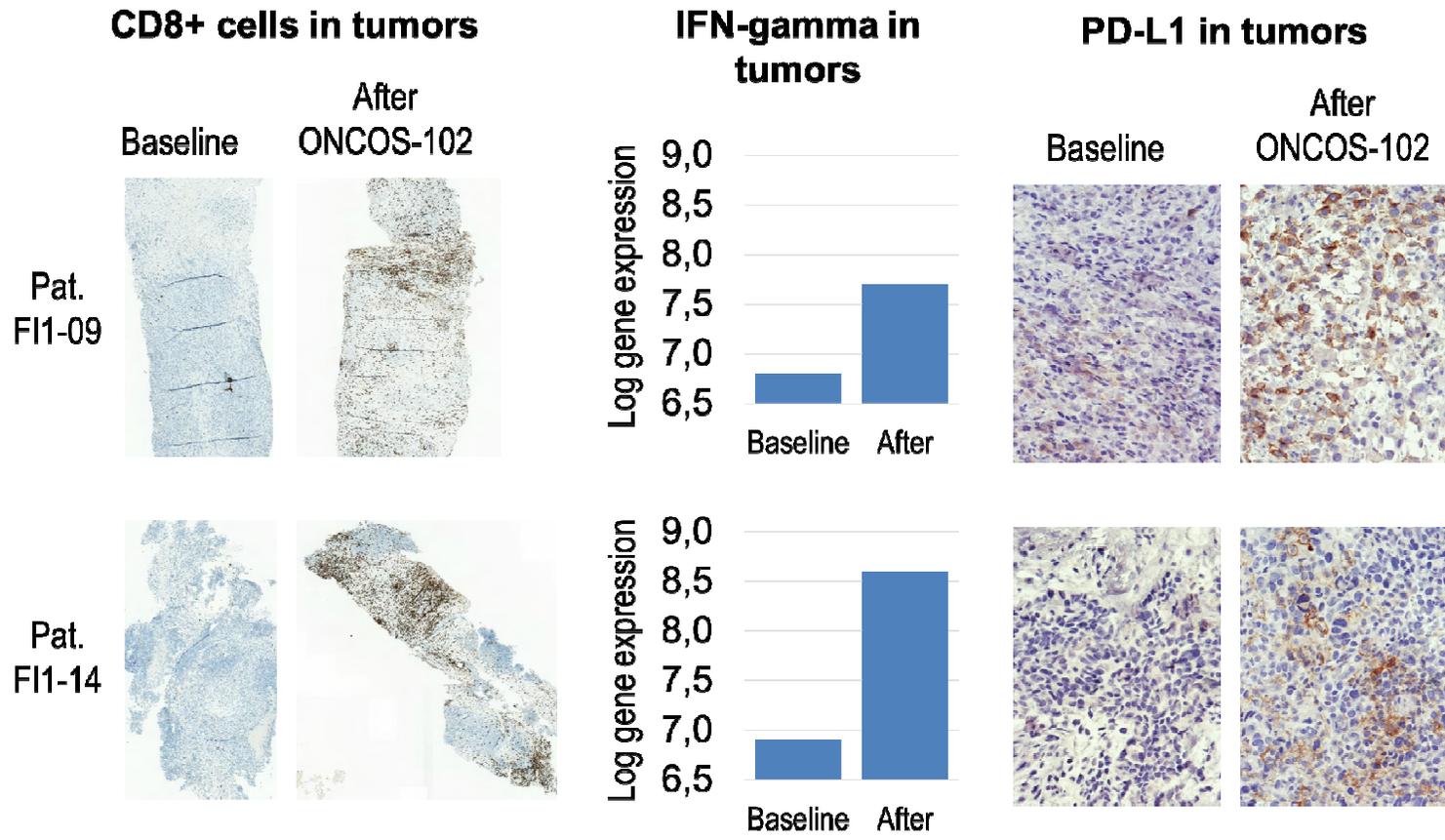
OvCa pt FI1-19: multiple tumor-specific CD8+ T cell populations induced by ONCOS-102



NY-ESO-1 specific CD8+ T cells present 17 mo after previous ONCOS-102 treatment, alive and SD >24 mo



CD8+ T cell infiltration was associated with an increased PD-L1 expression in mesothelioma tumors



Summary and Take Home Points

- Intratumoral administration of ONCOS-102 to patients with advanced solid tumors was safe and had evidence of clinical benefit
- High density of CD68+ TAMs in baseline tumor biopsies was associated with short survival
- Increase in CD68+ TAMs and other immune cells in post-treatment biopsies was associated with increased survival
- Treatment with ONCOS-102 converts tumors to "inflamed" phenotype with evidence of systemic tumor-specific immune response
- **Data suggest that ONCOS-102 may reduce local immune suppression by recruiting beneficial immune cells into tumors**
- **There is a rationale for evaluation of ONCOS-102 in combination with other immunotherapies (e.g. checkpoint inhibitors).**

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The patients and their families!!!