

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

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on behalf of ONCOS-102 investigators

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Presenter Disclosure Information

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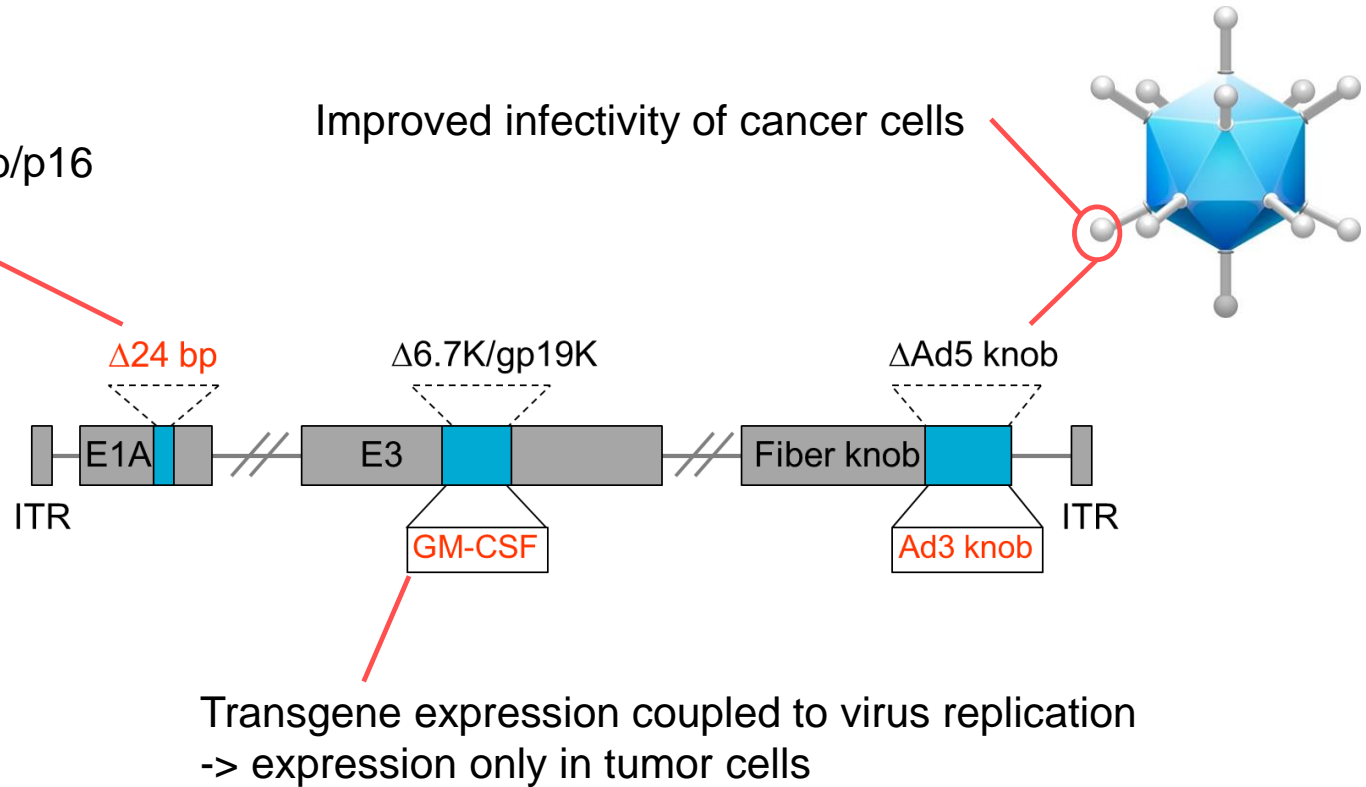
The following relationships exist related to this presentation:

No relationships to disclose

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

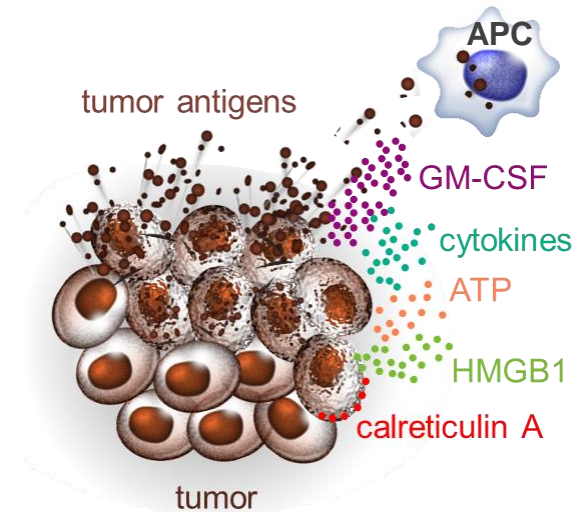
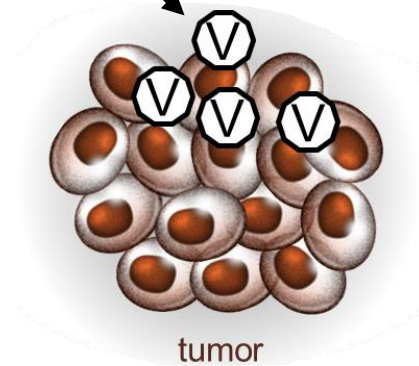
Selective replication in Rb/p16 defective cancer cells

Improved infectivity of cancer cells



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

Intratumoral administration

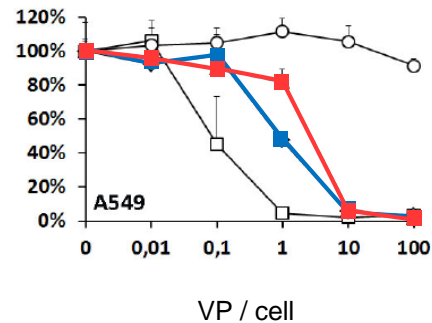
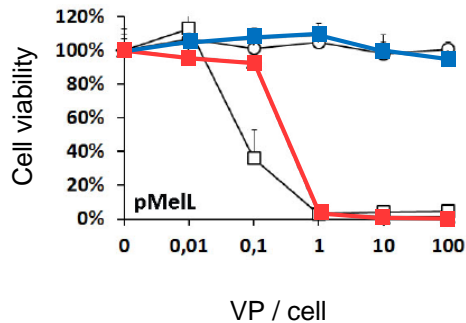


Ad5wt

ONCOS-102

Low passage melanoma

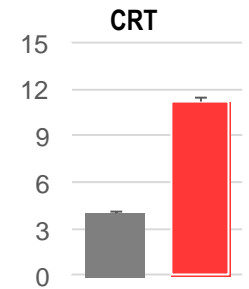
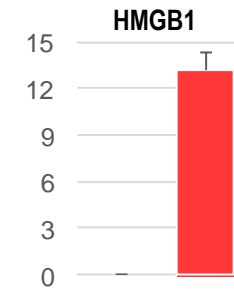
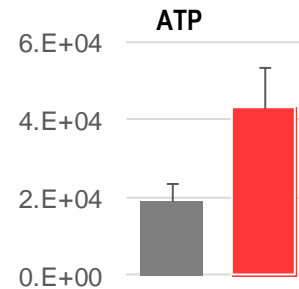
Lung cancer



H226 Mesothelioma

Untreated cells

ONCOS-102 treated cells

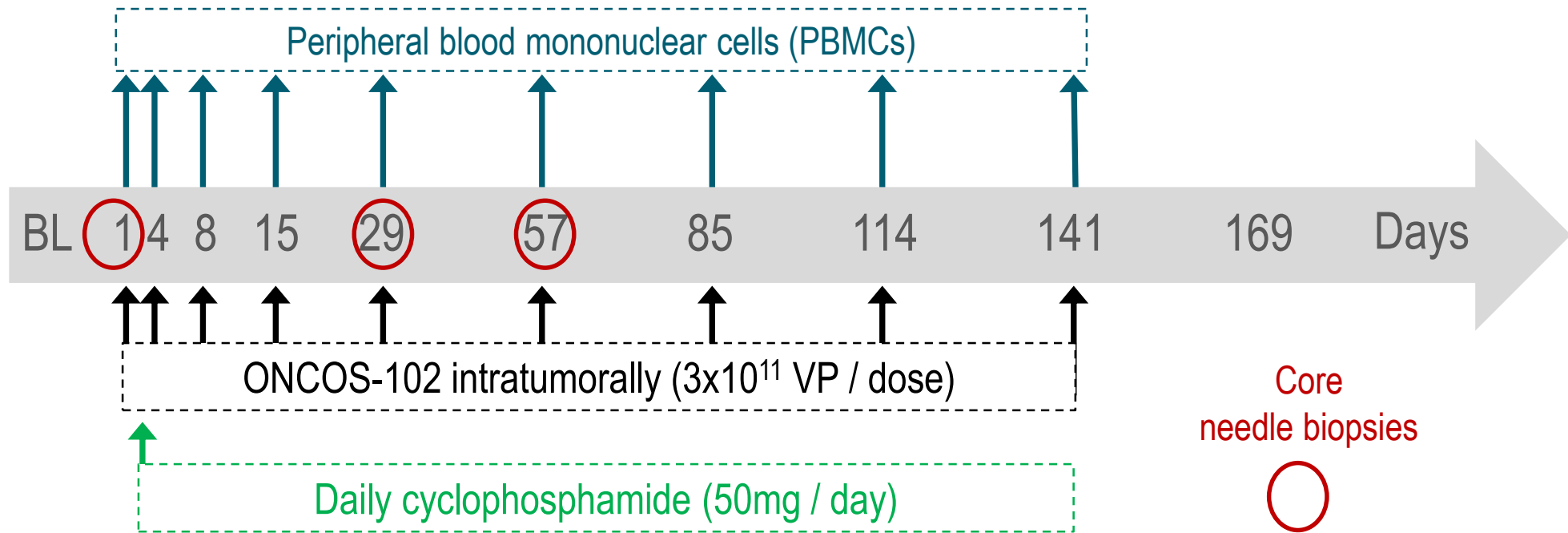


Phase I study of intratumoral ONCOS-102 with low dose cyclophosphamide in patients with advanced solid tumors

| Dose | Patient number | WHO score | Age/ Sex | Cancer type | Number of previous lines of therapy |
|-----------------------|----------------|-----------|----------|--------------|-------------------------------------|
| 3x10 ¹⁰ VP | FI1-01 | 1 | 64 / F | Ovarian | 16 |
| | FI1-02 | 0 | 61 / M | Colon | 3 |
| | FI1-04 | 0 | 55 / F | Colon | 4 |
| 1x10 ¹¹ VP | FI1-06 | 0 | 63 / M | Liver | 2 |
| | FI1-08 | 1 | 63 / F | Lung | 3 |
| | FI1-09 | 1 | 63 / M | Mesothelioma | 2 |
| 3x10 ¹¹ VP | FI1-13 | 0 | 53 / M | Rectum | 4 |
| | FI1-14 | 1 | 68 / M | Mesothelioma | 2 |
| | FI1-15 | 1 | 67 / F | Endometrial | 5 |
| | FI1-17 | 1 | 64 / F | STS | 6 |
| | FI1-18 | 1 | 51 / F | Breast | 11 |
| | FI1-19 | 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

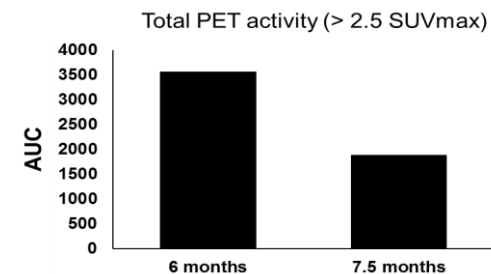
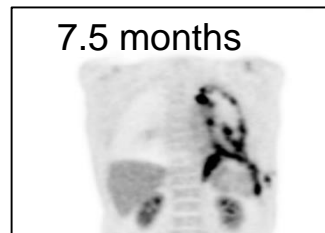
- 100% chemo refractory (up to 16 lines)
- 66% had prior surgery
- 50% had prior radiotherapy
- 2 pts died before 3 months

| 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

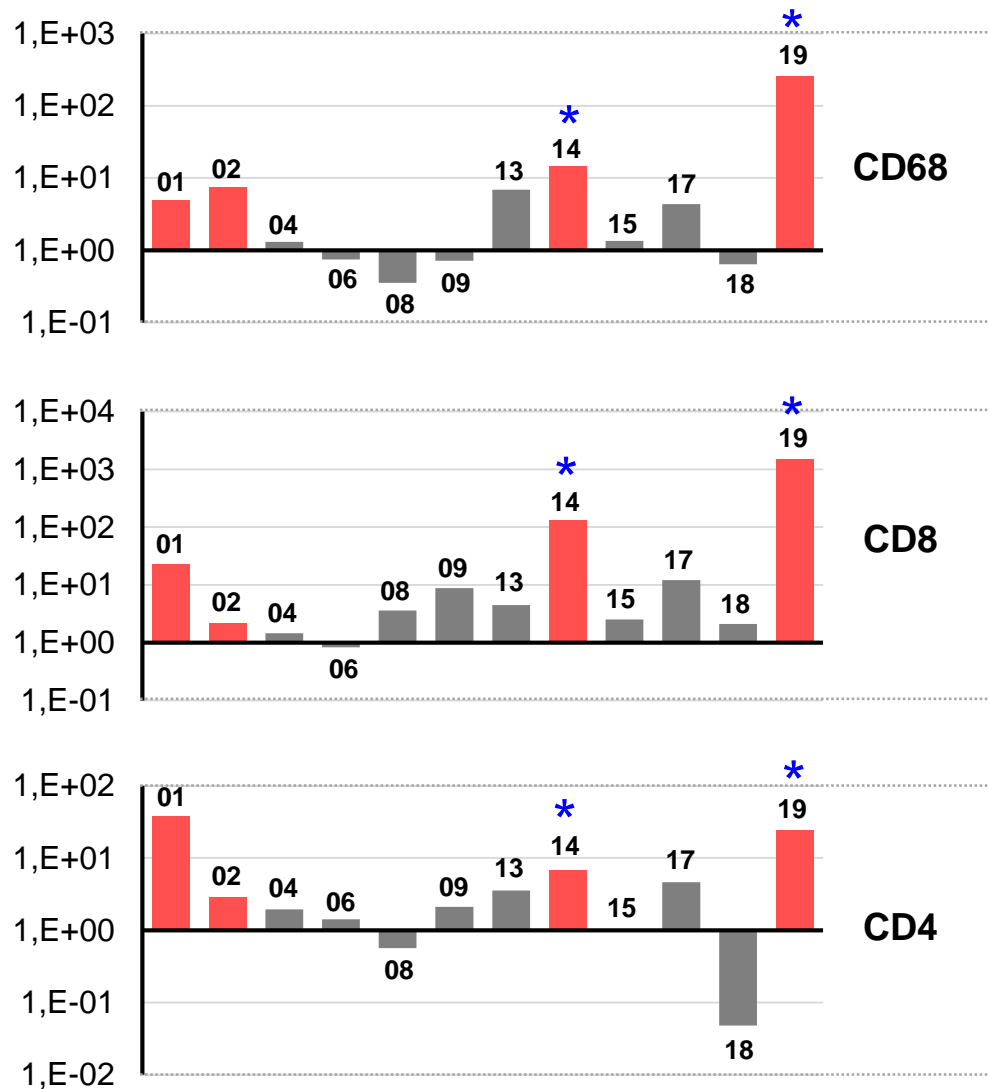
SD =Stable disease, PD =Progressive disease

FI1-14 Mesothelioma

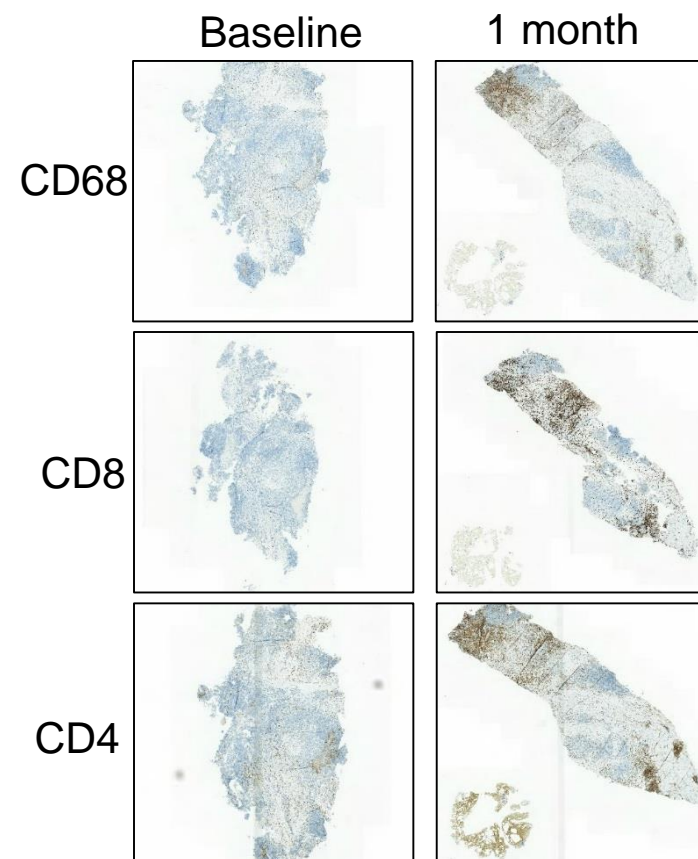


Several immune cell subsets were increased in tumors following ONCOS-102

Fold-change from baseline

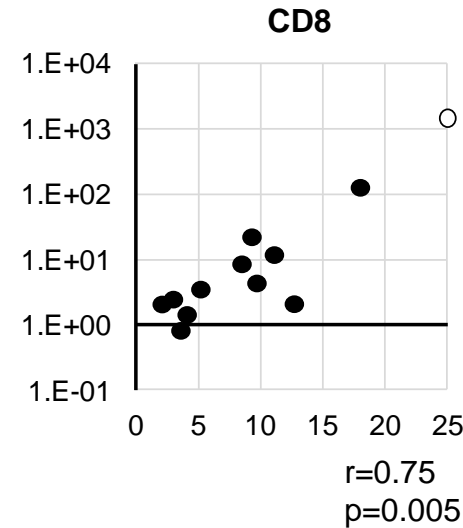
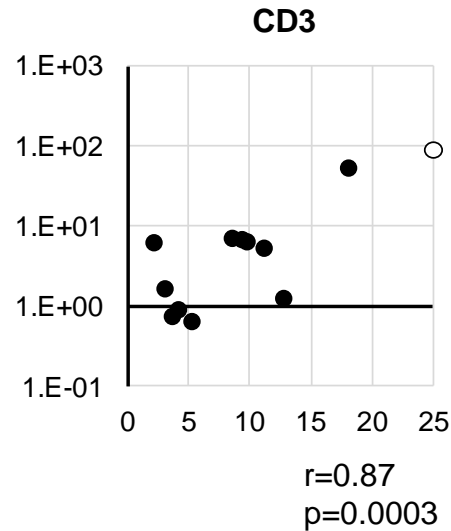


- SD at 3 months
- PD at 3 months
- * Tumor-specific CD8+ T cells in blood

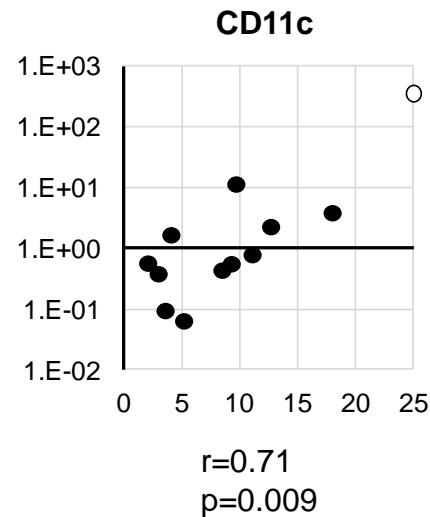
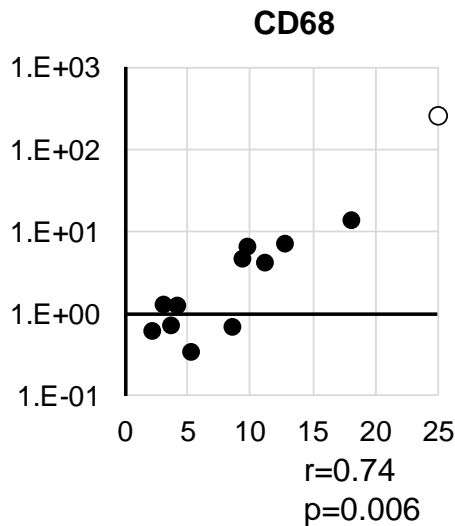


Increase in tumor-infiltrating immune cells following ONCOS-102 treatment is associated with increased survival

Fold change from baseline

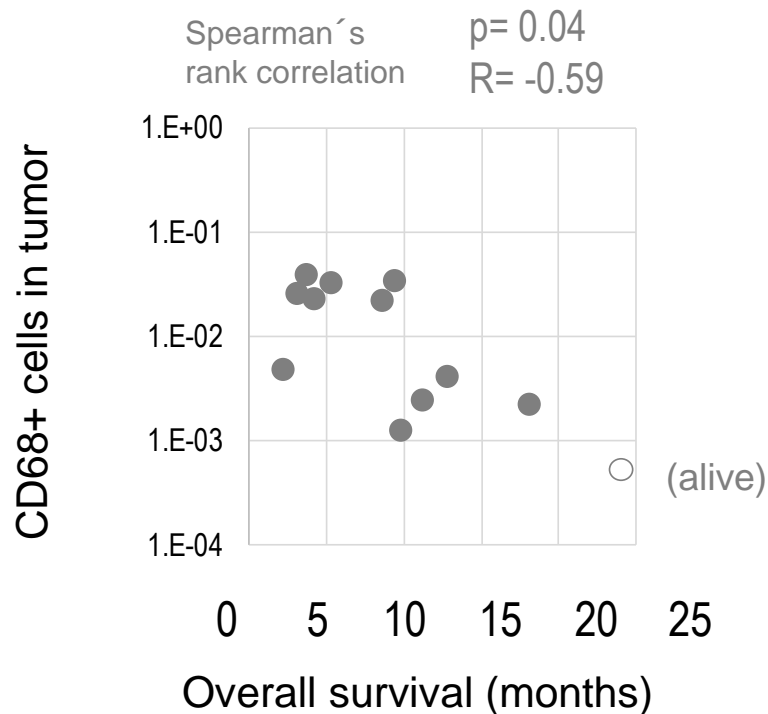


○ Pt FI1-19,
(alive)

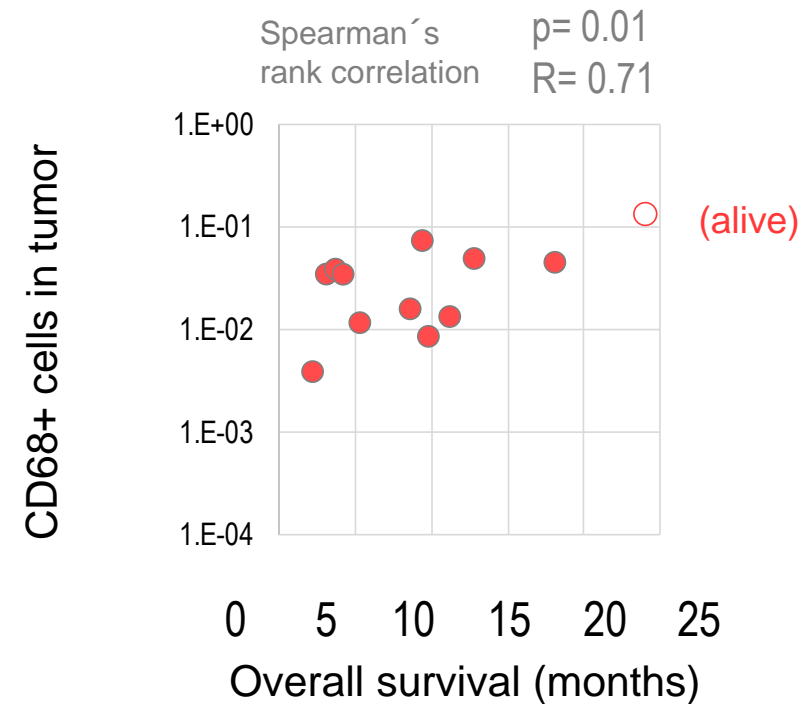


Absolute overall survival (months)

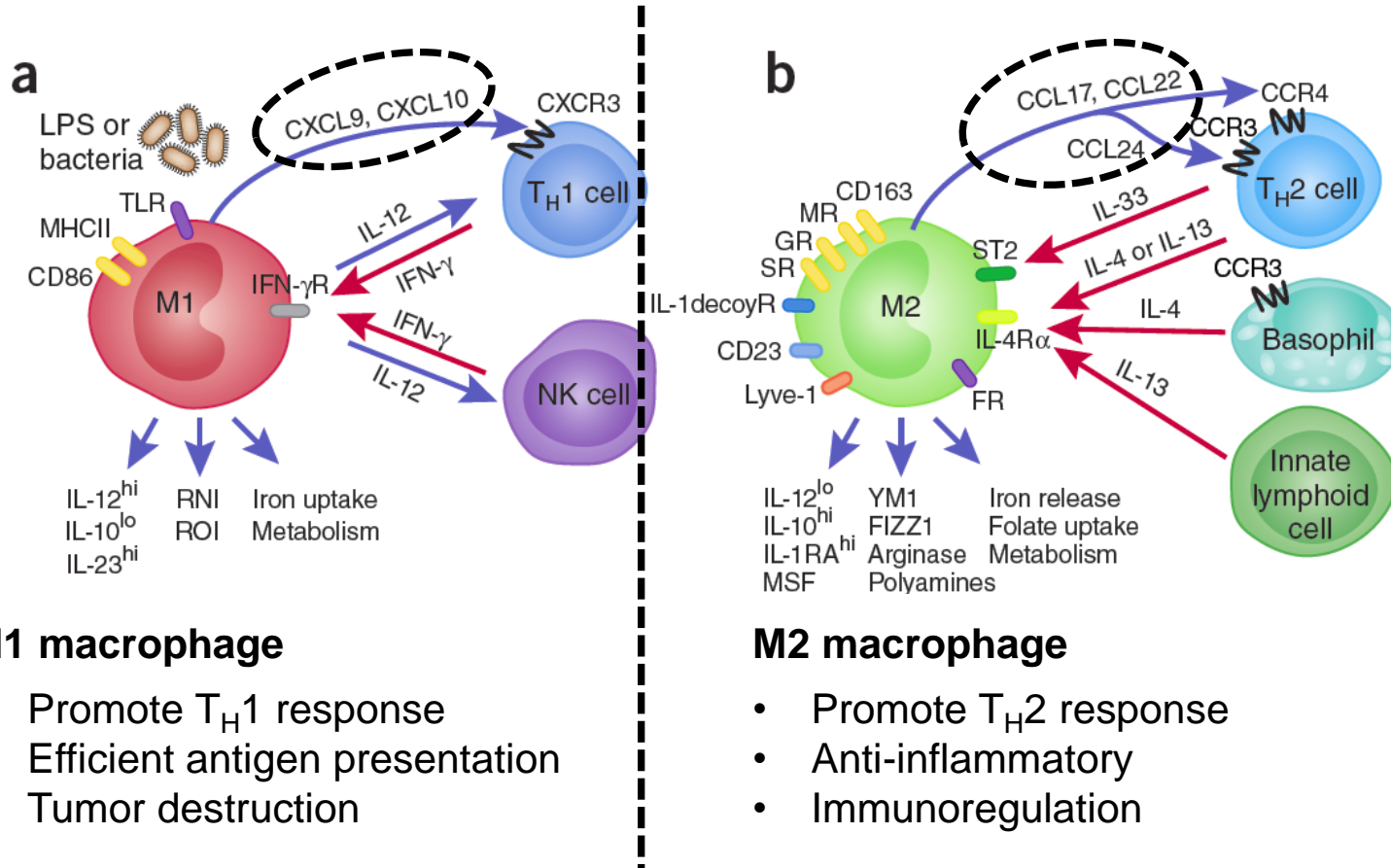
High number of CD68+ TAMs
in baseline tumors was
associated with short survival



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

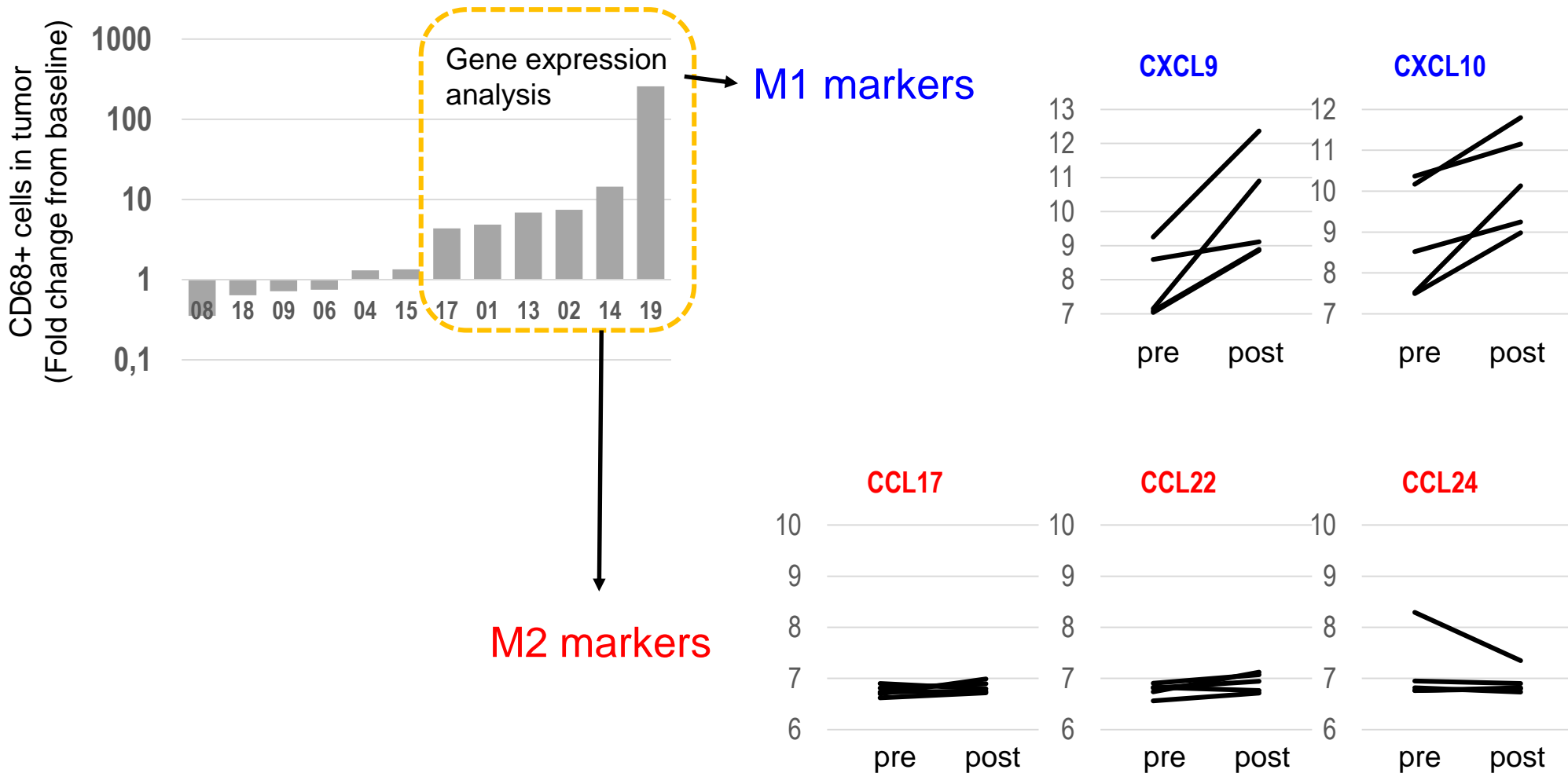


Macrophage plasticity



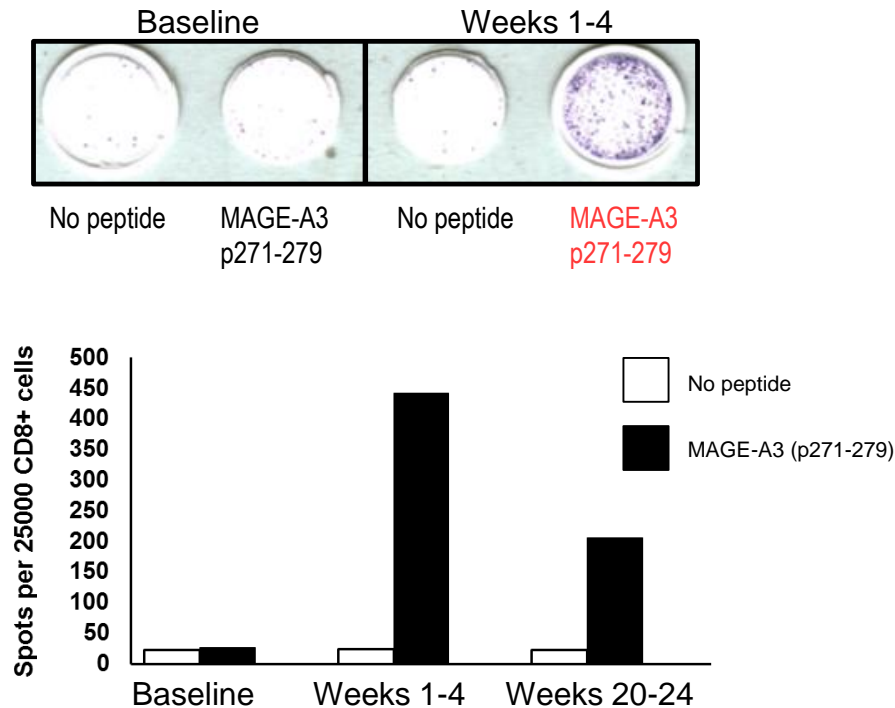
Adapted from Biswas and Mantovani Nature Immunol 2010

Tumors with increased CD68+ cells exhibit M1 macrophage transcriptional signature

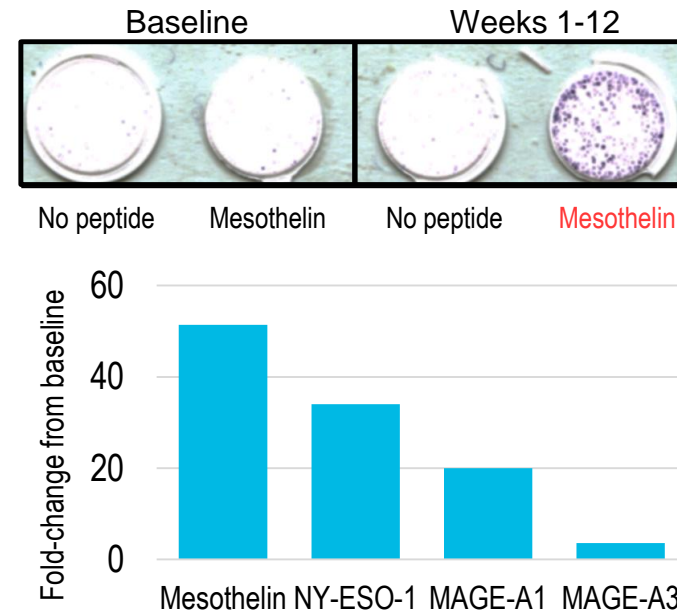


Local ONCOS-102 administration leads to induction of systemic tumor-specific CD8+ T cell response:

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

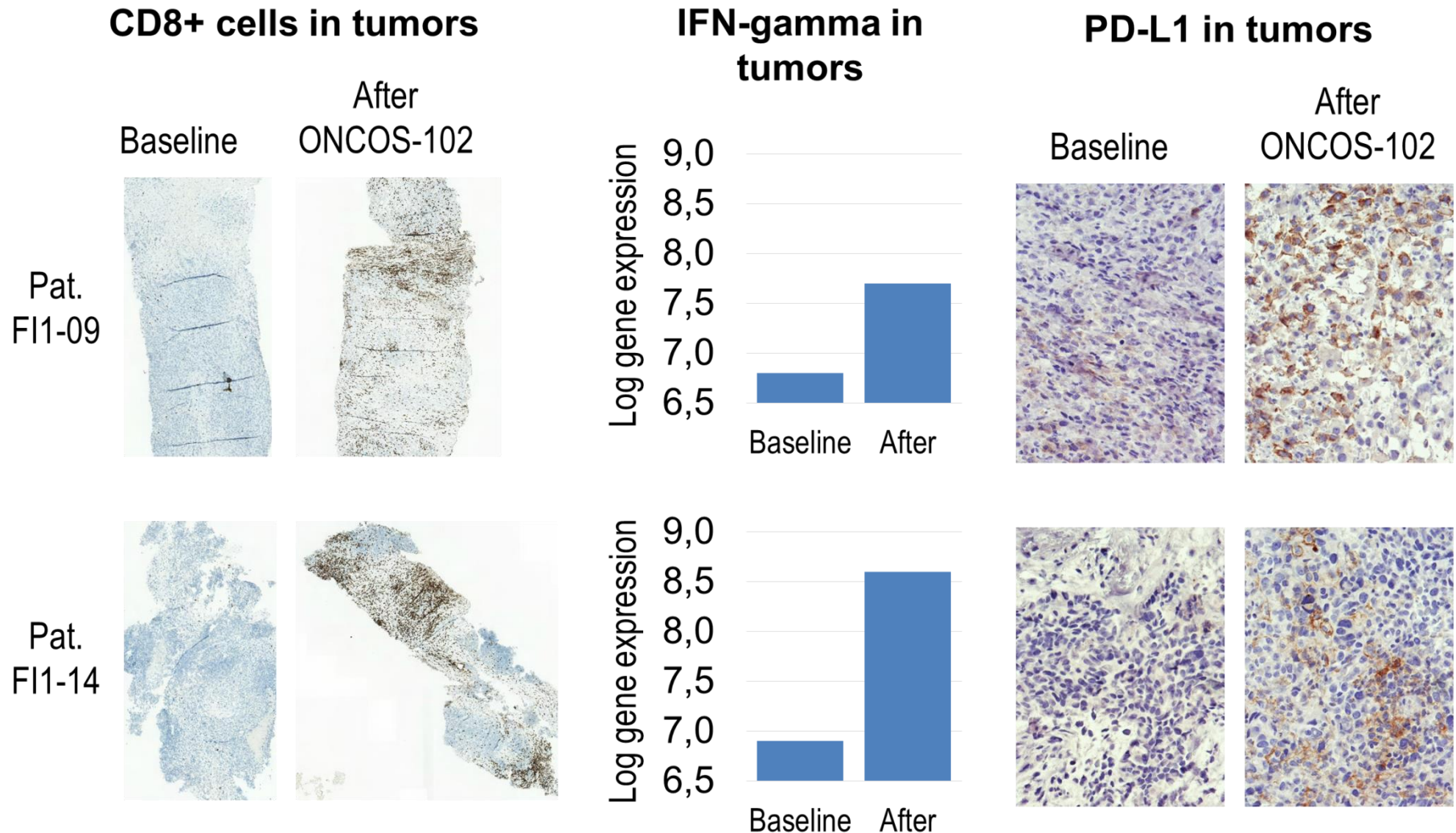


OvCa pt FI1-19: multiple tumor-specific CD8+ T cell populations induced by ONCOS-102



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).**

Acknowledgments

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The patients and their families!!!