4

Immune activation

5. Preclinical pipeline update
6. 4Q update
7. Closing remarks

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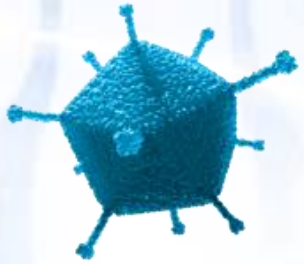
THE IMPORTANCE OF IMMUNOLOGICAL READ-OUTS

Function

- Understand **mechanism-of-action** of ONCOS-102
- Confirm **delivery** of ONCOS-102 into the tumor

Power

- **Strength** of immune responses
- **Breadth** of immunological **remodelling**



Duration

- **Persistence** of the immune response
- **Optimize dosing** and scheduling

Impact

- **Association** between immune response and **improved clinical outcome**

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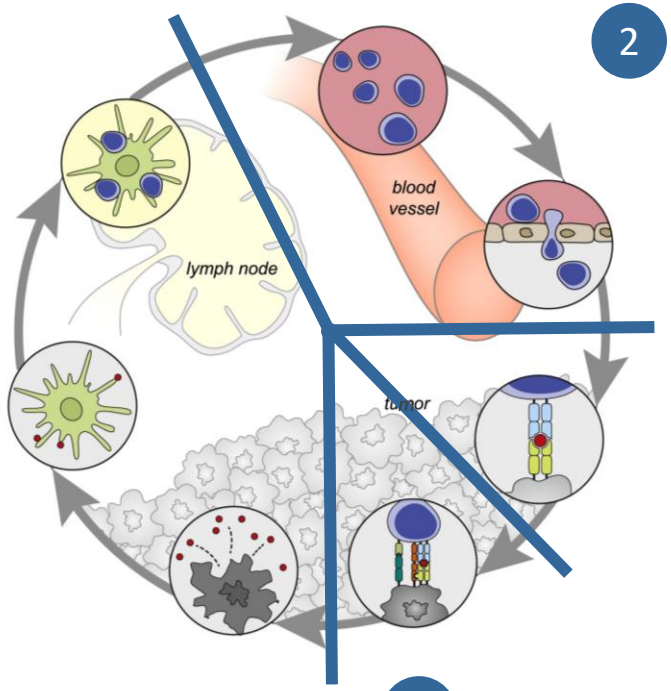
FOUR CRITICAL PHASES OF TUMOR-SPECIFIC IMMUNE RESPONSE

1 Access to tumor antigens, cross-presentation by APCs and priming of T-cells



2 T-cell migration and infiltration into the tumor

3 Expansion and survival of T-cells in the tumor

4 Tumor cell recognition and elimination

Adapted from Chen & Mellman, Immunity 2013

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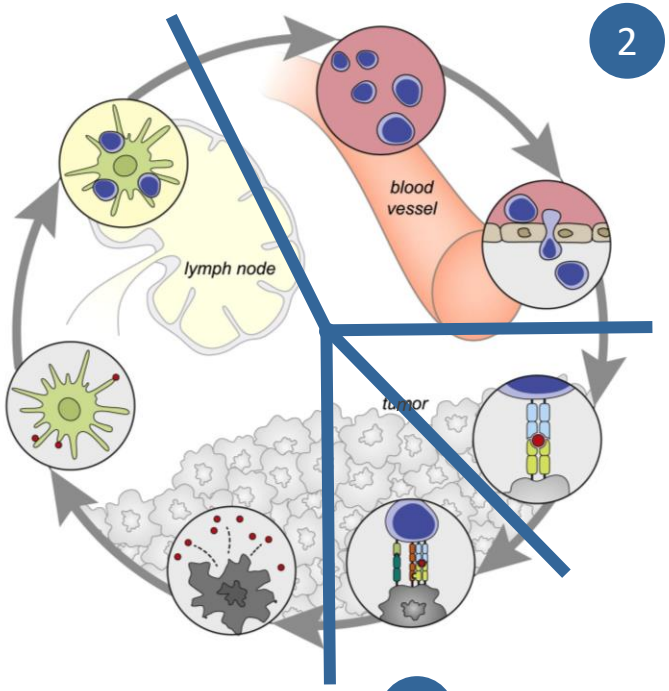
FOUR CRITICAL PHASES OF TUMOR-SPECIFIC IMMUNE RESPONSE

1 Access to tumor antigens, cross-presentation by APCs and priming of T-cells

Problem: *Low tumor immunogenicity and ineffective T-cell priming*



2 T-cell migration and infiltration into the tumor

Problem: *T-cells do not reach the tumor*

3 Expansion and survival of T-cells in the tumor

Problem: *Exhaustion of T-cells in the tumor*

4 Tumor cell recognition and elimination

Problem: *Immunosuppression in the tumor*

Adapted from Chen & Mellman, Immunity 2013

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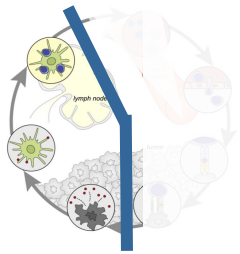
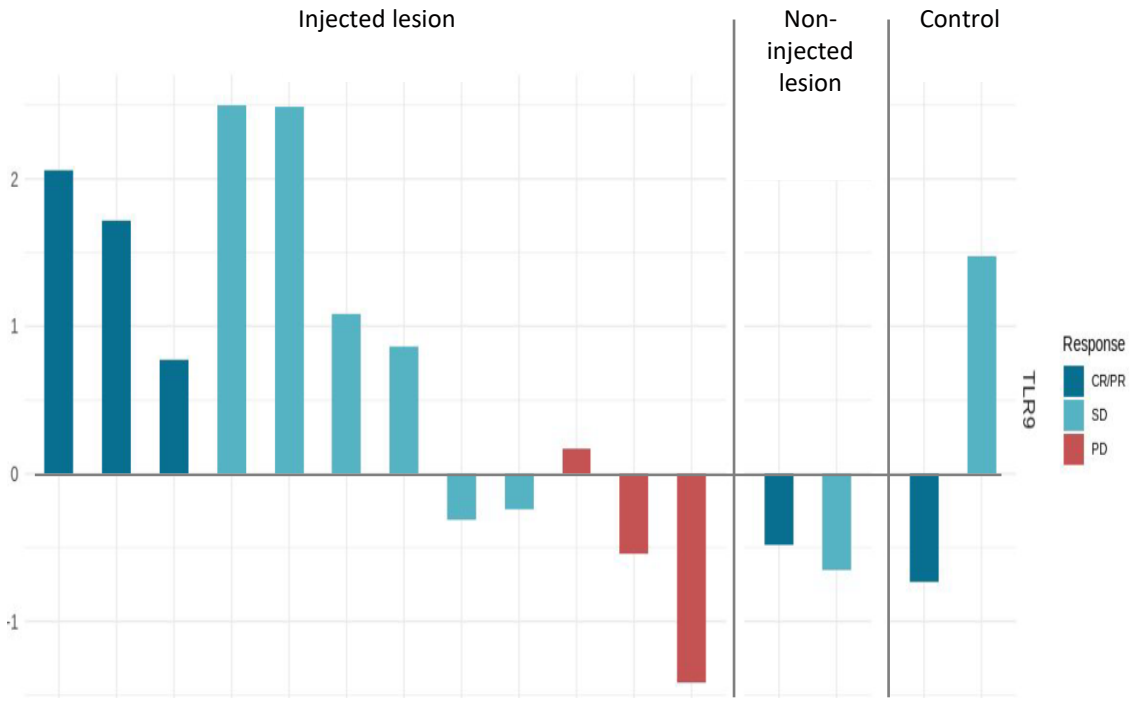
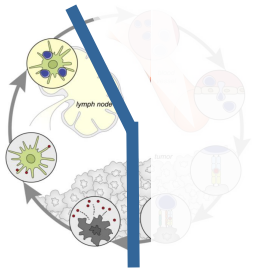


ONCOS-102 ACTIVATES DANGER SIGNALING: MESOTHELIOMA

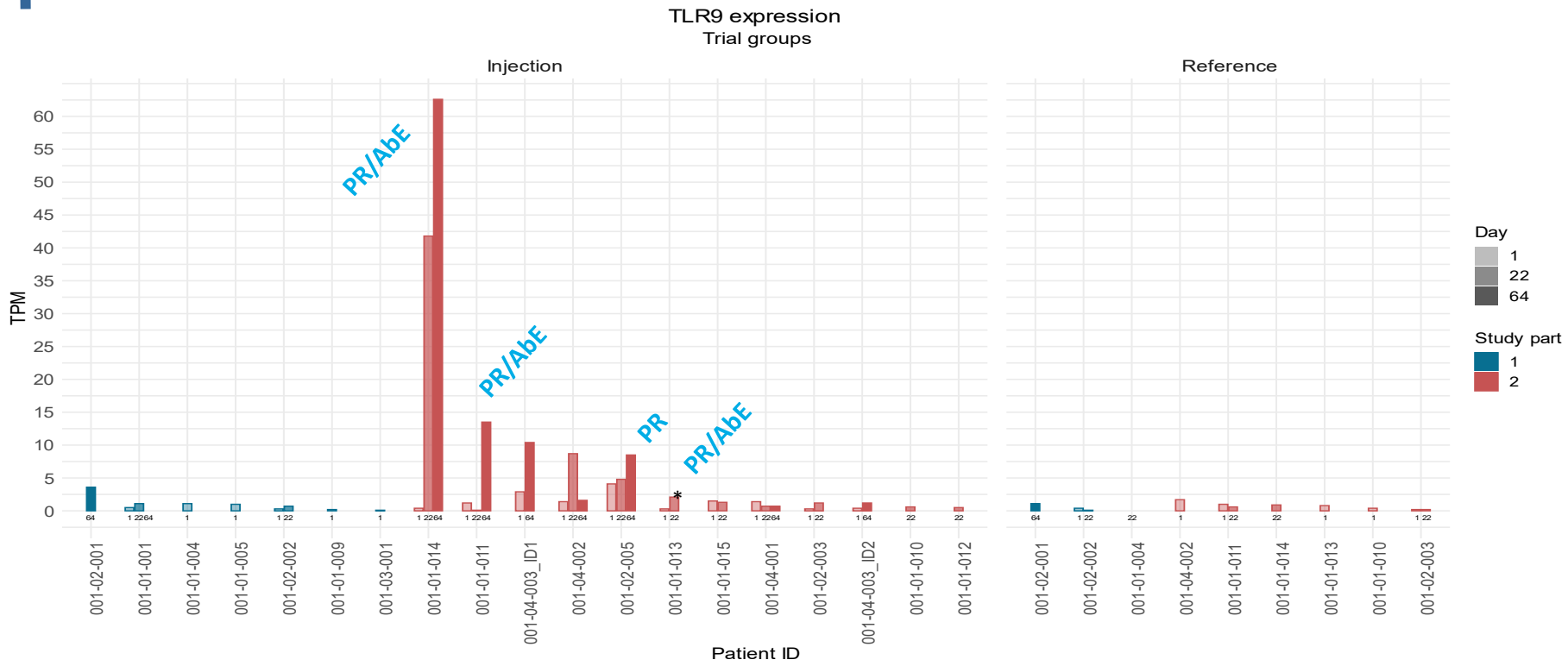
TLR9 expression in tumor RNAseq -fold change D36 vs. baseline[1], mesothelioma



1 Unpublished company data



ONCOS-102 ACTIVATES DANGER SIGNALING: MELANOMA



* 001-01-13 – no data for Day 64

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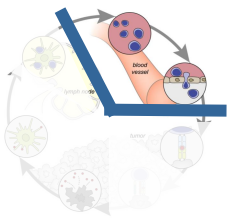
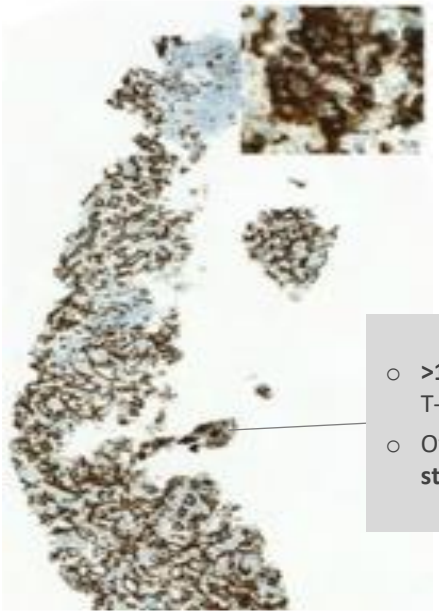


ROBUST INCREASE OF TUMOR INFILTRATION BY T-CELLS FOLLOWING ONCOS-102 TREATMENT

ONCOS-102 induced tumor T-cell infiltration
Ovarian cancer patient case example, monotherapy

Tumor biopsy mIHC – CD8+ T-cells

Pre-treatment
Baseline



Post-treatment
Week 8

- **>1000-fold increase** of CD8+ T-cells in tumor
- Ovarian cancer patient – **stable disease for three years**

Ranki et al. JITC 2016

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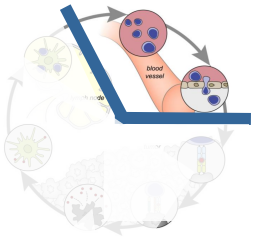
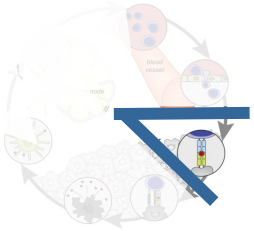
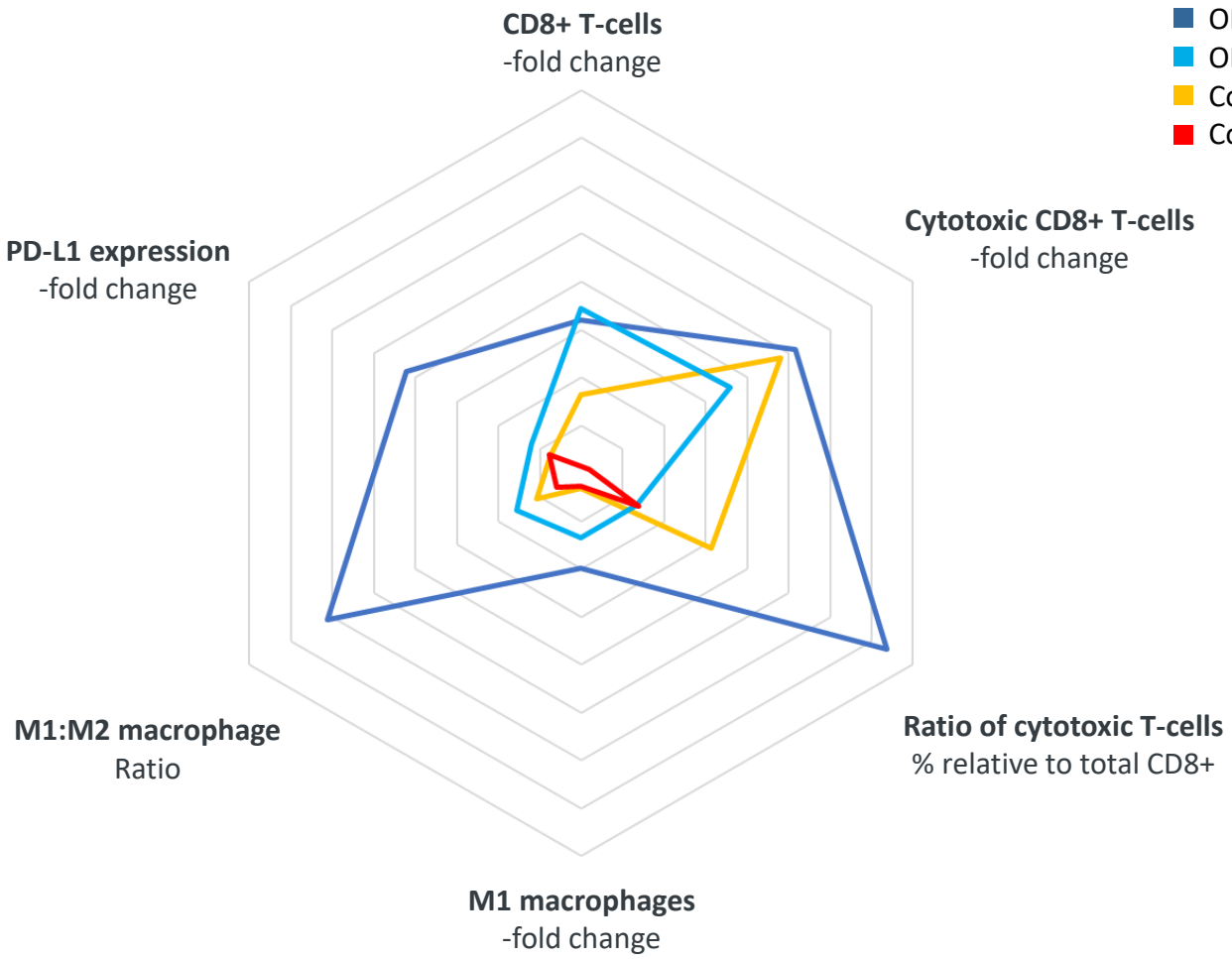




ROBUST INCREASE IN T-CELL TUMOR INFILTRATION FOLLOWING ONCOS-102 TREATMENT: MESOTHELIOMA



Unpublished company data

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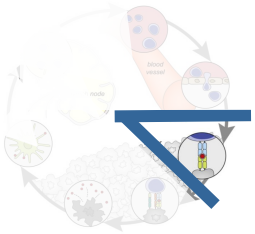
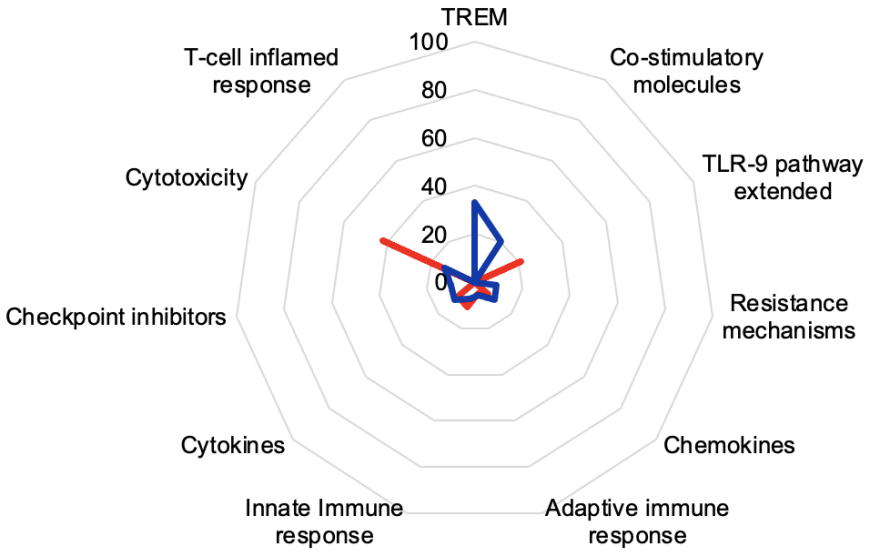


IMMUNE-PERMISSIVE RESHAPING OF TUMOR MICROENVIRONMENT BY ONCOS-102: MELANOMA

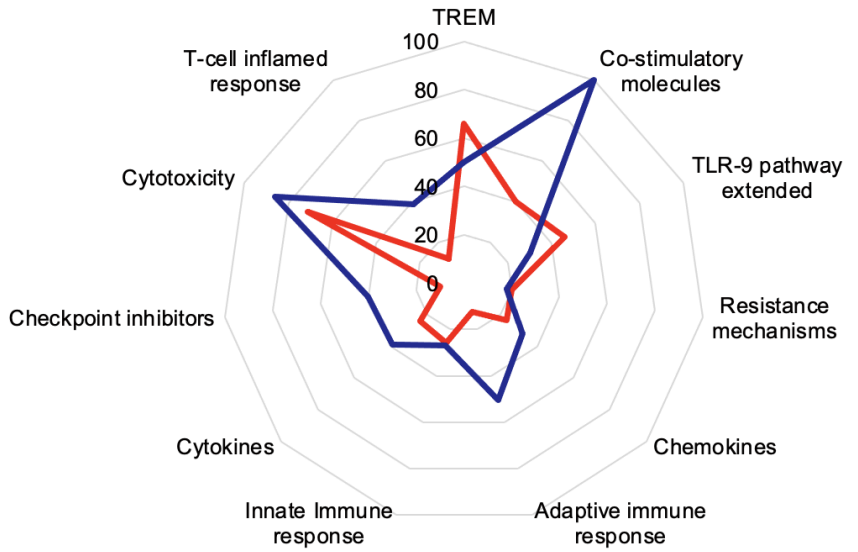
Modulation of gene expression; Fraction (%) of genes modulated within the indicated gene groups

Day 22 vs. Baseline
Day 64 vs. Baseline



Part 1

Day 22 & Day 64 (n=2)
Baseline (n=6)



Part 2

Day 22 (n=10) & Day 64 (n=7)
Baseline (n=10)

Unpublished company data

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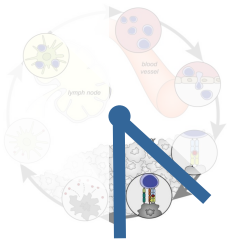
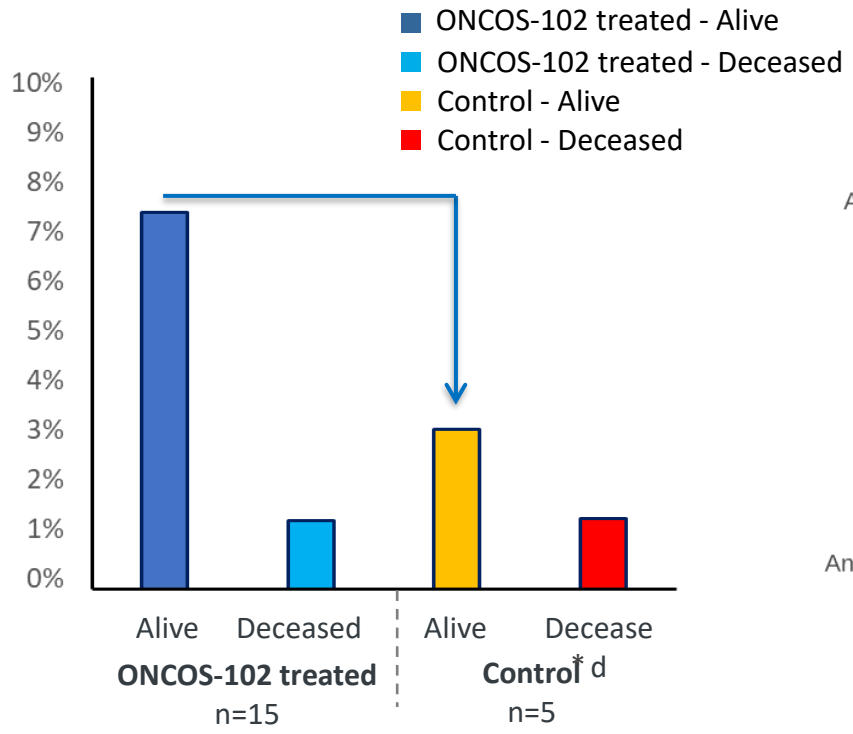
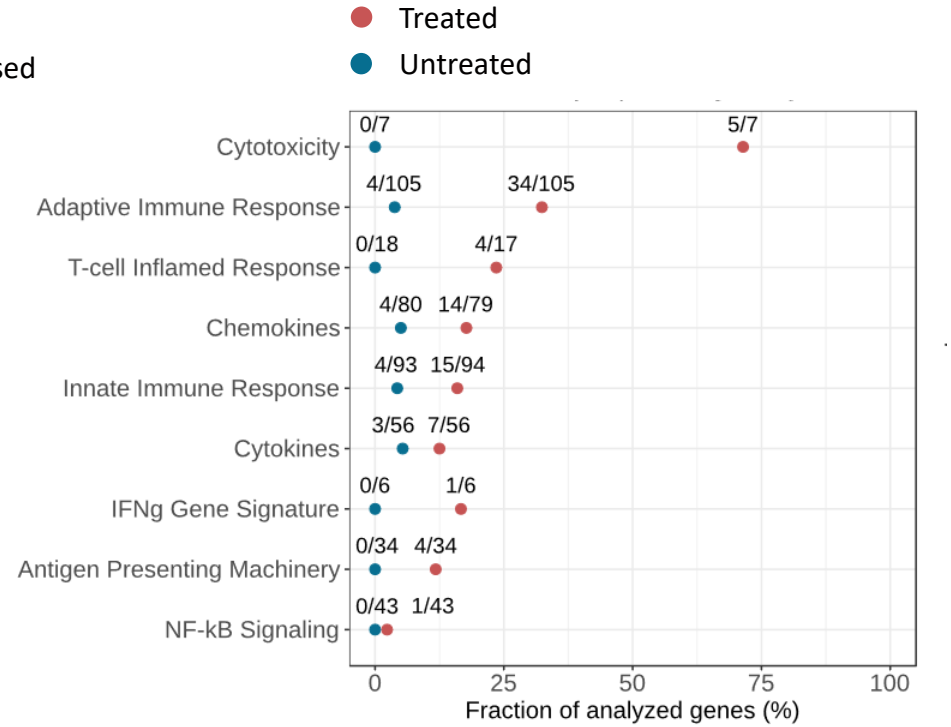


ONCOS-102 TREATMENT INCREASES CYTOTOXIC POTENTIAL OF INTRATUMORAL T-CELLS: MESOTHELIOMA

Relative level of cytotoxic GrB+ / CD8+ T-cells at day 36
Alive vs. deceased at 12 months, mesothelioma



Modulation of tumor gene expression, Fraction of genes
ONCOS-102 treated vs. untreated, mesothelioma



Unpublished company data
* Control patients treated with standard-of-care chemotherapy

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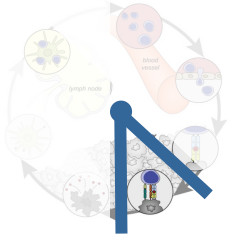
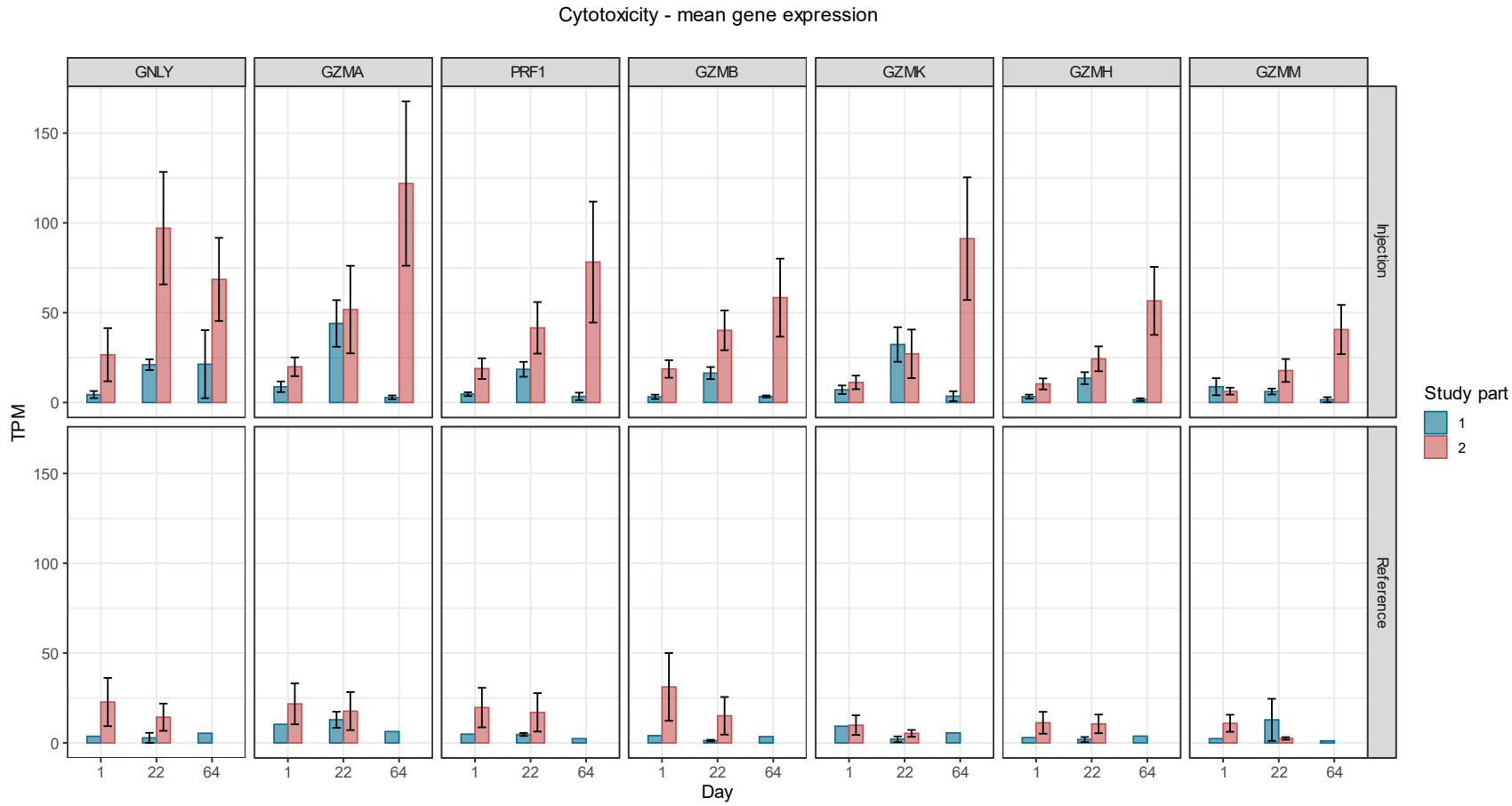
ONCOS-102 TREATMENT INCREASES CYTOTOXIC POTENTIAL ON INTRA-TUMORAL T-CELLS: MELANOMA





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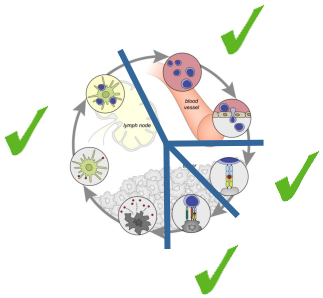
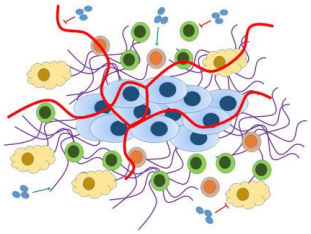
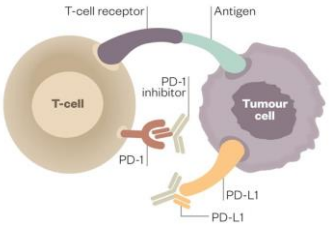
ONCOS-102 IMMUNE ACTIVATION - CONCLUSIONS



ONCOS-102 activates the immune system and counteracts multiple mechanisms of immuno-suppression operating at different steps of the cancer immunity cycle



Multifaceted **modulation of the tumor micro-environment induced by ONCOS-102 is linked to clinical benefit** in patients with different tumor types



ONCOS-102 induced immune activation provides **broad and powerful priming to sensitize patients** to respond to subsequent treatment with **checkpoint inhibitors**

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