SITC 2022

NOVEMBER 8-12 BOSTON MASSACHUSETTS

# The Society for Immunotherapy of Cancer 37th Annual Meeting and Pre-Conference Programs

THE LEADING CANCER IMMUNOTHERAPY AND TUMOR IMMUNOLOGY CONFERENCE

sitc

Society for Immunotherapy of Cancer

#SITC22

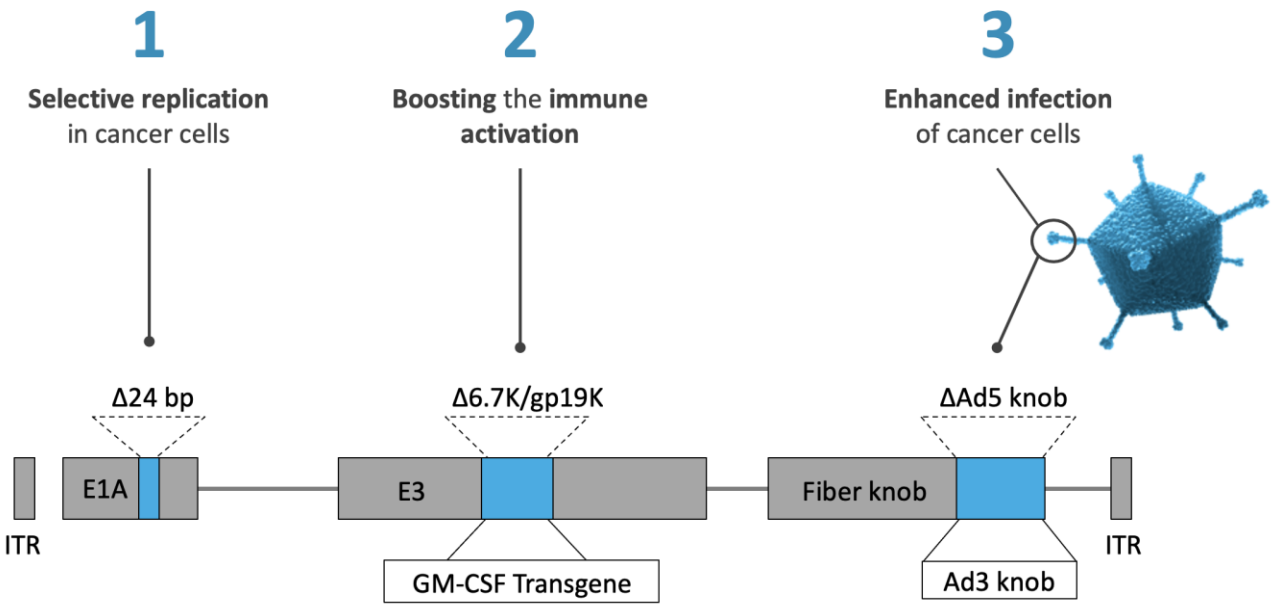
SITC 2022
NOVEMBER 8-12 BOSTON MASSACHUSETTS

# Repeat dosing of oncolytic adenovirus ONCOS-102 is associated with enhanced and persistent immune responses and improved systemic activity in anti-PD-1 resistant melanoma

**A. Shoushtari**[1,2], A. J. Olszanski[3], M. Nyakas[4], T. J. Hornyak[5], J. D. Wolchok[1,2,6,7], V. Levitsky[8], T. B. Hansen[8], and L. Ottesen[8]

**1** Department of Medicine (Melanoma Service), Memorial Sloan Kettering Cancer Center, New York, NY, USA. **2** Weill Cornell Medicine, New York, NY, USA. **3** Department of Medicine, Fox Chase Cancer Center, Philadelphia, PA, USA. **4** Department of Oncology, Oslo University Hospital, Oslo, Norway. **5** Department of Dermatology and University of Maryland Greenebaum Comprehensive Cancer Center, University of Maryland School of Medicine, Baltimore, USA. **6** Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, NY, USA. **7** Parker Institute for Cancer Immunotherapy, San Francisco, CA, USA. **8** Research and Development, Targovax ASA, Oslo, Norway

# ONCOS-102 is an engineered oncolytic immunotherapy based on an Adenovirus serotype 5 backbone

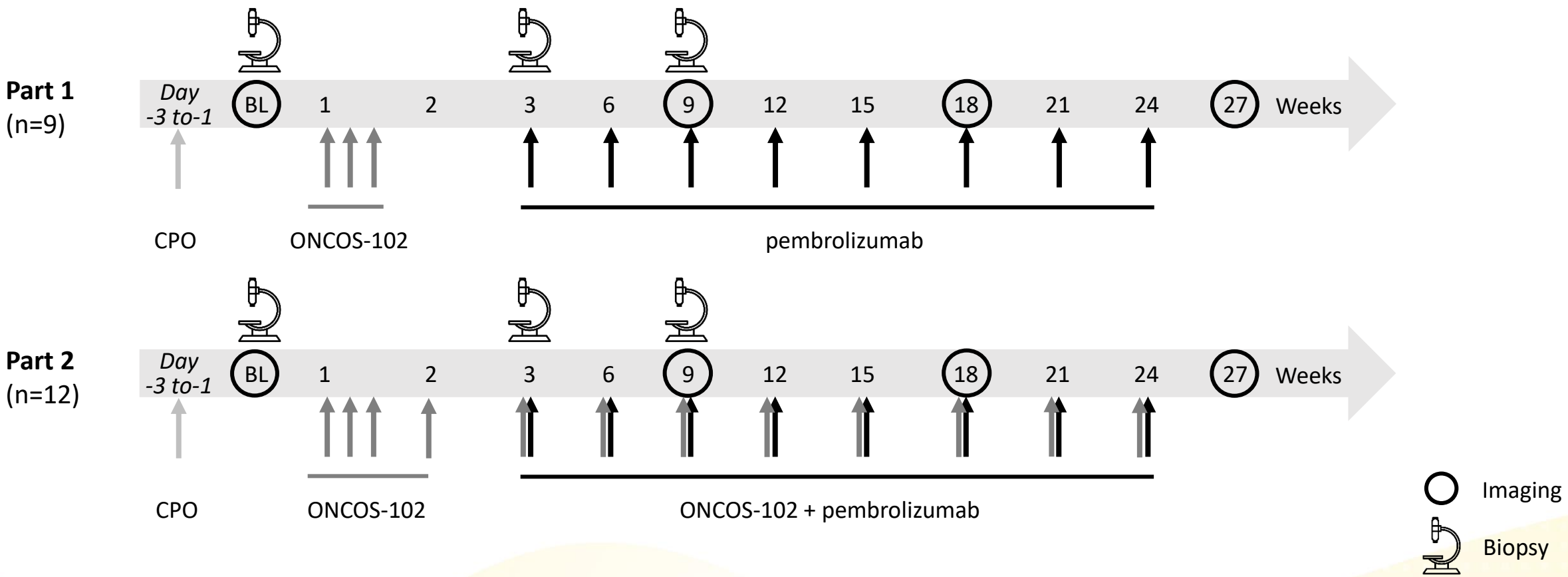



**Drives inflammatory response** to reverse immuno-suppressive defence mechanisms in the tumor

**Primes** tumor-antigen specific **T-cell responses**

**Delivers GM-CSF** as an immune stimulatory payload

# Two intra-tumoral ONCOS-102 dosing regimens were tested in 21 PD-1 resistant melanoma patients



# Patient characteristics: higher tumor burden and more stage IV disease in Part 2 patients

| | Part 1 (n=9) | Part 2 (n=12) | Total (N=21) |
|---|---|---|---|
| **Median age,** years (range) | 73 (40–87) | 72 (43–83) | 73 (40–87) |
| **Sex** (female/male), n | 4/5 | 6/6 | 10/11 |
| **EGOG performance status,** n (%) | | | |
| 0 | 1 (11) | 7 (58) | 8 (18) |
| 1 | 8 (89) | 5 (42) | 13 (62) |
| **Melanoma subtype,** n (%) | | | |
| Cutaneous | 8 (89) | 6 (50) | 14 (67) |
| Acral | 1 (11) | 1 (8) | 2 (10) |
| Mucosal | 0 | 2 (17) | 2 (10) |
| Unknown Primary | 0 | 3 (25) | 3 (14) |
| **AJCC stage[a], n (%)** | | | |
| III (any stage) | 6 (67) | 5 (42) | 11 (52) |
| IV | | | |
| IVM1a | 2 (22) | 2 (17) | 4 (19) |
| IVM1b | 0 | 2 (17) | 2 (10) |
| IVM1c | 1 (11) | 3 (25) | 4 (19) |
| **Tumor burden at baseline** | | | |
| Sum of the longest diameter of target lesions, mm (range) | 37.5 (15–117) | 73.5 (12–174) | 43 (12–174) |
| Median number of lesions (range)[b] | 3 (1–10) | 8.5 (3–17) | 7 (1–17) |

| | Part 1 (n=9) | Part 2 (n=12) | Total (N=21) |
|---|---|---|---|
| **Prior cancer therapy, n (%)** | | | |
| Surgery | 9 (100) | 11 (92) | 20 (95) |
| Radiotherapy | 2 (22) | 4 (33) | 6 (29) |
| Chemotherapy | 1 (11) | 6 (50) | 7 (33) |
| Anti-PD-1 agent | 9 (100) | 12 (100) | 21 (100) |
| Anti-CTLA-4 agent | 4 (45) | 8 (67) | 12 (57) |
| BRAF and/or MEK inhibitor | 2 (22) | 1 (8) | 3 (14) |
| Intralesional therapy[c] | 4 (45) | 2 (17) | 6 (29) |
| **Driver alterations[d], n (%)** | | | |
| BRAF V600 | 2 (22) | 0 | 2 (10) |
| NRAS Q61, *NRAS* other | 3 (33) | 7 (58) | 10 (48) |
| Other/Not tested | 4 (44) | 5(42) | 9 (42) |

[a]Disease stage at enrolment; [b]Includes all target and non-target lesions at baseline; [c]Includes talimogene laherparepvec (n=4), CMP-001 (n=1), and PV-10 (n=1); [d]Driver alterations were identified with ≥5% allele frequency in somatic tissue and cross-referenced with the Personalis Research Cancer Gene List

# Both regimens were well-tolerated with similar safety profiles and no dose limiting toxicities observed

*ONCOS-102-related AEs were mainly flu-like symptoms*

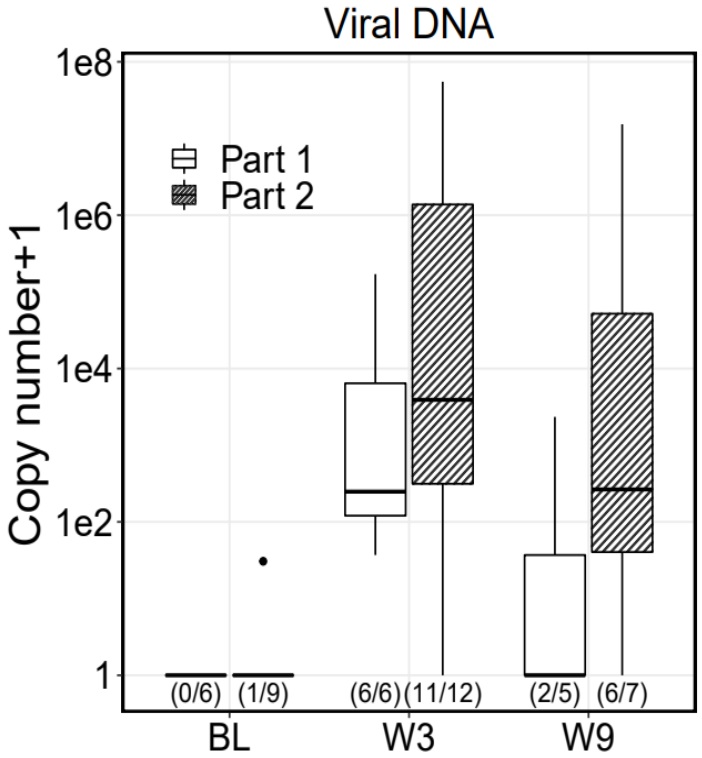
**Treatment related adverse events (≥1 patient)**

| Preferred term n (%) | AEs related[a] to ONCOS-102, only | | | AEs related[a] to ONCOS-102 and pembrolizumab | | |
|---|---|---|---|---|---|---|
| | Part 1 (N=9) | Part 2 (N=12) | Total (N=21) | Part 1 (N=9) | Part 2 (N=12) | Total (N=21) |
| All treatment-related AEs | 8 (89) | 9 (75) | 17 (81) | 3 (34) | 6 (50) | 9 (43) |
| Pyrexia | 3 (33) | 6 (50) | 9 (43) | 1 (11) | 2 (17) | 3 (14) |
| Chills | 5 (56) | 4 (33) | 9 (43) | 0 | 0 | 0 |
| Nausea | 3 (33) | 3 (25) | 6 (29) | 0 | 1 (8) | 1 (5) |
| Injection site pain | 1 (11) | 3 (25) | 4 (19) | 0 | 0 | 0 |
| Vomiting | 2 (22) | 2 (17) | 4 (19) | 0 | 0 | 0 |
| Injection site reaction | 0 | 3 (25) | 3 (14) | 0 | 0 | 0 |
| Myalgia | 3 (33) | 0 | 3 (14) | 0 | 0 | 0 |
| Fatigue | 2 (22) | 1 (8) | 3 (14) | 0 | 0 | 0 |
| Diarrhea | 2 (22) | 0 | 2 (10) | 0 | 0 | 0 |
| Pruritus | 1 (11) | 1 (8) | 2 (10) | 0 | 0 | 0 |
| Rash maculo-papular | 1 (11) | 1 (8) | 2 (10) | 0 | 0 | 0 |
| Hypotension | 0 | 2 (17) | 2 (10) | 0 | 0 | 0 |
| ALT increased | 1 (11) | 0 | 1 (5) | 0 | 1 (8) | 1 (5) |
| AST increased | 0 | 0 | 0 | 1 (11) | 1 (8) | 2 (10) |

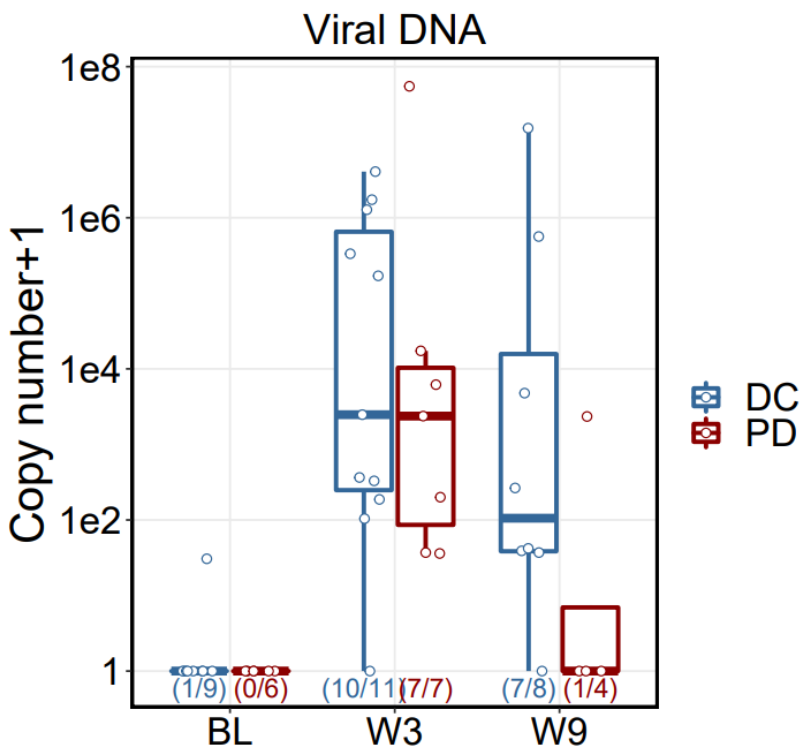
# Part 2 regimen supports prolonged ONCOS-102 tumor exposure which correlated with disease control

**ONCOS-102 viral particles (VP) in tumor,** qPCR on tumor biopsy DNA

Part 1 vs. Part 2 patients



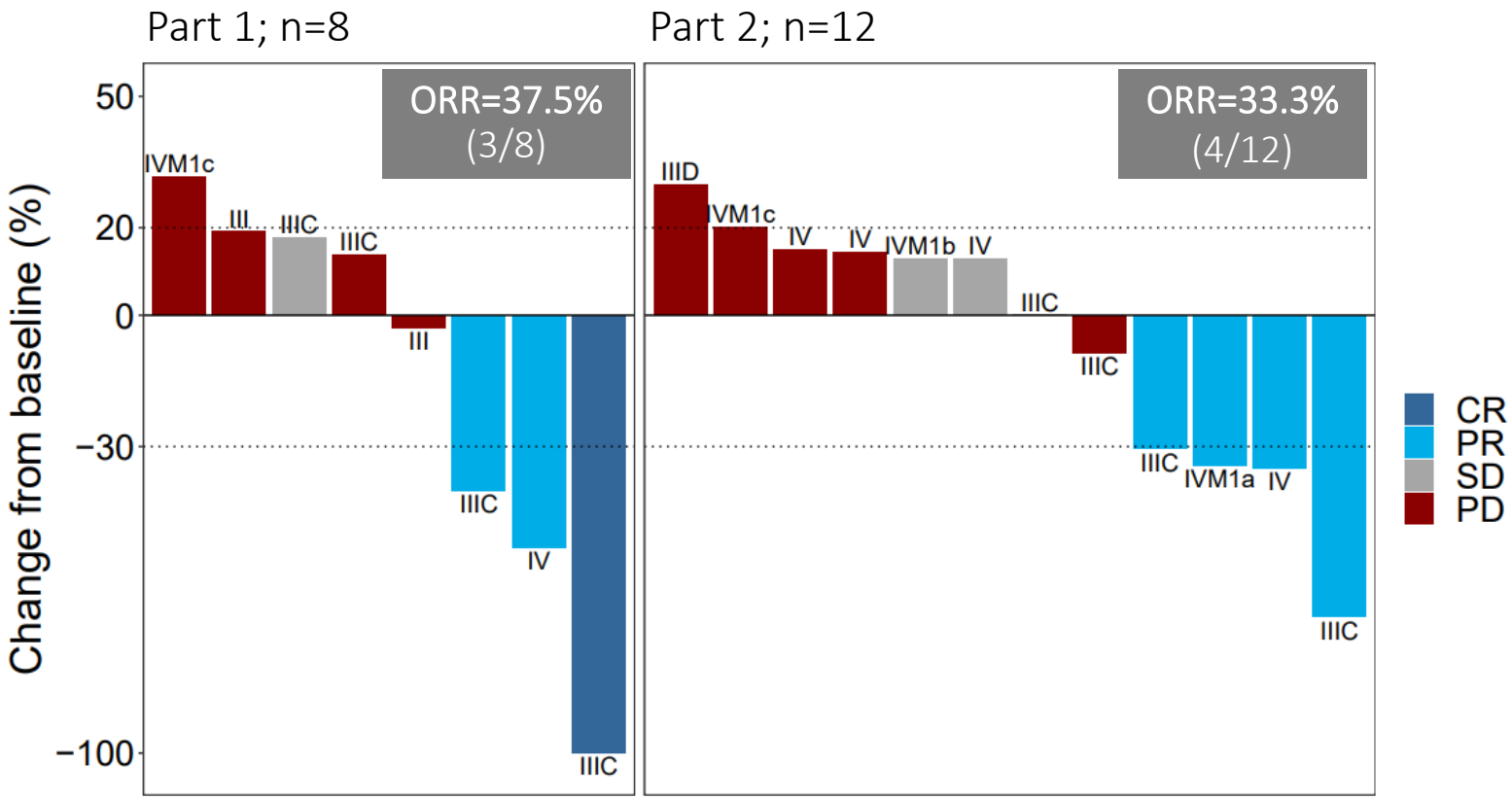

Patients w/DCR vs. PD




- **ONCOS-102 replication** supported in tumors for **at least 6 injections** and **until week 9**
- **Q3W schedule** ensures consistent virus exposure
- **Higher ONCOS-102** levels with Part 2 **concomitant dosing regimen**
- ONCOS-102 level at week 9 **correlated with tumor response**

# An overall ORR of 35% was observed with similar response rates in Part 1 and Part 2

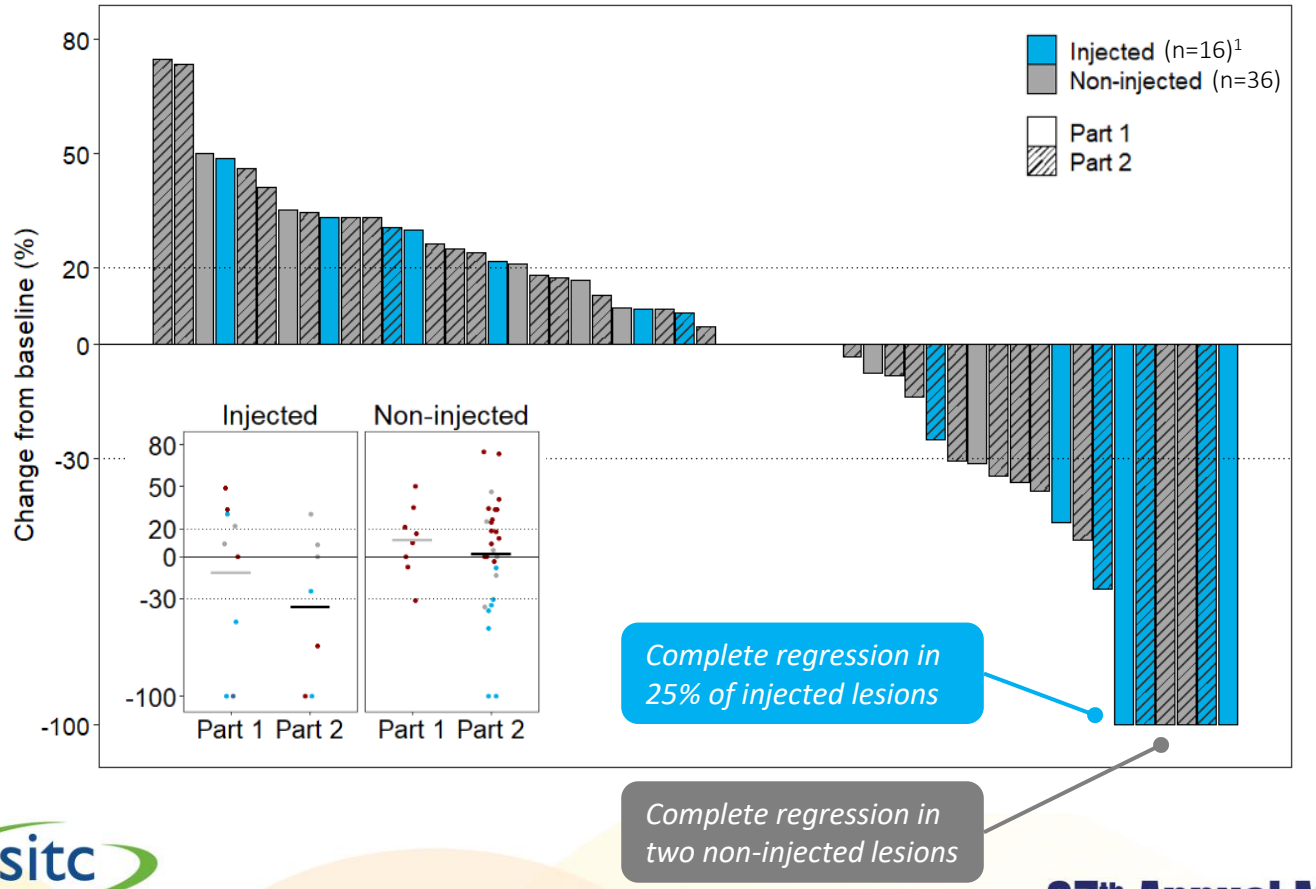
**Best response in target lesions (BOR)**, tumor burden change from baseline (%)



# Systemic activity was more pronounced with part 2 concomitant dosing regimen

**Response in individual tumors**

% change from baseline; injected and non-injected target lesions



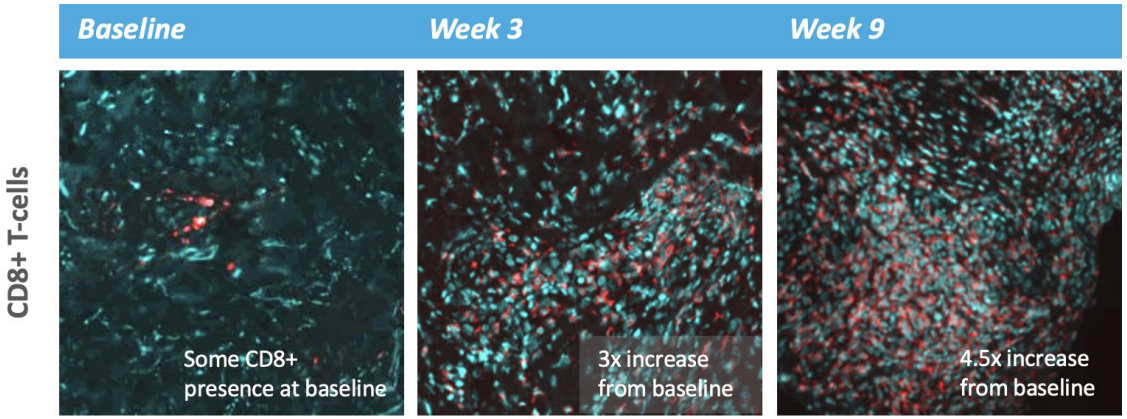

Observed systemic effect:

- **12 of 36 (33%) non-injected** target lesions **reduced in size**
- **8 of 15 (53%) patients** had reduction in non-injected target lesions
- **7 of 8 (88%) non-injected lesions** with ≥30% reduction in size were in **part 2 patients**

# Robust increase in T-cell infiltration in both Part 1 and 2, persisting at week 9 in patients with clinical benefit

2022 SITC NOVEMBER 8-12 BOSTON MASSACHUSETTS

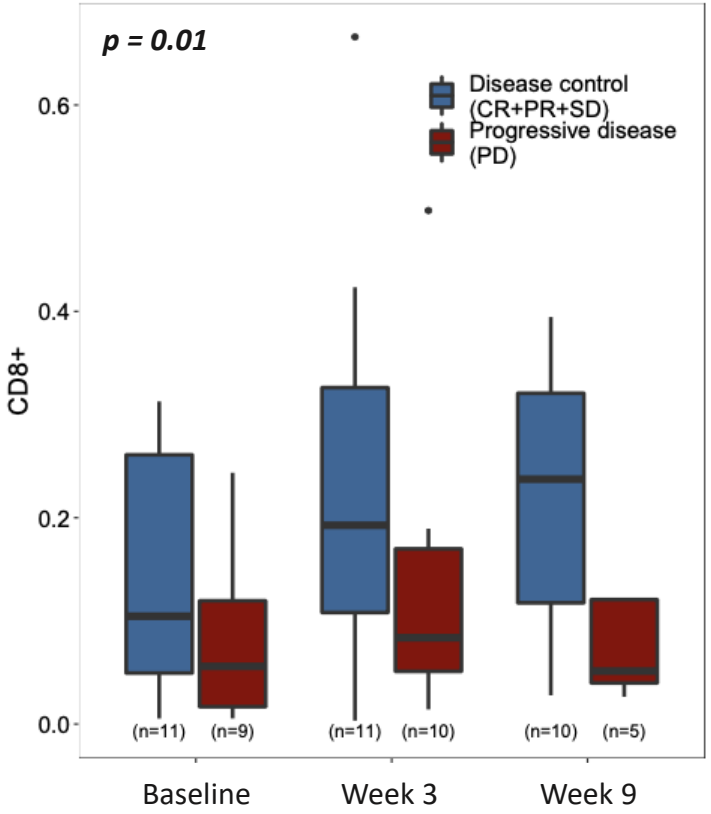
**CD8+ T-cell tumor infiltration**
Tumor biopsy IHC, patient case example




| Progression on pembrolizumab | 3x ONCOS-102 only monotherapy | 6x ONCOS-102 2x pembrolizumab |
|---|---|---|

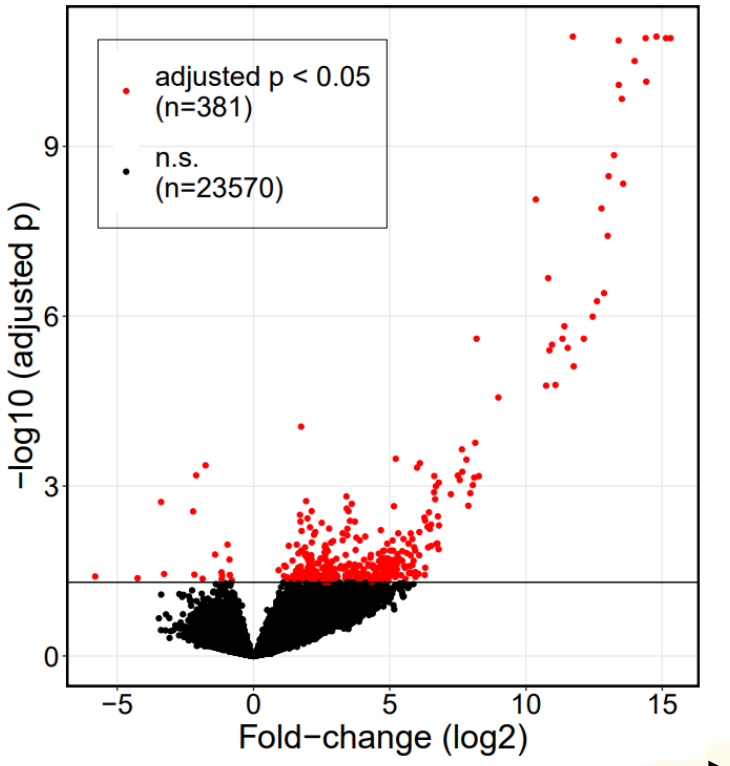
| | | | |
|---|---|---|---|
| **Prior therapies:** | T-vec (oncolytic virus)<br>Ipilimumab (CTLA-4)<br>Pembrolizumab (PD-1) | **Disease stage:**<br>**Outcome:** | T4a-M1<br>PR RECIST 1.1<br>Week 9 - EoS |

**CD8+ T-cell infiltration, aggregated**
Average level in biopsies per group



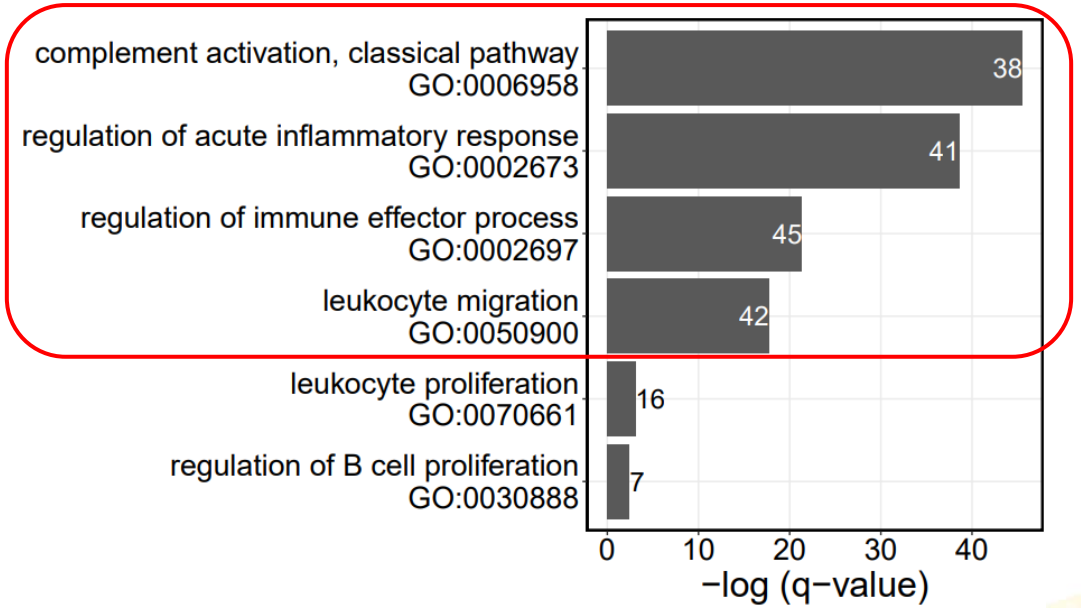
# Gene expression revealed specific up-regulation of immune related pathways in Part 2

**Gene expression profile**, total RNAseq on tumor biopsies
Changes at week 9 vs. baseline; Part 1 vs. Part 2




*Specifically upregulated in Part 2*

**Gene ontologies**
Categories of differentially expressed genes in Part 2



# Part 2 concomitant dosing regimen selected for Phase 2 development of ONCOS-102 in PD-1 resistant melanoma

SITC 2022
NOVEMBER 8-12 BOSTON MASSACHUSETTS

## Summary & conclusions

- **Both ONCOS-102 dosing regimens** were **safe and well-tolerated** in combination with pembrolizumab
- **35% ORR was observed**, with similar response rates in Part 1 and Part 2
- **Part 2 regimen supported high and long-lasting viral activity** in tumors, which correlated with clinical benefit
- Systemic activity was **more pronounced with Part 2 regimen**
- Several immunological pathways were **differentially up-regulated in Part 2**
- Data generated in this pilot study supports **taking the Part 2 concomitant dosing regimen forward** in phase 2 development in PD-1 resistant melanoma



Shoushtari et al. Clinical Cancer Research 2022