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Agenda & Speakers:

11:30AM-12:00PM
Registration & Lunch

12:00-12:10PM
Welcome Remarks
Øystein Soug, CEO, Targovax

12:10-12:50PM
Oncolytic Virus Overview and Q&A
Dmitriy Zamarin, MD, PhD

12:50-1:30PM
Melanoma: the disease, CPIs, and lack of treatment options; Early ONCOS-102 data
Alexander N. Shoushtari, MD

1:30-1:50PM
Mesothelioma ORR Data
Magnus Jaderberg, CMO, Targovax

1:50-2:00PM
Closing Remarks
Øystein Soug, CEO, Targovax

PLEASE JOIN US FOR A KOL EVENT

Leading experts discuss the oncolytic virus landscape and present interim data from Targovax's ongoing melanoma and mesothelioma trials

DATE	|	Thursday, October 11th, 2018
TIME	|	11:30 AM EST
LOCATION	|	The Maxwell (formerly The W Hotel) 541 Lexington Avenue, Great Room 1

KOL PARTICIPANTS:

Dmitriy Zamarin, MD, PhD
Medical Oncologist, Memorial Sloan Kettering

Alexander N. Shoushtari, MD
Medical Oncologist, Melanoma, Memorial Sloan Kettering

Important
NOTICE AND DISCLAIMER

This report contains certain forward-looking statements based on uncertainty, since they relate to events and depend on circumstances that will occur in future and which, by their nature, will have an impact on the results of operations and the financial condition of Targovax. Such forward-looking statements reflect the current views of Targovax and are based on the information currently available to the company. Targovax cannot give any assurance as to the correctness of such statements.

There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in these forward-looking statements. These factors include, among other things, risks or uncertainties associated with the success of future clinical trials; risks relating to personal injury or death in connection with clinical trials or following commercialization of the company's products, and liability in connection therewith; risks relating to the company's freedom to operate (competitors patents) in respect of the products it develops; risks of non-approval of patents not yet granted and the company's ability to adequately protect its intellectual property and know-how; risks relating to obtaining regulatory approval and other regulatory risks relating to the development and future commercialization of the company's products; risks that research and development will not yield new products that achieve commercial success; risks relating to the company's ability to successfully commercialize and gain market acceptance for Targovax's products; risks relating to the future development of the pricing environment and/or regulations for pharmaceutical products; risks relating to the company's ability to secure additional financing in the future, which may not be available on favorable terms or at all; risks relating to currency fluctuations; risks associated with technological development, growth management, general economic and business conditions; risks relating to the company's ability to retain key personnel; and risks relating to the impact of competition.

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1 Introduction

2. Oncolytic virus overview – Dr. Dmitriy Zamarin
3. ONCOS-102 in melanoma – Dr. Alexander Shoushtari
4. ONCOS-102 in mesothelioma – Dr. Magnus Jäderberg
5. Summary & closing

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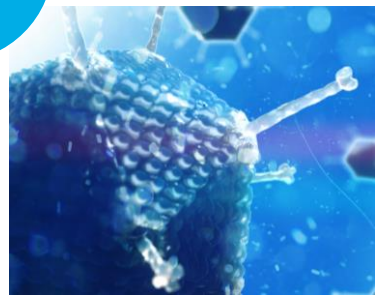
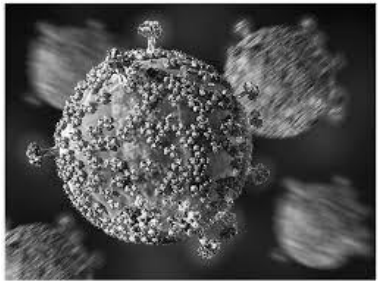
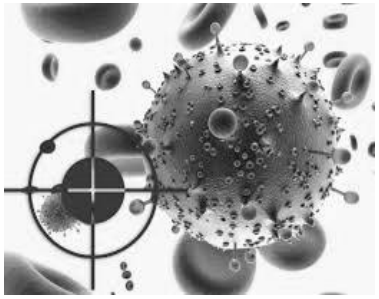
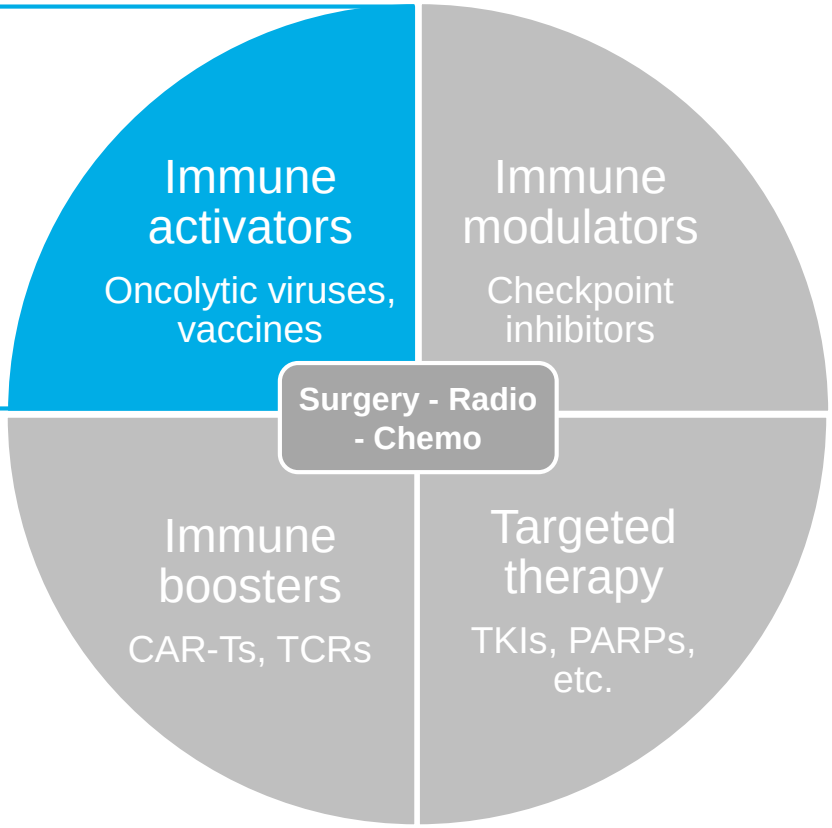
TARGOVAX AIM IS TO ACTIVATE THE PATIENT'S OWN IMMUNE SYSTEM TO FIGHT CANCER

Targovax focus









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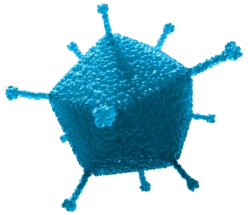
Targovax has two programs in clinical development, with an

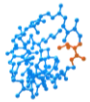
ONCOLYTIC VIRUS LEAD PRODUCT CANDIDATE



ONCOS
Oncolytic virus

Lead product candidate

- Genetically **armed adenovirus**
- **Alerts the immune system** to the presence of cancer antigens
- **Induces T-cells** specific to the patients' tumor
- **4 ongoing trials**



TG
Neoantigen vaccine

Pipeline product

- **Shared neoantigen**, therapeutic cancer vaccine
- Triggers the immune system to **recognize mutant RAS cancers**

Activates the immune system

Triggers patient-specific responses

No need for individualization

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ONCOS-102 is a cancer targeting adenovirus armed with an

IMMUNE STIMULATING TRANSGENE

1

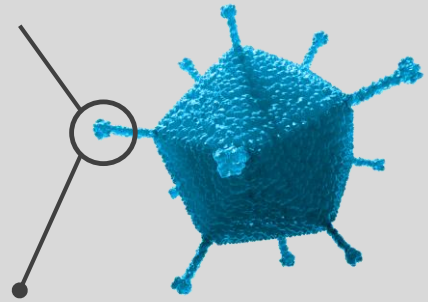
Selective replication
in cancer cells

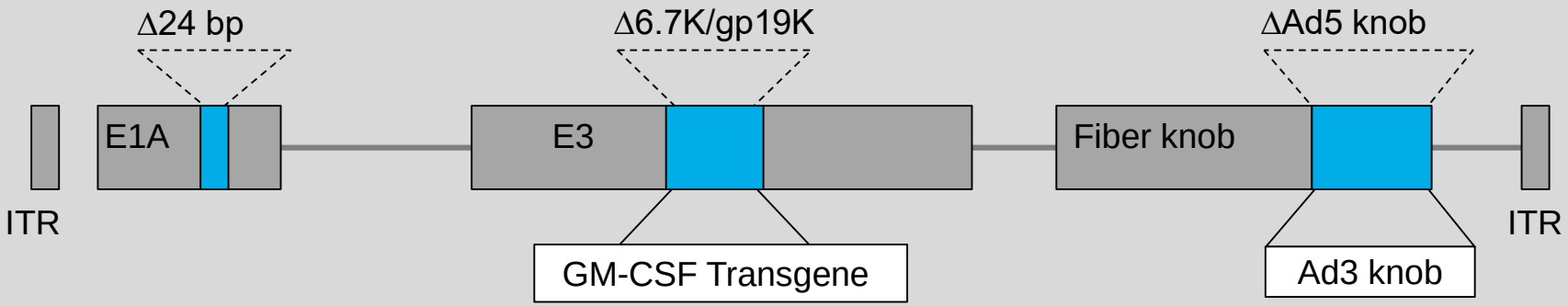
2

Boosting the **immune activation**

3

Enhanced infection
of cancer cells





ONCOS-102
Phase I proof of concept

IMMUNE ACTIVATION DEMONSTRATED

ONCOS-102 Phase I trial design:

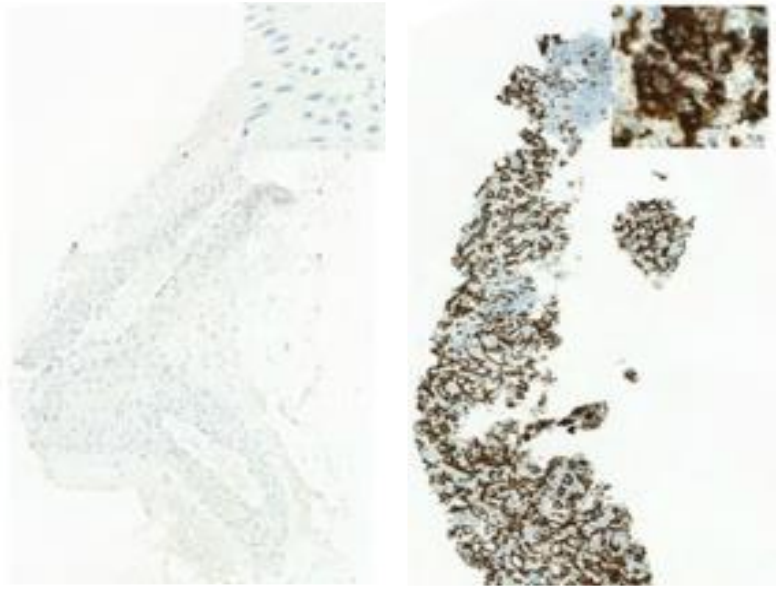
- 12 patients, 7 different solid tumors
- No other treatment options left
- Monotherapy 9 injections

Top-line results:

- 100% innate immune activation
- 11/12 patients increase in TILs
- Abscopal effect
- Tumor specific T-cells in blood
- Correlation with survival

Cold tumor turned hot

CD8+ T-cell staining



Pre-treatment **Post-treatment**

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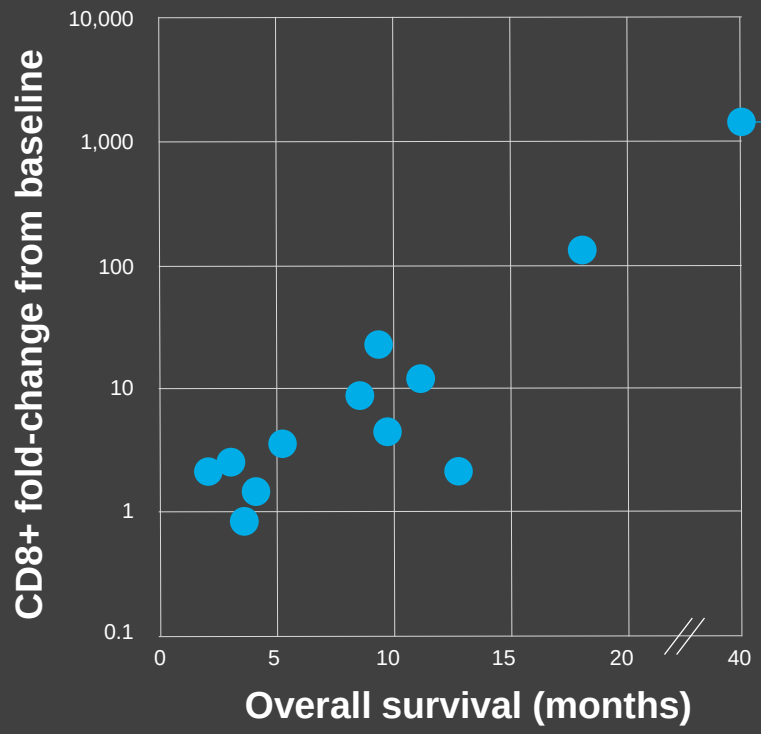
ONCOS-102

Phase I single agent proof of concept

CD8+ T-CELL INFILTRATION CORRELATES WITH SURVIVAL

Fold-change CD8+ T-cell count vs. survival

r = 0.75 p = 0.005



Case example

- Ovarian cancer
- Failed on 5 chemotherapies
- Tumor specific T-cells after 2 years
- Stable disease for 3 years
- Survived 3.5 years

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ONCOS

CLINICAL PROGRAM OVERVIEW

Compassionate use program
115 patients

→

Phase I trial
12 patients
7 indications

Mesothelioma
Phase I/II - randomized
30 patients

- Shortest path-to-market
- Orphan drug designation
- Combination with SoC chemo
- Randomized vs. SoC

Melanoma
Phase I
Up to 12+12 patients

- PoC in CPI refractory patients
- Combination with Keytruda®
- Memorial Sloan Kettering

Peritoneal cancer
Phase I/II
up to 78 patients

- Ovarian and colorectal cancers
- Combination with Imfinzi®
- Intraperitoneal administration
- Collaboration with MedImmune / AZ, CRI, & Ludwig

Prostate cancer
Phase I
up to 15 patients

- Combination with dendritic cell vaccine (DCVAC)
- Collaboration with Sotio

Completed

Ongoing trials sponsored by Targovax

Ongoing trials sponsored by partner

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2

Oncolytic virus overview
Dr. Dmitriy Zamarin

3. ONCOS-102 in melanoma – Dr. Alex Shoushtari
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Memorial Sloan Kettering Cancer Center™

Systemic immunomodulation with *in situ* oncolytic vaccines

Dmitriy Zamarin MD PhD

Assistant Attending, Gynecologic Medical Oncology /
Immune Therapeutics Center
Parker Institute for Cancer Immunotherapy
Memorial Sloan-Kettering Cancer Center
New York, NY

October 11, 2018

The idea of using pathogens for treating cancer

1800

1850

1900

1950

1970

1990

2005

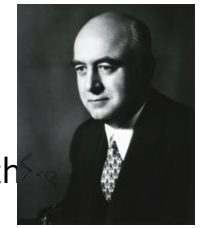
2015

1850-1900 – reports of natural tumor regressions coinciding with human infections

William Coley

1891-William B. Coley uses live Strep. pyogenes to treat head and neck cancer

1910-De Pace et. al - patient with advanced cervical cancer treated with rabies vaccine experiences complete remission



George T. Pack

1940's-George T. Pack – treated melanoma with rabies vaccine; some remissions were seen.

1950's- clinical trials with Hepatitis B, West Nile virus, Adenovirus, Russian Far Eastern Encephalitis viruses

Chester Southam

1960's-1990's-clinical trials with attenuated human viruses and animal viruses

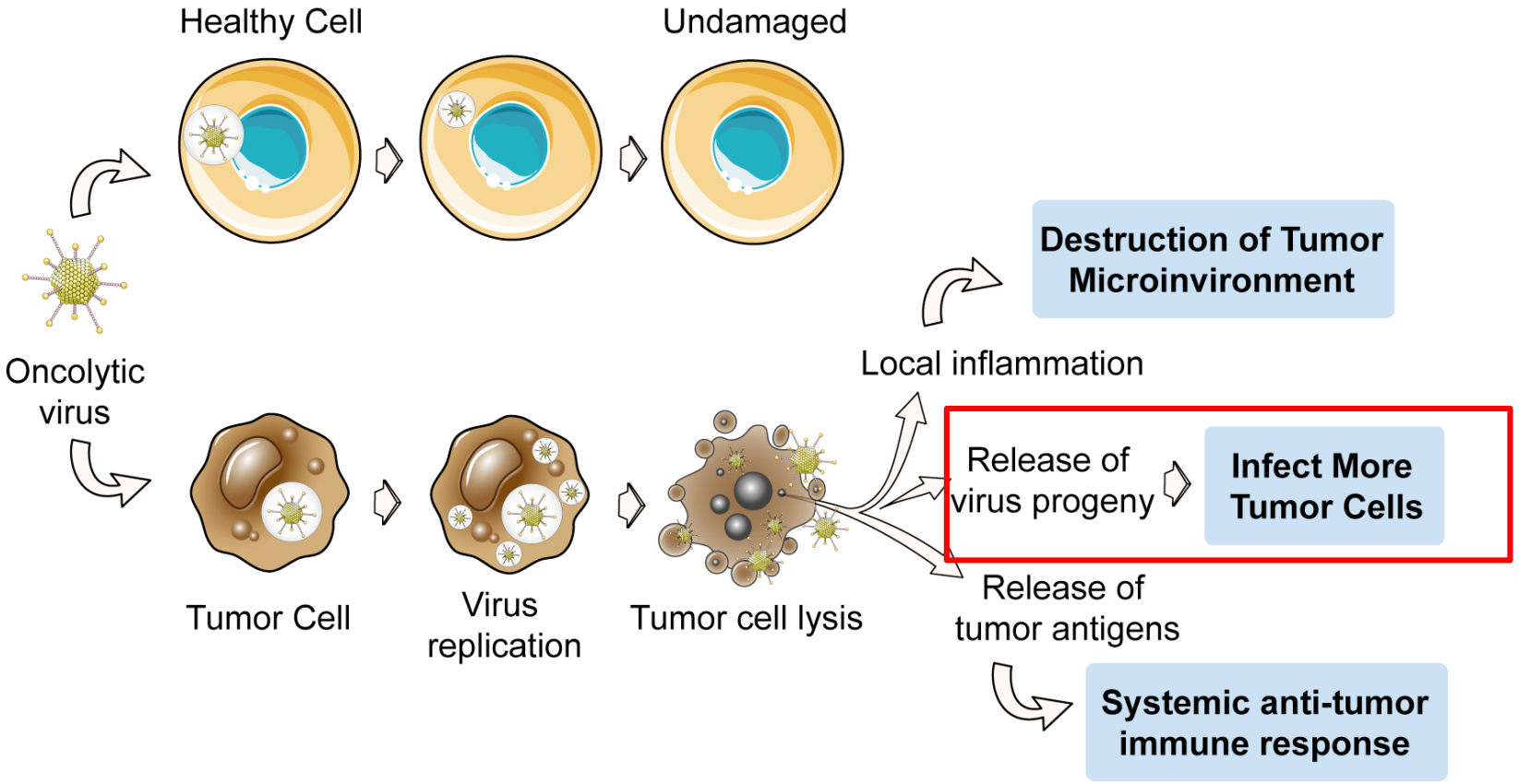
1990's-present – Genetically engineered viruses

2005- 1st approved oncolytic virus (China)

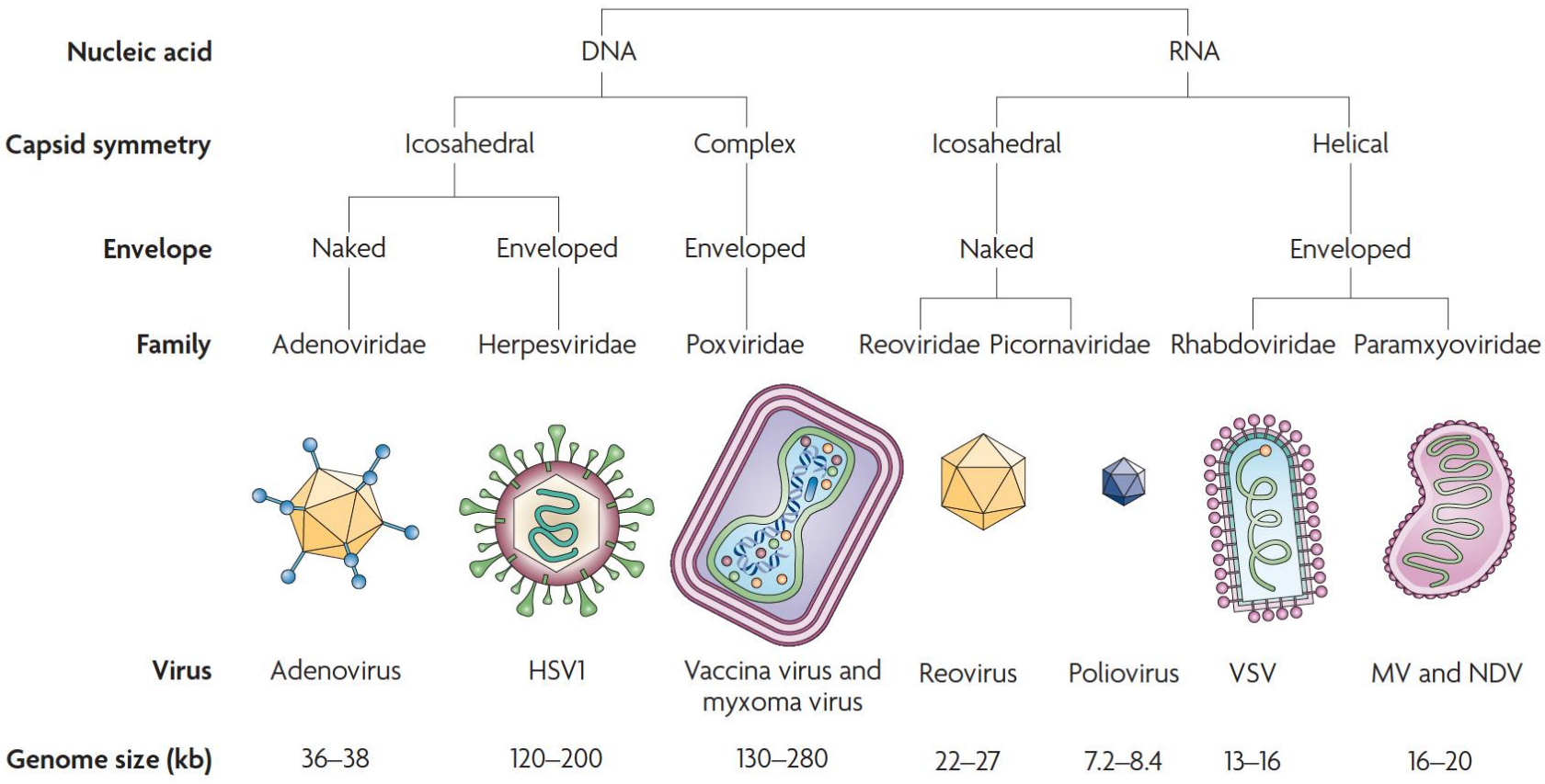
2013-1st positive phase III trial (talimogene laherparepvec)

2015- T-vec approved for advanced melanoma

How oncolytic viruses work



Not all oncolytic viruses are created equal



Dogma: replicating and lytic viruses are better anti-cancer agents than non-lytic viruses

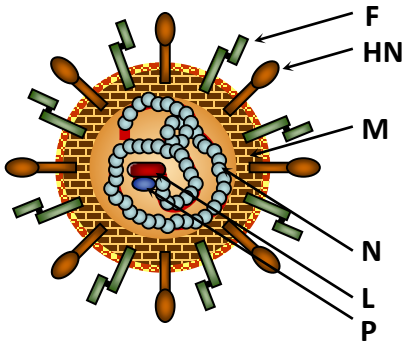
NATURE REVIEWS | MICROBIOLOGY VOLUME 6 | JULY 2008 | 529

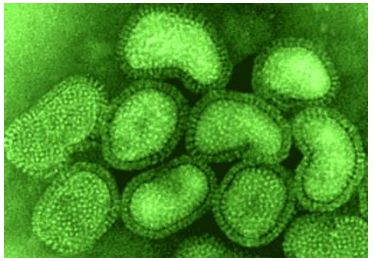
Current efforts (non-exhaustive list, closest to clinical development)

- **HSV-1 (Amgen and at least 5 other companies);** T-vec phase III in melanoma complete and FDA-approved; combination trials with anti-PD-1 and anti-CTLA-4 in melanoma ongoing. Head and neck Ph III trial terminated in 2011.
- **Vaccinia (Jennerex, Genelux, Western Oncolytics).** JX-594 had encouraging results in early trial with HCC; less promising in a later study. GL-ONC1 is in phase I for IP for carcinomatosis, intrapleural for mesothelioma, IV for solid tumors.
- **Myxoma (academic).** Pre-clinical
- **Reolysin (Oncolytics).** Multiple clinical trials in various indications; most recently in combination with chemotherapy.
- **Coxsackie A21 (Viralytics).** Phase II for intralesional administration (CALM study, melanoma) showed promise. Currently in phase I IV for different cancer types; including with pembro combination for lung.
- **Poliovirus (academic).** Encouraging data in glioblastoma (given intratumorally)
- **Adenovirus (Oncos, Cold Genesys, PsiOxus, academic).** Oncos: Ad5-GM-CSF; completed phase I study with IT administration, results pending (evidence of immune activation based on poster presentations). PsiOxus: chimeric Ad11p/Ad3, in phase I for colon cancer (IV).
- **VSV (Viread).** Phase I ongoing in HCC.
- **Maraba (Turnstone).** Phase I ongoing in combination with adenovirus prime-boost in patients with MAGE-A3 expressing cancers
- **Measles (academic).** Phase I in ovarian, head and neck, multiple myeloma, GBM, mesothelioma. Promising results in ovarian and multiple myeloma so far.
- **NDV (academic and industry).** Several phase I studies completed in multiple tumor types using virulent virus strain, with promising results. Currently in development with non-virulent strains.
- **Seneca Valley (Neotropix).** Phase I completed in neuroendocrine tumors.

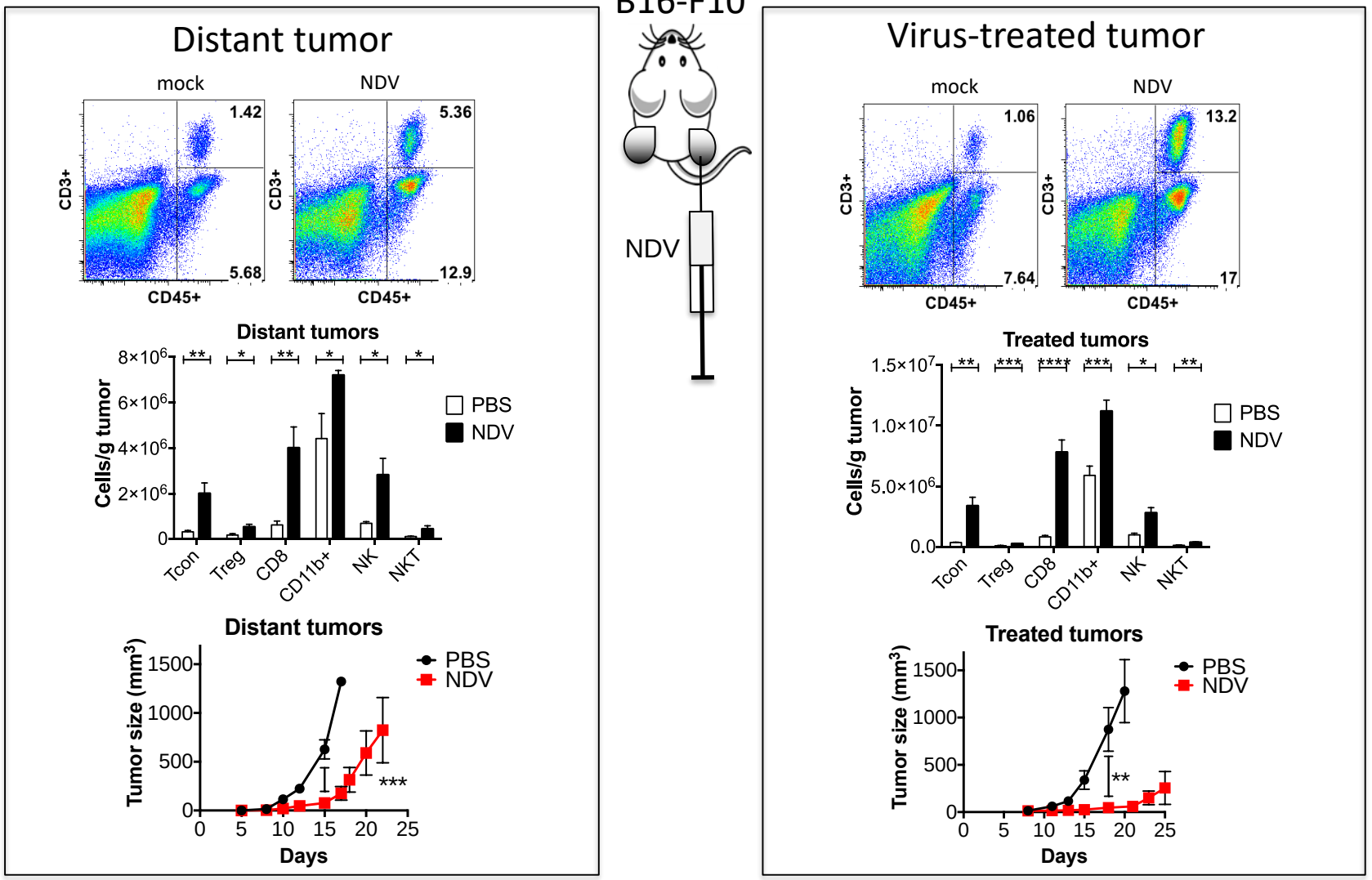
Newcastle Disease Virus (NDV)

- Negative-strand RNA virus, member of Paramyxoviridae family (same as mumps, HPIV, measles), which **do not integrate into mammalian genome**
- Causes contagious bird disease affecting many domestic and wild avian species, but poses **no hazard to human health**
- Readily **infects the majority of cancer cells** due to ubiquity of the receptor (sialic acid)
- Specificity for cancer cells is mediated by selective viral replication in cells with **deficient innate immune responses and cells resistant to apoptosis**
- Pathogenicity in birds is primarily determined by the fusion protein cleavage site sequence



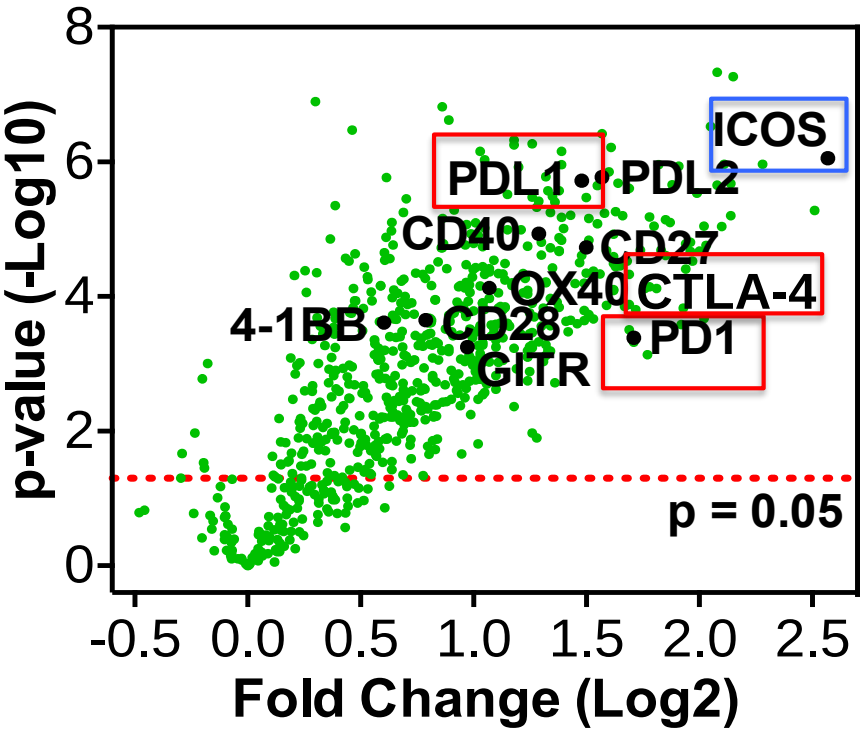


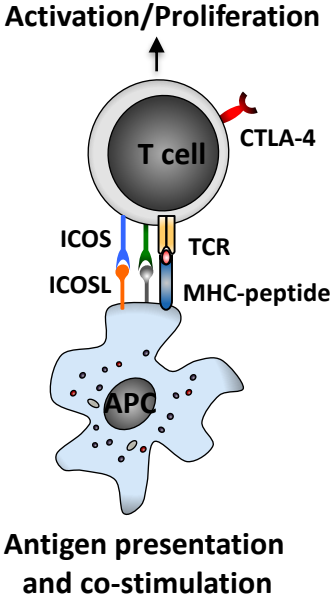
Intratumoral NDV induces local and distant TIL infiltration



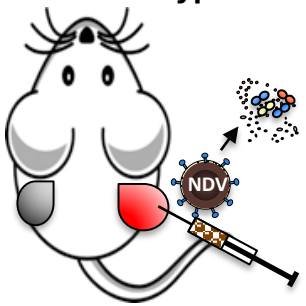
Zamarin D, Wolchok JD, Allison JP. *Science Translational Medicine.* 2014 5:226ra

NDV upregulates a range of immune inhibitory and activating pathways in tumors

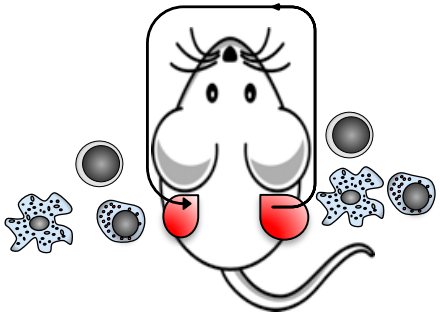


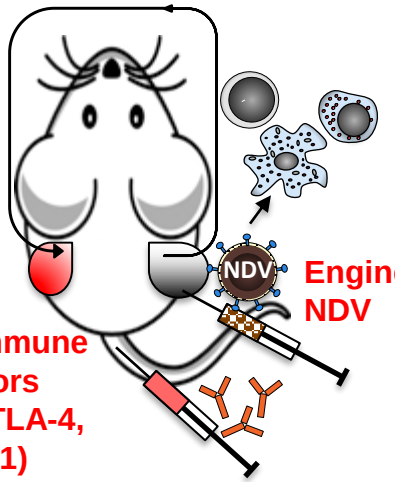


Early: direct action of type I IFN



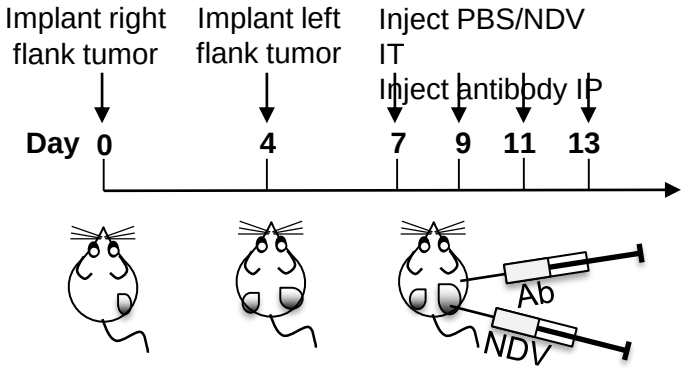
Late: response to TIL infiltration



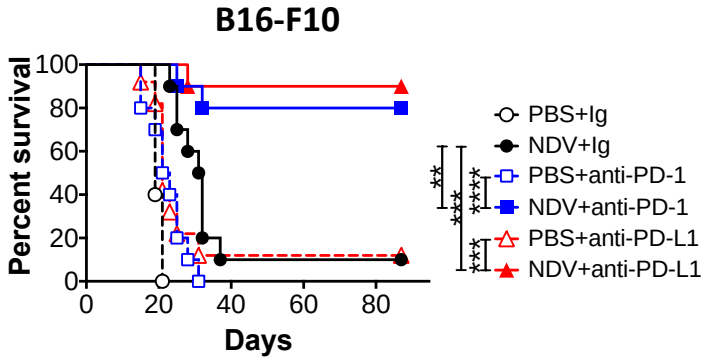


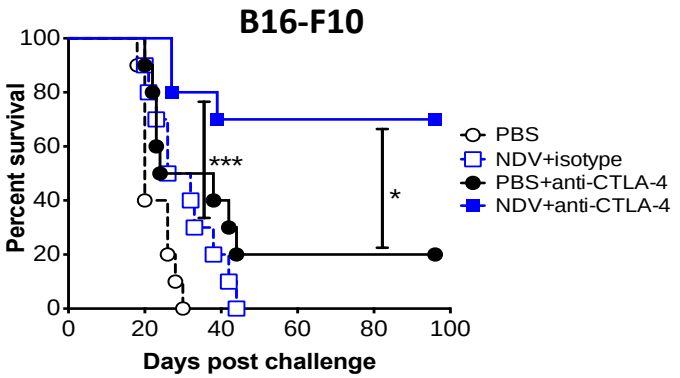
Zamarin et al., *J. Clin. Invest*. 2018 *in press*

NDV potentiates the efficacy of systemic immune checkpoint blockade in models sensitive and resistant to NDV lysis

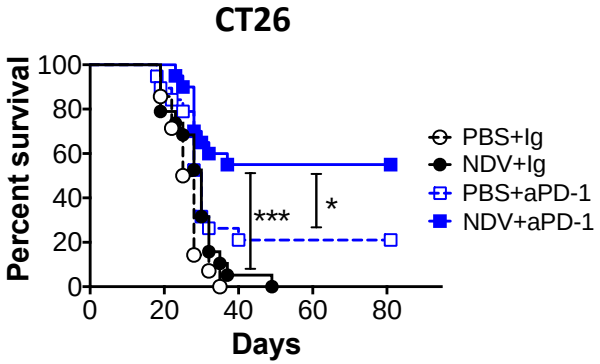


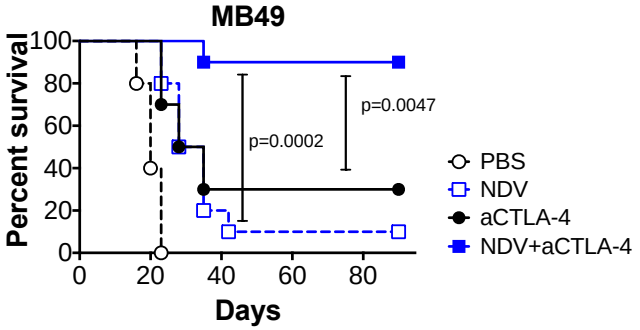
NDV-sensitive





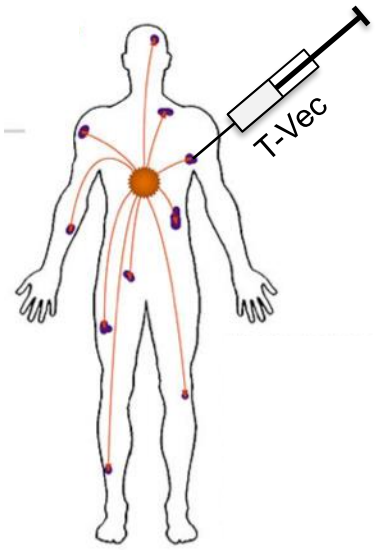
NDV-resistant

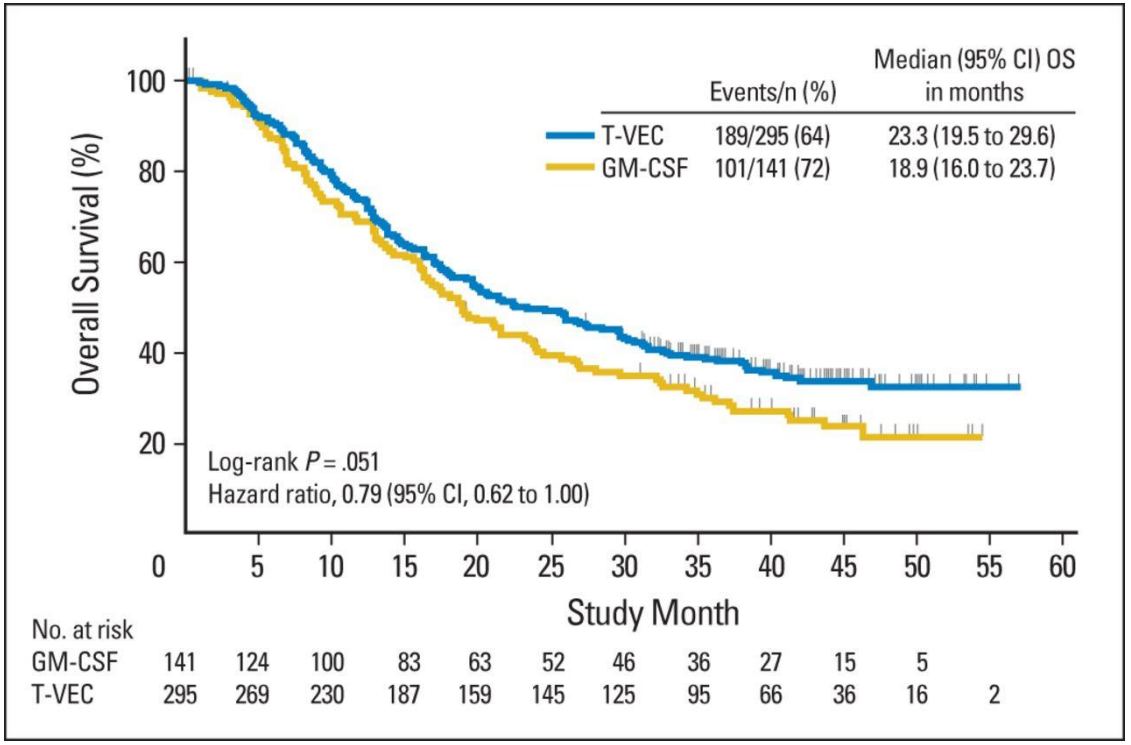




Zamarin et al., *J. Clin. Invest*. 2018 *in press;* Zamarin D, et al., *Science Translational Medicine.* 2014 5:226ra

OPTiM, a randomized phase III trial of talimogene laherparepvec (T-VEC: HSV-GM-CSF) versus subcutaneous GM-CSF for the treatment of advanced melanoma

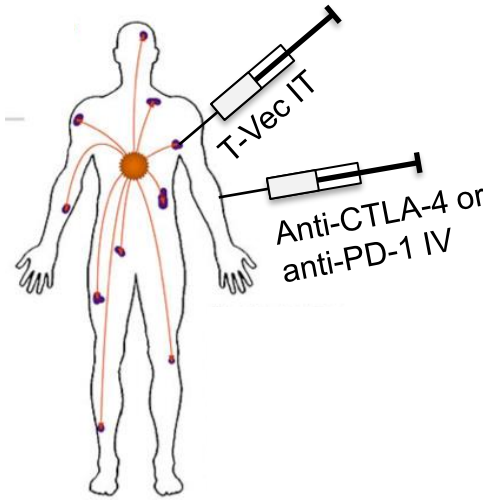




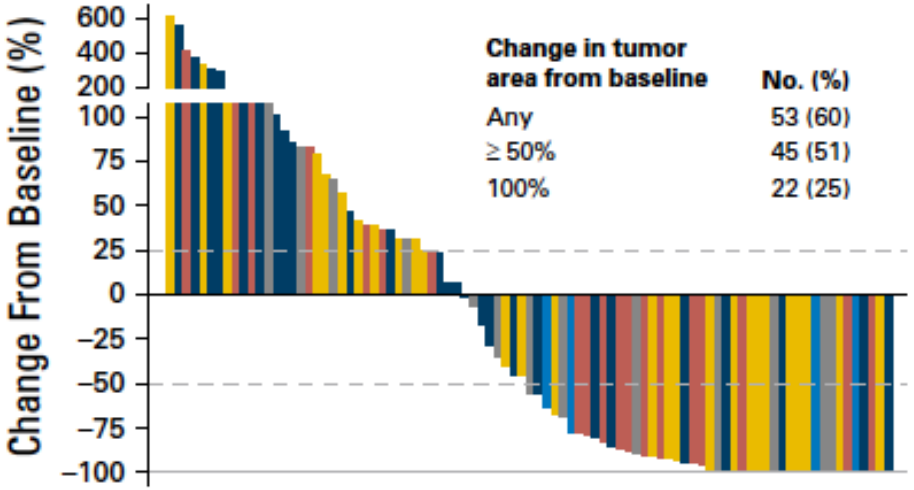
T-vec was approved by FDA in 10/2015

Andtbacka et al., JCO 2015

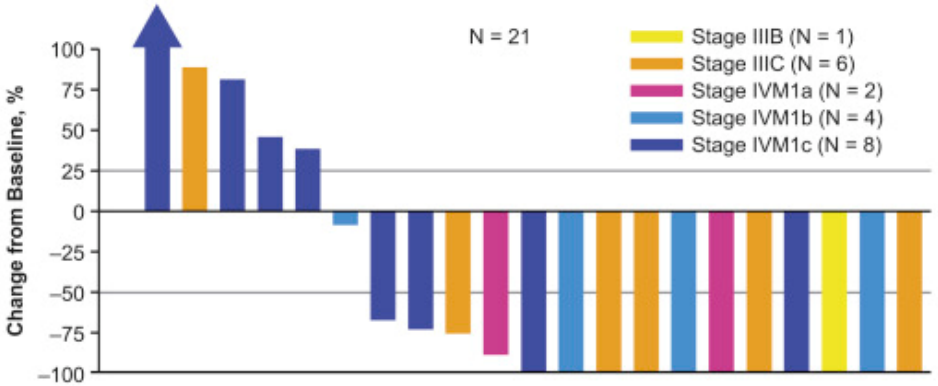
Intratumoral T-vec potentiates the efficacy of systemic anti-CTLA-4 and anti-PD-1 therapy in melanoma



Tvec + anti-CTLA-4 (ORR 39%)

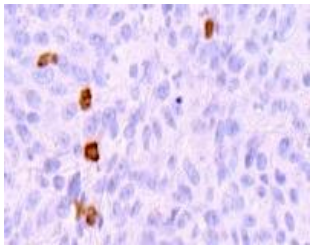


Tvec + anti-PD-1 (ORR 62%)

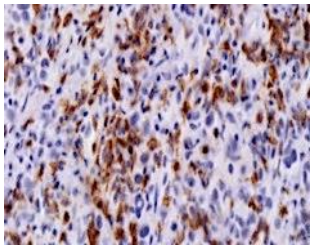


Chesney et al., JCO 2017; Ribas et al, Cell 2017

Summary: locoregional and systemic immune modulation approaches can lead to systemic anti-tumor immunity

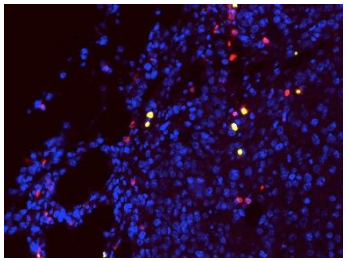


No response to CPI



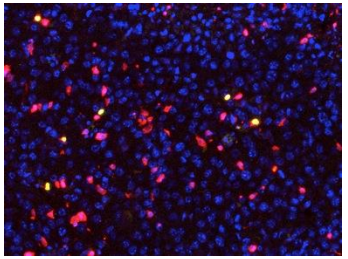
Response to CPI

PBS

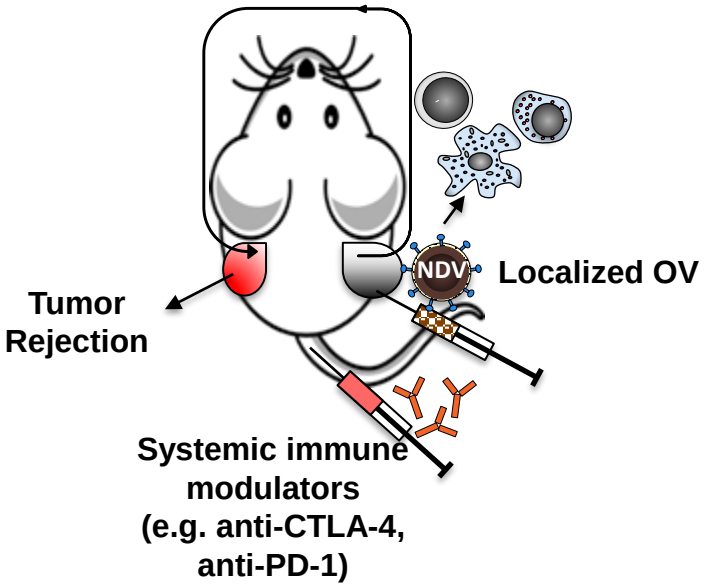


No response to CPI

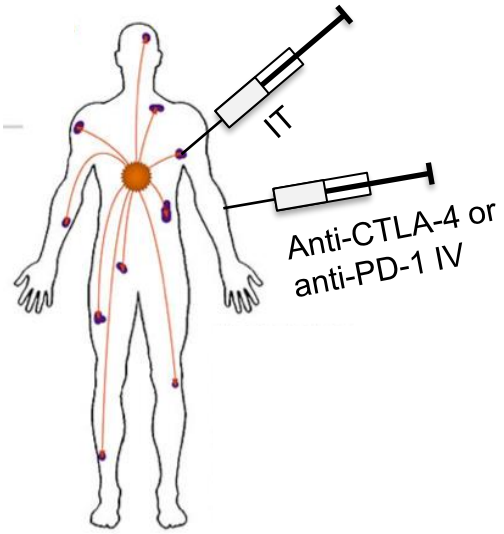
NDV



Response to CPI



In situ oncolytic vaccines in combination with ICB overcome the need for systemic oncolytic virus delivery

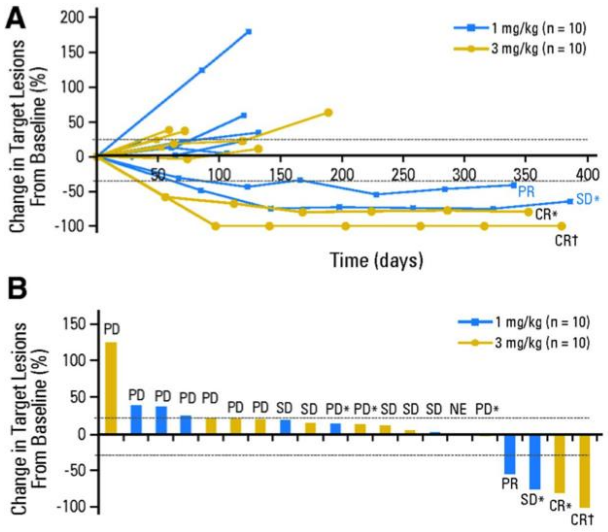


Methods for delivery of *in situ* oncolytic vaccines

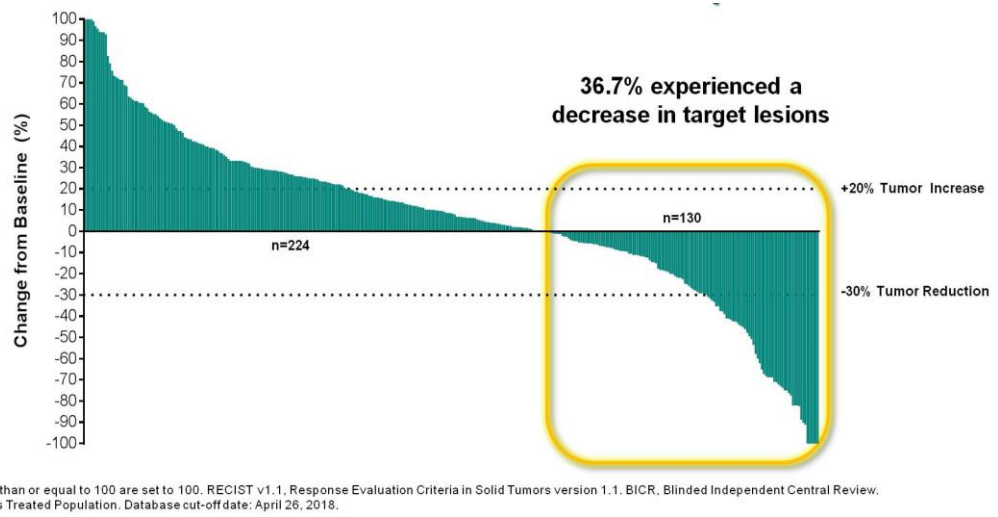
- Intravenous
- Intratumoral
  - Direct injection of accessible lesions
  - Image guided
  - Endoscopic
- Intraperitoneal catheter
- Intrapleural catheter
- Intraarterial
  - Hepatic artery infusion pump

Combination oncolytic immunotherapy for peritoneal cancers

PD-1 blockade as a single agent has limited activity in ovarian cancer



ORR 15%

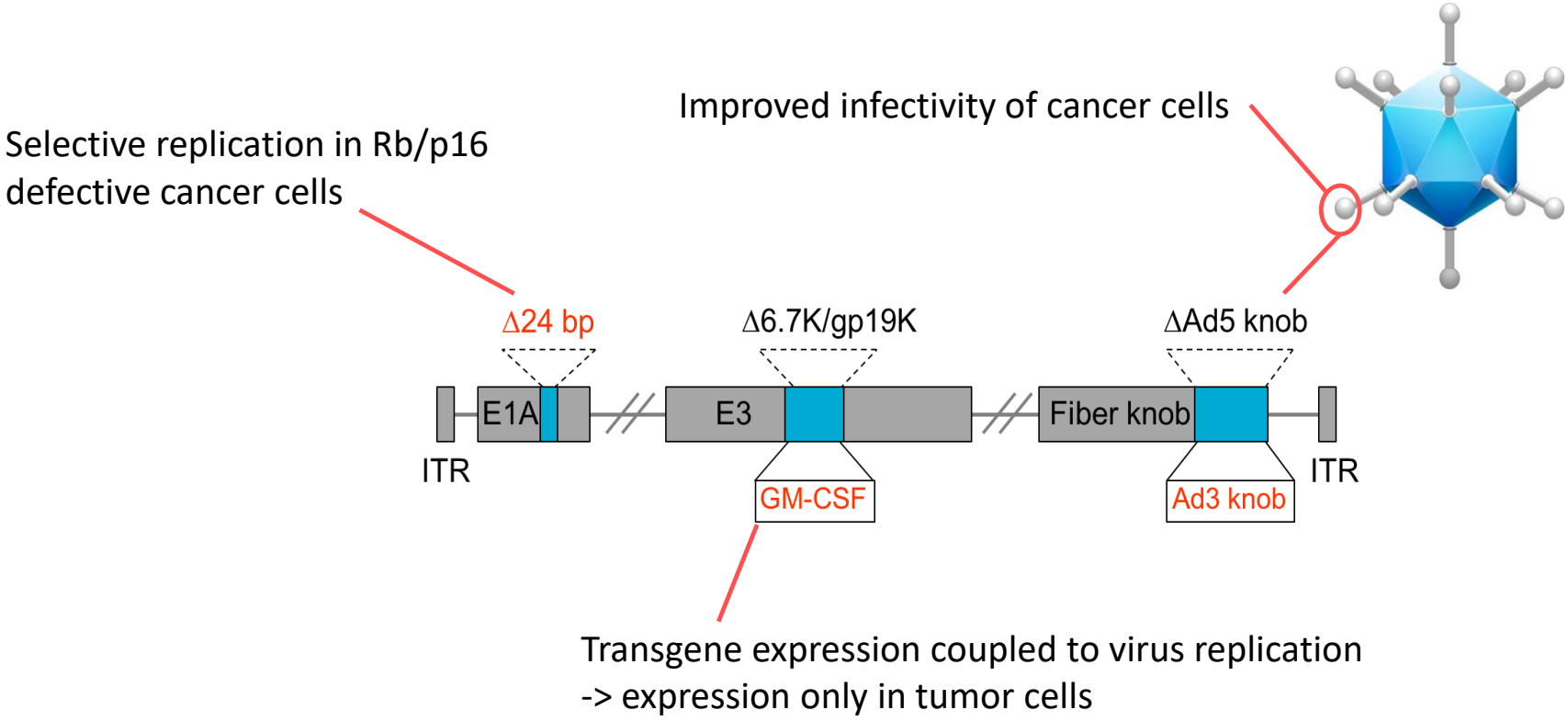


Values higher than or equal to 100 are set to 100. RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review. All Subjects as Treated Population. Database cut-off date: April 26, 2018.

ORR 9%

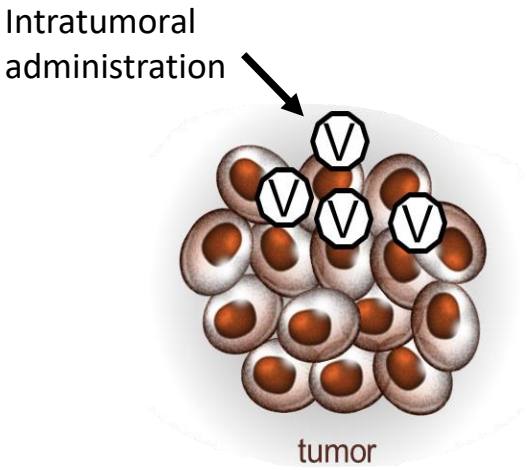
Hamanishi et al., JCO 2015, Matulonis et al., ASCO 2018

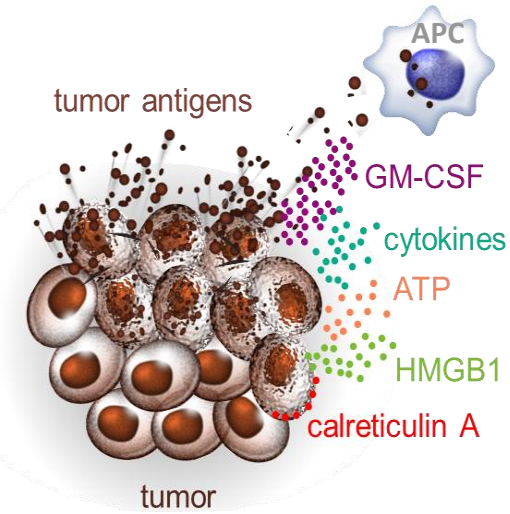
Background on ONCOS-102

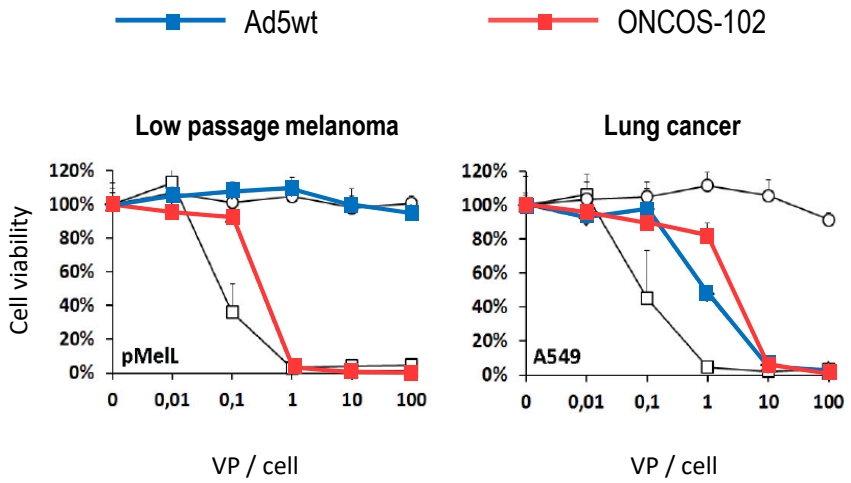


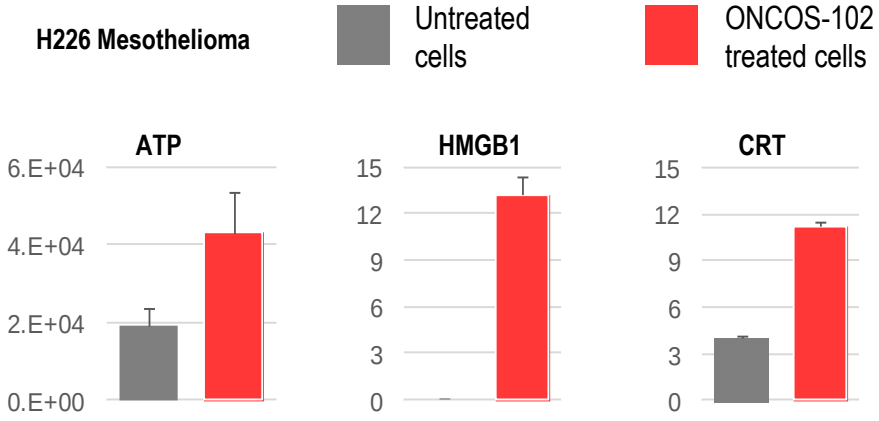
- 115 cancer patients with solid refractory tumors were treated with ONCOS-102 in Advanced Therapy Access Program (ATAP)
- ONCOS C1 trial

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

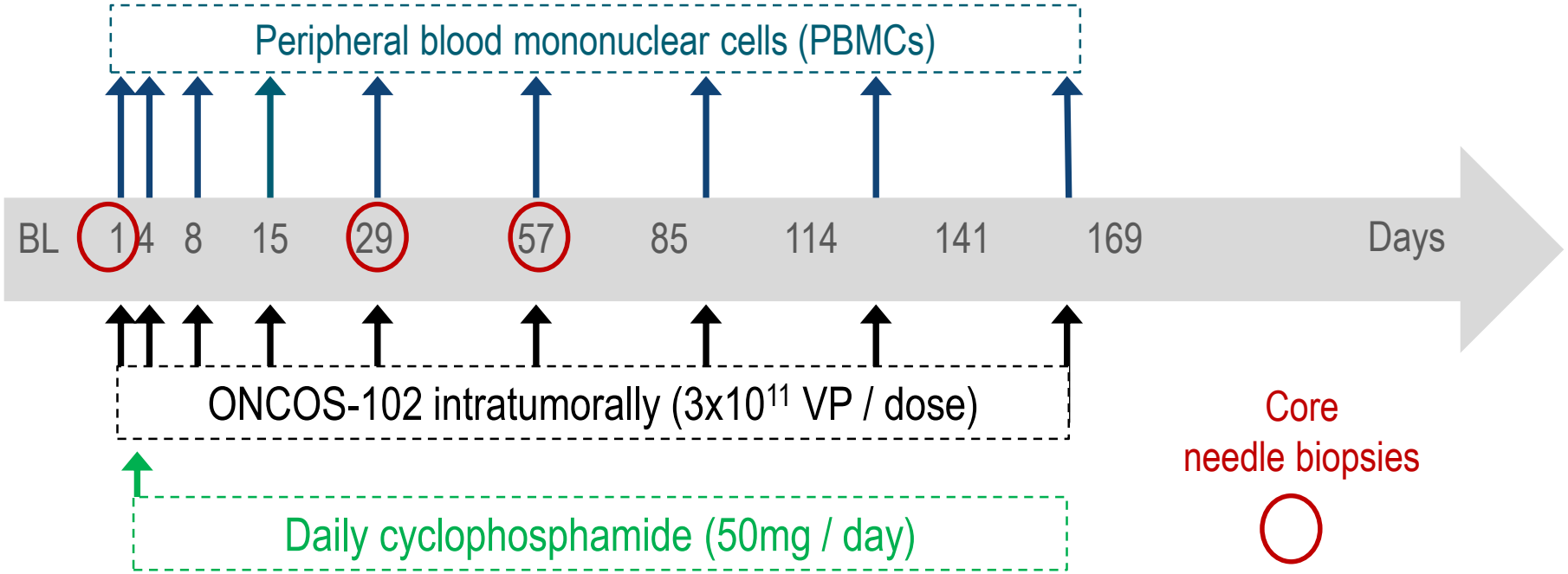




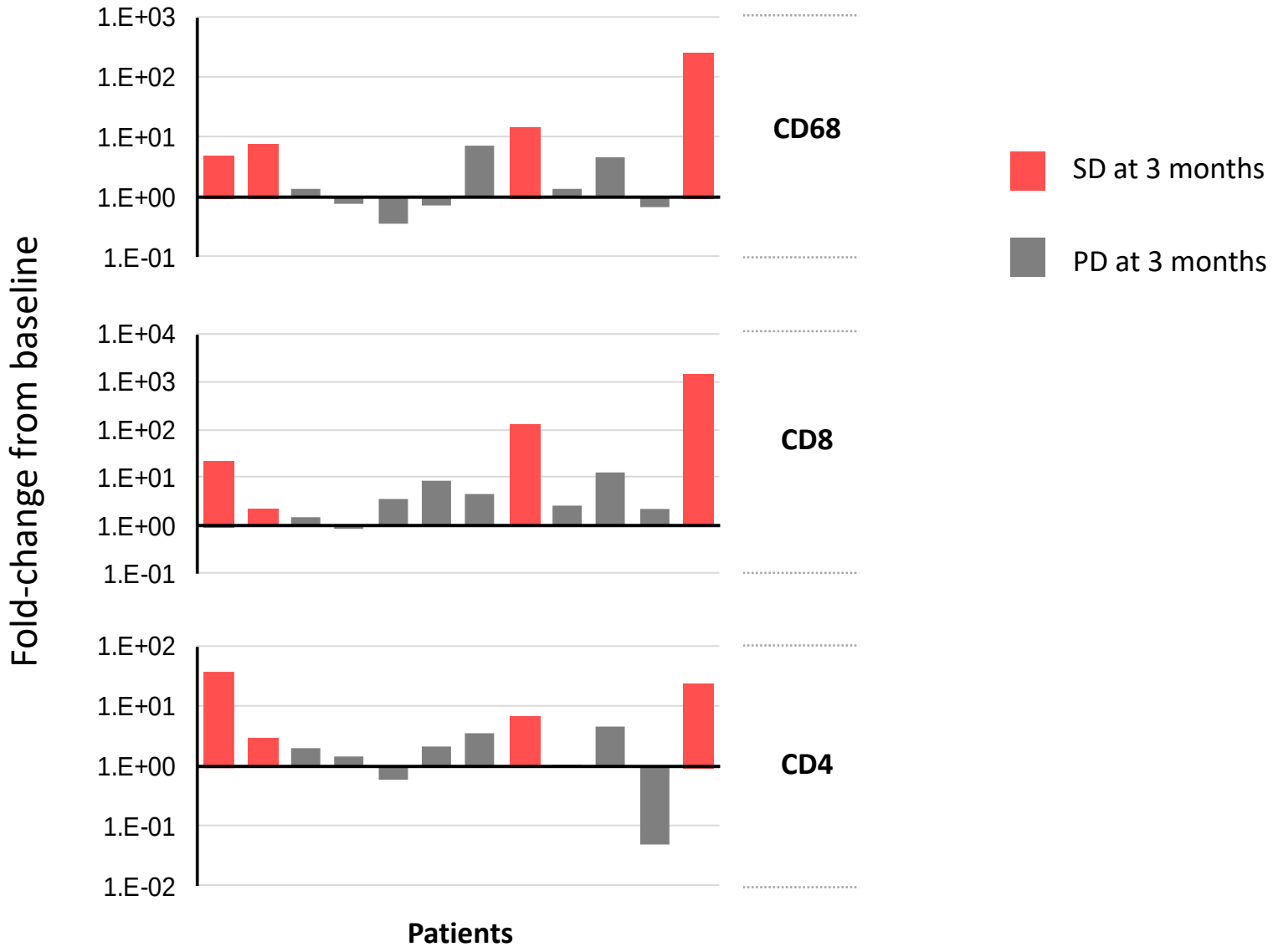




Phase I study of intratumoral ONCOS-102 with low dose cyclophosphamide in patients with advanced solid tumors

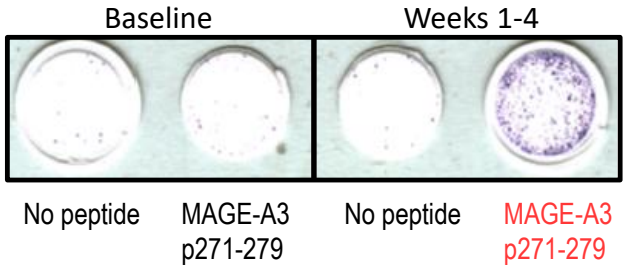


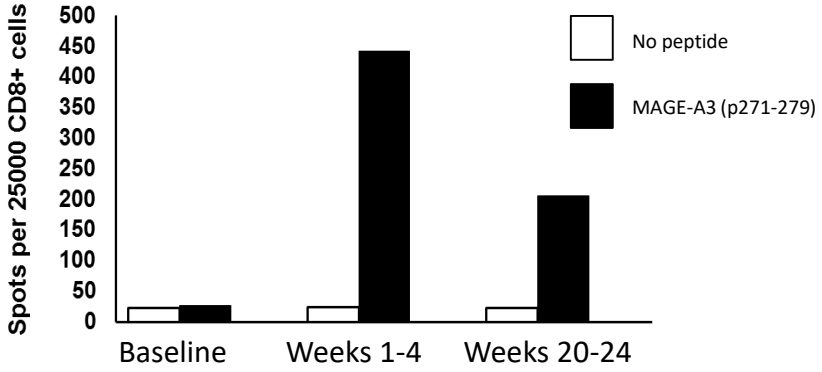
Several immune cell subsets were attracted into tumors following ONCOS-102



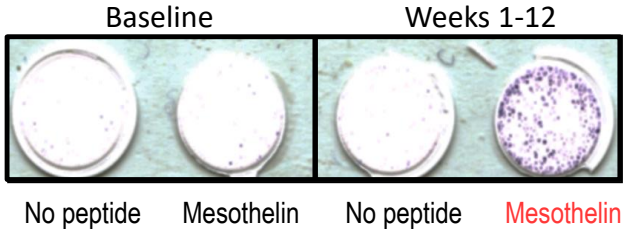
Local ONCOS-102 administration leads to induction of systemic tumor-specific CD8+ T cell response

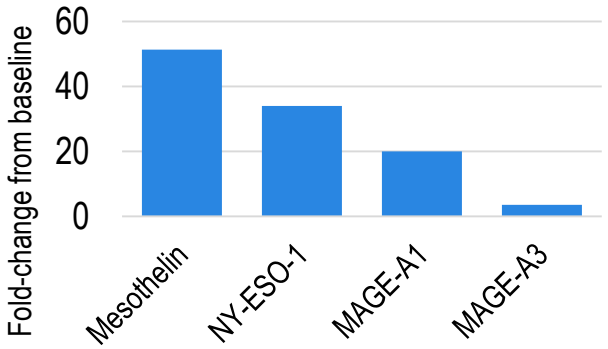
Mesothelioma pt FI1-14: induction of MAGE-A3 specific CD8+ T cells





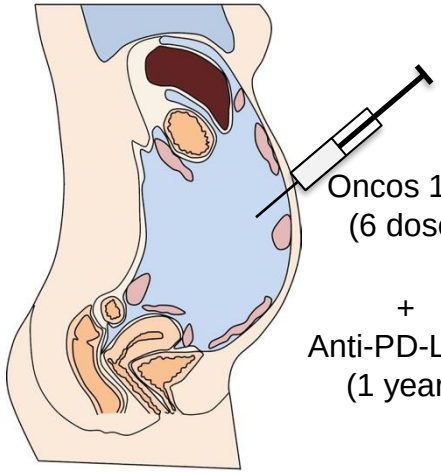
OvCa pt FI1-19: multiple tumor-specific CD8+ T cell populations induced by ONCOS-102





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

A Phase I/II study to investigate the safety and biologic and anti-tumor activity of ONCOS-102 in combination with PD-L1 blockade in patients with peritoneal malignancies



Oncos 102 IP
(6 doses)

+

Anti-PD-L1 IV
(1 year)

Phase I	Phase II	Endpoints
3 + 3 design	**Optimal Simon 2 stage design**	**Primary** • Feasibility • Safety **Secondary** • Efficacy (ORR, CBR at 24 weeks, PFS) **Exploratory** • Immune biomarkers
2 virus dose cohorts: 1. $1x10^{11}$ pfu 2. $3x10^{11}$ pfu (6-12)	1. Platinum-resistant/ refractory ovarian cancer (18+15) 2. Colorectal cancer (13+14) 3. Other intraperitoneal (e.g. mesothelioma, pancreas, endometrial) (30) Additional expansion cohorts?	

LUDWIG CANCER RESEARCH

CANCER RESEARCH INSTITUTE

PI: Zamarin

Update

- 7 patients enrolled and treated to date
- Dose escalation is ongoing

3

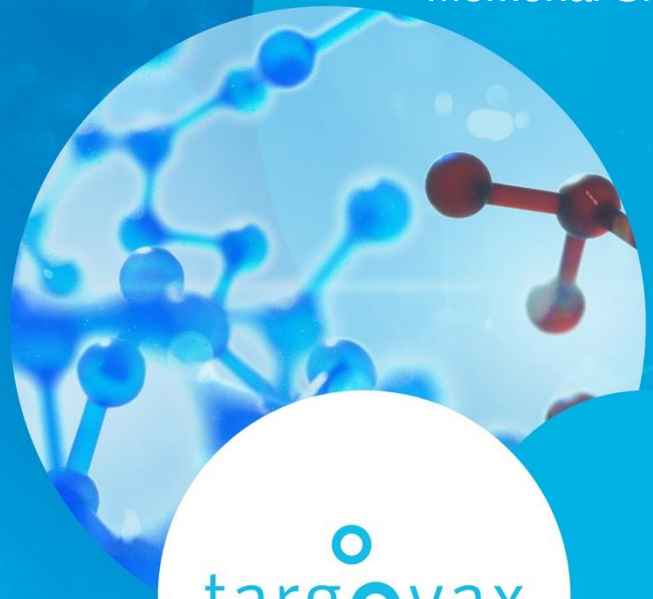
ONCOS-102 in melanoma
Dr. Alexander Shoushtari

4. ONCOS-102 in mesothelioma
5. Summary & closing

Preliminary data from C824

Alexander Shoushtari, MD
Assistant Attending Physician
Melanoma and Immunotherapeutics Service
Memorial Sloan Kettering Cancer Center

October 2018



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MELANOMA IN 2018: FRONTLINE THERAPY

PD-1 based therapy

- **2 choices**
  - Monotherapy: Pembrolizumab or Nivolumab
  - Combined Nivolumab plus Ipilimumab (CTLA-4 inhibitor)
- **45 - 60% objective response rate**
- **Responses last years, but not forever**
- **Overactive immune system leads to immune-related adverse events (irAEs)**
  - Diarrhea / Colitis
  - Liver inflammation
  - Pneumonitis
  - Thyroid, Pituitary dysfunction
- **iRAE rate varies by monotherapy versus combined therapy**
  - Monotherapy: 1 in 4 require steroids
  - Combined Nivo + Ipi: 3 in 4 require steroids

MELANOMA IN 2018: FRONTLINE THERAPY

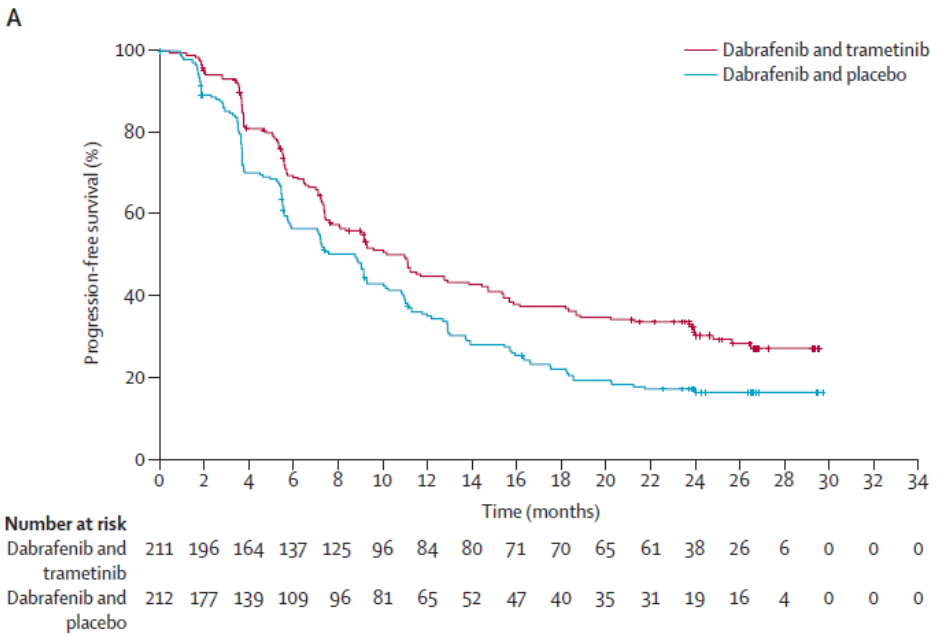
BRAF-MEK Inhibition

- **Only available for 40-50% with BRAF V600 mutant melanoma**
- **60-70% objective response rate**
- **Responses last average of 12-15 months**
- **Adverse events (AEs) not directly related to immune system**
  - Diarrhea
  - Liver inflammation
  - Rash
  - Fevers, chills
  - Muscle/joint aches
- **If BRAF-MEK stopped, adverse events stop**

MELANOMA IN 2018: NEEDS

Resistance to Standard Therapies

- **BRAF-MEK therapy:** majority of initial responders will progress (secondary resistance)



Long et al, Lancet 2015

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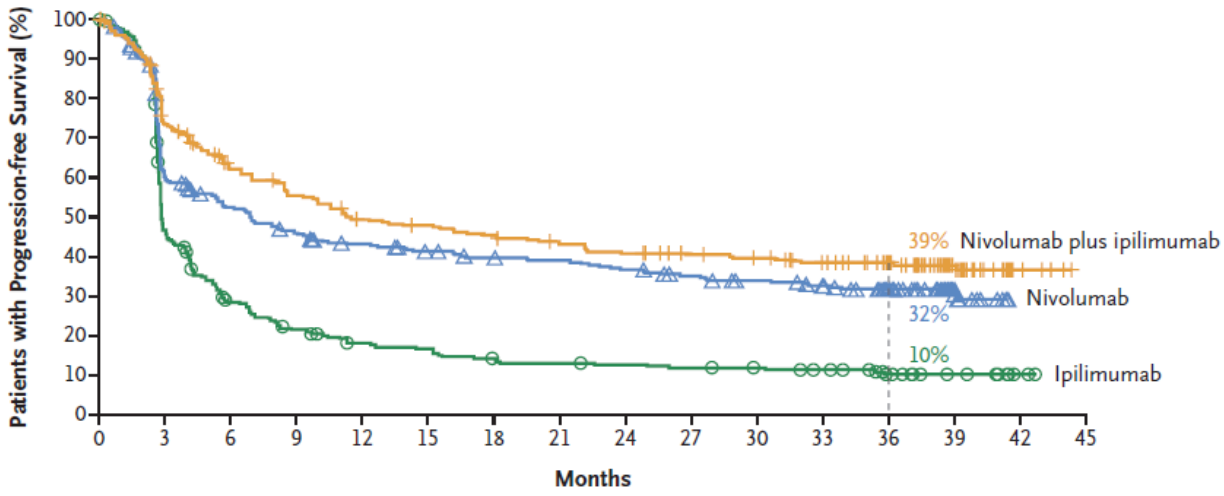
MELANOMA IN 2018: NEEDS

Resistance to Standard Therapies

- **BRAF-MEK therapy:** majority of initial responders will progress (secondary resistance)

- **PD-1 based therapy:**
  - 30-40% will have primary resistance
  - 25-35% will have secondary resistance



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MELANOMA IN 2018: NEEDS

Resistance to Standard Therapies

- **BRAF-MEK therapy:** majority of initi
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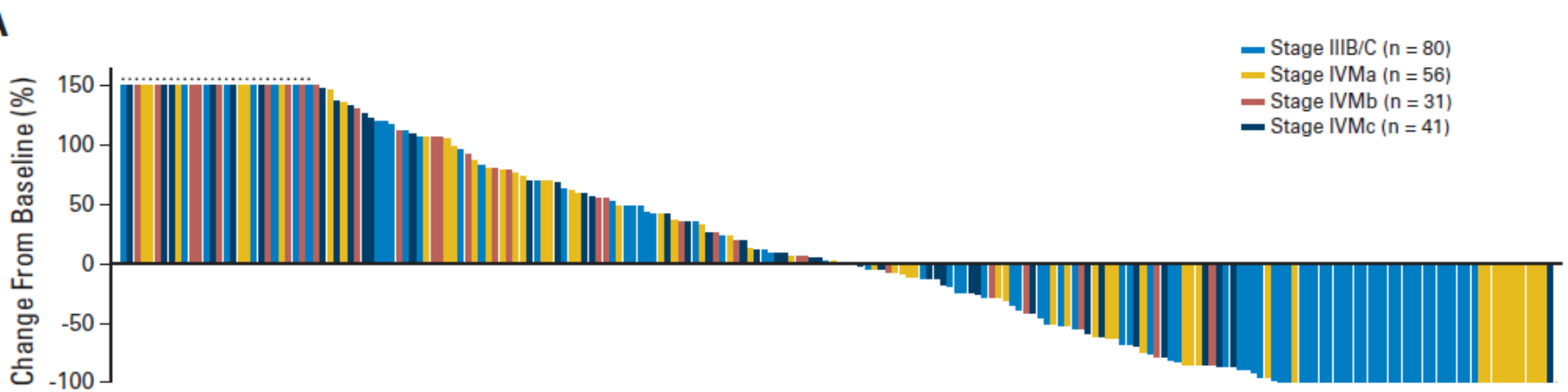

- PD
  -
  - resistance

- **Talimogene Laherparepvec**
  - 40% primary resistance in injected lesions
  - 85% resistant in distant lesions
  - Takes 10 injections on average to respond as monotherapy

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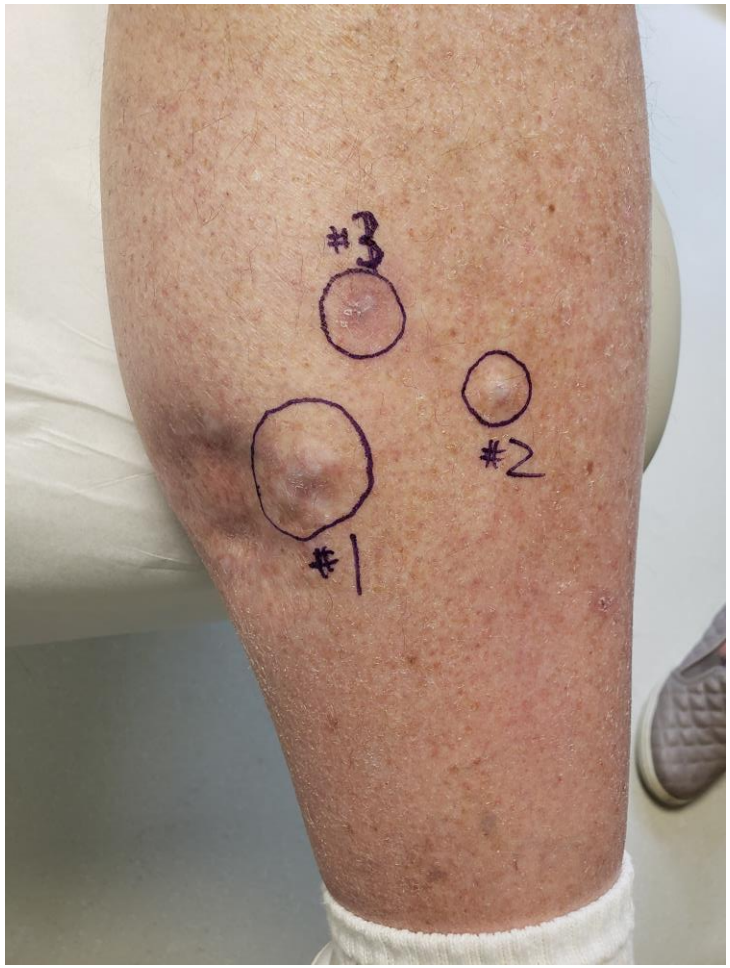
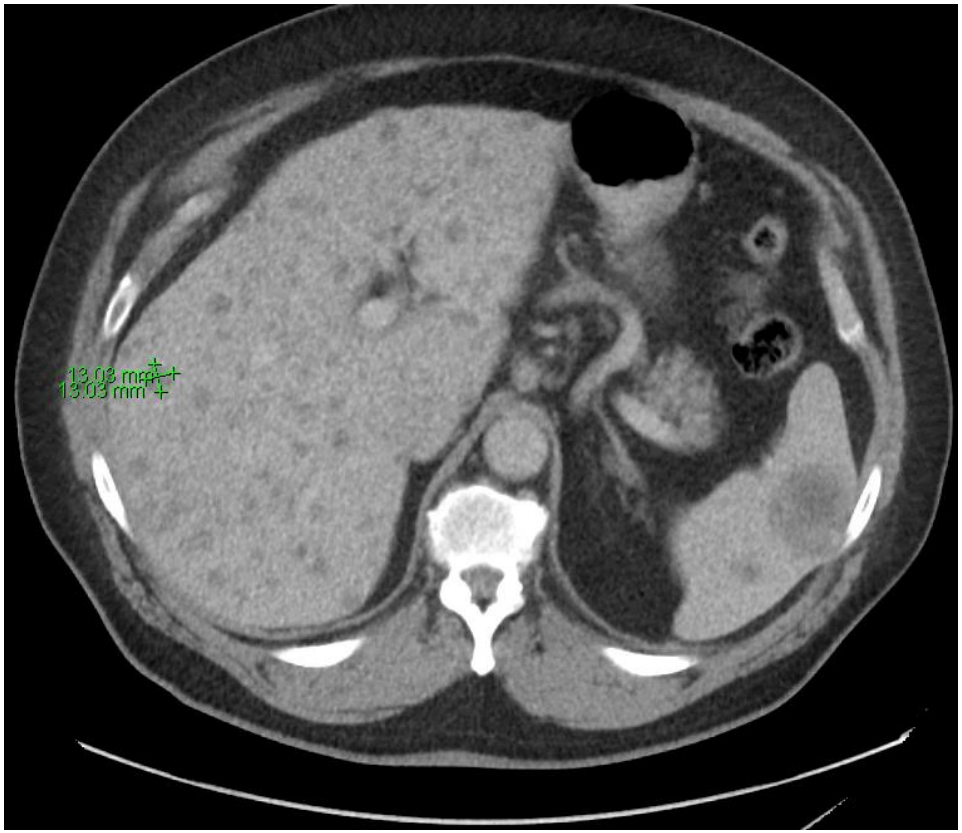
MELANOMA IN 2018: NEEDS

Not all resistance is treated alike!





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MELANOMA IN 2018: OPTIONS POST-PD-1

Standard Options

- **After PD-1 monotherapy**
  - BRAF-MEK, if V600 mutant
  - Nivolumab plus ipilimumab
  - Ipilimumab alone
  - Cytotoxic chemotherapy
  - T-VEC if injectable
- **After Nivolumab plus Ipilimumab**
  - BRAF-MEK, if V600 mutant
  - Cytotoxic chemotherapy
  - T-VEC if injectable
- **If local progression only**
  - Surgery
  - Radiation therapy

Non-standard options

- **Clinical Trials (selected)**
  - PD-1 plus
    - LAG-3 inhibitor
    - OX40 agonist
    - GITR agonist
  - Tumor Infiltrating Lymphocyte trials
  - Injectable trials
    - ONCOS-102 + pembro
    - TVEC + pembro
    - Coxsackievirus + pembro
    - TLR9 agonist (tilsotolimod) + ipilimumab
- **Off-label uses**
  - BRAF + MEK + PD-1
  - T-VEC + PD-1 inhibitor
  - Radiation + PD-1 +/- Ipilimumab

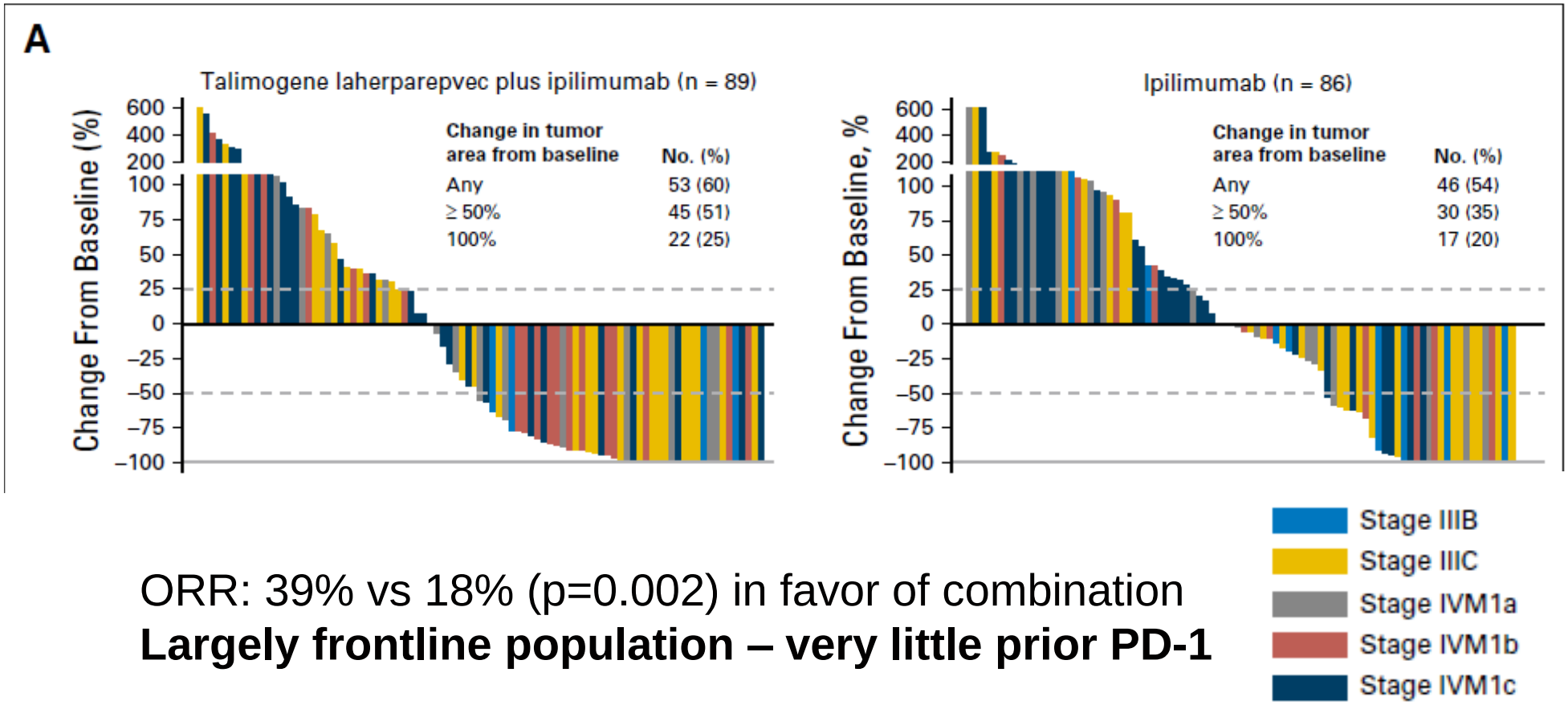
MELANOMA IN 2018: CHALLENGES

- **After PD-1 progression, no "one size fits all" approach**
  - Nivolumab plus LAG-3 – 10-15% response rate
  - IDO inhibitors had a negative frontline trial
- **Rightly or wrongly, many physicians want an excuse to avoid ipilimumab**
  - 20-30% response rate, can be durable
  - Significant toxicity
- **Injectable combinations may represent a happy medium**
  - Overcome lack of recognition by direct injection of agent into tumor
  - Activate innate and adaptive immune system → "domino effect"
  - ?Fewer off-target effects to reduce systemic toxicity

MELANOMA: INJECTABLE COMBINATIONS TO DATE

T-VEC +/- Ipilimumab (Chesney et al, J Clin Oncol 2017)

TVEC: day 1, 22, then every 2 weeks



ORR: 39% vs 18% (p=0.002) in favor of combination

Largely frontline population – very little prior PD-1

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MELANOMA: INJECTABLE COMBINATIONS TO DATE

Cocksackie virus CVA21 + pembro (CAPRA, Silk et al, AACR 2017)

- **Largely PD-1 naïve**
- Injections: D1, 3, 5, 8, every 3 weeks for up to 19 total
- 8 of first 11 evaluable patients with objective responses

Toll-Like Receptor 8/9 Agonist + Ipilimumab (Diab et al, ASCO 2018)

- **Already received PD-1 blockade** – only study to date
- Only 3 of 26 were stage 3; 11 (42%) M1c
- 8 of 21 patients responded (38%)
  - 2 CR
  - 6 PR
  - 8 SD
  - 5 PD

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ONGOING TARGOVAX STUDY at MSKCC

A Pilot Study of Sequential ONCOS-102 and Pembrolizumab in Patients with Advanced or Unresectable Melanoma Progressing after PD1 Blockade

Deliveries:
- ORR data on 6 patients
- 4/4 patients biopsy data: TILs (CD3+, CD4+ and CD8+ T cells) – Day 1, 22 and 64
- 4/4 patients cytokines: IFNgamma, TNFa, IL6 - Day 1, 4, 8/W3/W9/W18
- 4/4 patients PBMC: T cell activation/exhaustion - Day 1, W 3, 8/9
- 1st safety review of 4 pats – there were no issues

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STUDY OBJECTIVES

Primary Endpoint

- Safety of sequential administration of 3 doses of ONCOS-102 followed by 8 doses of pembrolizumab

Exploratory Endpoints

- Analysis of mutation rate in relation to response
- Changes in T cell receptor clonality
- Gene expression analysis in biopsied tissue

Secondary Objectives

- Objective responses by RECIST 1.1 and irRECIST
- Progression-free survival
- Change in size of individual lesions
- Immune subsets in tumor and plasma, changes over time

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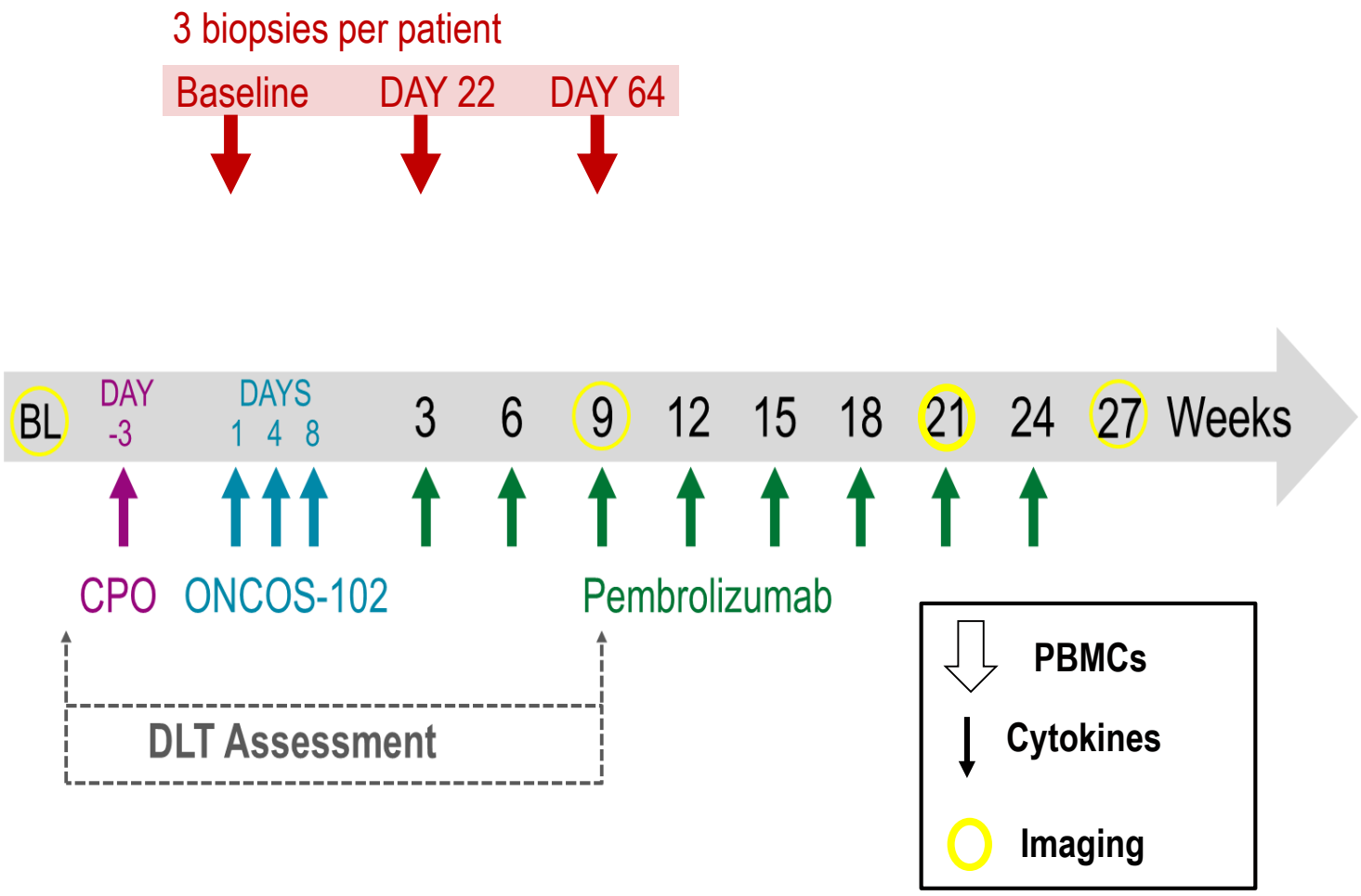
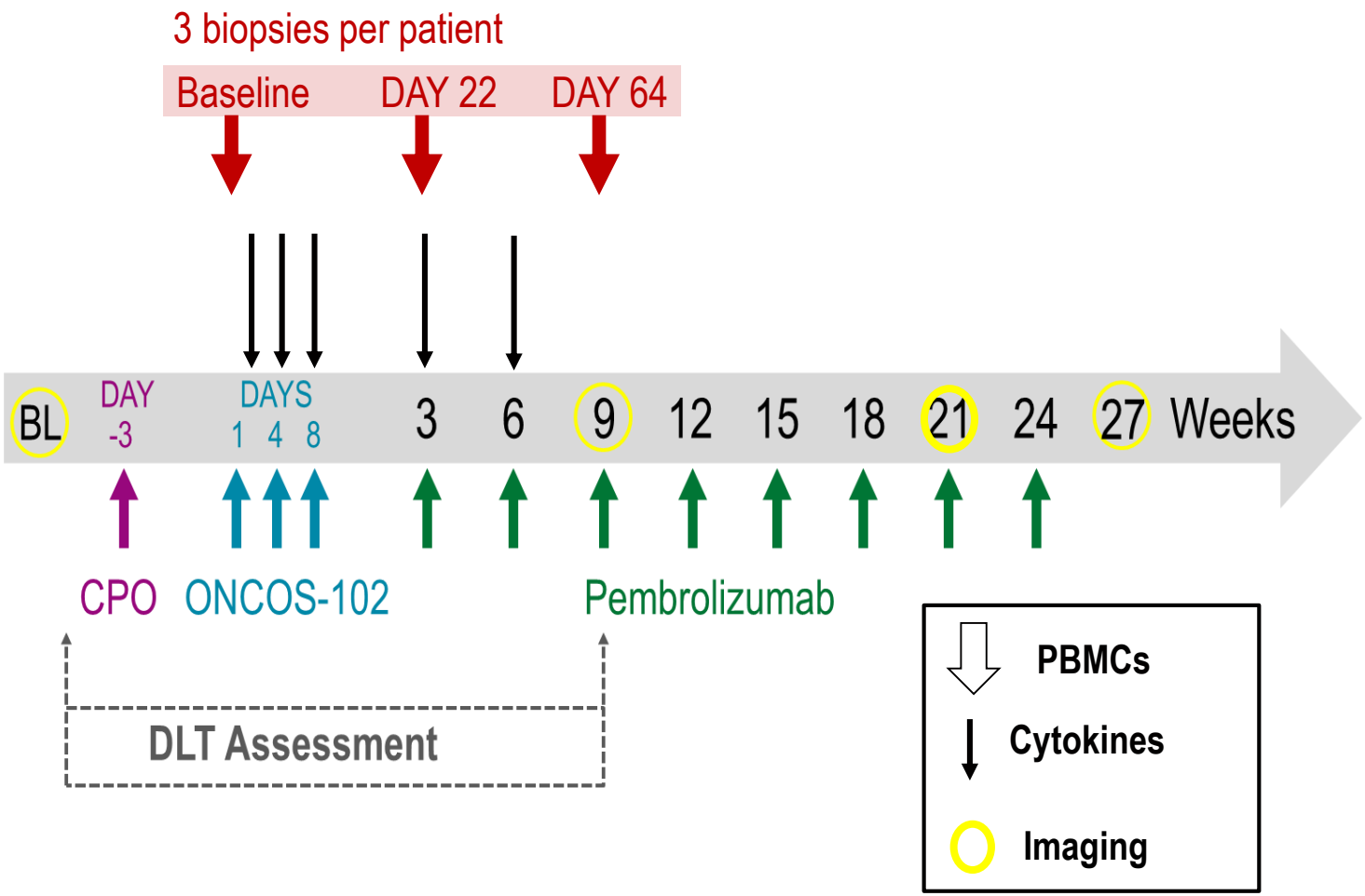
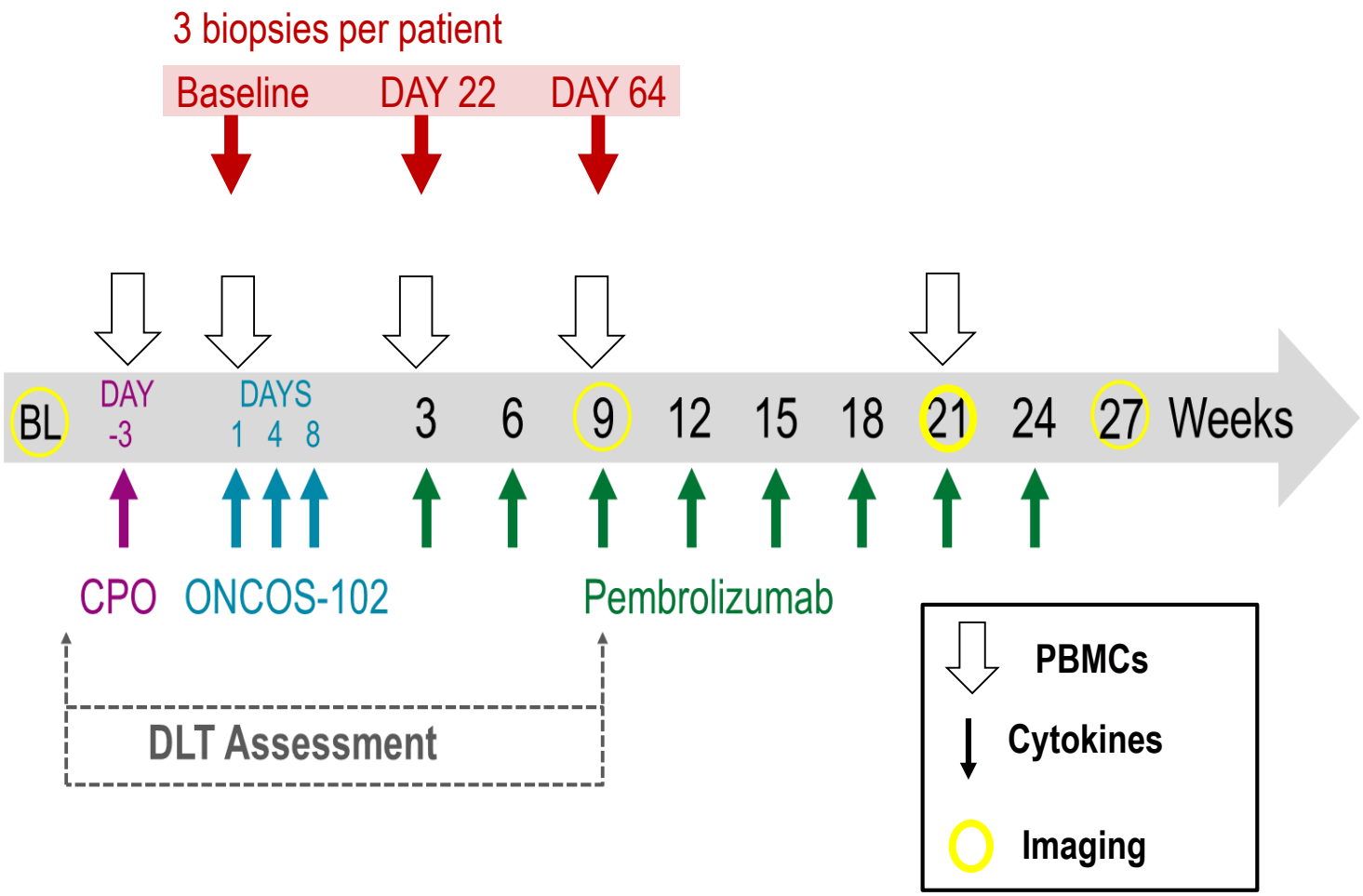
STUDY SCHEMA



STUDY SCHEMA



STUDY SCHEMA



WHAT REPRESENTS SUCCESS (TO A MELANOMA ONCOLOGIST)?

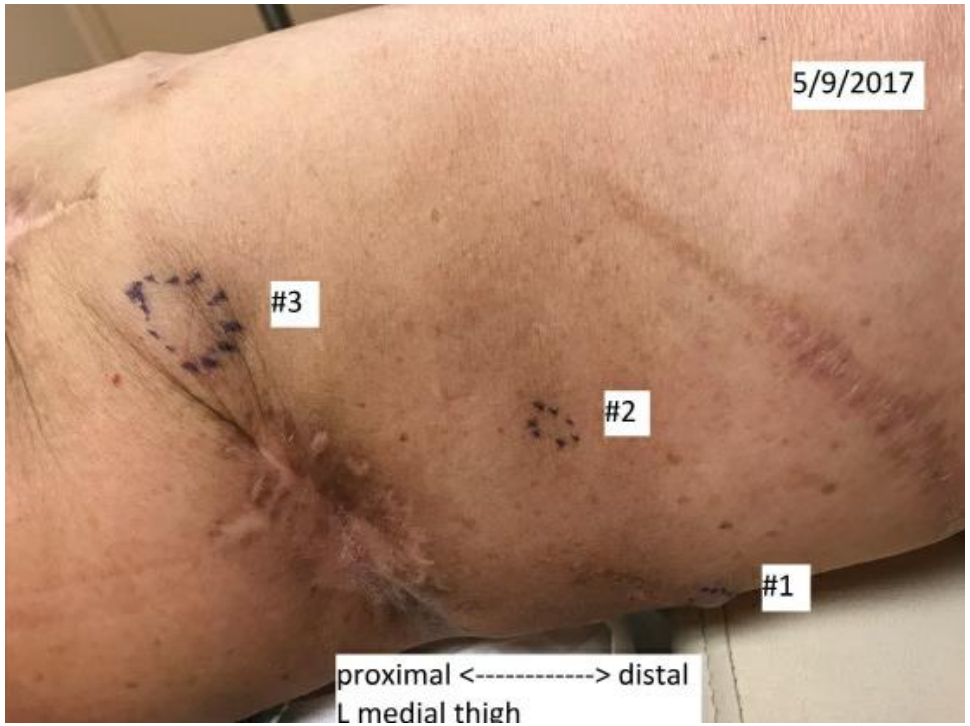
- Ability to administer the drug safely
- Evidence of preliminary efficacy
- Access to tissue and biomarker data to refine your therapeutic strategy moving forward

87 year old female

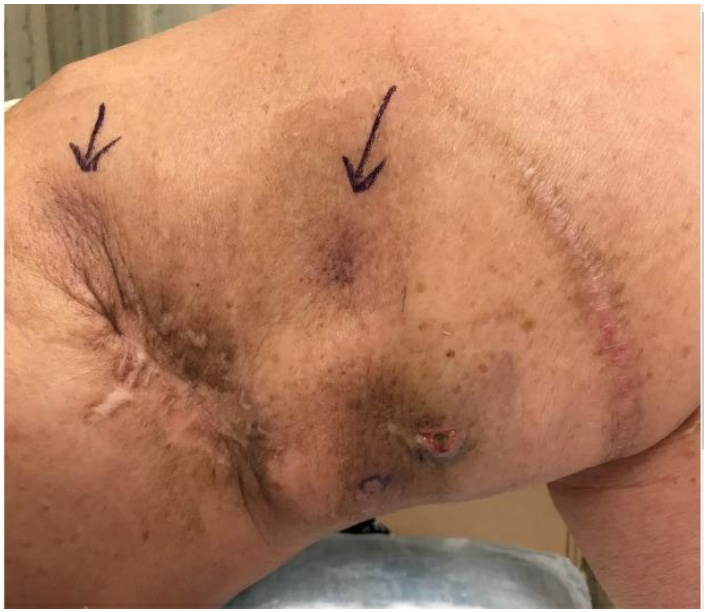
Surgery, Keytruda, T-VEC, Radiotherapy prior study

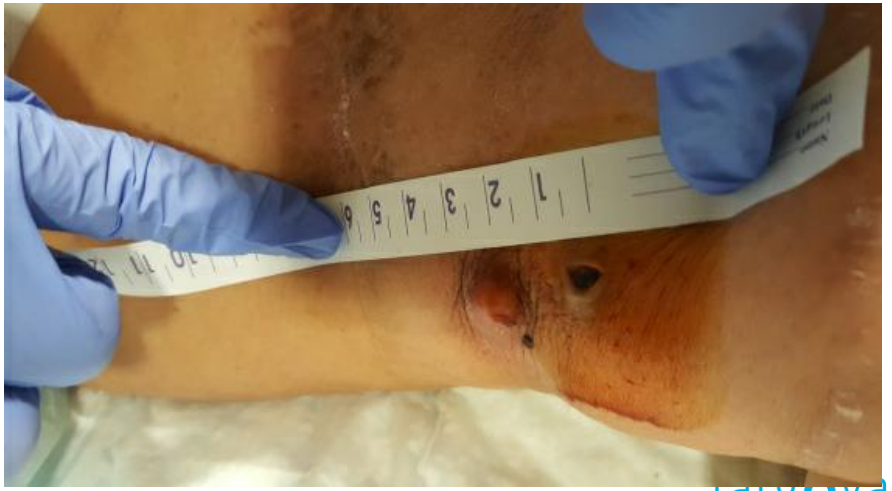
ORR: PD (not received full dose of ONCOS-102)

Baseline



Day 10





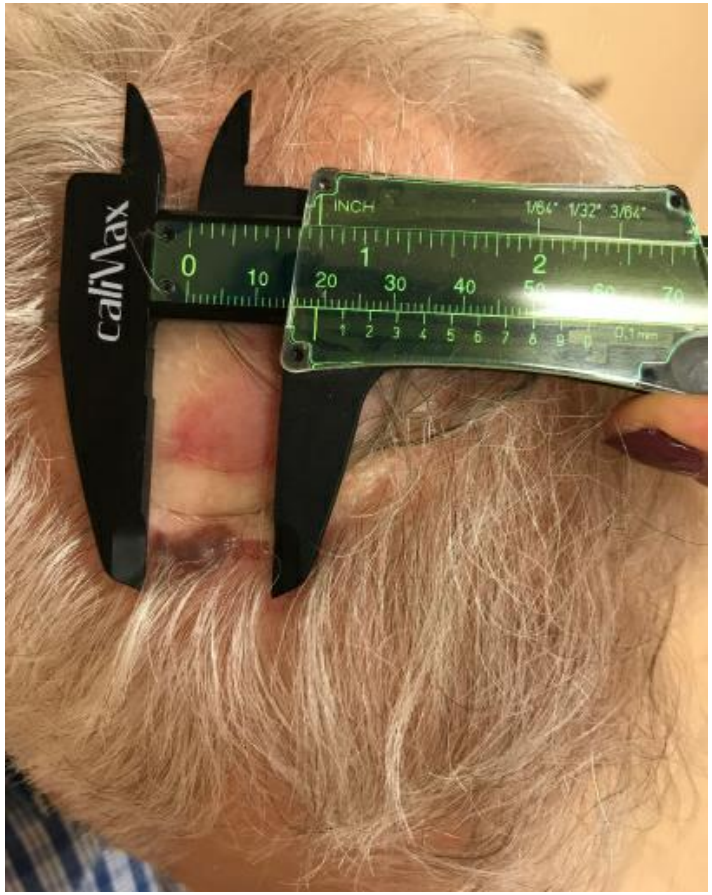
Day 22

73 year old male

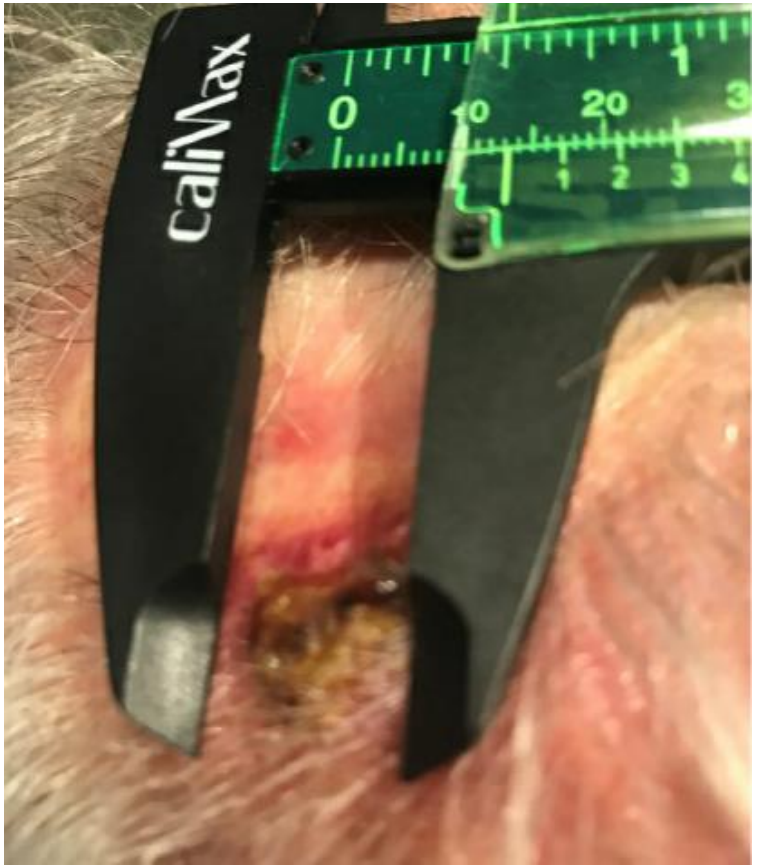
Surgery, Keytruda prior study

ORR: PD (not received full dose of ONCOS-102)

Baseline



Day 22



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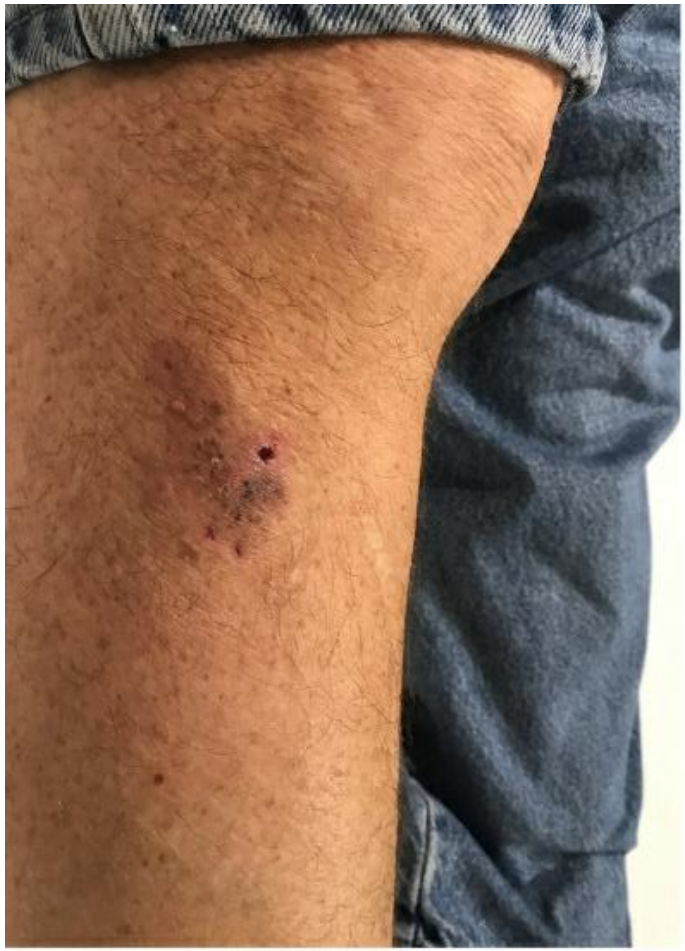
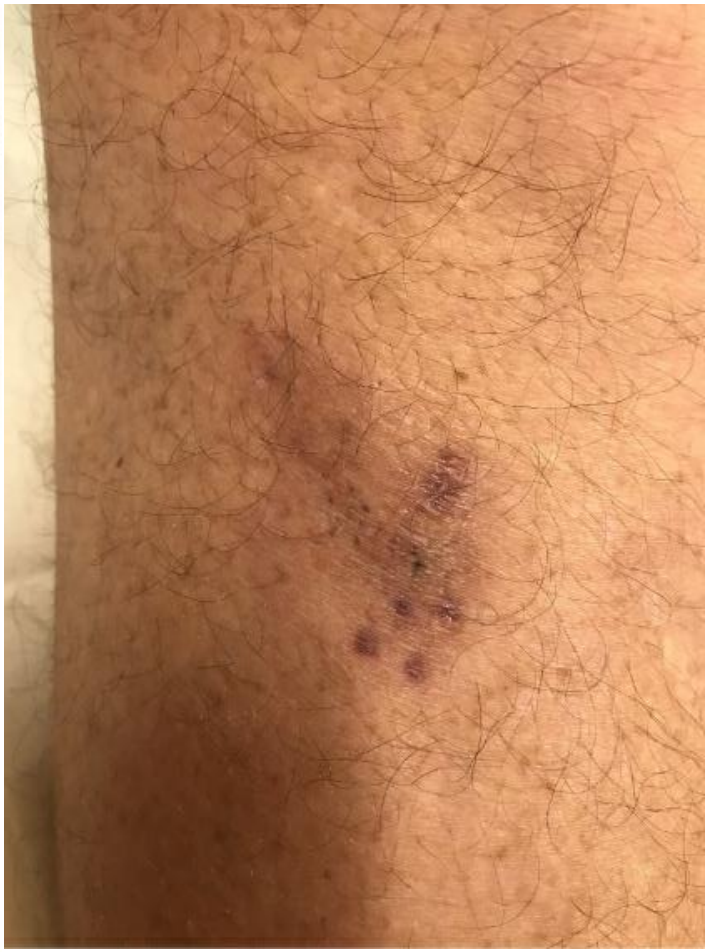
60 year old male

Surgery, Yervoy, Keytruda prior study

ORR: CR (after only 2 Keytruda infusions)

Baseline **Day 22** **Day 63**





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3 MORE PATIENTS

79 year old male; had Yervoy, Keytruda, T-VEC prior study

- Shrinkage in injected lesion but new distant lesion
- ORR: PD

74 year old female; had surgery and Opdivo prior study

- ORR: PD

78 year old female; had Yervoy, Opdivo, Keytruda prior study

- ORR: PD

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EFFICACY, N=6

Demographics

- **Age:** 60 – 87 (median 76)
- **Stage**
  - IIIB/C: 5 of 6
  - IV: M1C, 1 of 6
- **Prior PD-1 blockade:** 100%
- **Prior Ipilimumab:** 50%
- **Prior Injectable:** 50%
- **Prior BRAF:** 50% (2 of 3 intolerant)
- **Median prior lines**: 2.5 (range: 1-4)

Efficacy

- **Complete Response: 1/6, 12+ mo**
- **Partial Response: 0/6**
- **SD: 0/6**
- **PD: 5/6**

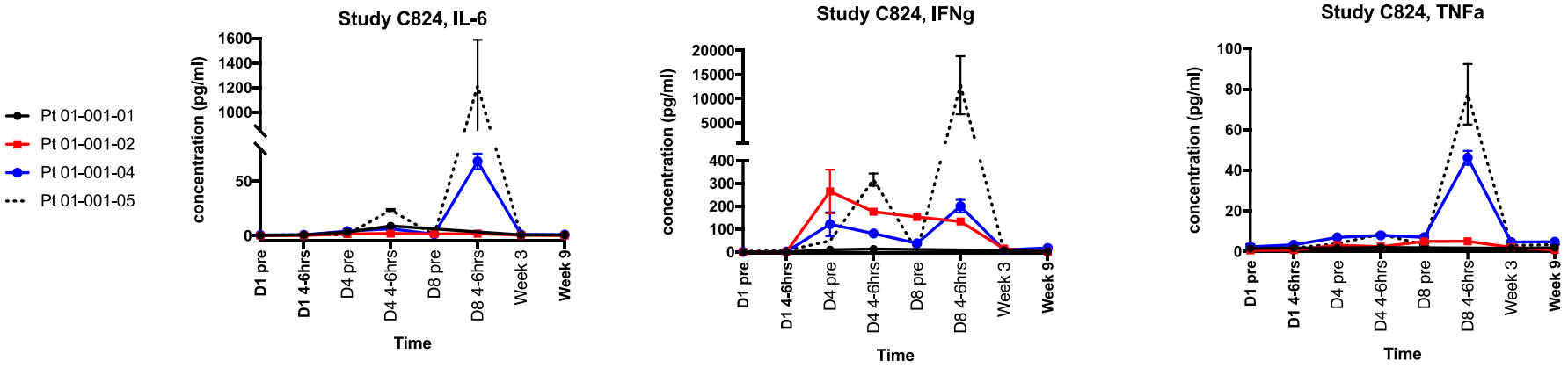
- **Anecdotally:** At least 3 patients with “PD” had transient shrinkage in the injected tumor

ONCOS-102 INDUCED INCREASE OF CYTOKINES IN ALL PATIENTS (tested to date n=4)

Summary on cytokines analyses (D 1, 4, 8, W3, 9/18):

- Increase of pro-inflammatory cytokines (IFN-y, TNF-a, IL-12p40, GM-CSF) after ONCOS-102 administration (4 out of 4)
- Increase of pro-inflammatory cytokines (IL-6 and IL-8) after ONCOS-102 administration (3 out of 4)
- Temporarily elevation level of IL-10 after second ONCOS-102 administration (3 out of 4 patients)
- Profound increase of IL-6, TNFa and IFNg (001-01-005)

The treatment with ONCOS-102 induces innate immune responses



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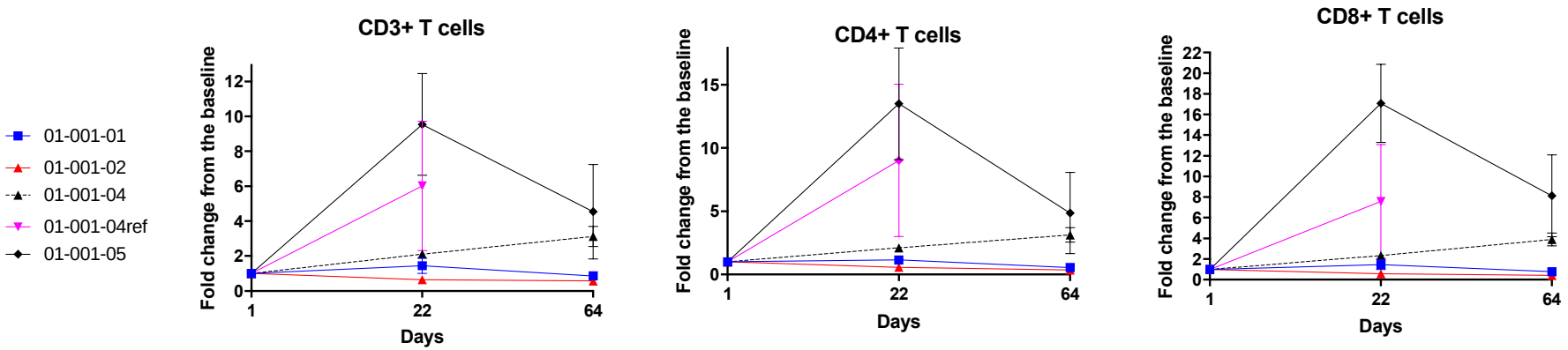
T CELL INFILTRATES ON MULTIPLEX IHC INCREASE WITH ONCOS-102



Patient with CR had highest relative increase of CD3+, CD4+, CD8+ cells

2 patients with reduced dose of ONCOS-102 had lower relative increases

Non-injected lesion seen with increase of CD3=, CD4= and CD8+ cells

PINK: un-injected lesion

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ONCOS-102 INDUCED CANCER ANTIGEN SPECIFIC T-CELLS

Measured by IFN gamma ELISPOT in PBMCs (baseline vs. post-treatment samples)

- Patient with CR had de novo induction and development of tumor specific T cells against NY-ESO-1 and MAGE-A1 present in the PBMC on Week 3 and 9

LESSONS LEARNT AND NEXT STEPS

- We can inject ONCOS-102 safely and follow with pembrolizumab in patients with melanoma that has recurred despite prior PD-1 blockade
- There is preliminary efficacy in a patient with PD-1 refractory in-transit disease – associated with the most profound activation of both innate and adaptive immune cells
- Correlative analyses in the first 4 patients provide evidence supporting the proposed mechanism of action
- For larger baseline lesions, transient shrinkage is seen when injected with 3 doses of ONCOS-102, but it does not appear to persist
- If we could inject more doses of ONCOS-102, more lesions are likely to respond

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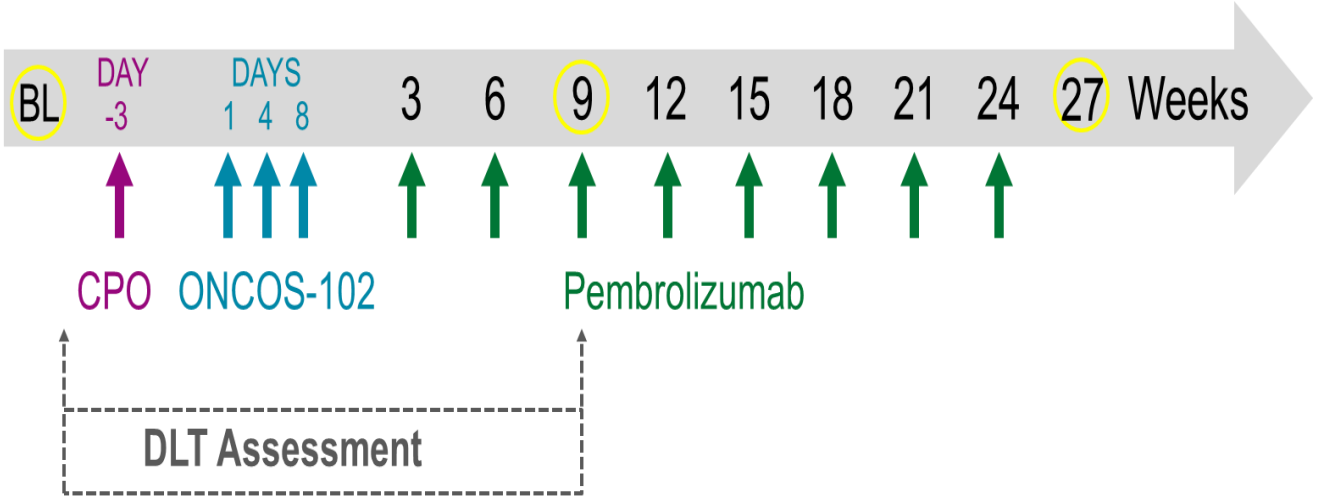
NEW SCHEMA: 12 ADDITIONAL PATIENTS

From



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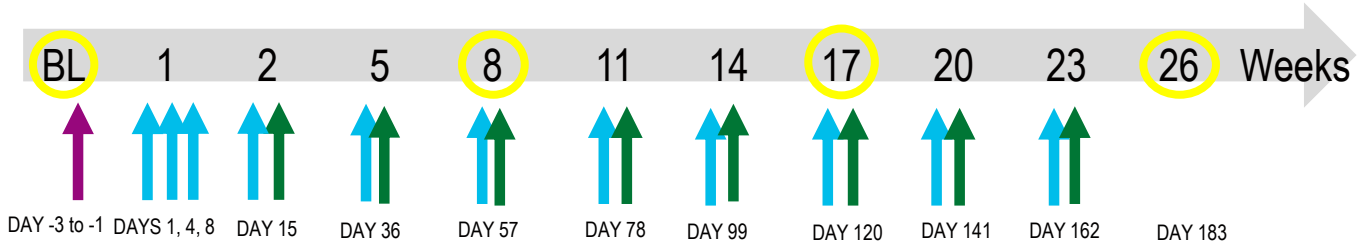

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SUMMARY

- ONCOS-102 safe and well tolerated
- ORR in 1/6 patients in pre-treated population
  - Patients were not ”cherry-picked” and likely to represent true population
  - The only variable that we changed is 3 doses of ONCOS-102
- Mechanism of action is supported by preliminary correlative data
  - Increase in pro-inflammatory cytokines associated with improved outcomes to PD-1
  - Increase in tumor-infiltrating CD4+/8+ T cells
- Solid rationale for increasing the number of ONCOS-102 injections
  - Increase ability to shrink injected tumor
  - Mirror other trials (e.g. TVEC, TLR9) that have shown some visceral efficacy
  - now being approved at 2 additional US sites

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4

ONCOS-102 in mesothelioma

Dr Magnus Jaderberg
Chief Medical Officer
Targovax

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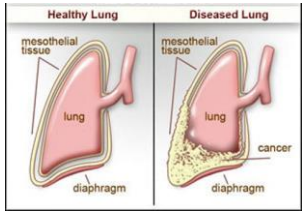
ONCOS

CLINICAL DEVELOPMENT STRATEGY

1

Path-to-market
Mesothelioma

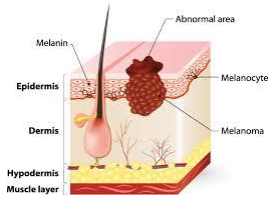


Target launch indication

- Ongoing Phase I/II

2

Proof-of-concept
CPI refractory

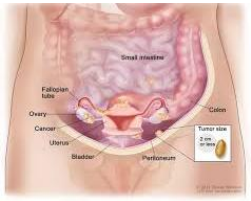


Indications with no/ limited effect of CPIs

- Ongoing melanoma Phase I

3

Proof-of-concept
New CPI indication

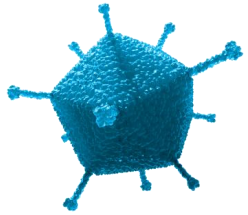


Peritoneal malignancies

- Ongoing Phase I/II in ovarian and colorectal

4

Next generation
oncolytic viruses



Targeting new indications

- Novel targets and mode-of-action

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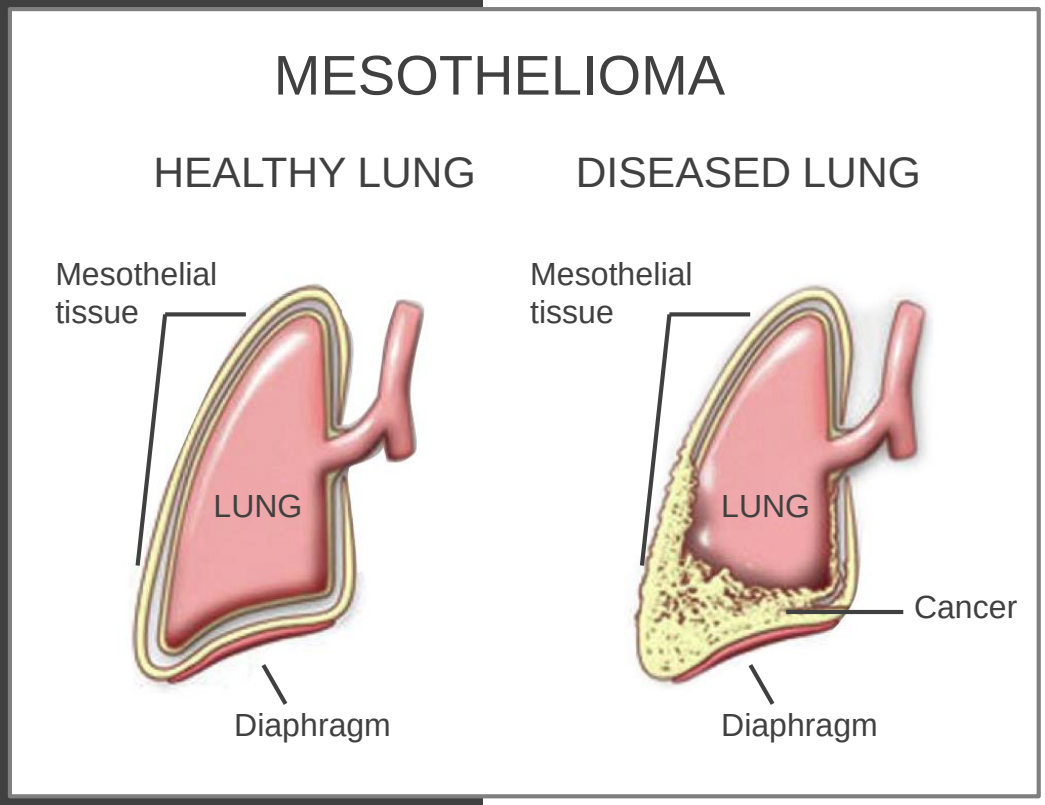
ONCOS-102 target launch indication

MALIGNANT PLEURAL MESOTHELIOMA

- **Orphan disease**, estimated 15,000 new cases per year (EU, USA, Australia)
- **Incidence is increasing** worldwide and is predicted to peak in 5-10 years
- Often **caused by asbestos** exposure, with a latency period of up to 40 years before diagnosis
- Aggressive cancer form with **median survival of 12 months**
- **No significant treatment advance** in the last decade



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MESOTHELIOMA IS SHORTEST PATH-TO-MARKET

Rationale for ONCOS-102 opportunity in mesothelioma:

Become frontline therapy

- **Phase I results** indicate potential of ONCOS-102 in mesothelioma
- **Ongoing randomized phase I/II trial** combining ONCOS-102 with SoC chemotherapy
- **Good safety profile**

Orphan Drug Designation

- High unmet medical need, ONCOS-102 has **orphan drug designation**
- Opportunity for priority regulatory review, and **quick route-to-market**
- 7 year **market exclusivity** in the US and 10 years in the EU

Limited competition

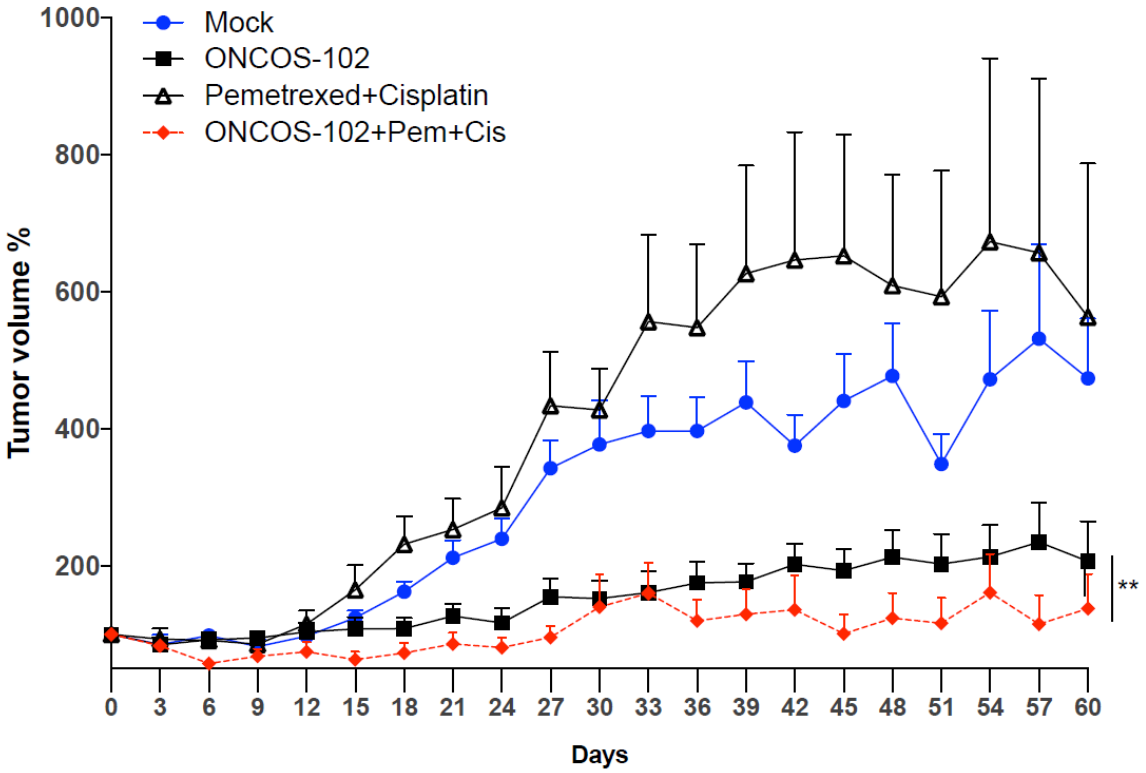
- CPIs show some early signs of efficacy, but are **potential ONCOS-102 combinations**, rather than competitors
- **No competing viruses** and few vaccines in current clinical development in mesothelioma

SYNERGY BETWEEN ONCOS-102 AND CHEMOTHERAPY

mesothelioma mouse model

Anticancer effect of ONCOS-102 and standard of care chemotherapy in xenograft mouse mesothelioma model

% change in tumor volume, 7 animals per group (14 tumors/group)



Effects observed at Day 60:

ONCOS vs. mock

56% tumor volume reduction
p < 0.01

ONCOS vs. pem/cis

63% tumor volume reduction
p < 0.01

ONCOS+pem/cis vs. pem/cis

75% tumor volume reduction
p < 0.001

ONCOS+pem/cis vs ONCOS

33% tumor volume reduction p < 0.01

SOURCE: Kuryk et al., Int J Cancer, 10 June 2016

ONCOS-102 CAN TURN MESOTHELIOMA LESIONS HOT

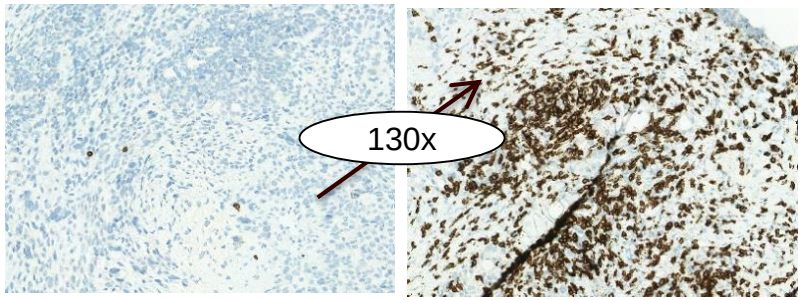
Phase I

CD8+ T-cells in tumor
Tumor biopsy staining

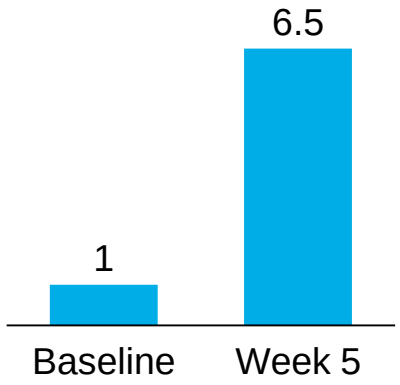
CD4+ T-cells in tumor
Fold change

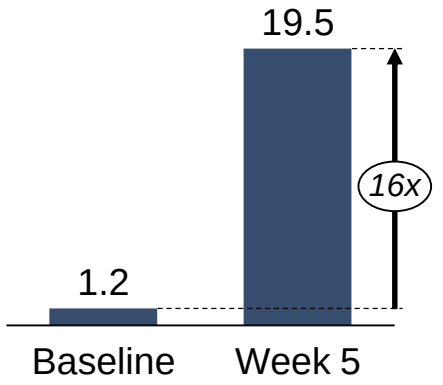
PD-L1 positive tumor cells
% of total

Mesothelioma *– Phase I, patient 14*

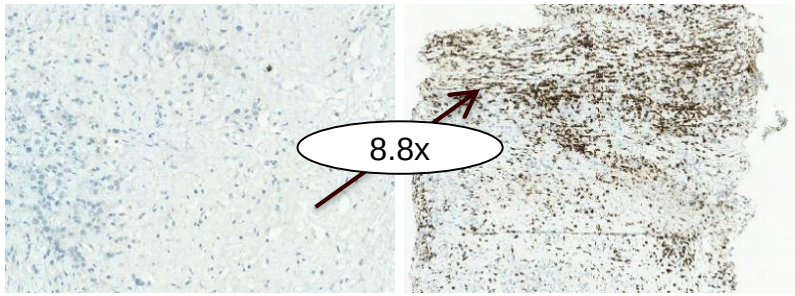


Baseline Week 5

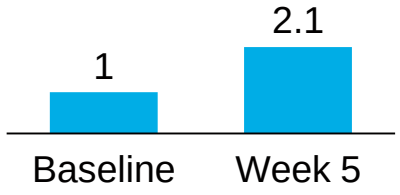


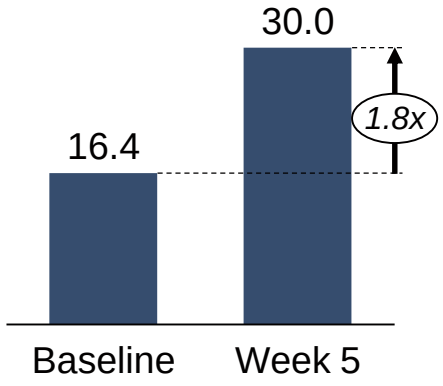


Mesothelioma *– Phase I, patient 9*



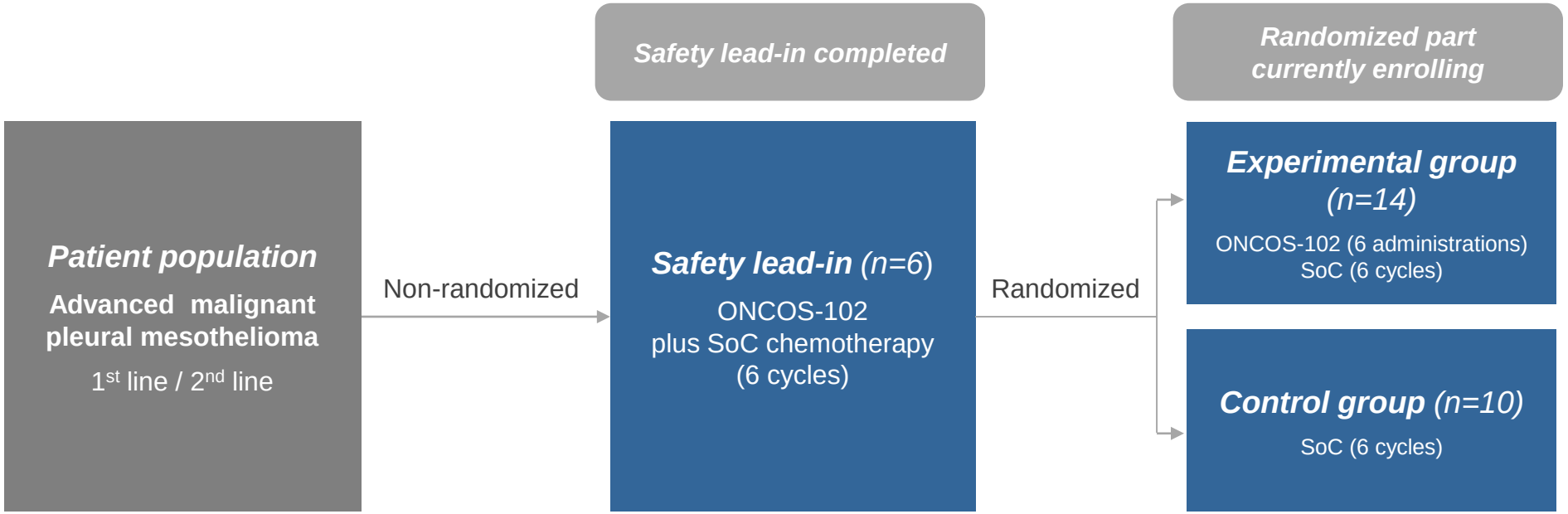
Baseline Week 5





Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC



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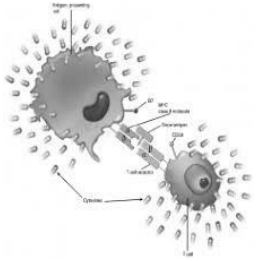
SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1
Safety

- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**

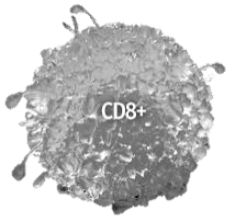
2
Innate immune activation

- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients (IL-6, TNFα and IFNγ)



3
Adaptive immune activation

- ✓ Increase in **tumor infiltration of CD4+ and CD8+ T-cells** in 3/4 patients



4
Clinical benefit

- ✓ **Signal of clinical benefit** seen in **3/6 patients** after 6 months
- ✓ **50% disease control rate**

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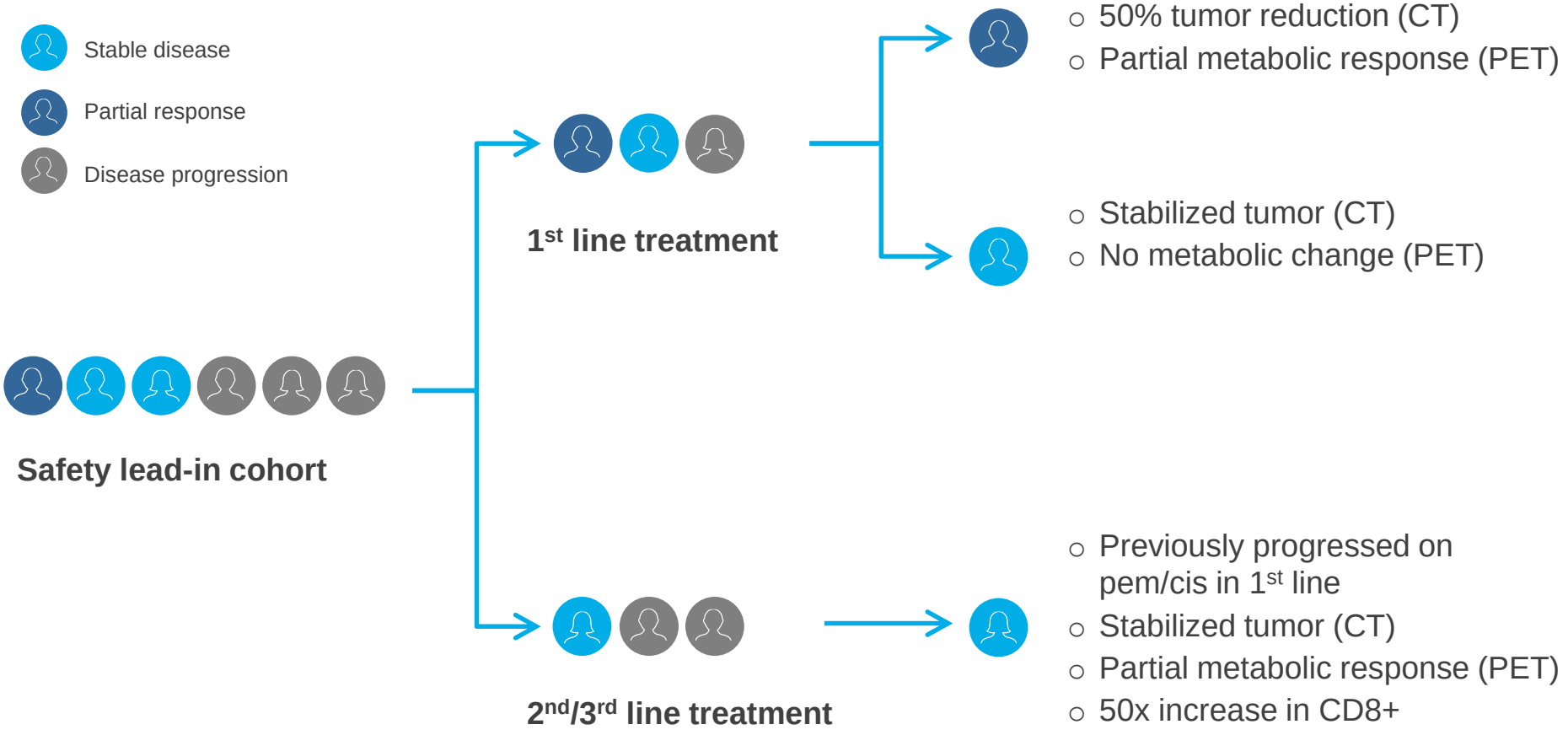
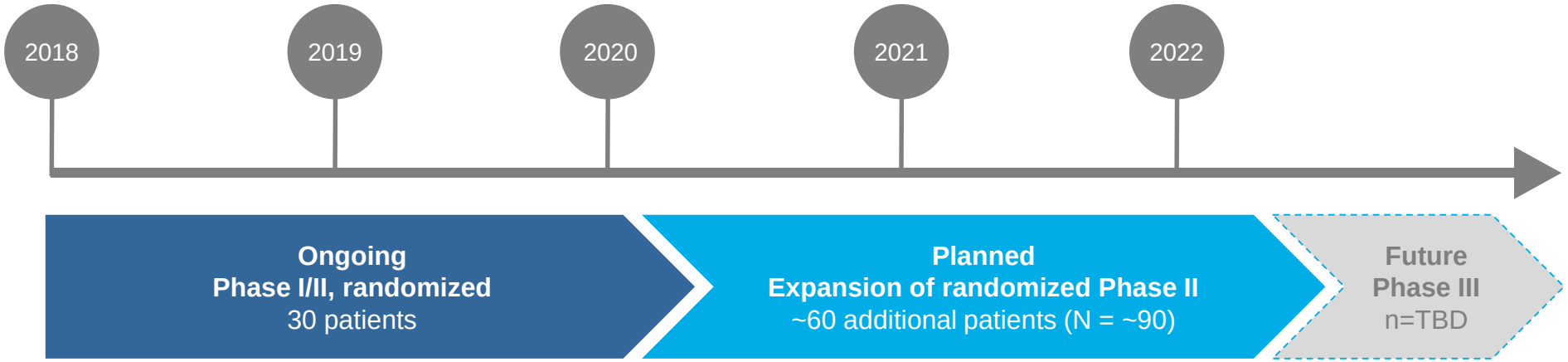
CLINICAL RESPONSES IN SAFETY COHORT



ONCOS-102 in malignant pleural mesothelioma

DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES



- Randomized ORR and OS data 30 patients
- Decide on possible CPI combination arm
- EMA & FDA advisory meetings

- Randomized ORR and OS data 90 patients
- Potentially use as basis for a submission for conditional approval
- Start Phase III OS trial for full MAA

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5 Summary & Closing

R&D PIPELINE OVERVIEW AND MILESTONES

Platform	Product candidate	Preclinical / Phase I / Phase II / Phase III	Last event	Next expected event
ONCOS oncolytic adenovirus	ONCOS-102	**Mesothelioma** Comb. w/ pemetrexed/cisplatin[1]	Phase Ib safety lead-in cohort, incl. immune activation and ORR data (6 pts)	**1H 2020** Randomized ORR data 30 pts
		Melanoma Comb. w/KEYTRUDA®	ORR and immune activation (6 pts), 1/6 CR	**1H 2019** ORR and immune data first cohort (n=8)
		Peritoneal cancers[2,3] Partner: Ludwig, CRI & AZ Comb. w/IMFINZI®	First dose escalation cohort safety review (4 pts)	*Update by partner, expected 2019*
		Prostate[3] Partner: Sotio Comb. w/DCVAC	First patient dosed	*Update by partner, expected 2019*
	Next-gen ONCOS	**3 viruses** undisclosed	Virus construct cloning and *in vitro* validation	**2H 2019** Target disclosure and *in vivo* data
TG neo-antigen cancer vaccine	**TG01**	**Pancreatic cancer** Comb. w/gemcitabine	mOS 33.4 months Demonstrated mutant RAS-specific immune activation	TBD
	TG02	**Colorectal cancer** Proof-of-mechanism Comb. w/KEYTRUDA®	First safety review, incl. immune activation data (3 pts)	**1H 2019** Immune activation and mechanistic data
	TG02	**CPI synergy** TG + PD-1		**1H 2019** TG02 + PD-1 combination *in vivo* data

1. Current standard of care chemotherapy for patients with unresectable malignant pleural mesothelioma
2. Patients with advanced peritoneal disease, who have failed prior standard chemotherapy and have histologically confirmed platinum-resistant or refractory epithelial ovarian or colorectal cancer
3. Partner sponsored trials

Ongoing partner sponsored trials

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ONCOS-102 phase I/II development strategy

COVERING THE BASES

Delivery route

Local
Intra-tumoral injection ✓

Compartmental
Intra-peritoneal infusion ✓

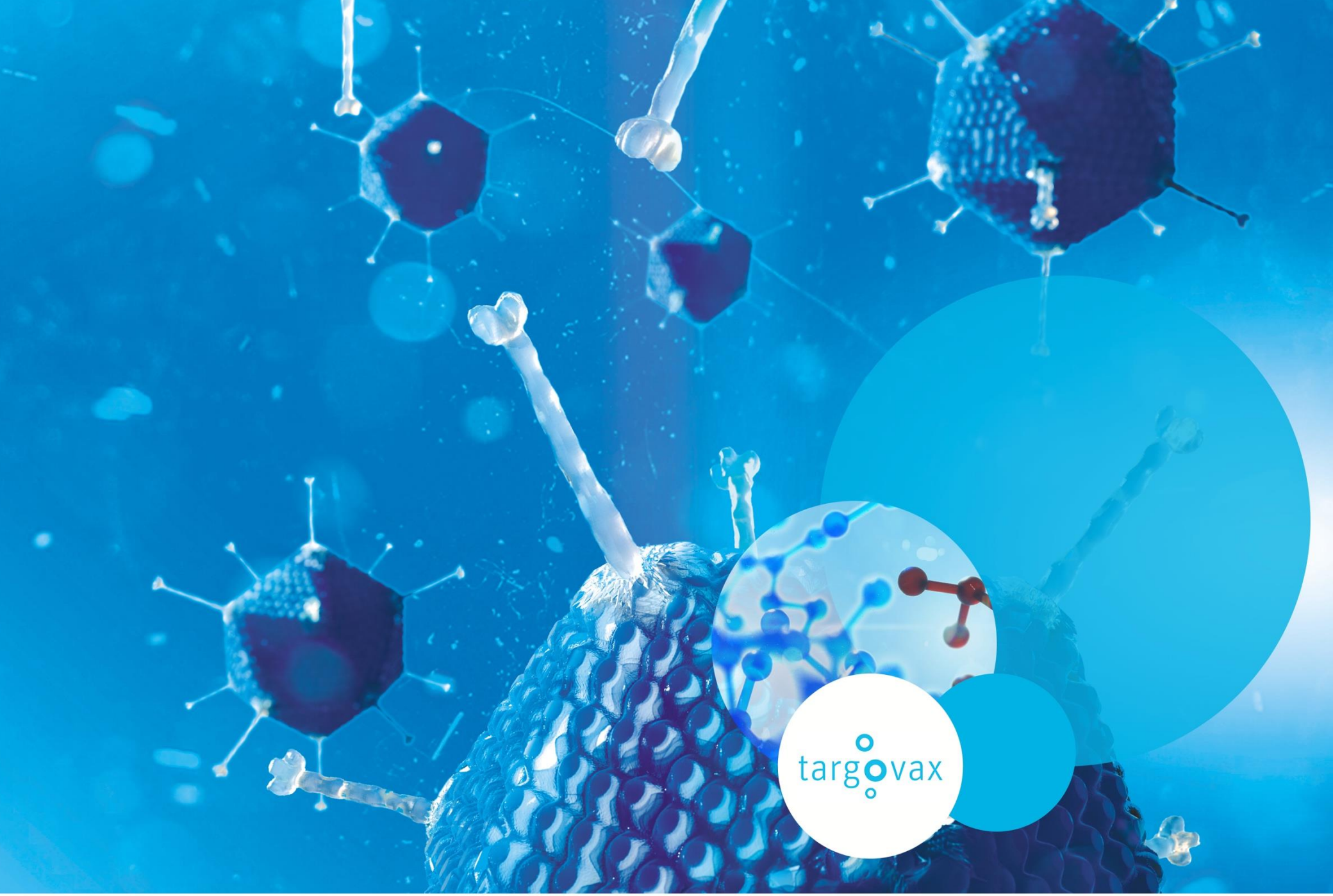
Systemic
Intra-venous infusion *TBD future*

Combination therapy

Chemotherapy
Cytostatics, SoC ✓

Checkpoint inhibitor
PD-1 & PD-L1 blockade ✓

Cell therapy
DC vaccine ✓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Backup

Major deals over the past 6 months are driving increasing

INDUSTRY INTEREST IN ONCOLYTIC VIRUSES

Acquirer	Target	Type of deal	Deal value
Boehringer Ingelheim	ViraTherapeutics	**M&A** Phase I/II oncolytic virus	**USD 250m** up-front cash
MERCK	Viralytics Developers of Oncolytic Immunotherapies	**M&A** Phase I/II oncolytic virus	**USD 400m** up-front cash
janssen PHARMACEUTICAL COMPANIES OF Johnson&Johnson	BeneVir	**M&A** Pre-clinical oncolytic virus	**USD 140m** up-front cash **Up to USD 1b** total value
Bristol-Myers Squibb	PsiOxus THERAPEUTICS	**BD partnership** IV delivered oncolytic virus	**USD 15m** milestone payment **Up to USD 1b** total value

TARGOVAX HAS A SOUND FINANCIAL POSITION

with cash to complete the planned clinical program well into 2H 2019

Operations

Cash end of Q2 - Jun 30th 2018

201 / **25**

NOK million **USD million**

Net cash flow - total Q2

-28 / **-3**

NOK million **USD million**

Annual run rate - last four quarters

109 / **13**

NOK million **USD million**

The share

Market Cap - at share price NOK ~10

600 / **70**

NOK million **USD million**

Daily turnover - rolling 6 month avg.

2.6 / **0.3** / **0.5**

NOK million **USD million** **% of share capital**

Analyst coverage

DNB, ABG Sundal Collier, Arctic, Redeye, Edison

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