TCR2 THERAPEUTICS

The Solid Tumor T Cell Company

Phase 1 Dataset

September 2022

Forward Looking Statements

This presentation has been prepared by TCR2 Therapeutics Inc. ("we," "us," or "our") and contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our clinical results and other future conditions. All statements, other than statements of historical facts, contained in this presentation, including express or implied statements regarding our expectations for the Phase 2 clinical trial of gavo-cel and the Phase 1/2 clinical trial of TC-510, including expected progress and timing of updates; our expectations for the safety and efficacy of, and enhancements to, gavo-cel, TC-510 and our other product candidates including compared to other T-cell therapy approaches; our expectations regarding the estimated patient populations and related market opportunities in gavo-cel's, TC-510's and our other product candidates' targeted indications; our expectations regarding manufacturing of gavo-cel, TC-510 and our other product candidates, our expectations regarding our development programs and IND-enabling studies; our expectations regarding expansion opportunities for our TRuC platform; and our expectations regarding our financial position are forward-looking statements. These statements are based on management's current expectations and beliefs and are forward-looking statements which involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements.

Such risks and uncertainties include, among others: uncertainties inherent in clinical studies and in the availability and timing of data from ongoing clinical studies; whether interim results from a clinical trial will be predictive of the final results of a trial; the possibility that positive results from preclinical studies and correlative studies may not necessarily be predictive of the results of our planned clinical trials, including the Phase 2 clinical trial of gavo-cel and Phase 1/2 clinical trial of TC-510; the risk that the results from the Phase 2 clinical trial of gavo-cel and Phase 1/2 clinical trial of TC-510 will not support further development and marketing approval; the risk that we may be unable to gain approval of gavo-cel, TC-510 and our other product candidates on a timely basis, if at all; the risk that we have over-estimated the potential patient population for our product candidates, if approved; the risk that the current COVID-19 pandemic will impact our clinical trials and other operations; and the other risks set forth under the caption "Risk Factors" in our most recent Annual Report on Form 10-K for the year ended December 31, 2021, as filed with the SEC on March 22, 2022, as updated in our most recent Quarterly Report on Form 10-Q for the quarter ended June 30, 2022, as filed with the SEC on August 8, 2022, and in our future filings with the SEC available at the SEC's website at www.sec.gov. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. You should not place undue reliance on any forward-looking statements, which speak only as of the date they are made.

While we may elect to update these forward-looking statements at some point in the future, we assume no obligation to update or revise any forward-looking statements except to the extent required by applicable law. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. Accordingly, readers are cautioned not to place undue reliance on these forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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Agenda

- **Phase 1 Key Takeaways |** Garry Menzel, PhD
- **Gavo-cel Phase 1 Data |** Alfonso Quintás-Cardama, MD
- **KOL: Gavo-cel Experience in the Clinic |** Raffit Hassan, MD
- **KOL: Standard of Care in Mesothelioma |** Patrick Forde, MD
- **Gavo-cel Phase 2 Trial Design |** Garry Menzel, PhD
- **Q&A**

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Phase 1 Key Takeaways

Efficacy Data

- 93% - Heavily pretreated patients that experienced tumor regression
- 77% - Disease Control Rate (DCR)
- New RECIST Responses in ovarian cancer (29% ORR), MPM (21% ORR)
- MPM: 5.6 PFS, 11.2 OS

Safety Data

- RP2D: manageable safety profile and reversible adverse events
- Most frequent Grade ≥ 3 AE: CRS in 15% of patients

Path Forward

- Ovarian Cancer: earlier focus due to encouraging early activity
- MPM: potential frontline setting if CPI combo improves durability of benefit
- NSCLC: expansion opportunity with new MSLN threshold

Baseline Established

Additional strategies in the Phase 2 clinical trial are designed to improve preliminary profile

✓ Combination with checkpoint inhibitors

✓ Redosing

✓ Earlier lines of therapy

DCR, Disease Control Rate; ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; RP2D, Recommended Phase 2 Dose; AE, Adverse Event; CRS, Cytokine Release Syndrome; MPM, Malignant Pleural/Peritoneal Mesothelioma; CPI, Checkpoint Inhibitor; NSCLC, Non-Small Cell Lung Cancer; MSLN, Mesothelin

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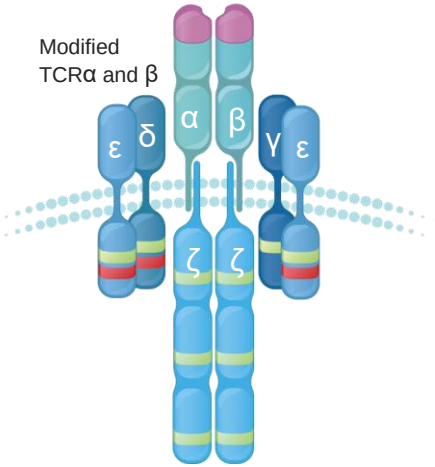
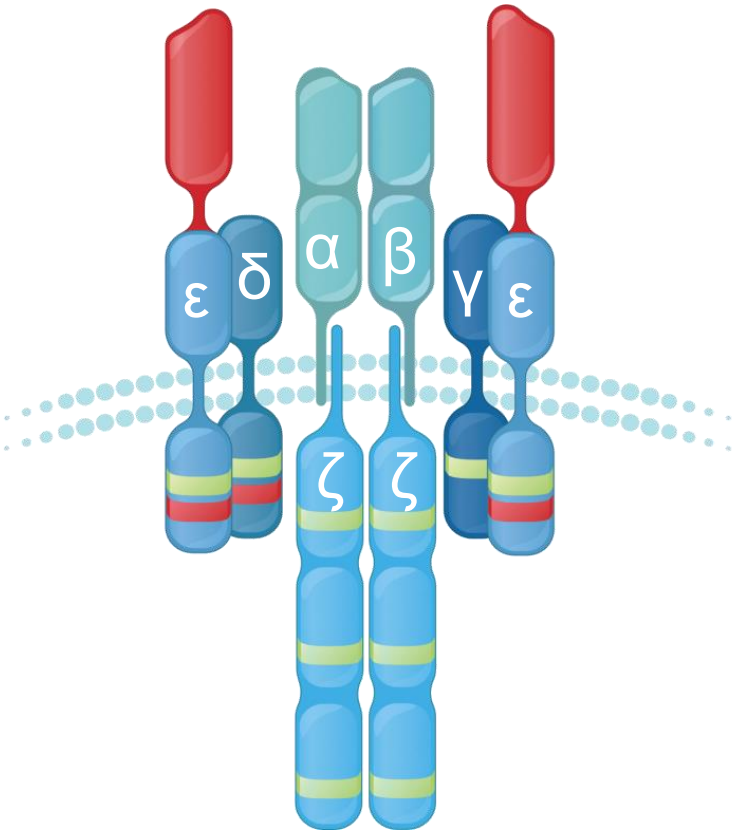
TRuCs Represent Advancement Upon Existing T Cell Therapies

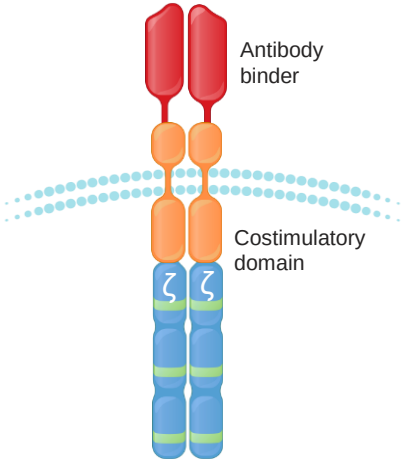
TCR-T Cell
(T Cell Receptor)



TRuC-T Cell
(T Cell Receptor Fusion Construct)



CAR-T Cell
(Chimeric Antigen Receptor)



- Utilizes Full TCR Complex Signaling
- HLA Independent

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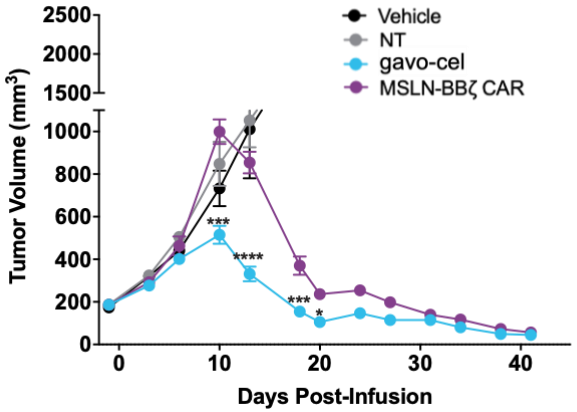
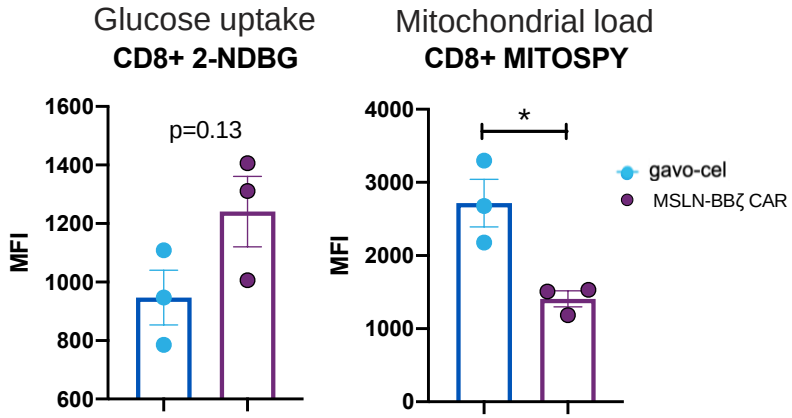
Preclinically, TRuCs Show Superiority Over CARs

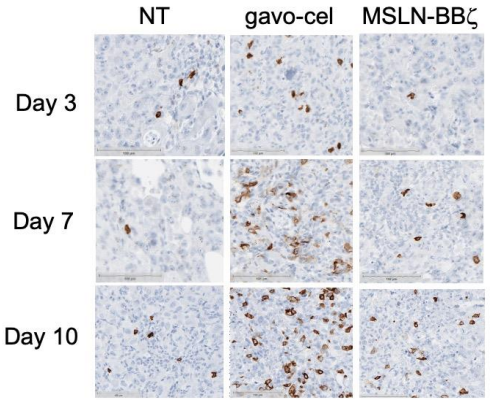
Superior Tumor Control vs. CAR-Ts



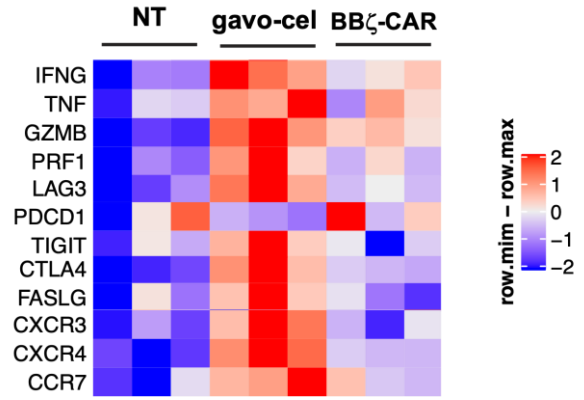
Optimal Metabolic Profile for Enhanced Fitness



Superior Intratumoral Infiltration



Higher Gene Expression Associated with T Cell Activation and Migration



Clinically, gavo-cel Has Shown Activity Where Others Have Failed

First Anti-Mesothelin Cell Therapy to Demonstrate Tolerability and Clinical Benefit

Penn
University of Pennsylvania

Memorial Sloan Kettering Cancer Center

ATARA BIO®

74 Patients treated with anti-mesothelin CAR-T monotherapy

1 Total RECIST Responses reported

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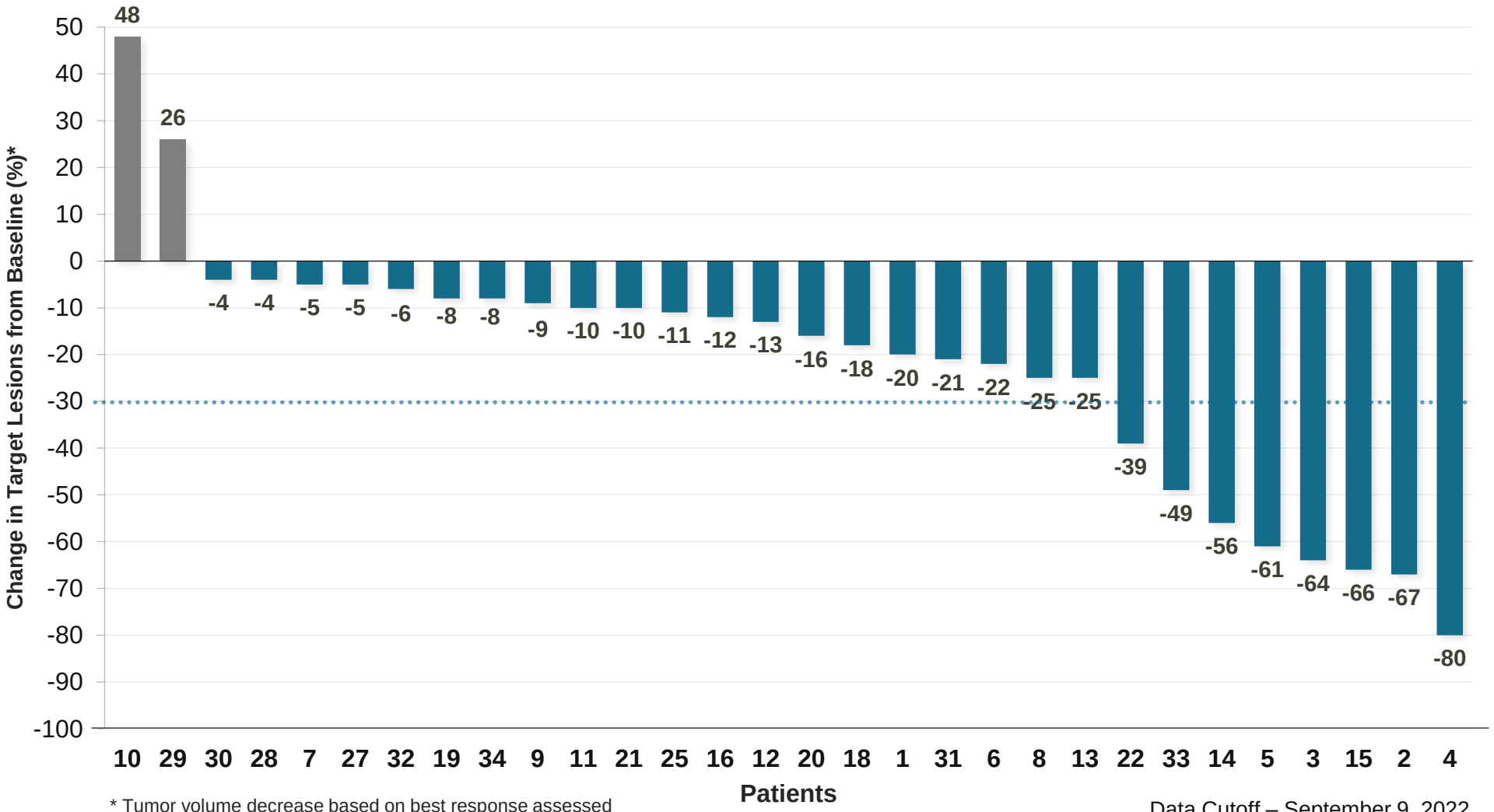
30 Patients evaluable treated with gavo-cel (TRuC-T cell) monotherapy

6 Total RECIST Responses reported

[1]Maus et al., 2013, Cancer Immunol. Res.; [2]Beatty et al., 2014, Cancer Immunol. Res.; [3]Hass et al., 2019, Mol. Therapy.; [4]www.med.upenn.edu/cellicon2021/assets/user-content/documents/tanyi.pdf; [5]Adusumilli et al., 2021, Cancer Discovery; [6]Wang et al., 2021, Cell Mol. Immunol.

gavo-cel Achieved Consistent Tumor Regression in 93% of Evaluable Patients



MPM

21/22

Ovarian

6/7

CHO

1/1

** CHO PR by Investigator Assessment

* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

MPM, Malignant Pleural/Peritoneal Mesothelioma; CHO, Cholangiocarcinoma

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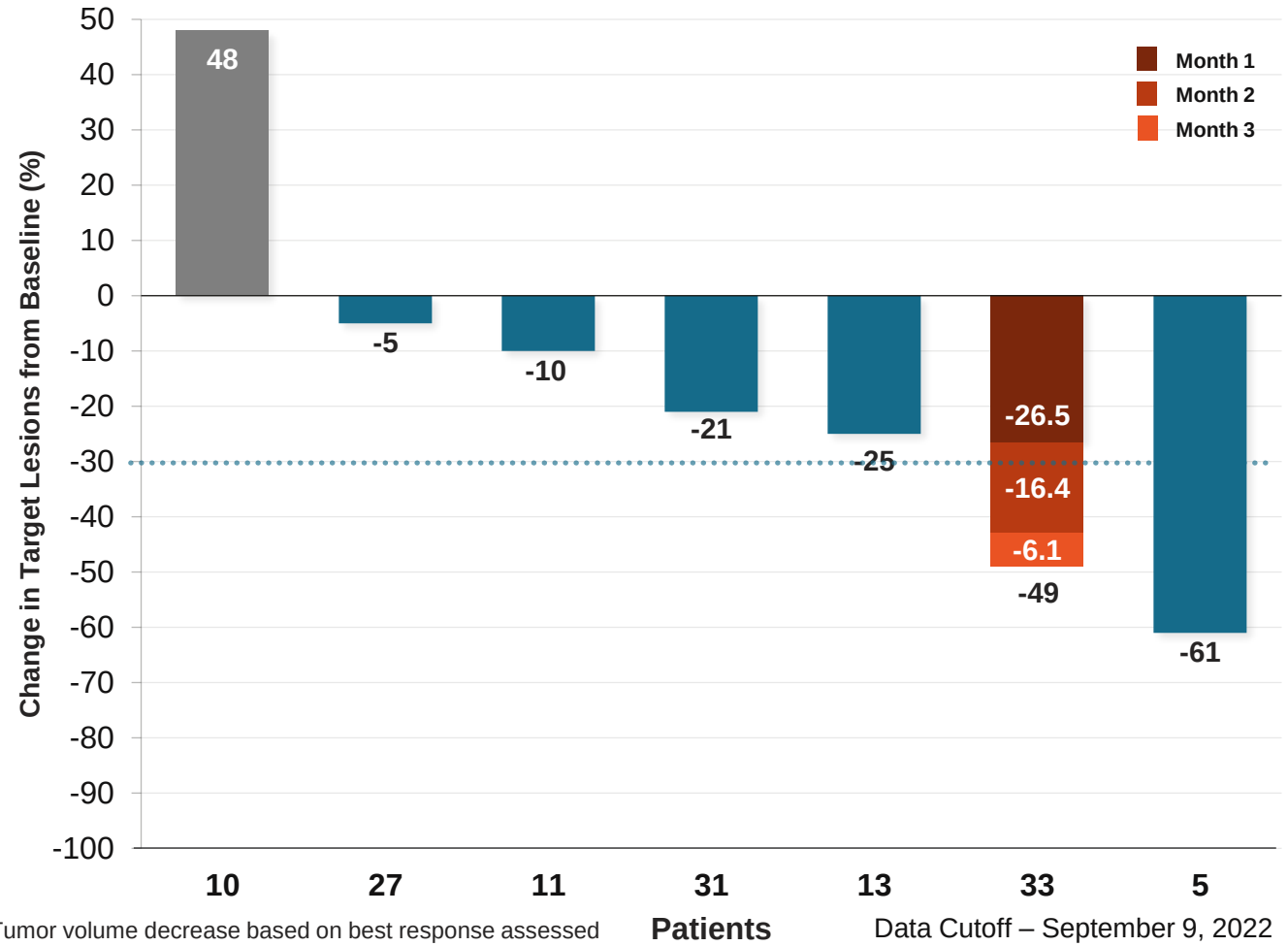
Promising Signal in Platinum Refractory Ovarian Cancer

Ovarian Highlights

- 6/7 patients experienced tumor regression
- 2/7 patients experienced RECIST partial responses
- Most recent RECIST response (Patient 33) is ongoing at month 4; experiencing continuous monthly improvement of radiological response

Efficacy Data

- ORR: 29% (gavo-cel + LD)
- PFS: 5.8 months
- OS: 8.1 months



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; LD, Lymphodepletion

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Patient 33 – Platinum Refractory Ovarian Cancer

Partial Response (RECIST v1.1), Tumor Regression Deepened Over 3 Months (49%)

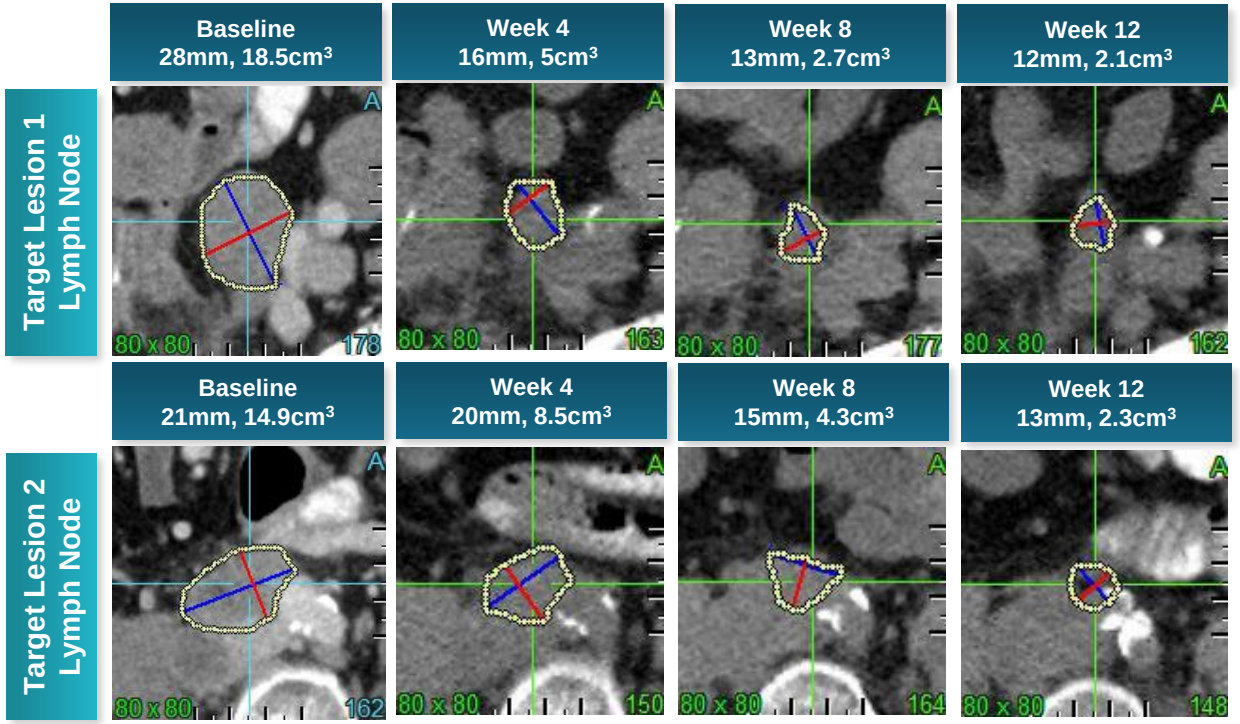
66-year-old female,

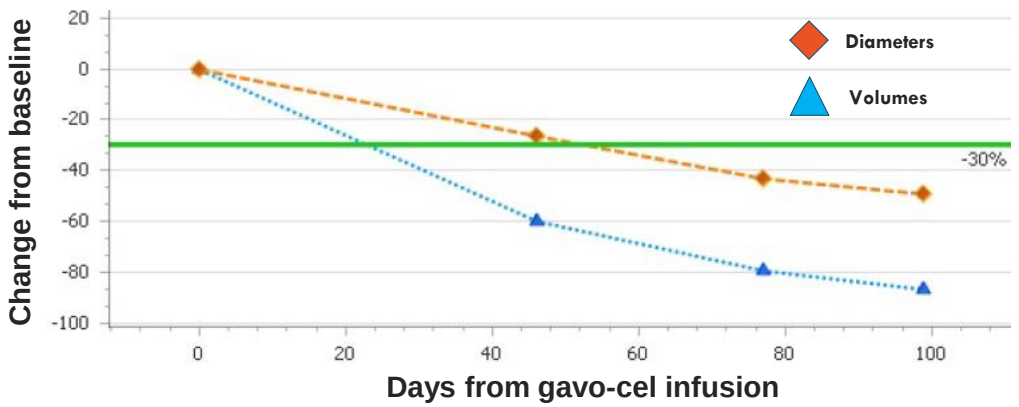
High grade, Stage IV serous ovarian cancer

- *TP53 mutated*
- Total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy
- Carboplatin/paclitaxel
- Bevacizumab/Paclitaxel
- Bevacizumab maintenance
- Weekly Paclitaxel

Enrolled in gavo-cel Clinical Trial

- Lymphodepletion with Flu/Cy
- gavo-cel at $1x10^8/m^2$ (RP2D)





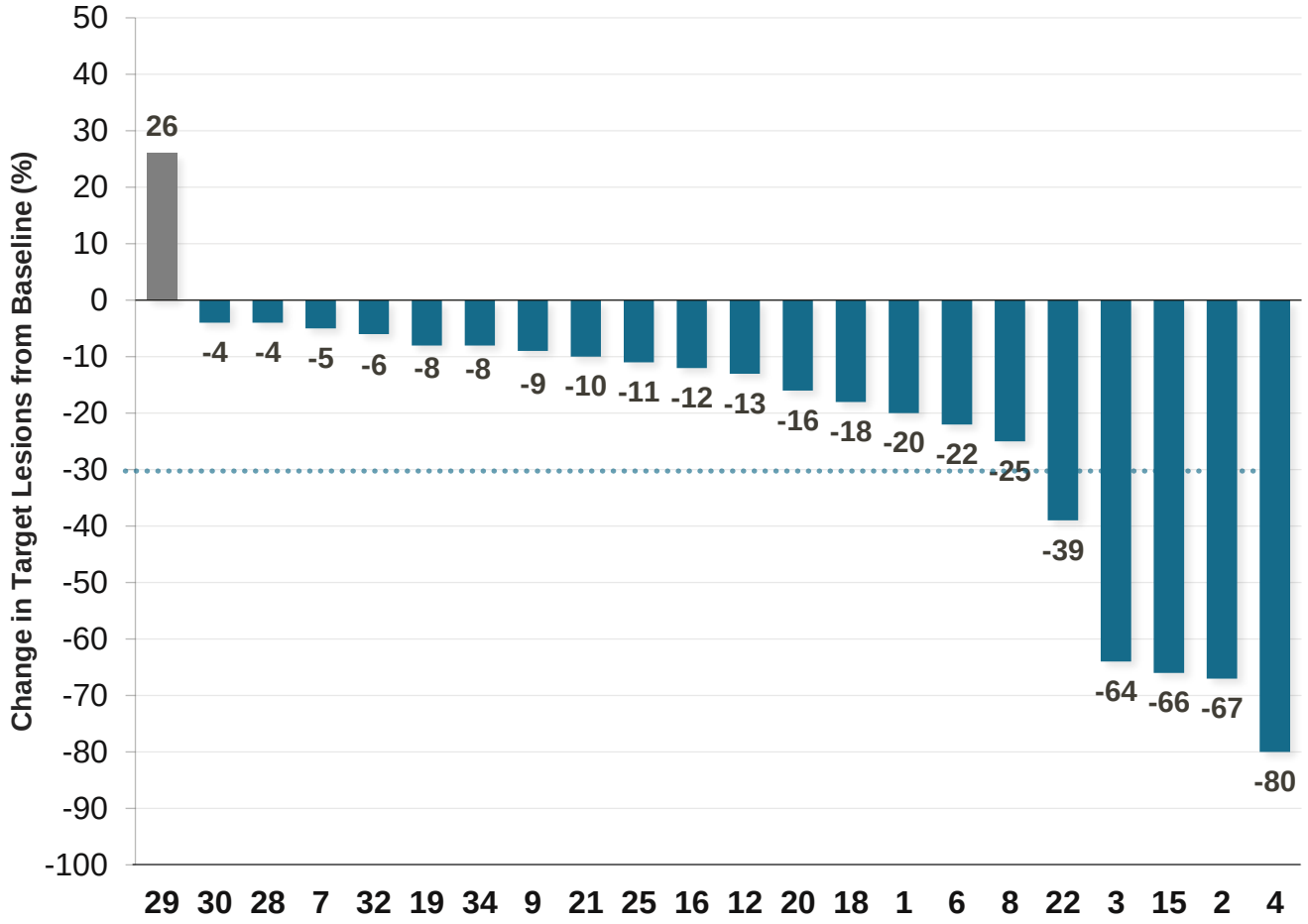
Phase 1 Data Support a Path Forward as Mesothelioma Leader

MPM Highlights

- 21/22 patients experienced tumor regression
- 5/22 patient partial responses by target lesion assessment; 4/22 experienced RECIST partial responses
- 1 patient experienced complete metabolic response

Efficacy Data

- ORR: 21% (gavo-cel + LD)
- PFS: 5.6 months
- OS: 11.2 months



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; LD, Lymphodepletion

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Significant Potential Opportunity in Mesothelin-Expressing Solid Tumors

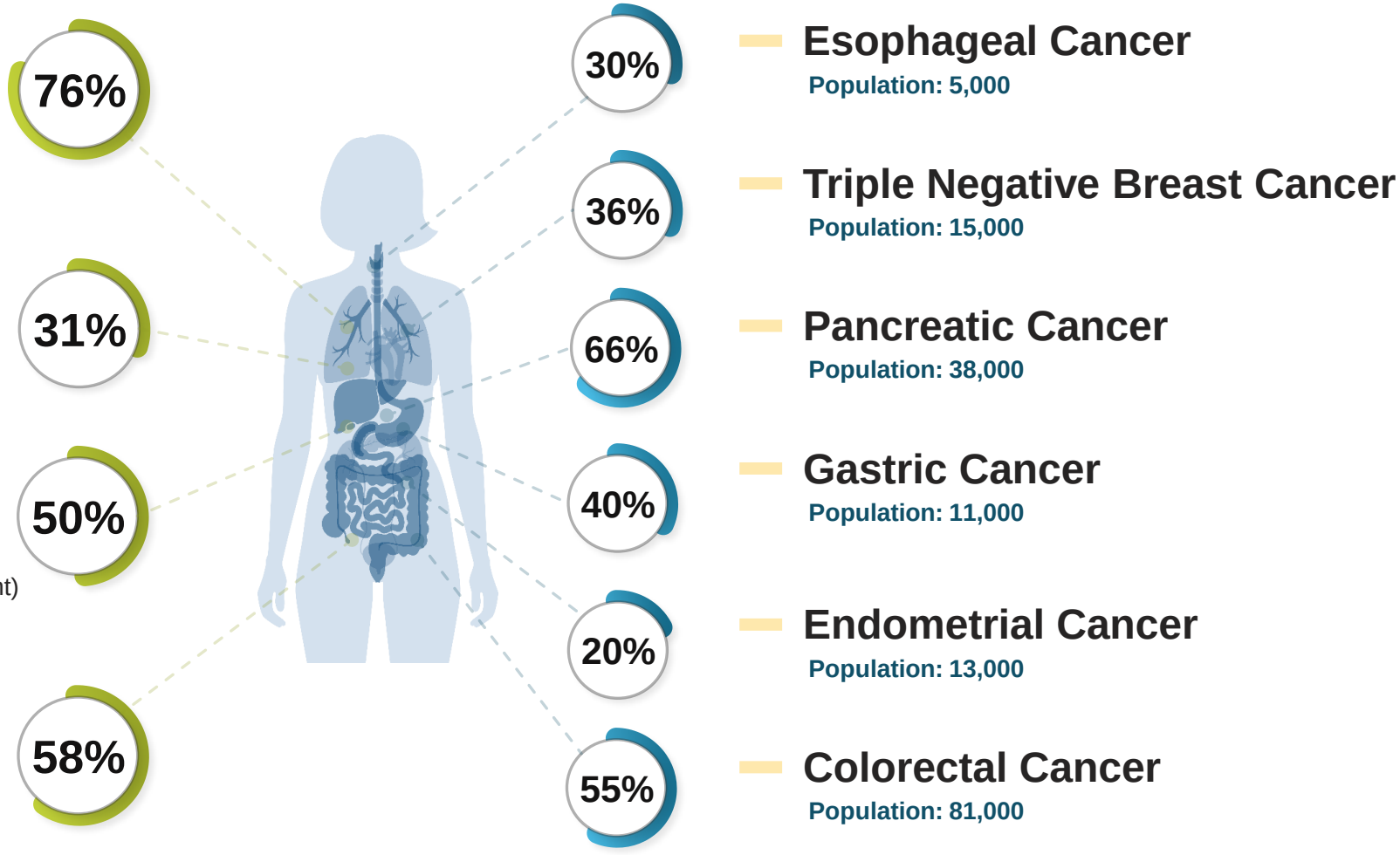
~215,000 Patients Across Multiple Target Indications

Mesothelioma
Population: 1,800
- Orphan Drug Designation
- 4 RECIST Partial Responses
- 21/22 Tumor Regression
- ORR 21%

NSCLC
Population: 62,600

Cholangiocarcinoma
Population: 4,000
- Orphan Drug Designation
- 1 Partial Response (by Investigator Assessment)
- 1/1 Tumor Regression

Ovarian Cancer
Population: 12,400
- 2 RECIST Partial Responses
- 6/7 Tumor Regression
- ORR 29%



Esophageal Cancer
Population: 5,000

Triple Negative Breast Cancer
Population: 15,000

Pancreatic Cancer
Population: 38,000

Gastric Cancer
Population: 11,000

Endometrial Cancer
Population: 13,000

Colorectal Cancer
Population: 81,000

Percent of Patients with Mesothelin Surface Expression

NSCLC, Non-Small Cell Lung Cancer; ORR, Overall Response Rate
Refs: Inaguma 2017, SEER Statistics, Morello 2016, Tozbikian 2014

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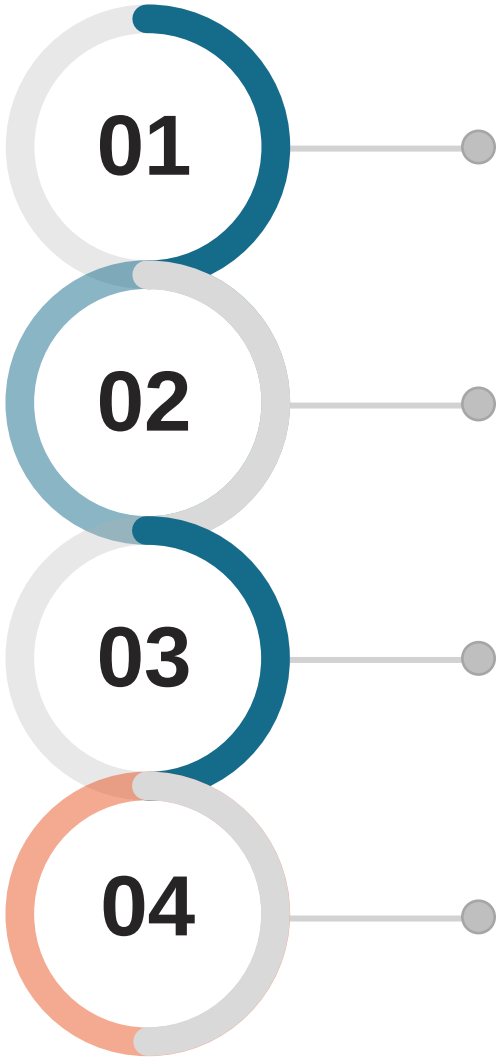
Phase 2 Modifications Aim to Further Improve Outcomes and Patient Access

Ovarian Cancer + Mesothelioma



01 CPI Combination
Better Clinical Responses and Persistence

02 Redosing
Increasing Depth and Duration of Response

03 Limit Prior Lines of Therapy
Improved Immune Health

04 New Mesothelin Threshold
Increased Patient Eligibility

NSCLC + Cholangiocarcinoma

NSCLC, Non-Small Cell Lung Cancer

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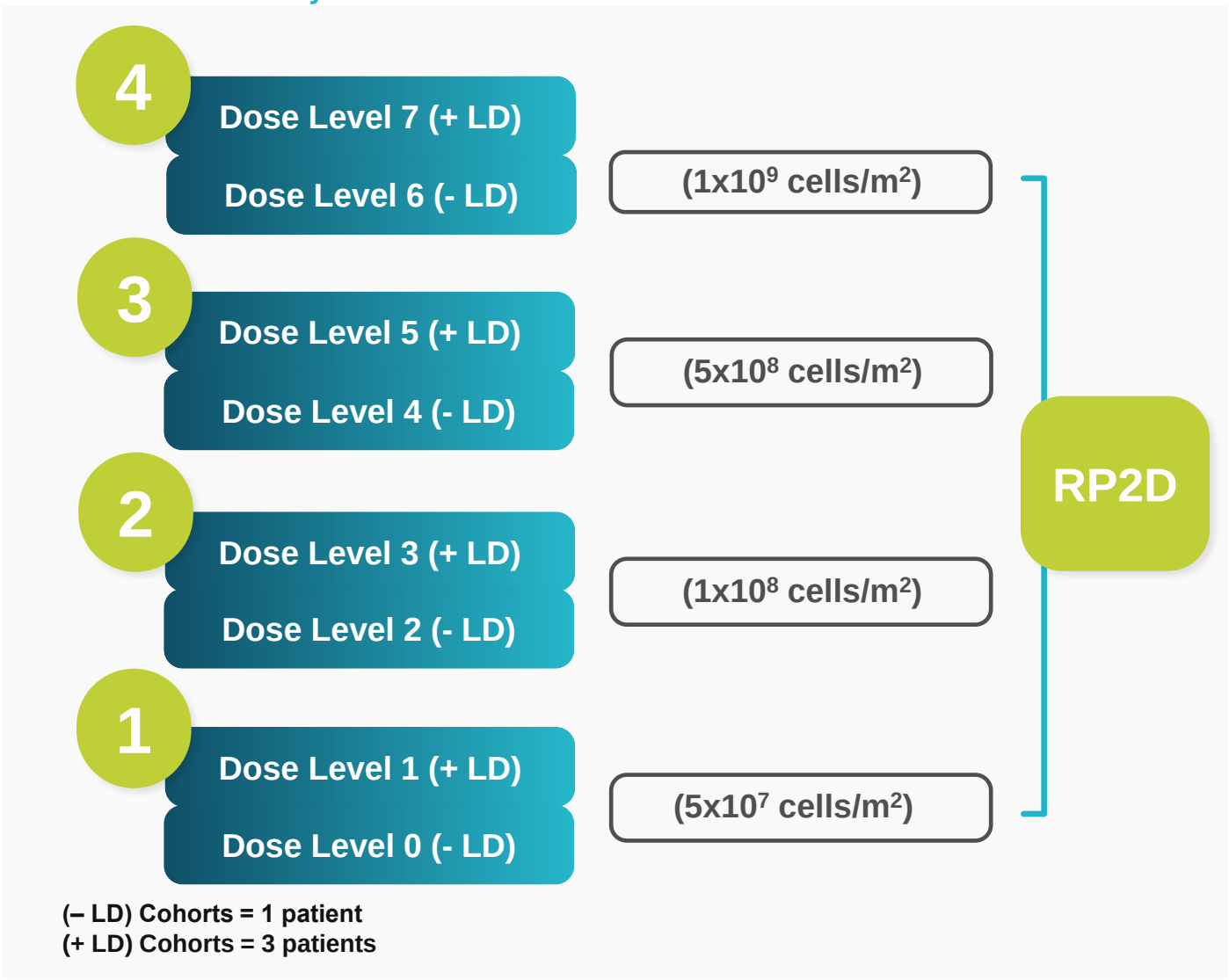
Phase 1 Data

gavo-cel Phase 1 Trial in MSLN+ Solid Tumors

Phase 1 Objective: Determine RP2D



Phase 1: Dose Finding

Indications

- MPM
- Ovarian cancer
- NSCLC
- Cholangiocarcinoma

Mesothelin Expression

- IHC assay
- Central lab (Roche/Ventana)
- Cut-off: ≥50% 2+/3+

Lymphodepletion (LD)

- Fludarabine: 30 mg/m^2 x4d
- Cyclophosphamide: 600 mg/m^2 x3d

LD, Lymphodepletion; RP2D, Recommended Phase 2 Dose; MPM, Malignant Pleural/Peritoneal Mesothelioma; NSCLC, Non-Small Cell Lung Cancer

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Patient Tumor Characteristics

Dose Level (gavo-cel dose) No. Patients	DL 0 (no LD) $5x10^7/m^2$ n=1	DL 1 $5x10^7/m^2$ n=8	DL 2 (no LD) $1x10^8/m^2$ n=1	RP2D DL 3 $1x10^8/m^2$ n=13	DL 3.5 $3x10^8/m^2$ n=5	DL 4 (no LD) $5x10^8/m^2$ n=1	DL 5 $5x10^8/m^2$ n=3	Overall n=32 (%)
Age, Median (Range)	61	70 (36-84)	46	59 (28-70)	63 (43-69)	67	52 (37-66)	63 (28-84)
Diagnosis	1 MPM	7 MPM 1 Ovarian	1 MPM	6 MPM, 6 Ovarian 1 Cholangio	4 MPM, 1 Ovarian	1 MPM	3 MPM	23 MPM 8 Ovarian 1 Cholangio
MSLN 2+/3+	90	72 (55-100)	90	70 (50-95)	75 (50-92)	60	65 (65-73)	70 (50-100)
Median No. Prior Rx	8	5	9	5	7	7	4	5 (1-13)
Prior ICI, n (%)	1 (100)	6 (75)	1 (100)	6 (46)	4 (80)	1 (100)	2 (66)	21 (66)
Prior Anti-MSLN Therapy, n (%)	1 (100)	1 (13)	1 (100)	1 (8)	2 (40)	0	1 (33)	6 (19)
Bridging Therapy, n (%)	0	6 (75)	0	12 (92)	5 (100)	1 (100)	1 (33)	25 (78)

Data Cutoff – September 9, 2022

DL, Dose Level; RP2D, Recommended Phase 2 Dose; MSLN, Mesothelin; ICI, Immune Checkpoint Inhibitors; MPM, MPM, Malignant Pleural/Peritoneal Mesothelioma; Cholangio, Cholangiocarcinoma

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Grade ≥3 Treatment Emergent Adverse Events

Adverse Event	DL 0 (no LD) $5x10^7/m^2$ n=1 (%)	DL 1 $5x10^7/m^2$ n=8 (%)	DL 2 (no LD) $1x10^8/m^2$ n=1 (%)	RP2D DL 3 $1x10^8/m^2$ n=13 (%)	DL 3.5 $3x10^8/m^2$ n=5	DL 4 (no LD) $5x10^8/m^2$ n=1 (%)	DL 5 $5x10^8/m^2$ n=3 (%)	Overall n=32 (%)
Hematologic								
Lymphopenia	0	8 (100)	0	13 (100)	5 (100)	0	3 (100)	29 (91)
Neutropenia	1 (100)	8 (100)	0	13 (100)	5 (100)	1 (100)	3 (100)	31 (97)
Thrombocytopenia	0	2 (25)	0	2 (15)	1 (20)	0	2 (67)	7 (22)
On Target / On Tumor								
CRS	0	2 (25)	0	2 (15)	1 (20)	0	3 (100)	8 (25)
HLH/ MAS	0	0	0	0	0	0	0	0
Neurotoxicity	0	0	0	0	0	0	0	0
On Target / Off Tumor								
Pericarditis / Pericardial effusion	0	0	0	0	1 (20)	0	0	1 (3)
Pleuritis / Pleural effusion	0	0	0	1 (8)	1 (20)	0	0	2 (6)
Peritonitis / Ascites	0	0	0	1 (8)	0	0	0	1 (3)
Other								
Pneumonitis	0	1 (13)*	*0	0	3 (60)	0	1 (33)	5 (16)
Sepsis	0	1 (13)	0	0	0	0	0	1 (3)
Hemorrhage	0	0	0	0	0	0	1 (33)*	1 (3)

*Dose Limiting Toxicity

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DL, Dose Level; LD, Lymphodepletion; RP2D, Recommended Phase 2 Dose; HLH, Hemophagocytic Lymphohistiocytosis; MAS, Macrophage Activation Syndrome

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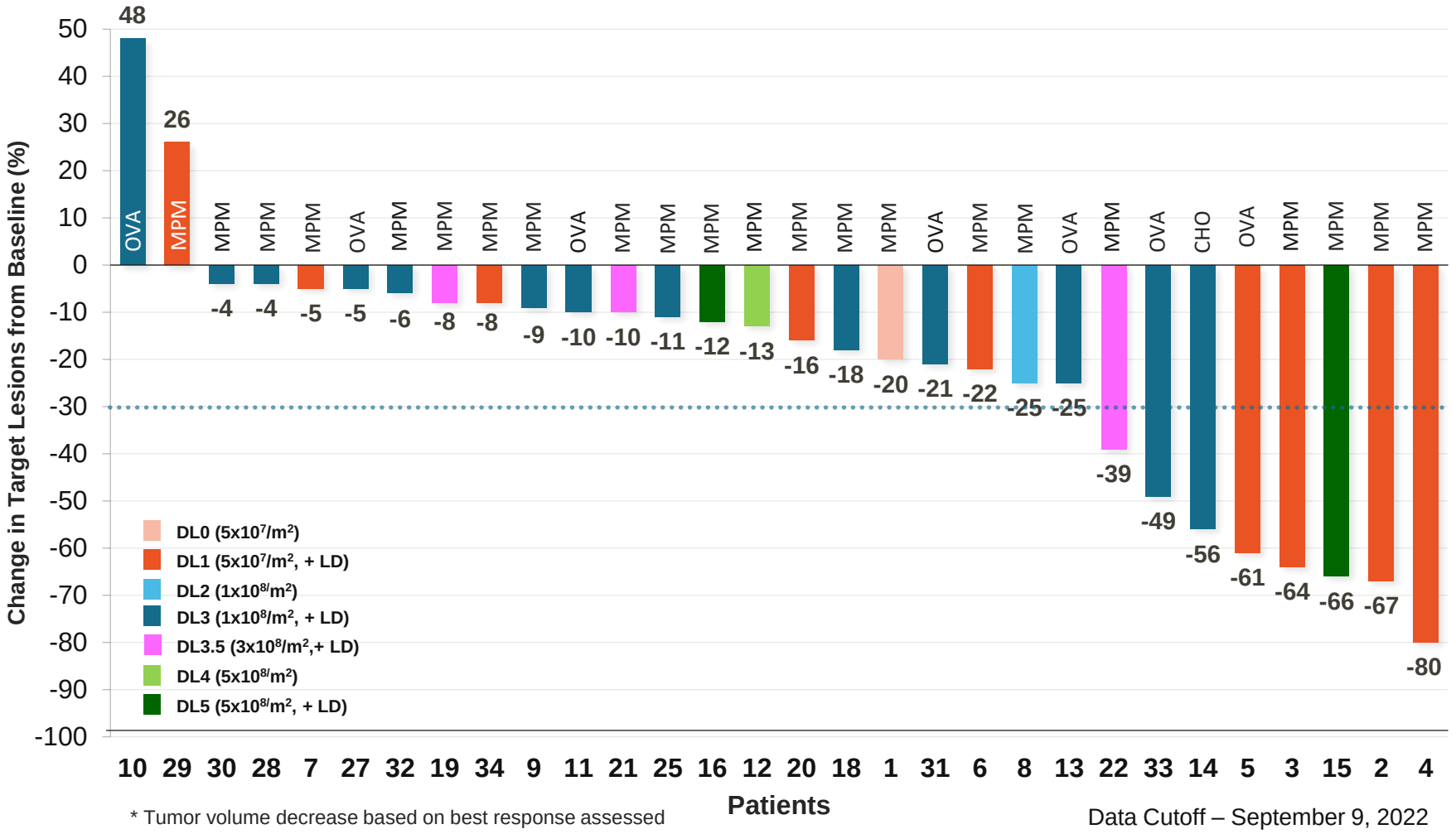
Consistent Tumor Regression in Patients with gavo-cel

Tumor Regression in 93% of Patients, Disease Control Rate 77%



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022

Blinded Independent Central Review

	All	gavo-cel + LD
ORR	20%	22%
MPM ORR	18%	21%
Ovarian ORR	29%	29%

DCR = PR or SD lasting at least 3 months

DL, Dose Level; LD, Lymphodepletion; DCR, Disease Control Rate; ORR, Overall Response Rate; PR, Partial Response; SD, Stable Disease

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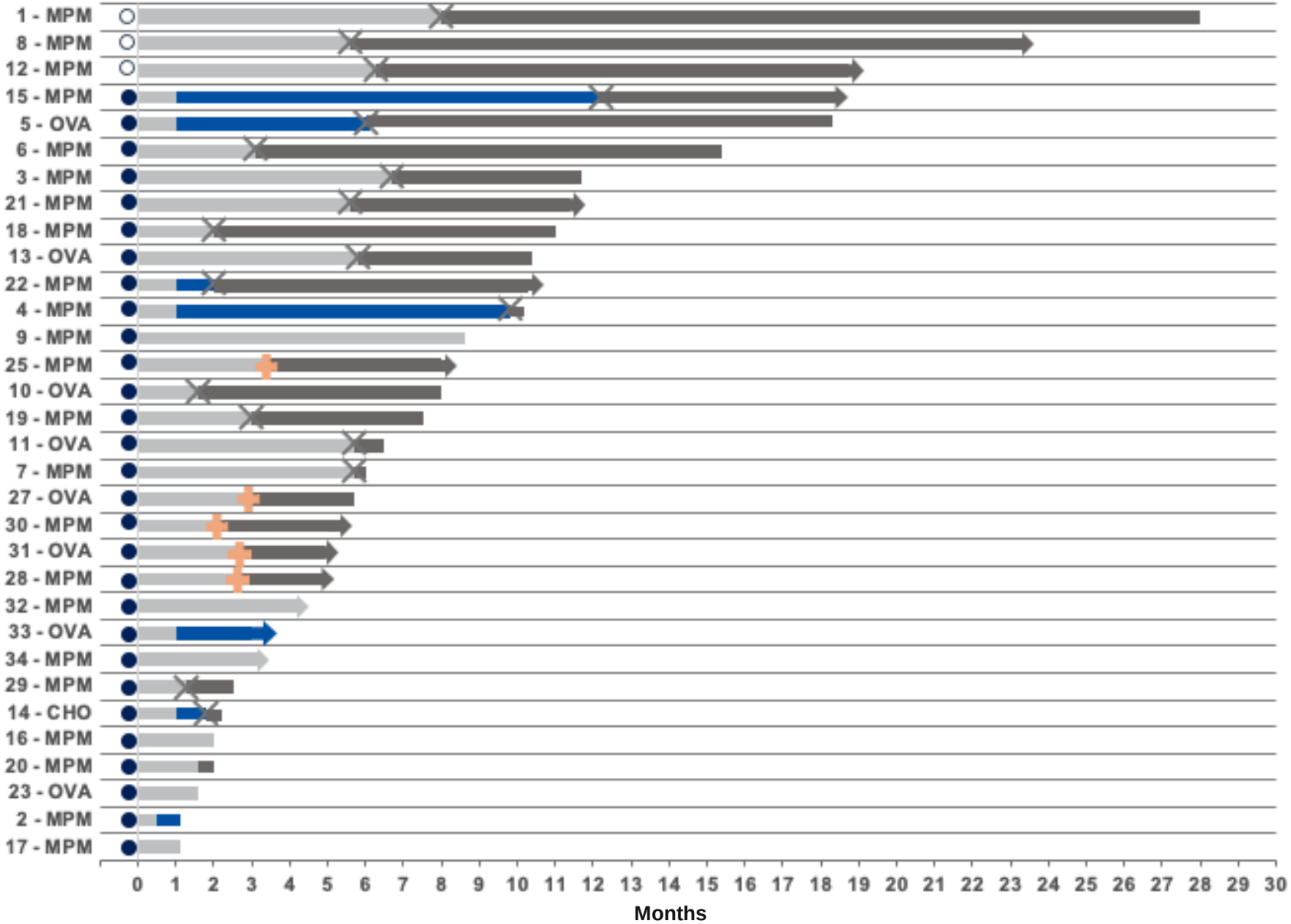
Patient Response and Follow-up as of September 9th, 2022



Patients alive at 6 months *	70%
Patients alive at 1 year *	31%
Patients alive as of cutoff	12

Data Cutoff – September 9, 2022

*Kaplan-Meier survival estimates
** CHO PR by Investigator Assessment

Lymphodepletion: ● LD ○ No LD

Response: SD PR CR × PD

✚ **Off Active FU (Unconfirmed PD) (e.g. Clinical prog/inv. decision)**

Alive (ongoing) **Deceased**

CHO, Cholangiocarcinoma; SD, Stable Disease; PR, Partial Response; CR, Complete Response; PD, Progressive Disease; FU, Follow-Up

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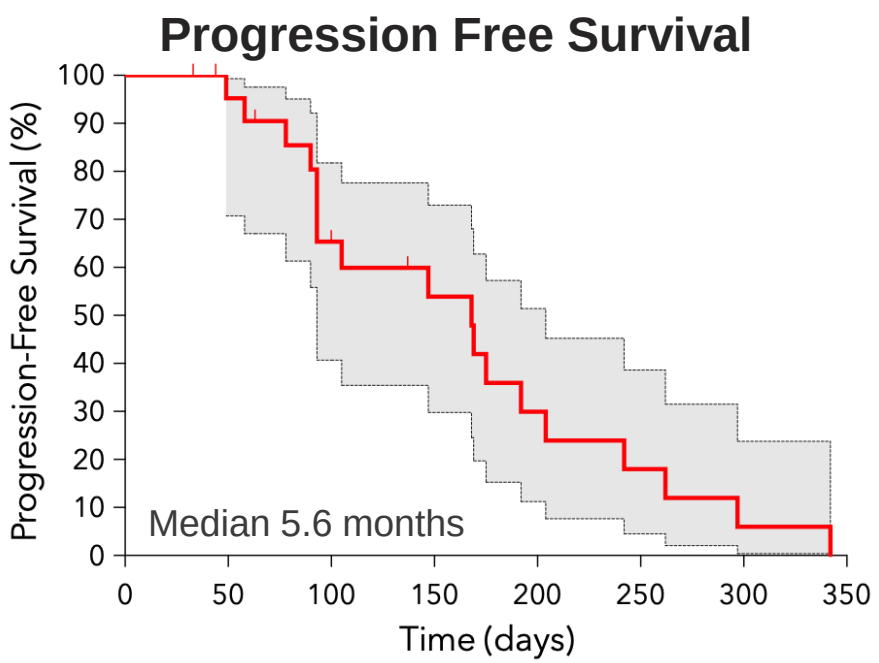
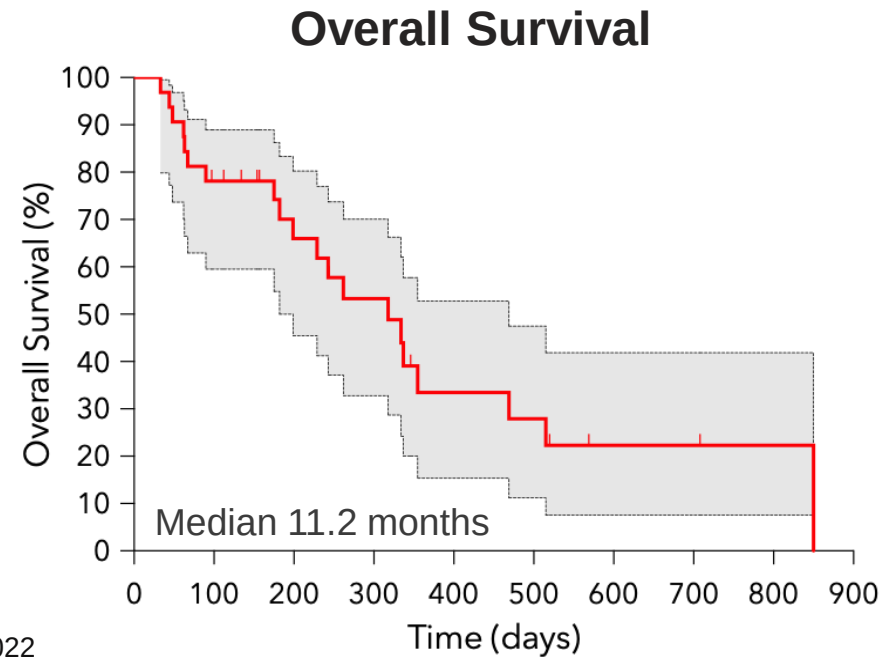
Survival in Mesothelioma

ORR 21%, PFS 5.6 Months, OS 11.2 Months





Data Cutoff – September 9, 2022

Study	n	ORR (%)	PFS (mo)	OS (mo)
Vinorelbine	98	3.1	4.2	9.3
vs **Supportive Care[1]**	56	1.8	2.8	9.1
Pembrolizumab	73	22	2.5	10.7
vs **Vinorelbine or Gemcitabine[2]**	71	6	3.4	12.4
Nivolumab	221	11	3	10.2
vs **Placebo[3]**	111	1	1.8	6.9

Benchmarks in Second Line Post Platinum-Based Therapy

1. Fennell et al Phase 2 VIM Study. ASCO 2021
2. Popat et al Phase 3 PROMISE-meso Study. Ann Oncol 2020
3. Fennell et al Phase 3 CONFIRM Study. Lancet Oncol 2021

ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival

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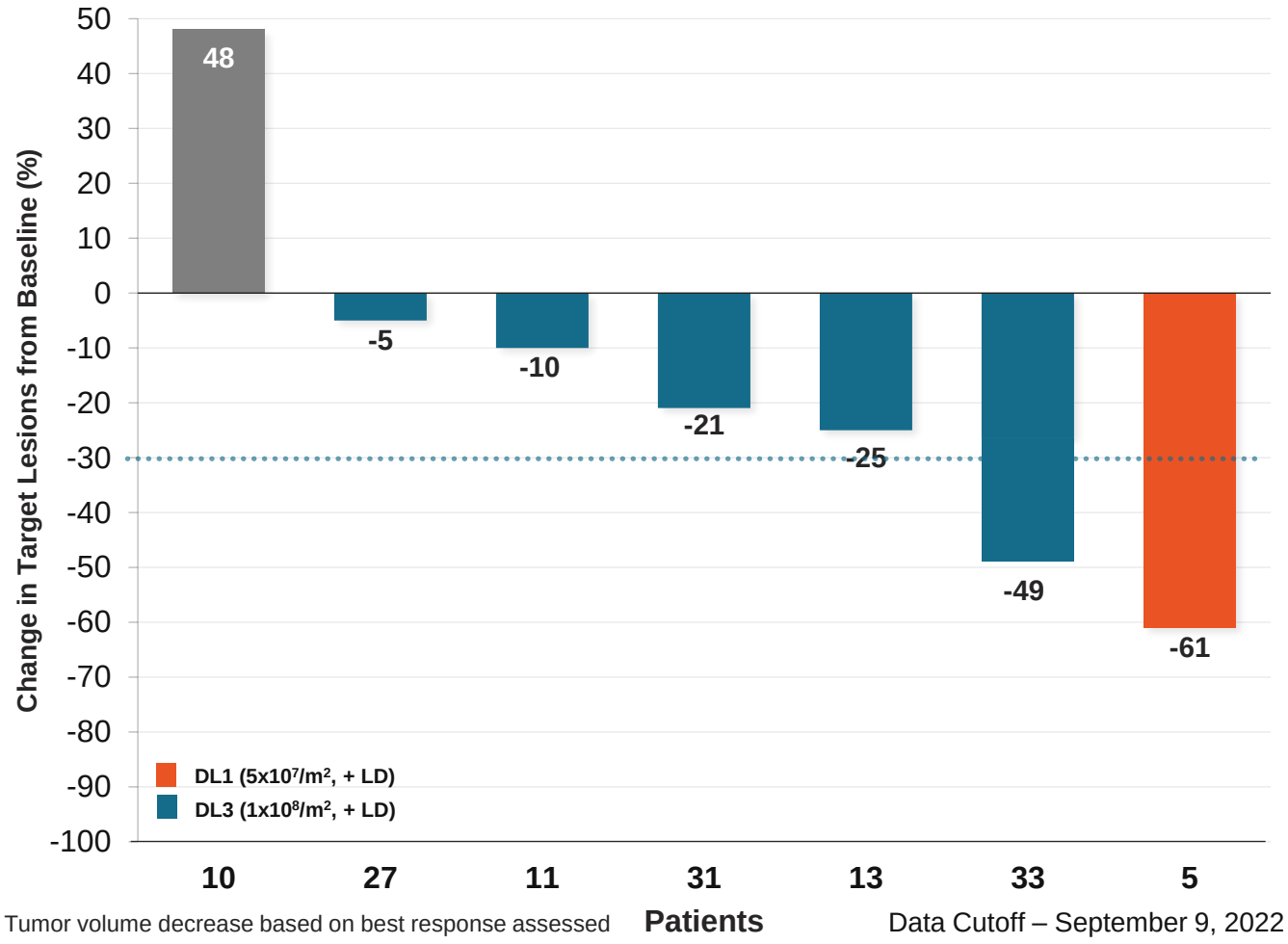
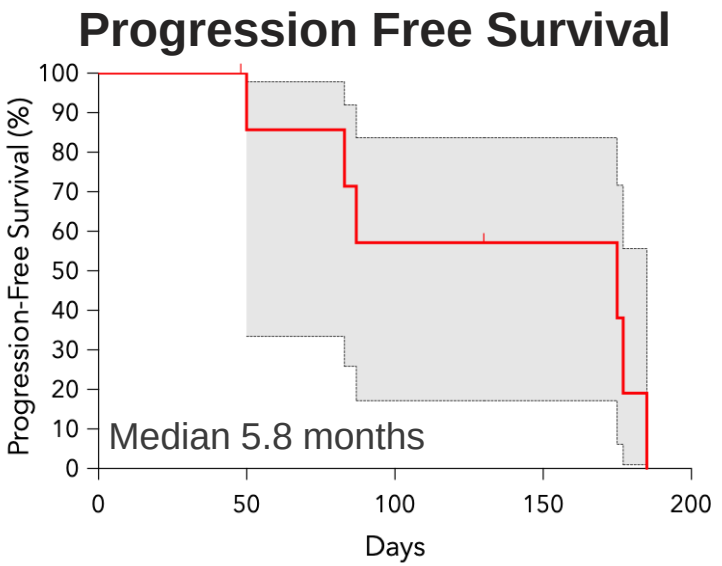
Survival in Ovarian Cancer after gavo-cel Infusion

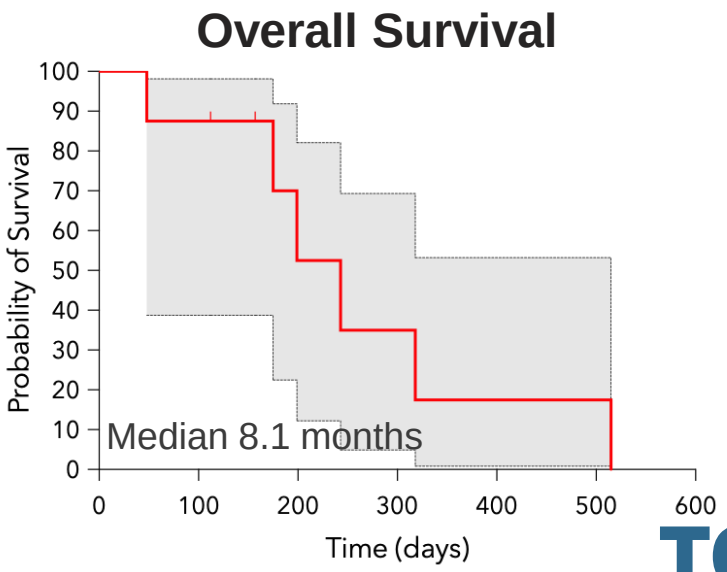
ORR 29%, PFS 5.8 Months, OS 8.1 Months



* Tumor volume decrease based on best response assessed

Data Cutoff – September 9, 2022





ORR, Overall Response Rate; PFS, Progression Free Survival; OS, Overall Survival; DL, Dose Level; LD, Lymphodepletion

Patient 5 – Platinum Refractory Ovarian Cancer

Partial Response (RECIST v1.1), Tumor Regression (61%)

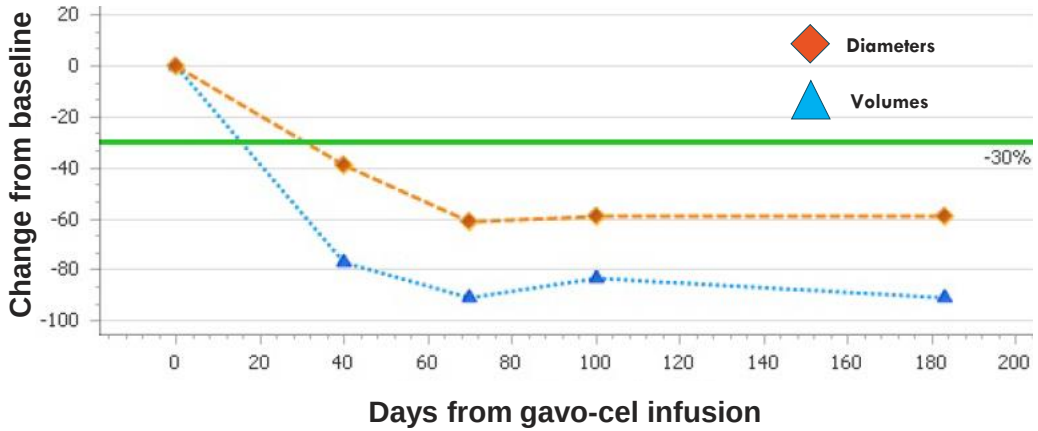
70-year-old female

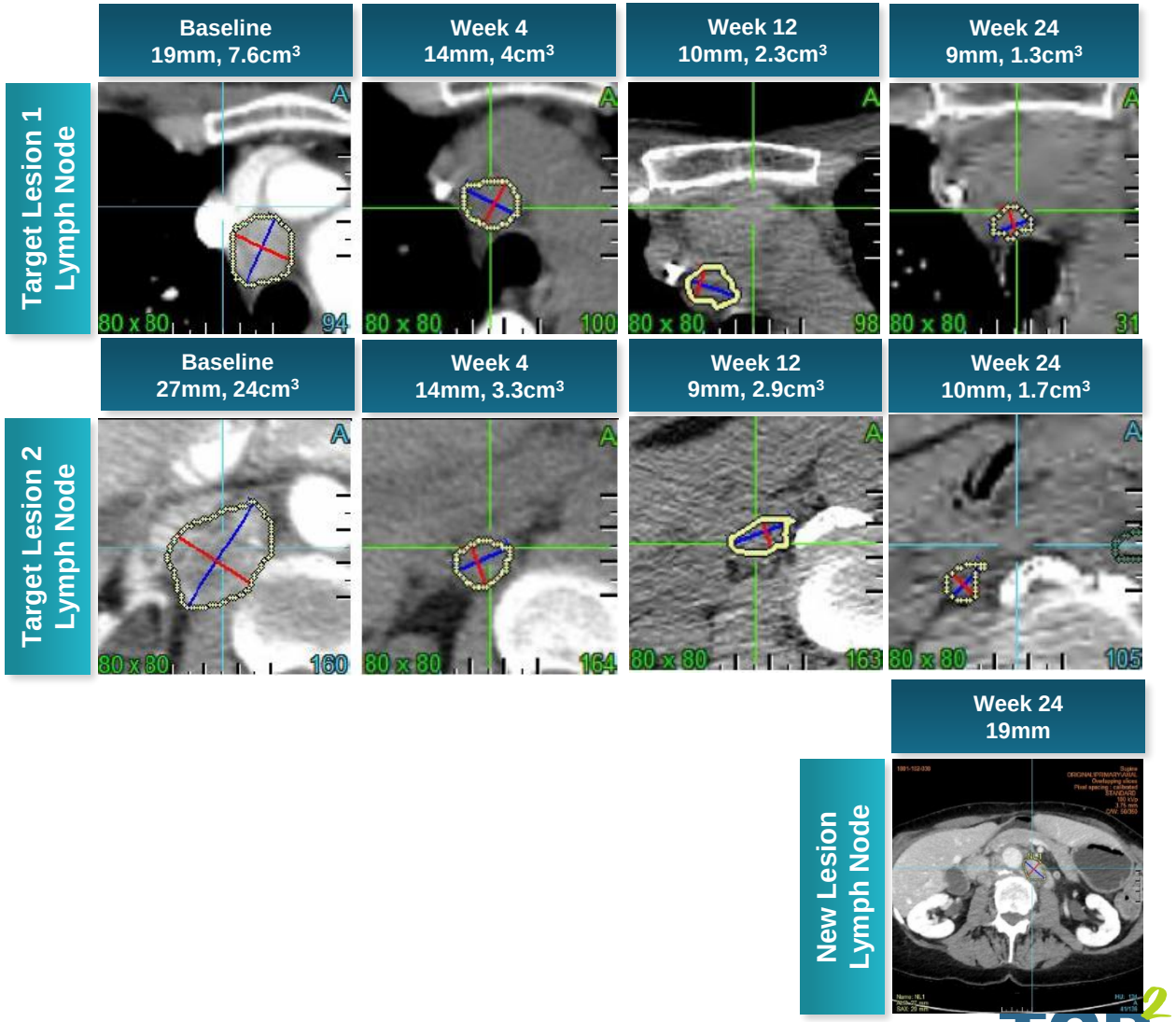
High grade, Stage IV serous ovarian cancer

- *TP53*^{R248Q}, *CCNE1* amplified, wild type *BRCA1/2*
- Failed 6 prior lines of chemotherapy

Enrolled in gavo-cel Clinical Trial

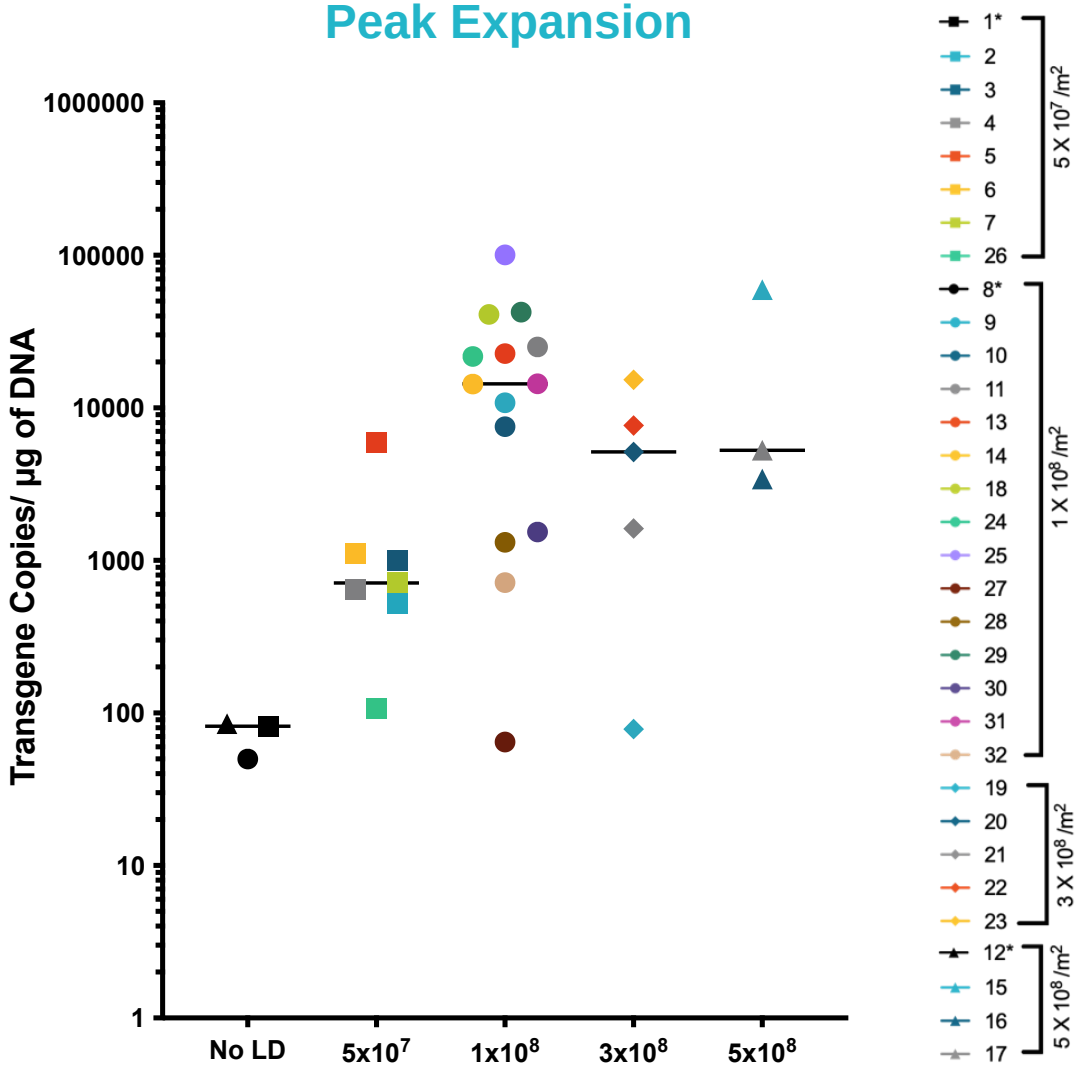
- Lymphodepletion with Flu/Cy
- gavo-cel at 5x10^{7}/m^{2} (Dose Level 1)



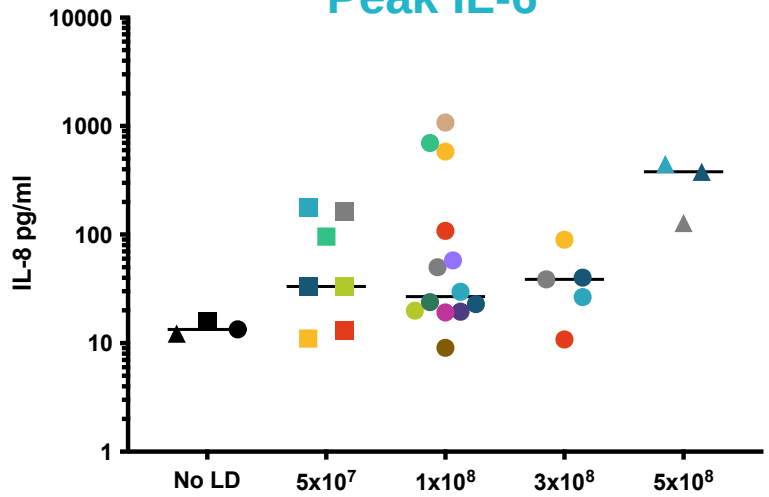


gavo-cel Displayed Dose-Dependent Expansion and Cytokine Release

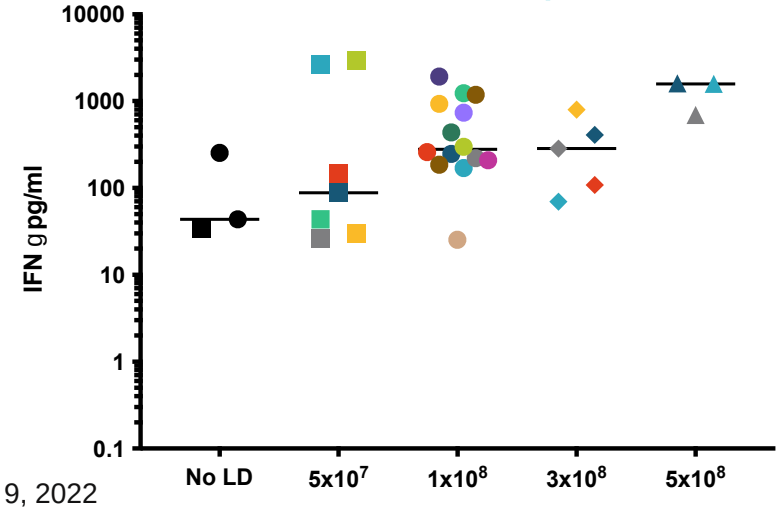
Peak Expansion



Peak IL-6



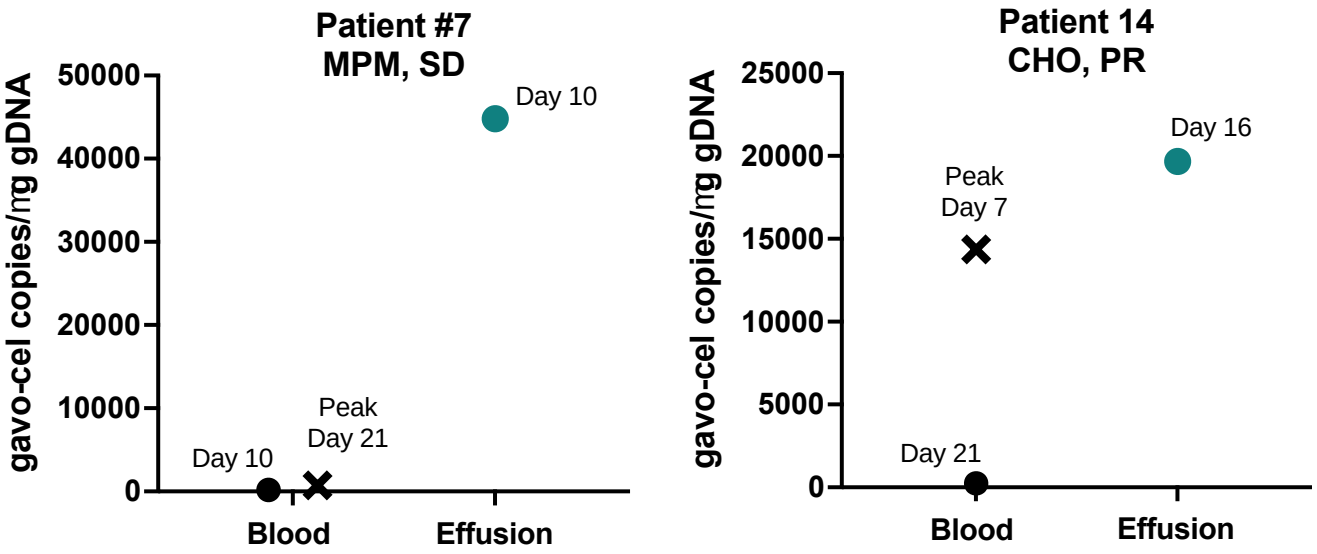
Peak IFN-γ



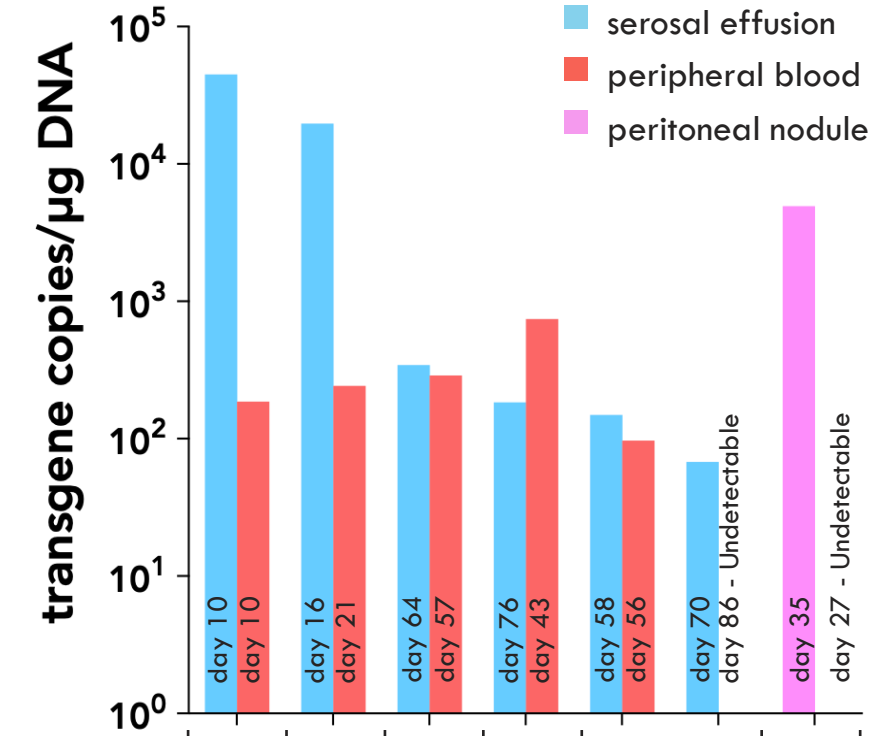
Data Cutoff – September 9, 2022

Intratumor Infiltration and Persistence Greater Than in Blood

TRuC-T Cell Migration and Infiltration Evident from Serous Effusions



Analysis performed in a subset of patients (n=6); all analyzable samples showed detectable levels of gavo-cel, but not all showed increased expansion at disease sites



	7	14	15	20	27	27	2
Diagnosis	MPM	CHO	MPM	MPM	Ovarian		MPM
Response	SD	PR*	PR	SD	SD		PR

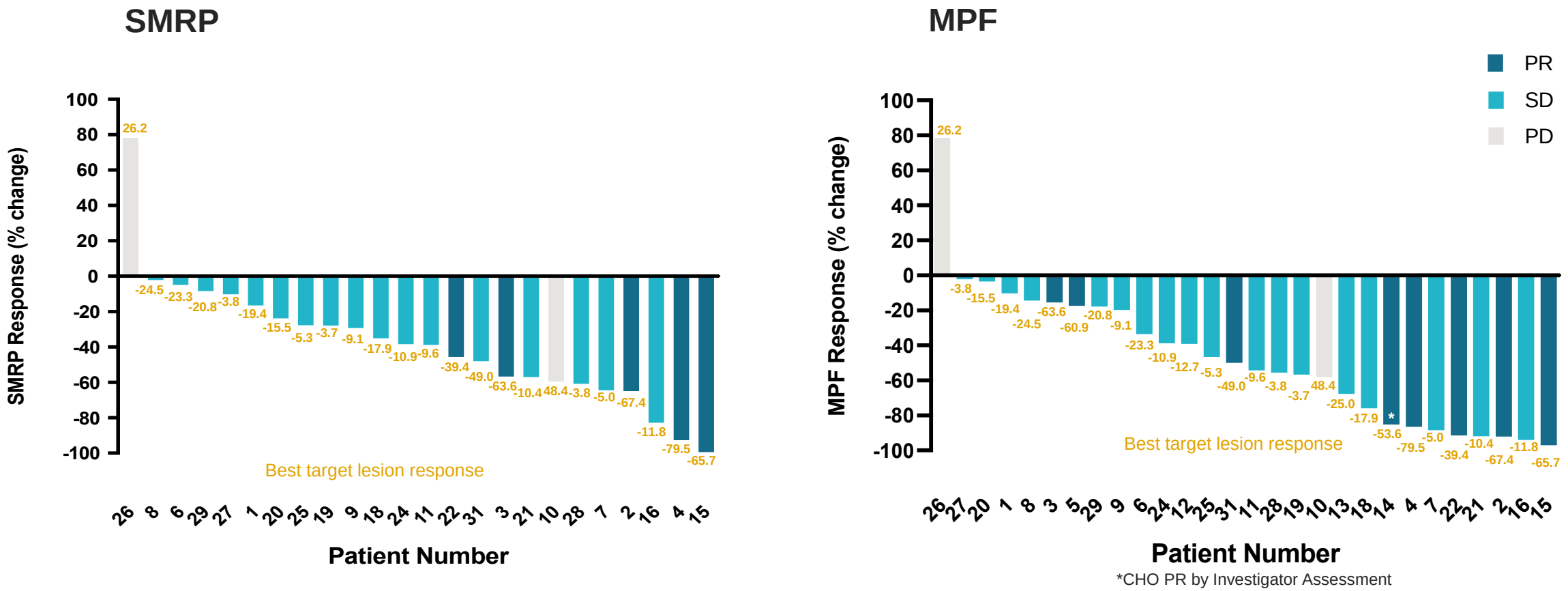
Data Cutoff – September 9, 2022

* PR by Investigator Assessment

MPM: Malignant Pleural/Peritoneal Mesothelioma; CHO: Cholangiocarcinoma; PR: Partial Response; SD: Stable Disease

TCR2 THERAPEUTICS

gavo-cel: SMRP and MPF Data vs. Best Target Lesion Response



*CHO PR by Investigator Assessment

Patients with baseline levels of SMRP in normal range were excluded

Data Cutoff – September 9, 2022

SMRP, Soluble Mesothelin-Related Peptides; MPF, Megakaryocyte Potentiating Factor; PR, Partial Response; SD, Stable Disease; PD, Progressive Disease; CHO, Cholangiocarcinoma

TCR2 THERAPEUTICS

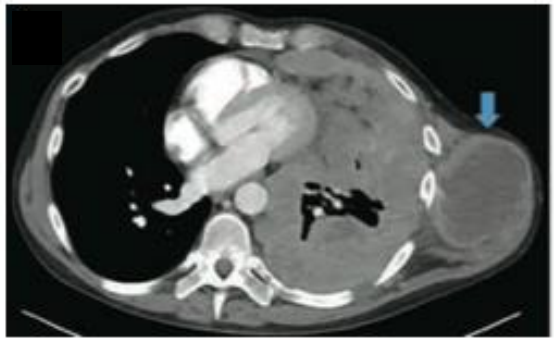
NIH NATIONAL CANCER INSTITUTE

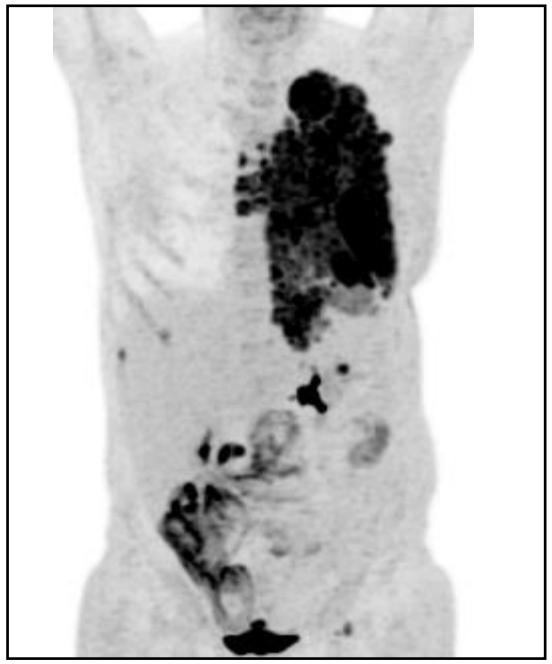
Thoracic and GI Malignancies Branch

Phase I Study of Gavo-cel to Treat Mesothelioma and other Mesothelin Expressing Solid Tumors

Raffit Hassan, M.D.

Malignant mesothelioma is an aggressive cancer with poor prognosis





- 3,000 new cases in US each year
- Many patients not candidates for surgery
- FDA approved therapies:

  Pemetrexed plus cisplatin, 2004

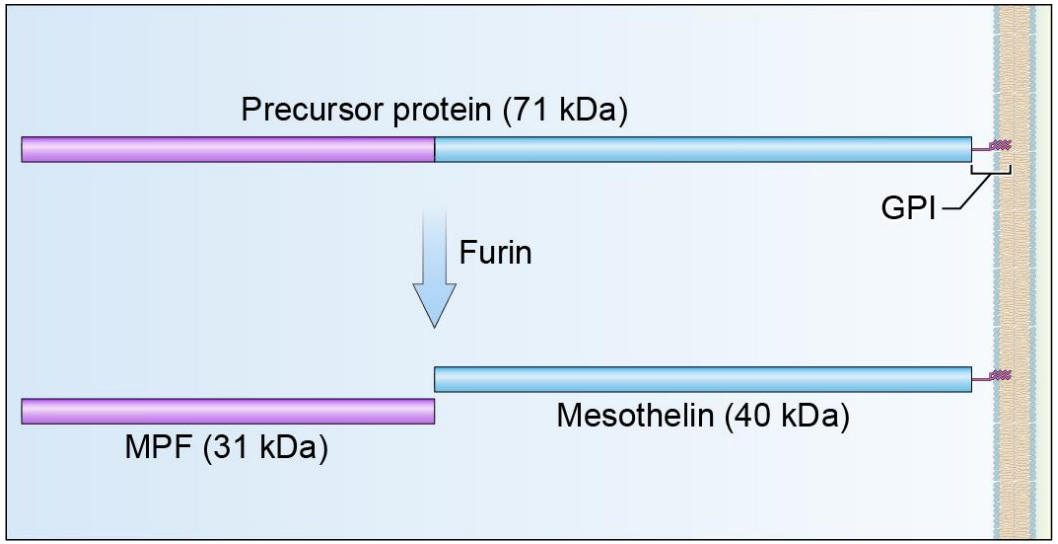
  Nivolumab plus Ipilimumab, 2020
- Median overall survival about 18 months

Kindler H,…Hassan R, *J Clin Oncol*., 2018
Vogelzang NJ et. al., *J Clin Oncol*., 2003
Baas P et. al., *Lancet*, 2021

Mesothelin Targeted Immunotherapy for Malignant Mesothelioma and other Solid Tumors

Mesothelin

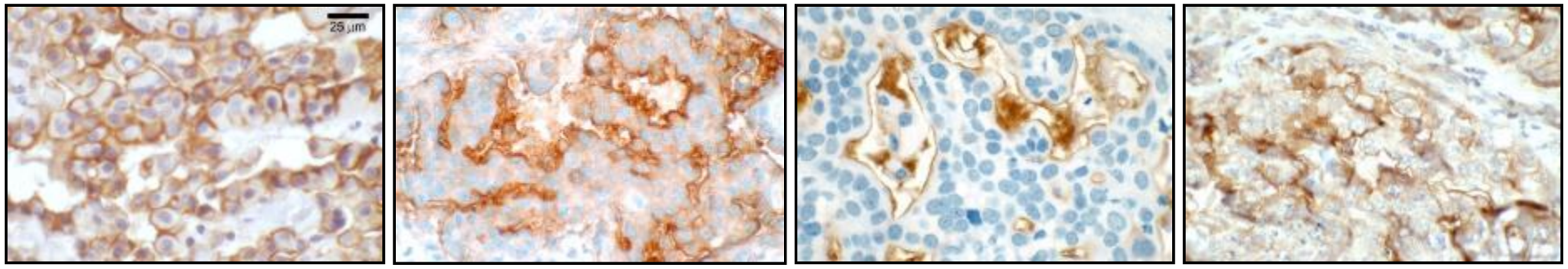
- Cell surface glycoprotein
- Expression in normal human tissues limited to mesothelial cells lining pleura, peritoneum and pericardium
- Mesothelin binds MUC16 and may play a role in tumor metastases



Chang K, Pastan I., PNAS 1996
Hassan R., Bera T., Pastan I. Clin. Cancer Res. 2004

Mesothelin is highly expressed in most solid tumors

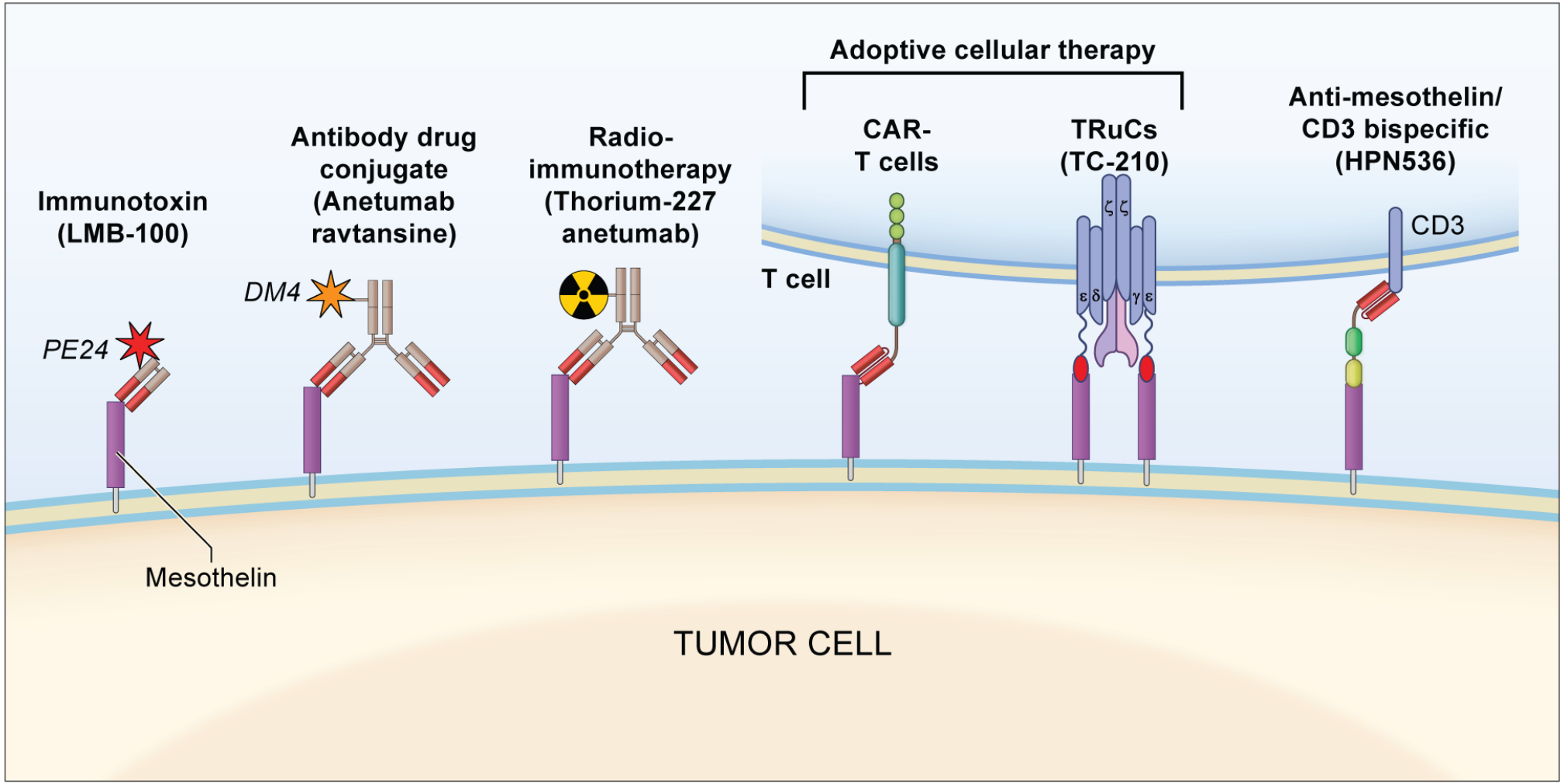
- **Mesothelioma (epithelial)** **~ 100%**
- **Pancreatic Cancer** **~ 80%**
- **Ovarian Cancer** **67-71%**
- **Lung adenocarcinoma** **41-53%**
- **Gastric cancer, colorectal cancers, TNBC, biliary cancers, thymic**



Mesothelioma **Ovarian Cancer** **Pancreatic Cancer** **Lung Cancer**

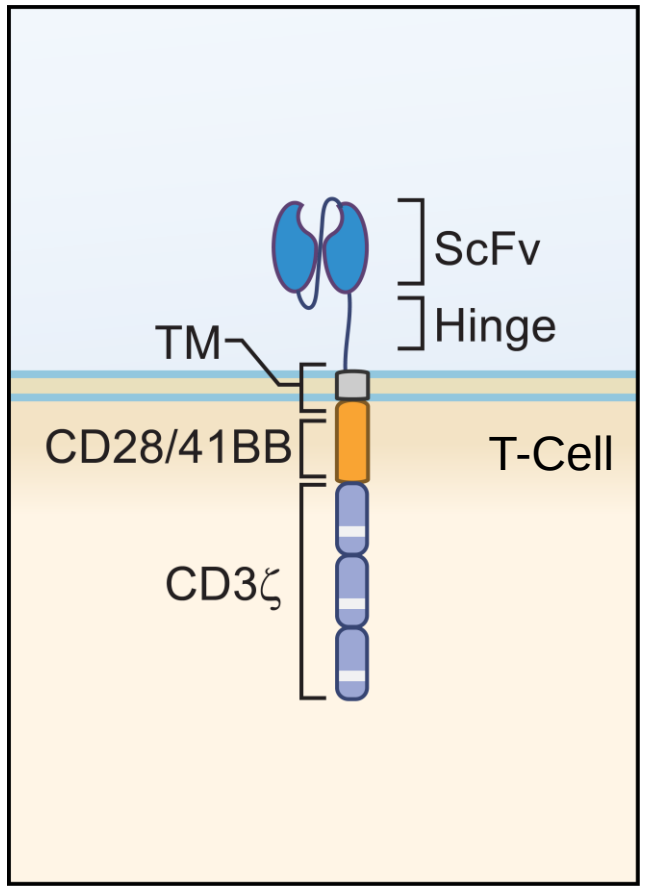
Hassan et al. Clin. Cancer Res., 2004
Ordonez NG. Am J Surg Pathol, 2003.
Ho M et al. Clin Cancer Res, 2007

Mesothelin targeted therapies evaluated in clinical trials



Hassan R et. al. *Journal of Clinical Oncology*, 2016

Chimeric Receptor Antigen (CAR)-T cell therapy for cancer



CAR-T cell

- **Very effective for hematologic cancers**
- **Limited efficacy in epithelial cancers**

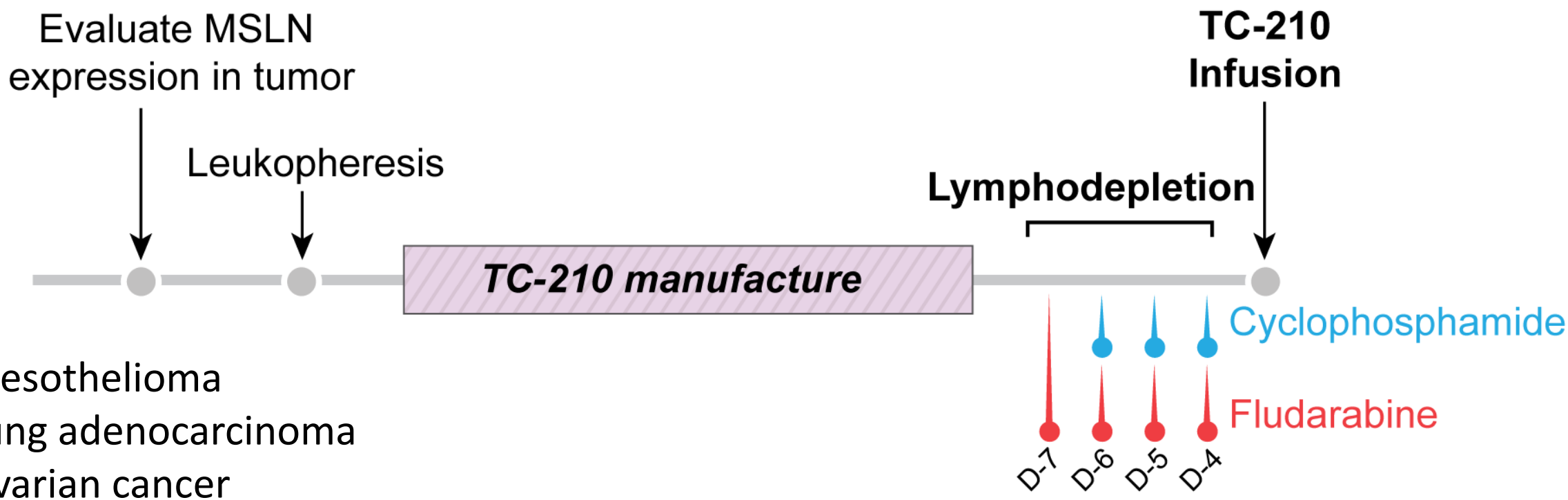
Anti-mesothelin CAR-T cells have limited activity in patients

CAR-T cell product	Description	Delivery route	Malignancies (N)	Partial/Complete Response
CART-Meso (mRNA)	Murine αMSLN, SS1 scFv fused to 41BB and CD3ζ signaling domains	multiple IV infusion	MPM (3) PDAC (1)	**1 out of 4** (Ref. 1 and 2)
CART-Meso (lentivirus)	Murine αMSLN, SS1 scFv fused to 41BB and CD3ζ signaling domains	single IV infusion, +/- Cytoxan	MPM (5), ovarian cancer (5) and PDAC (5)	**0 out of 15** (Ref. 3)
huCART-meso (lentivirus)	Humanized M5 scFv from human phage library, fused to 41BB and CD3ζ	multiple IV infusion with LD	MPM, lung, ovarian and pancreatic cancers	**0 out of 17** (Ref. 4)
M28z Anti-mesothelin CAR-T (retrovirus)	Anti-MSLN scFv, m912, fused to CD28 and CD3ζ signaling domain	Intra-pleural administration with LD	MPM (23)	**0 out of 23** (Ref. 5)
MPTK-CAR-T (lentivirus)	Anti-MSLN CAR, PD1 and TCR deficient	multiple IV infusion w/out LD	Mesothelin expressing cancer (15)	**0 out of 15** (Ref. 6)

LD, lymphodepletion; MPM, malignant pleural mesothelioma

[1]Maus et al., 2013, Cancer Immunol. Res.; [2]Beatty et al., 2014, Cancer Immunol. Res.; [3]Hass et al., 2019, Mol. Therapy.;
[4]www.med.upenn.edu/cellicon2021/assets/user-content/documents/tanyi.pdf; [5]Adusumilli et al., 2021, Cancer Discovery; [6]Wang et al., 2021, Cell Mol. Immunol.

Phase I study of gavo-cel (TC-210)



Mesothelioma
Lung adenocarcinoma
Ovarian cancer
Cholangiocarcinoma

Gavo-cel: Tumor response by blinded independent radiologic review

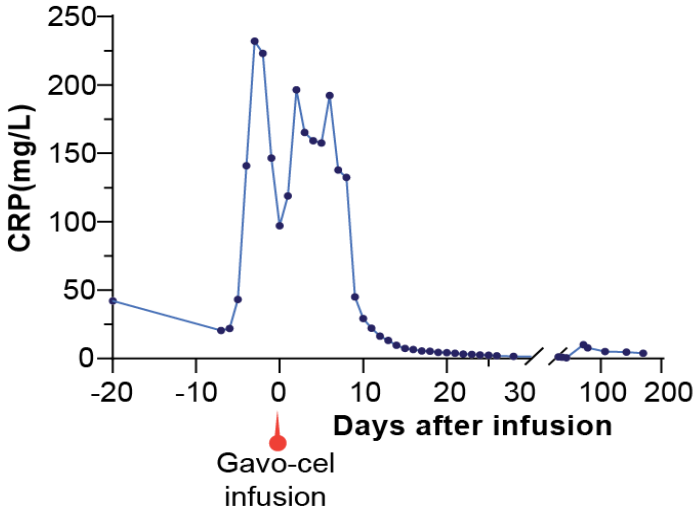
	All	gavo-cel + LD
ORR	20%	22%
MPM ORR	18%	21%
Ovarian ORR	29%	29%

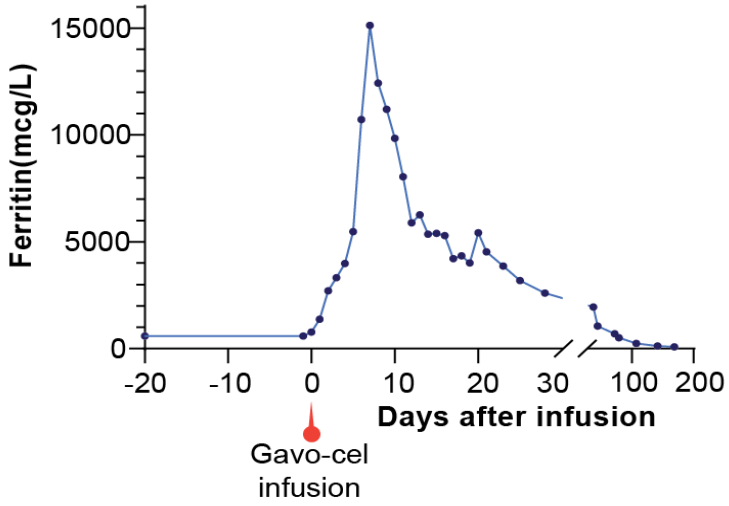
LD, lymphodepletion; MPM, malignant mesothelioma; ORR, overall response rate

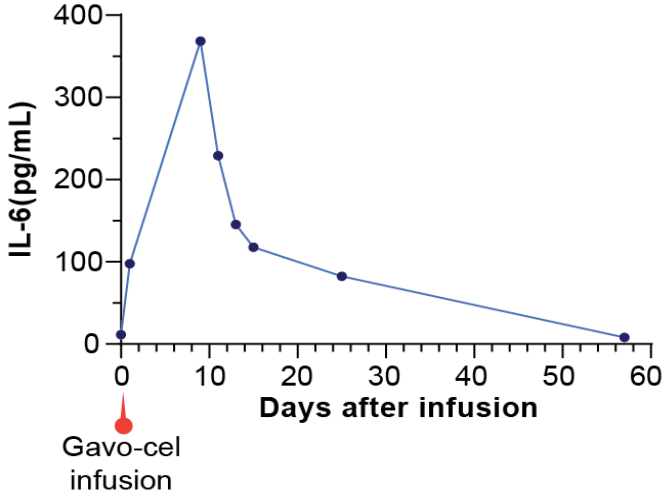
Patient 15: 67 year old female with metastatic pleural mesothelioma

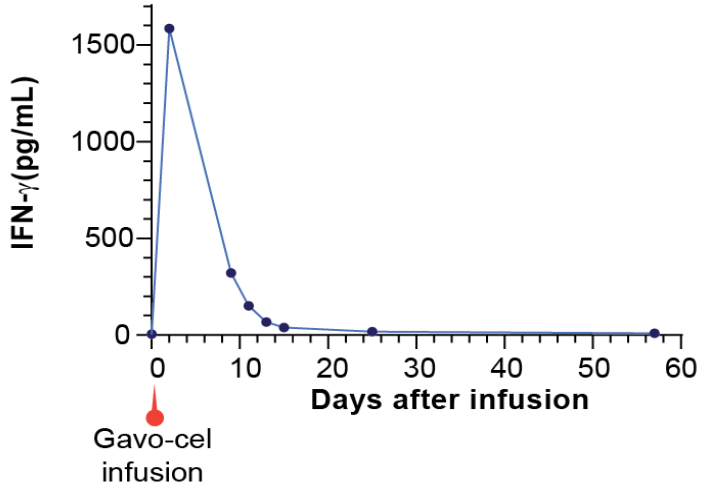
June 2018:	**Diagnosed with unresectable disease**
August to October 2019:	**Carboplatin/Pemetrexed/bevacizumab x 5 cycles with SD**
December 2019 to June 2020:	**Maintenance bevacizumab with disease progression**
June to September 2020:	**Nivolumab plus Ipilimumab x 2 cycles with disease progression**
November 2020:	**Treated on clinical trial of another mesothelin targeted agent but developed anti-drug antibodies**
February 2021:	**Disease progression and enrolled on this study**
April 2021:	**Infused with gavo-cel**

Administration of gavo-cel led to CRS managed by tocilizumab and steroids

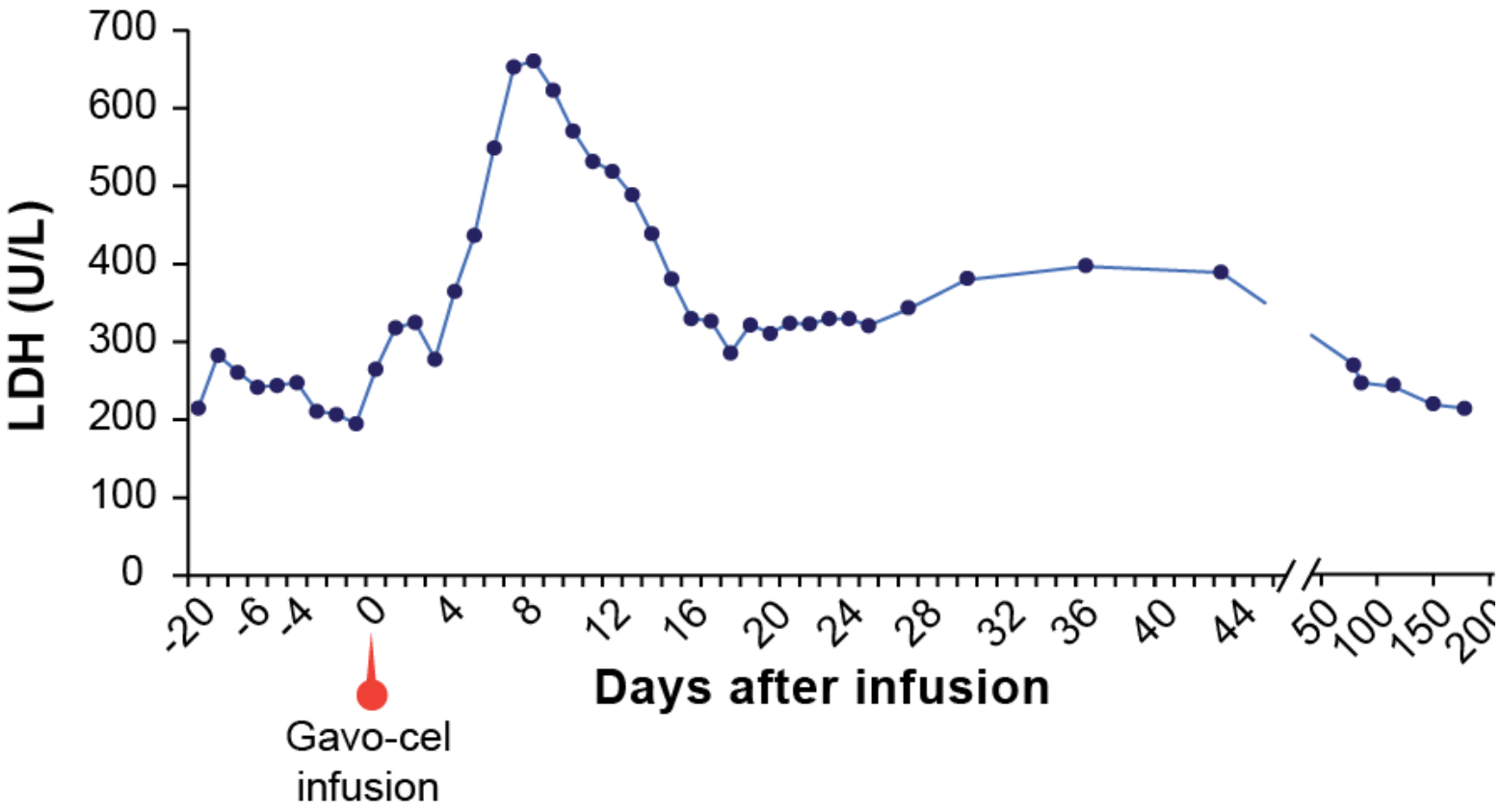




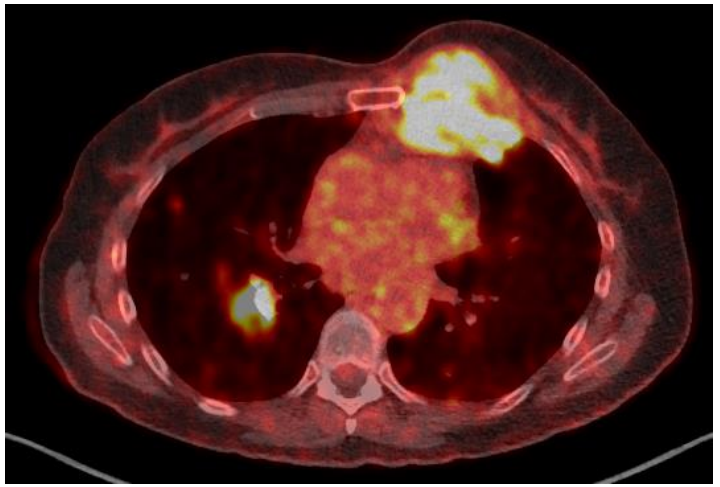


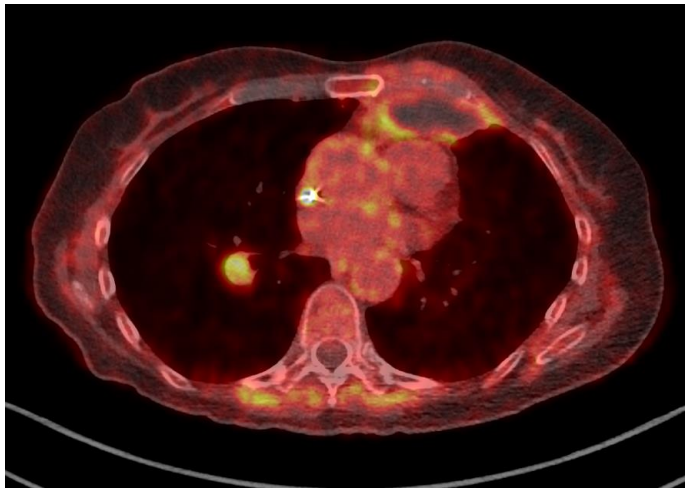


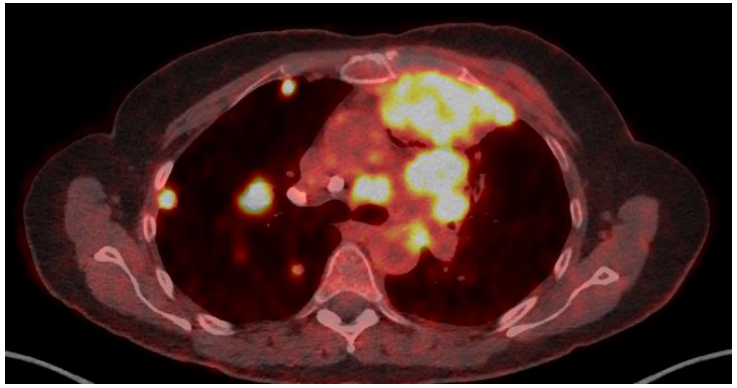
Rapid increase in serum LDH after gavo-cel infusion

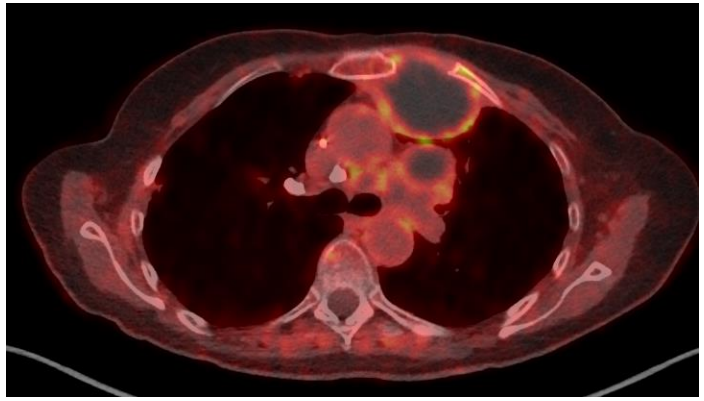


Treatment response with single infusion of gavo-cel







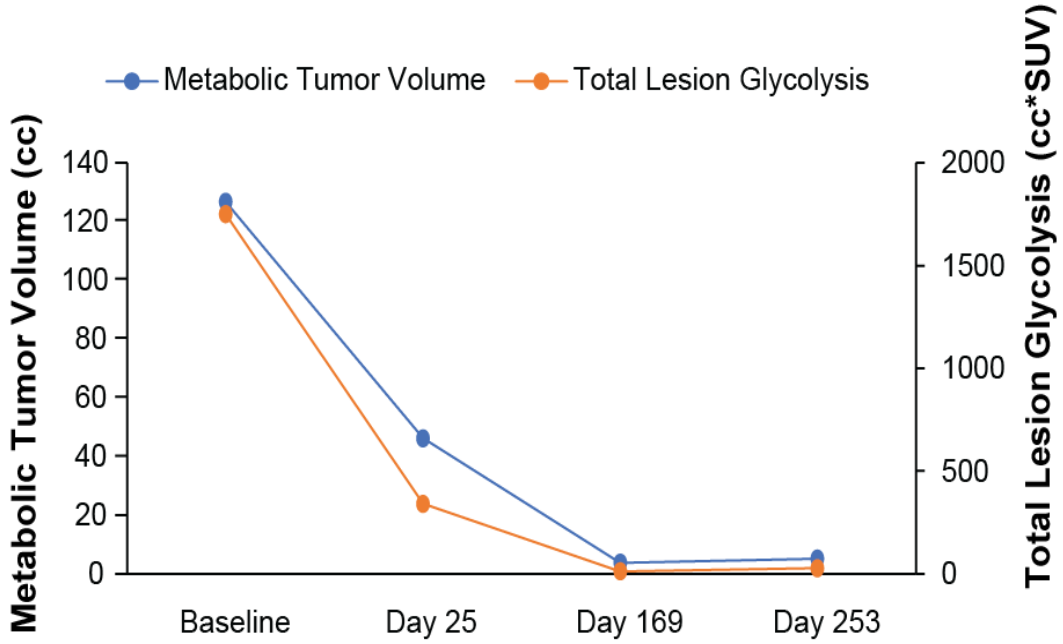


Baseline

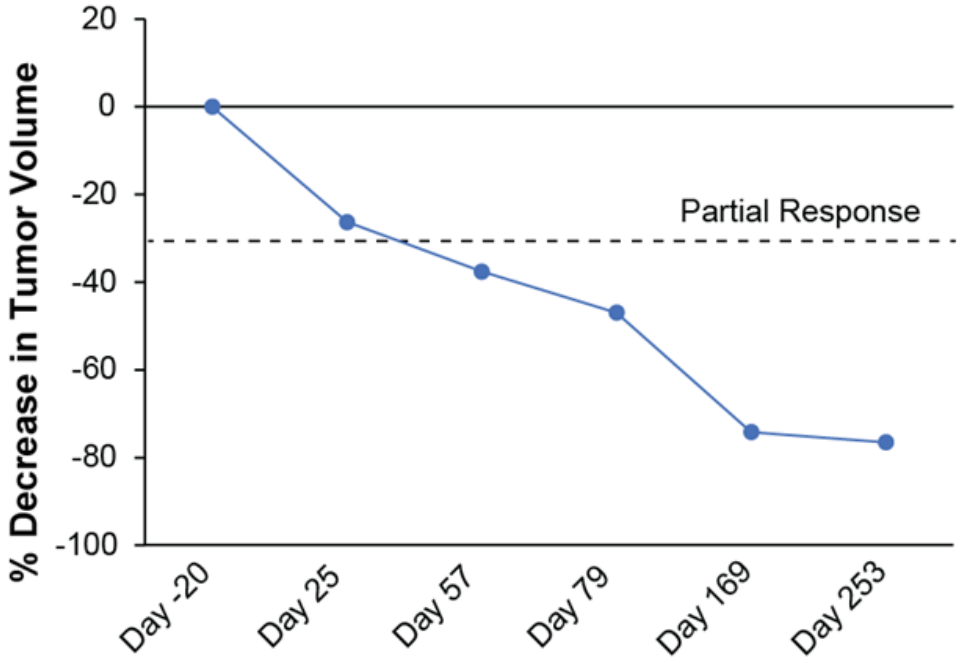
Day 28

Durable metabolic and tumor response after single infusion of gavo-cel

Metabolic tumor volume and total lesion glycolysis

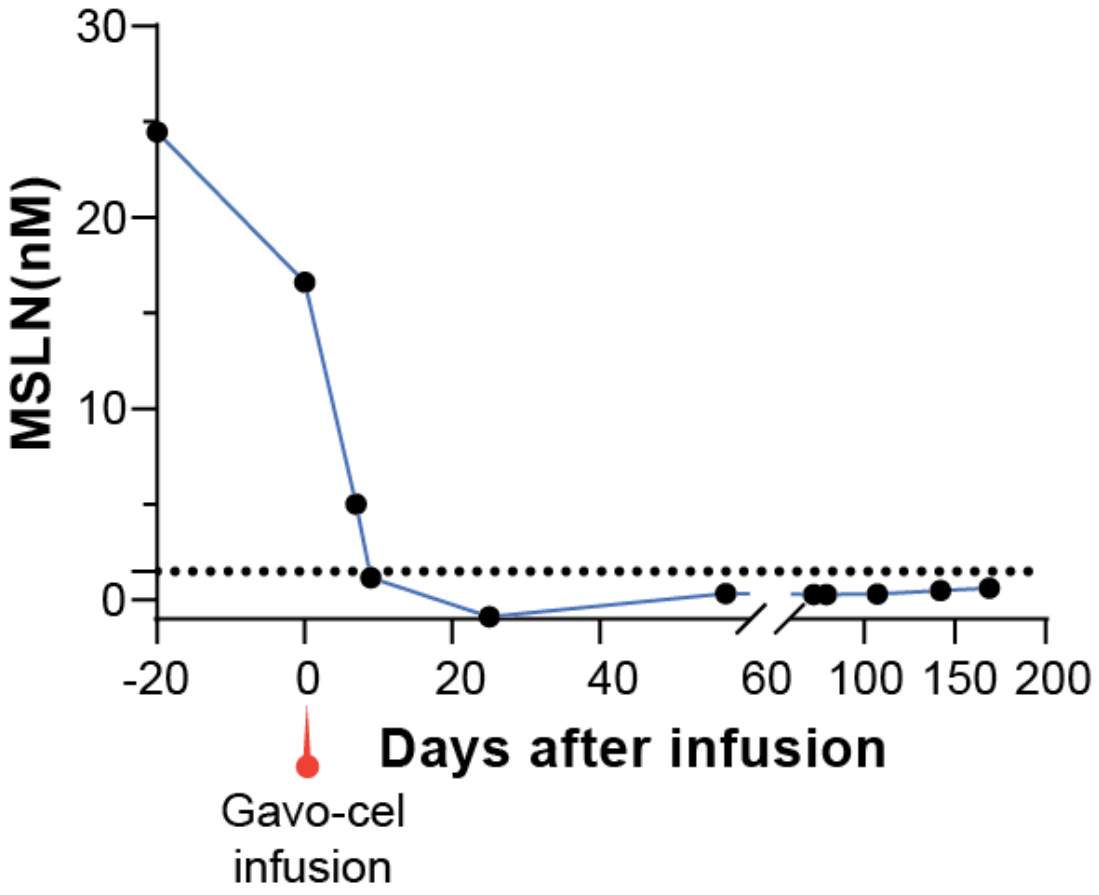


Change in tumor volume

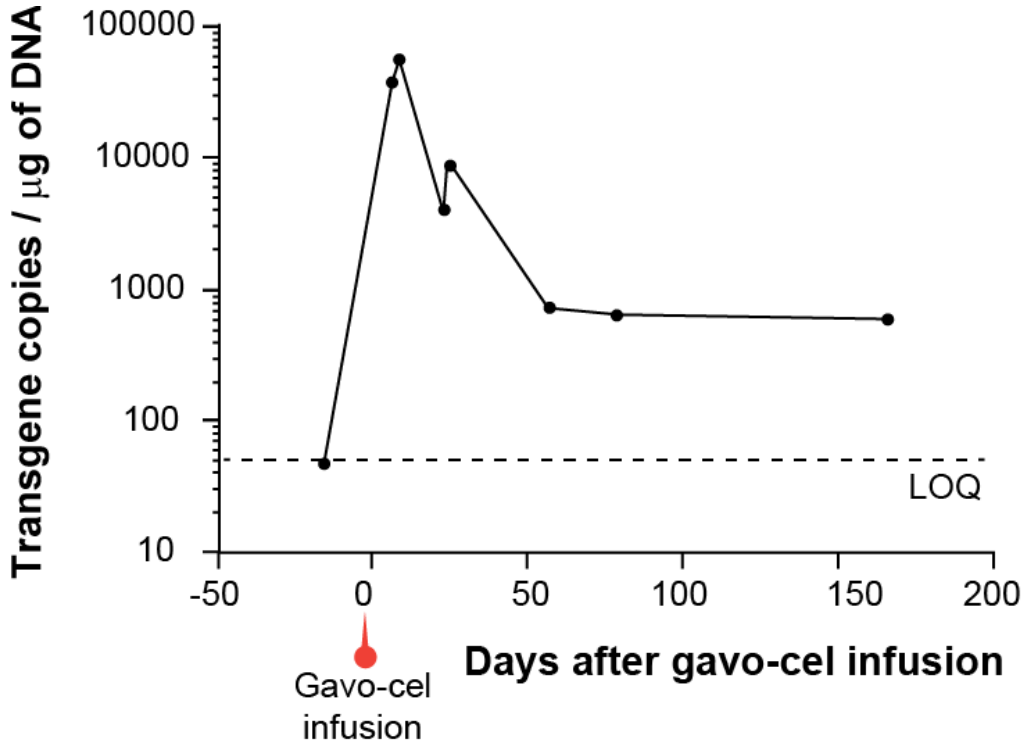


Response duration: 12 months

Rapid drop in serum mesothelin after gavo-cel



Persistence of gavo-cel in peripheral blood



Phase I Gavo-cel: summary

- Phase I dose-escalation completed, RP2D defined
- Cytokine release syndrome is common but manageable
- Objective tumor responses seen in heavily pre-treated patients
- Randomized phase II study in mesothelioma with and without immune checkpoint blockade has been initiated

Systemic Therapy for Mesothelioma

Patrick Forde MB BCh
Director, Thoracic Oncology Clinical Research Program
Co-Director, Division of Upper Aerodigestive Malignancies
Johns Hopkins University

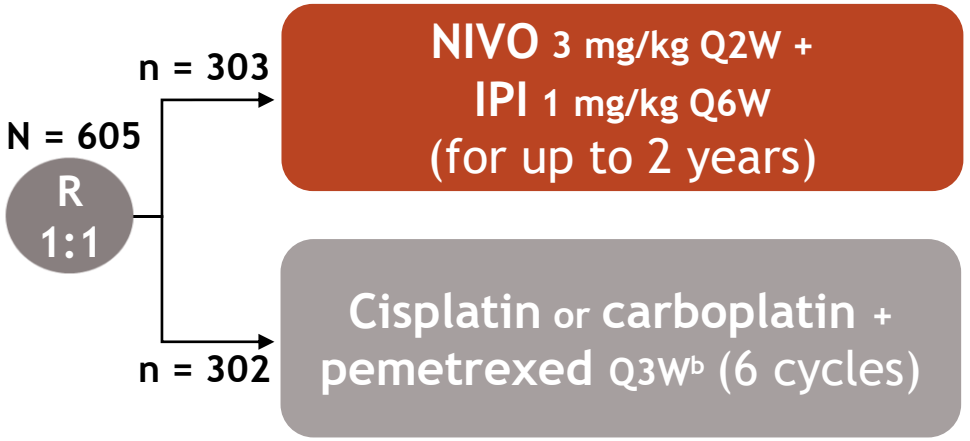
Recent studies in unresectable mesothelioma

- 1st line Standard of Care: CheckMate 743
- 2nd line studies: RAMES, Promise-Meso, CONFIRM

CheckMate 743 Study Design

Key Eligibility Criteria
- Unresectable pleural mesothelioma
- No prior systemic therapy
- ECOG performance status 0–1

Stratified by:
histology (epithelioid vs non-epithelioid) and gender

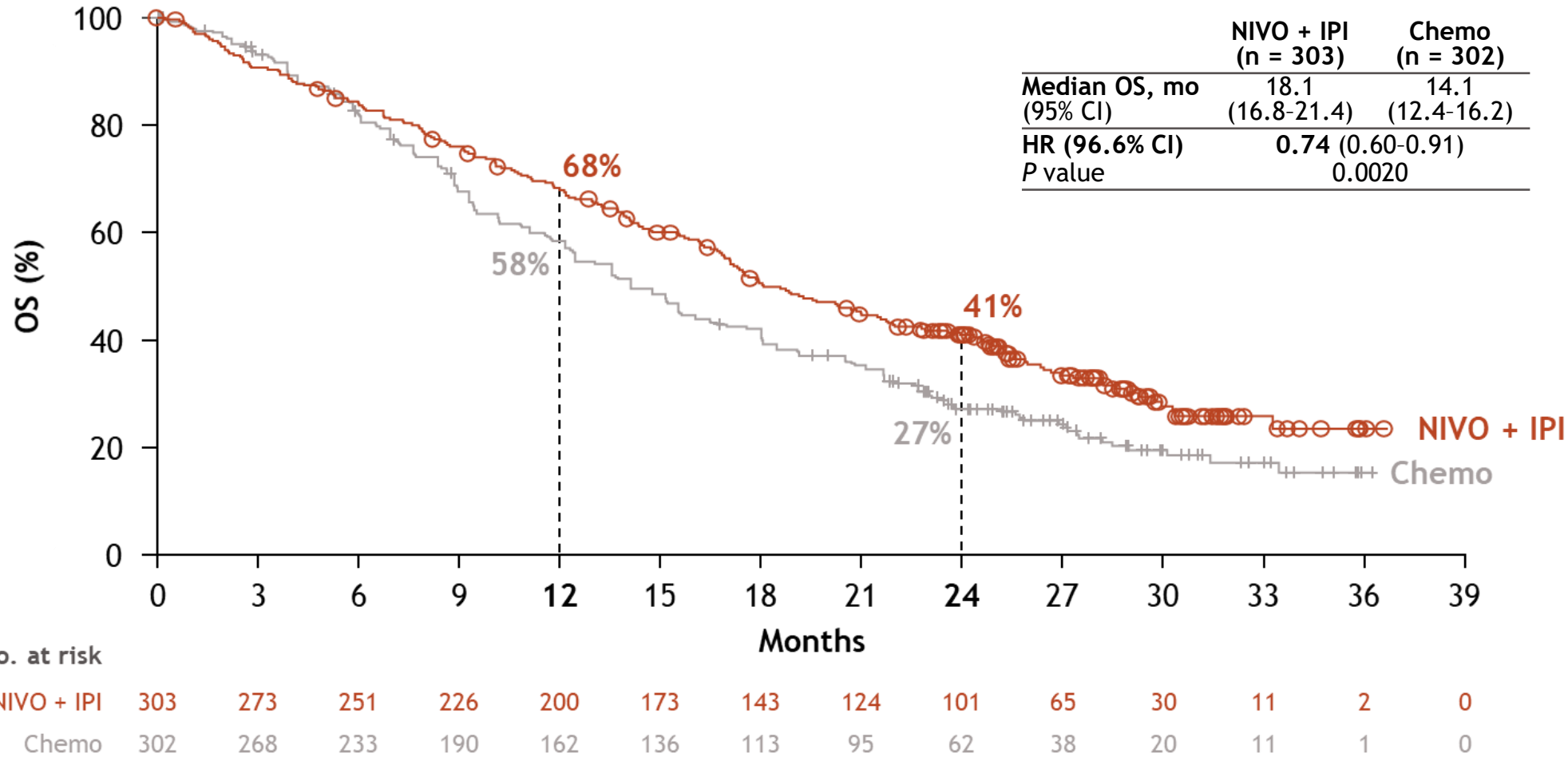


Until disease progression, unacceptable toxicity *or* for 2 years for immunotherapy arm

Primary Endpoint
- OS

Secondary Endpoints
- ORR, DCR, and PFS by BICR
- PD-L1[c] expression as a predictive biomarker

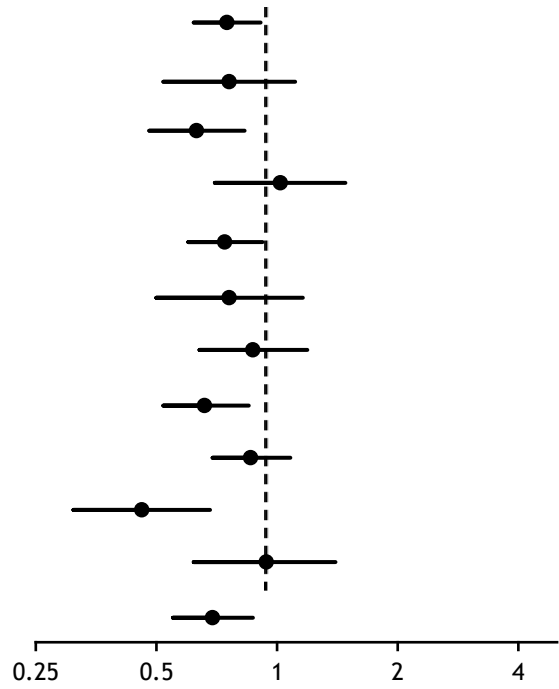
Overall survival CM-743



	NIVO + IPI (n = 303)	Chemo (n = 302)
Median OS, mo (95% CI)	18.1 (16.8-21.4)	14.1 (12.4-16.2)
HR (96.6% CI)	**0.74** (0.60-0.91)	
P value	0.0020	

OS by Subgroup in CM-743

Subgroup	Median OS, mo		Unstratified HR	Unstratified HR (95% CI)
	NIVO + IPI n = 303	Chemo n = 302		
All randomized (N = 605)	18.1	14.1	0.75[a]	
< 65 years (n = 167)	17.2	13.3	0.76	
≥ 65 to < 75 years (n = 281)	20.3	14.9	0.63	
≥ 75 years (n = 157)	16.9	15.4	1.02	
Male (n = 467)	**17.5**	**13.7**	**0.74**	
Female (n = 138)	**21.4**	**18.0**	**0.76**	
ECOG performance status 0 (n = 242)	20.7	19.5	0.87	
ECOG performance status ≥ 1 (n = 363)	17.0	11.6	0.66	
Epithelioid (n = 456)	**18.7**	**16.5**	**0.86**	
Non-epithelioid (n = 149)	**18.1**	**8.8**	**0.46**	
PD-L1 < 1% (n = 135)	17.3	16.5	0.94	
PD-L1 ≥ 1% (n = 451)	18.0	13.3	0.69	



Summary of ongoing phase 3 chemo-IO studies for 1st line unresectable mesothelioma

Study	Phase	N	Regimen(s)	Primary Endpoint(s)	Geographic Locations
DREAM3R/PrE0506 (ALTG/PrECOG)	3	480	Cis-pem-durva vs. Cis-pem	OS	USA/Aus/NZ
NCT02784171 (CCTG)	2/3	390 (Ph 3)	Cis-pem-pembro vs. Cis-pem	OS (Ph 3)	Canada & Europe/UK
BEAT-meso (ETOP)	3	320	Carbo-pem-bev-atezo vs. carbo-pem-bev	PFS/OS	Europe/UK

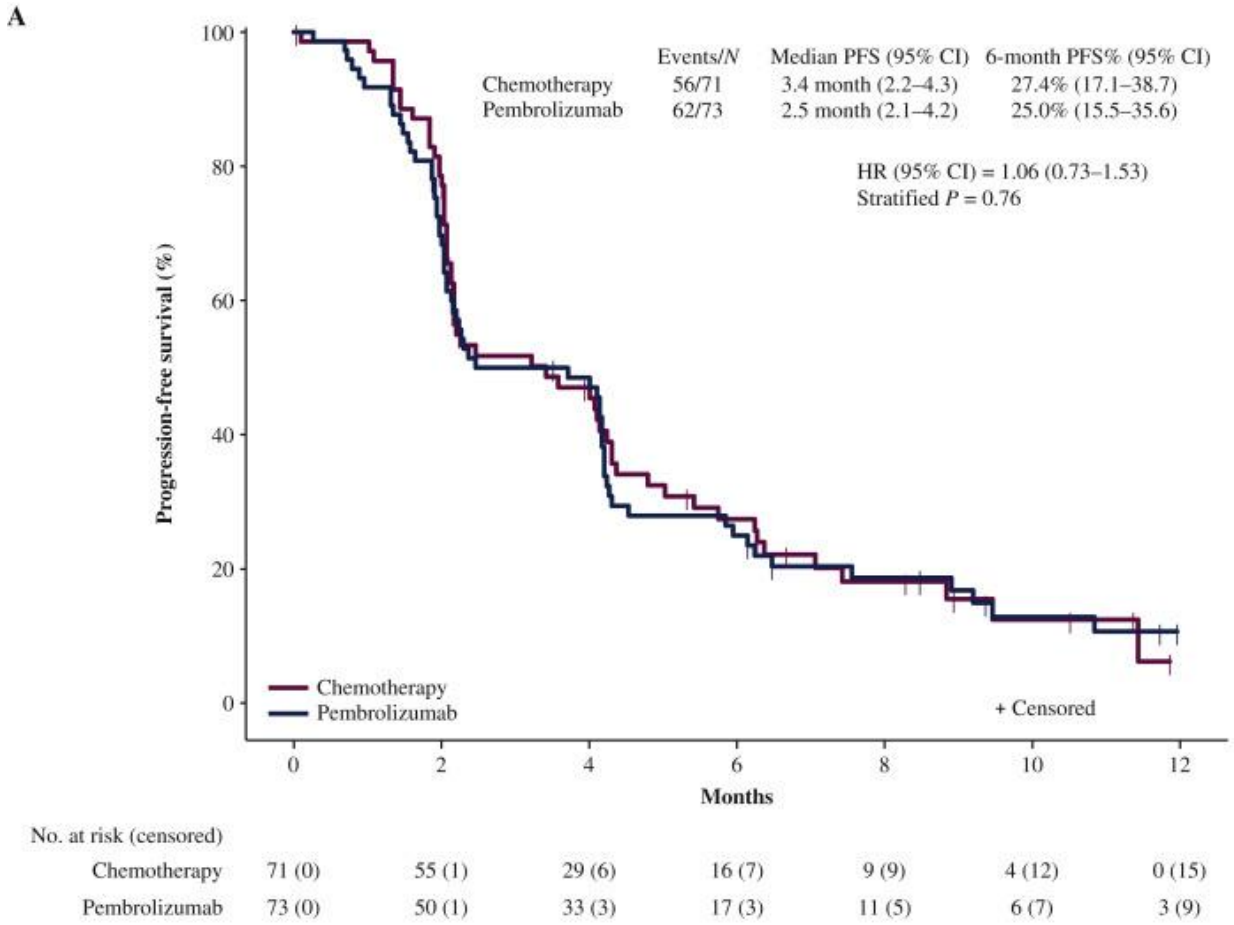
Anti-PD-(L)1 in pretreated MPM

JOHNS HOPKINS MEDICINE

Target (s)	Drug(s) (reference)	NCT	Population	N (pts)	ORR (%)	DCR (%)	PFS (months)	OS (months)	PD-L1 IHC status
PD-1	**Pembrolizumab (KEYNOTE-028) (43)**	02054806	Second line	25	20	72	5.4	18	All patients were PD-L1 IHC positive
PD-1	**Pembrolizumab (48)**	02399371	Second line	35	21	77	6.2	NR (not reached)	Did not correlate to response
PD-1	**Nivolumab (NivoMES trial) (47)**	02497508	Beyond first line	33	24	50	3.6	NR	Trend for correlation with OR
PD-L1	**Avelumab (JAVELIN) (46)**	01772004	Salvage, any line	53	9.4	57	4.3	NR	Trend to correlate with median PFS
PD-1 ± CTLA-4	**Nivolumab + Ipilimumab vs Nivo alone (MAPS-2) (44-45)**	02716272	Second/ third line	125 (62 vs 63)	25.9 vs 18.5	50 vs 44.1	5.6 vs 4	15.9 vs 11.9	Correlation with OR (p=0.003 if ≥1%)

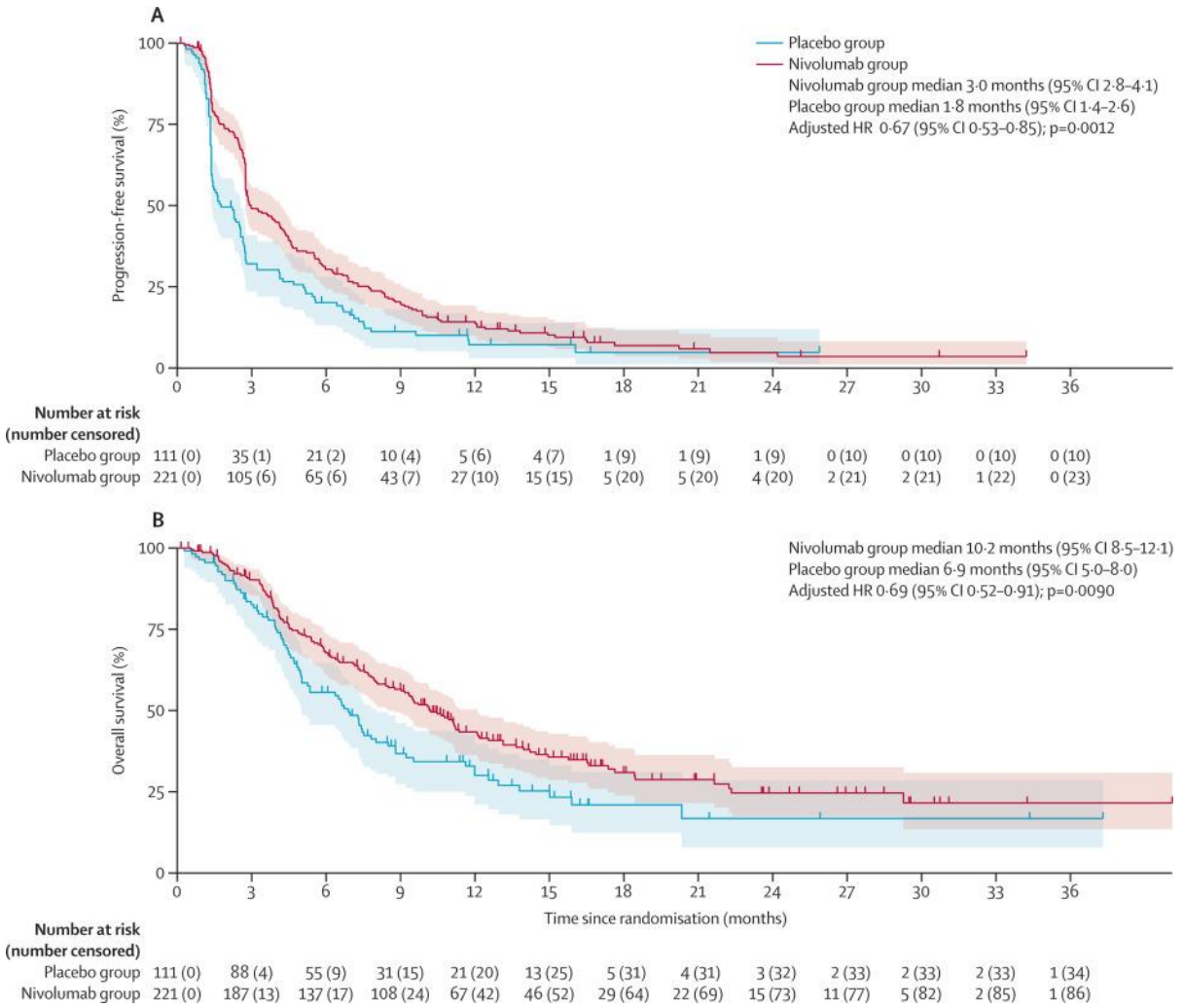
(unfulfilled) PROMISE-MESO

- Randomized phase 2 study, enrolled 143 patients pretreated with platinum pemetrexed, randomized 1:1 to either pembrolizumab or investigators choice of single agent chemotherapy
- ORR increased from 6% (chemo) to 22% (pembro)
- Primary endpoint: PFS no difference
- Also no OS difference between the two arms



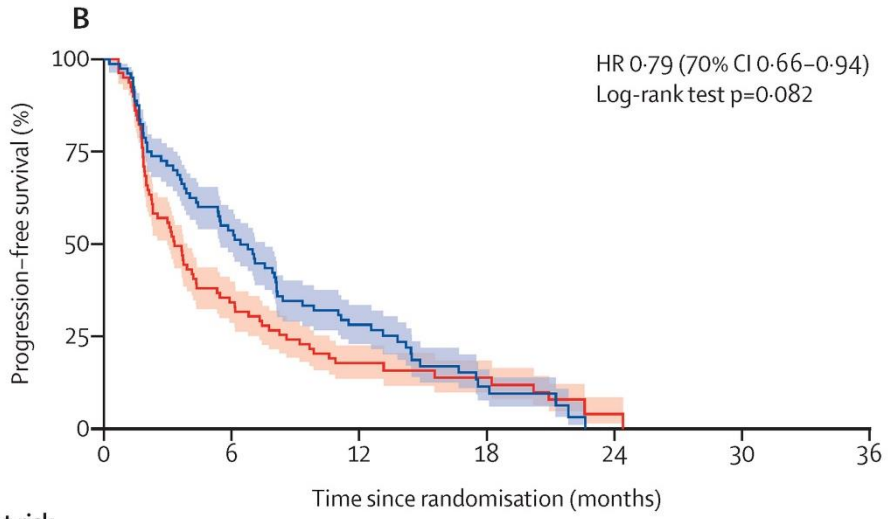
CONFIRM – Phase 3 trial of nivo vs. placebo in mesothelioma after chemo

- 332 pts randomized to either nivo or placebo for 1 yr; 87% epithelioid; 96% 3rd line or later
- Co-primary endpoints: PFS and OS
- PFS significantly improved with nivo (3.0m vs. 1.8m, HR 0.62, p<0.001)
- OS improved (9.2m vs. 6.6m, HR 0.72, p=0.02)



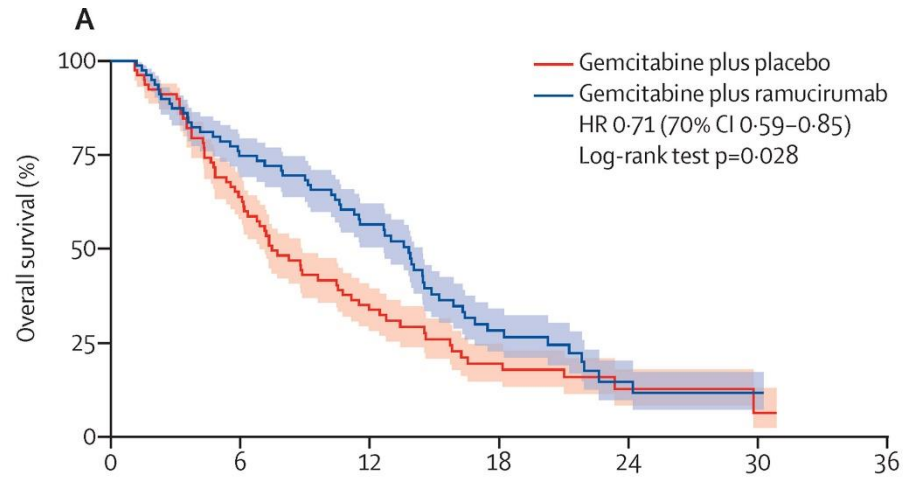
RAMES Trial - Gemcitabine with or without ramucirumab as second-line treatment for malignant pleural mesothelioma

Median PFS – 6.4m



Number at risk (number censored)							
Gemcitabine plus placebo	81 (0)	27 (2)	13 (3)	7 (7)	1 (9)	0 (9)	0 (9)
Gemcitabine plus ramucirumab	80 (0)	42 (1)	21 (2)	6 (7)	0 (9)	0 (9)	0 (9)

Median OS – 13.8m



Number at risk (number censored)							
Gemcitabine plus placebo	81 (0)	49 (4)	25 (5)	12 (9)	4 (14)	1 (16)	0 (17)
Gemcitabine plus ramucirumab	80 (0)	58 (2)	41 (5)	16 (12)	5 (17)	1 (20)	0 (21)

2nd and Subsequent Line Options in NCCN

- Either of the following as single agent – vinorelbine, gemcitabine
- ORR 7-18%, median OS (mainly 2nd line pts) - 4.7-11.2m

Systemic therapy for mesothelioma

- Nivolumab improves PFS & OS in chemo-pretreated mesothelioma
- First line Nivo-Ipi is FDA-approved – doubling of survival for non-epithelioid MPM; benefit less clear for epithelioid
- No approved agent after prior Nivo-Ipi & Platinum Pemetrexed

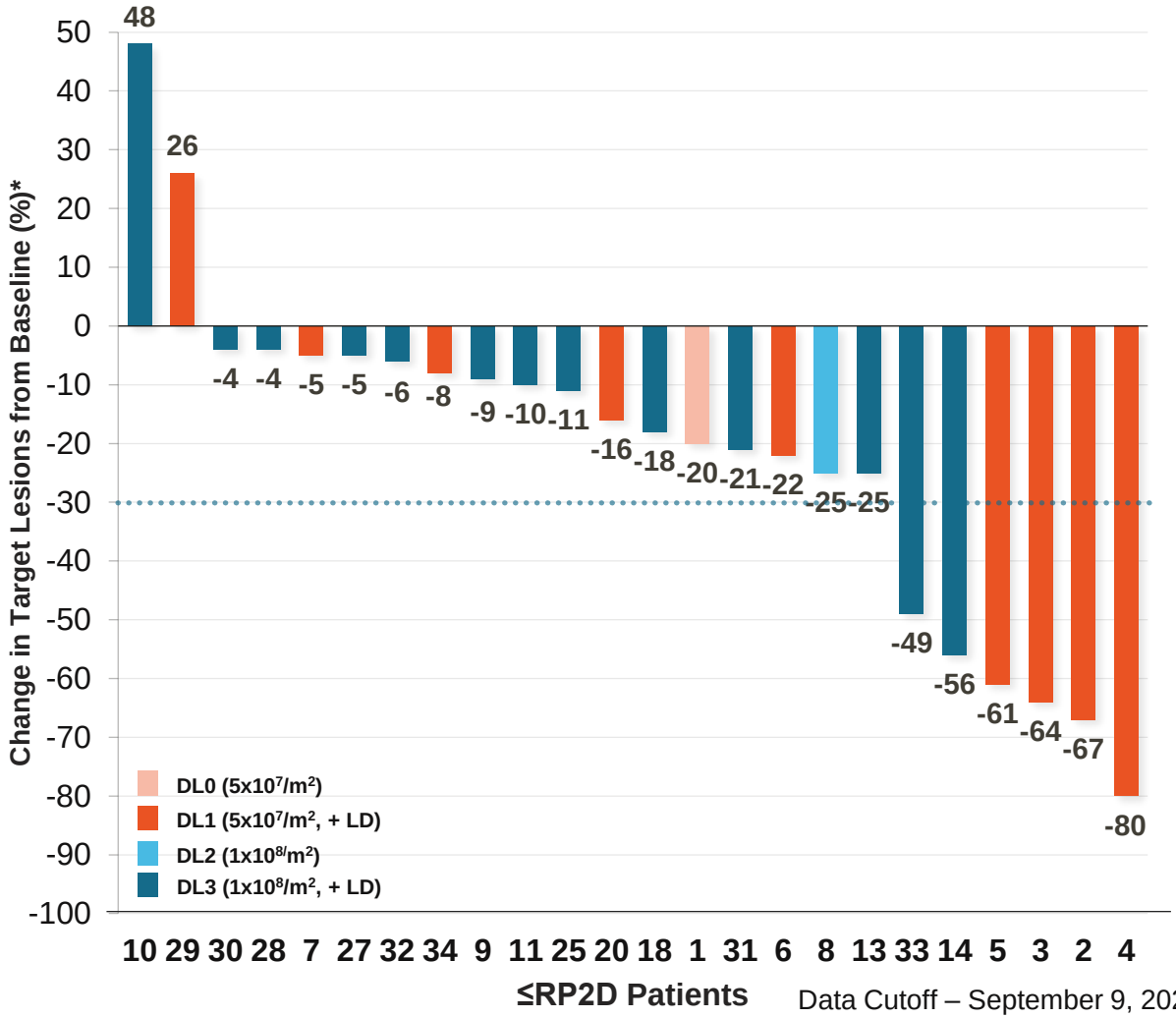
Phase 2 Trial

Trial Modifications & Design

TCR2 THERAPEUTICS

Clinical Activity At or Below gavo-cel RP2D

- Manageable safety profile
- Clinical activity at ≤RP2D in 3/3 tumor indications
- 5 RECIST PRs
- Multiple patients near 30% tumor regression



Data Cutoff – September 9, 2022

* Tumor volume decrease based on best response assessed

DL, Dose Level; LD, Lymphodepletion; RP2D, Recommended Phase 2 Dose; PR, Partial Response

TCR2 THERAPEUTICS

Phase 2 Incorporates Four Changes Aiming to Boost Patient Outcomes

Broadening Patient Access

1 Increased Patient Eligibility with New MSLN Threshold for NSCLC and Cholangiocarcinoma

Durability and Persistence

2 Redosing (LD + gavo-cel)

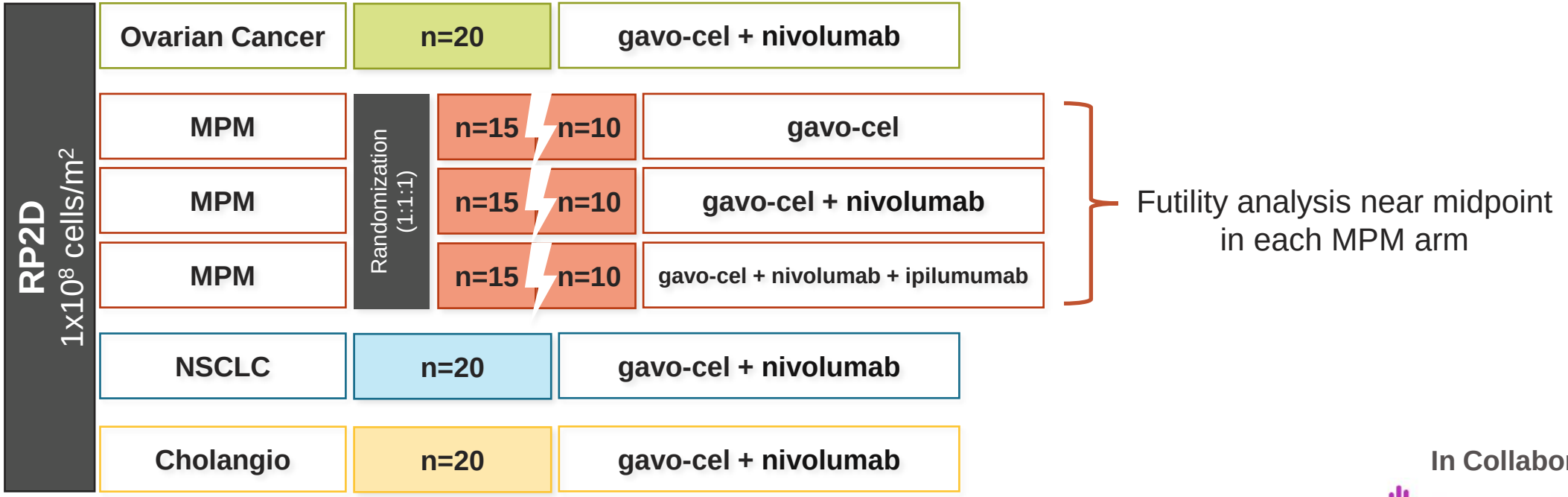
3 Checkpoint Inhibitor Combinations

4 Limit Prior Lines of Therapy ≤5

MSLN, Mesothelin, NSCLC, Non-Small Cell Lung Cancer; LD, Lymphodepletion

Phase 2 Expansion Cohorts in MSLN+ Solid Tumors

PATIENT POPULATION: ≤5 PRIOR LINES OF THERAPY



In Collaboration with Bristol Myers Squibb™

Key Objectives

- Primary: ORR (RECIST v1.1), DCR (ORR+SD)
- Secondary: PFS, OS

Mesothelin Expression

- MPM, Ovarian: ≥50%, 2+/3+
- NSCLC, Cholangio: ≥50%, 1+/2+/3+

Retreatment

- Patient with a confirmed response (i.e. PR or CR) and then exhibits symptoms or signs of PD
- Patients with SD for at least 8 weeks

LD, Lymphodepletion; CPI, Checkpoint Inhibitor; RP2D, Recommended Phase 2 dose; MPM, Malignant Pleural/Peritoneal Mesothelioma; NSCLC, Non-Small Cell Lung Cancer; Cholangio, Cholangiocarcinoma

TCR2 THERAPEUTICS

Increase in Patient Eligibility with New MSLN Threshold

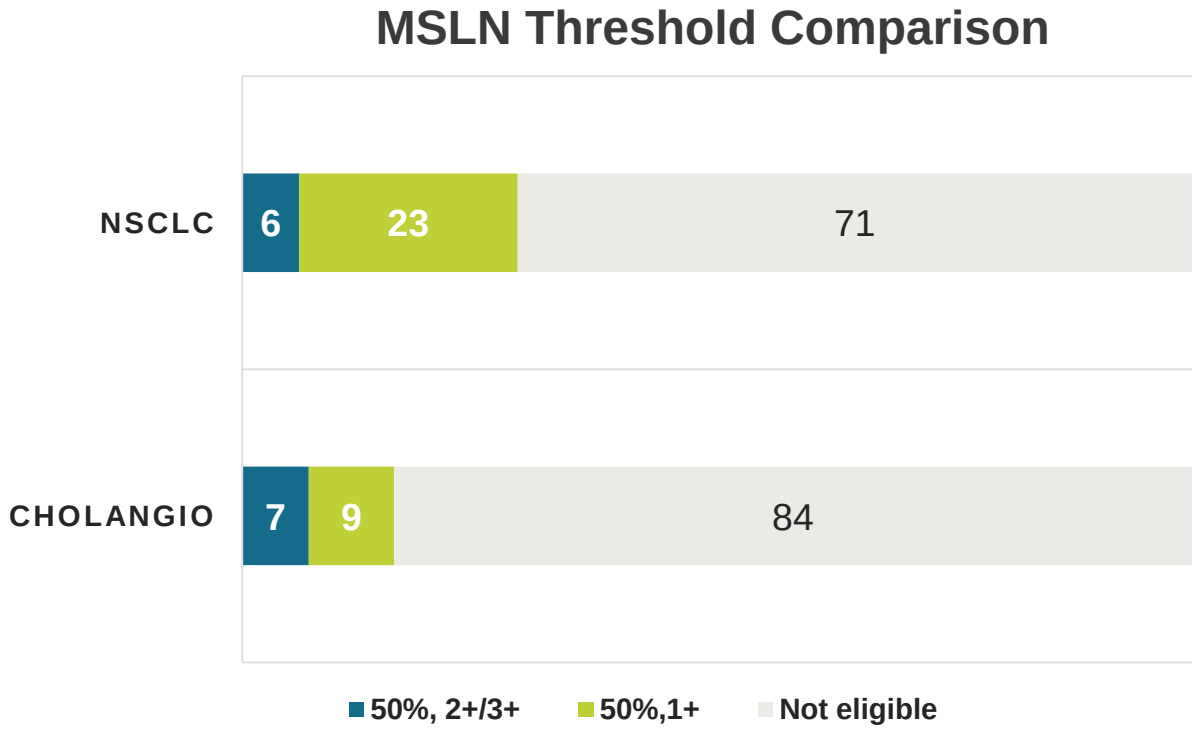
New Threshold:
≥50% tumor cells irrespective of MSLN intensity (1+/2+/3+)

Non-Small Cell Lung Cancer

29% patients eligible for therapy based on Phase 2 threshold

Cholangiocarcinoma

16% patients eligible for therapy based on Phase 2 threshold



Data based on internal analysis in September 2022

MSLN, Mesothelin

TCR2 THERAPEUTICS

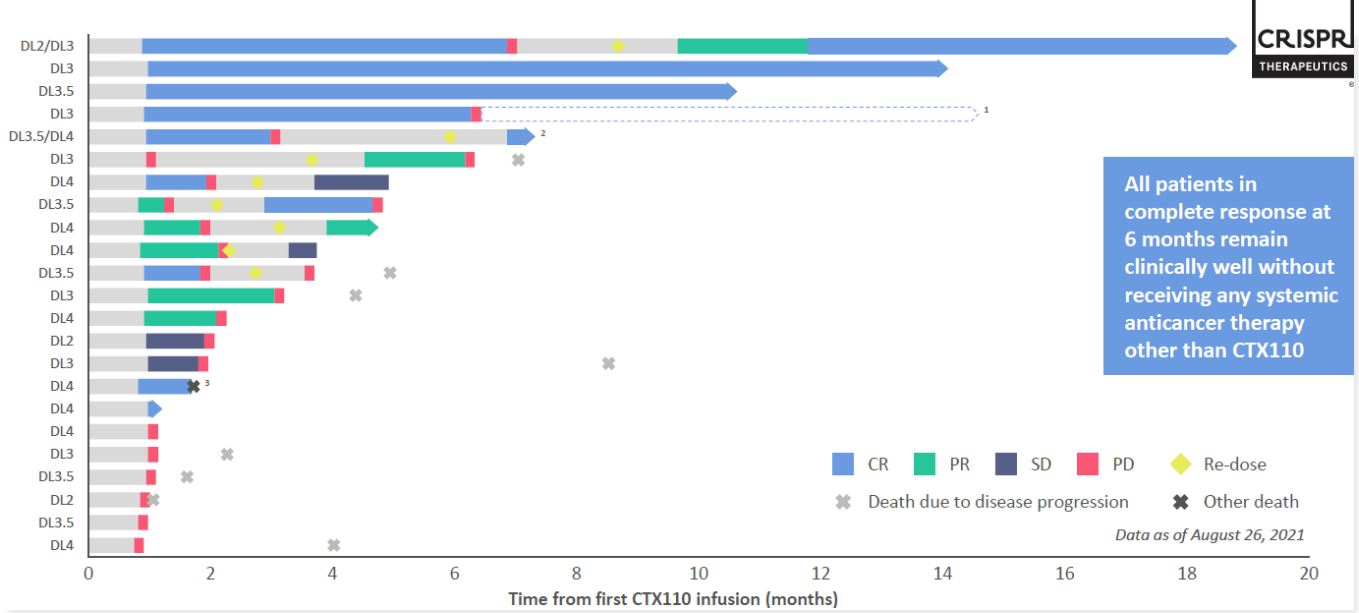
Redosing Allowed from 12 Weeks, Could Deepen Patient Responses

Based on gavo-cel Phase 1 manufacturing experience:

100% Patients had 2 doses from one manufacturing run

97% Patients had 3 doses from one manufacturing run

46% Patients eligible for a redosing based on Phase 2 protocols



CRISPR Highlights:

- Evaluated safety and efficacy of CTX110 with the option of as second consolidation dose in aggressive 2L+ LBCL; n=29
- Option for 2nd CTX110 infusion with LD following disease progression
- 5 out of 8 patients receiving a second dose saw an improved response

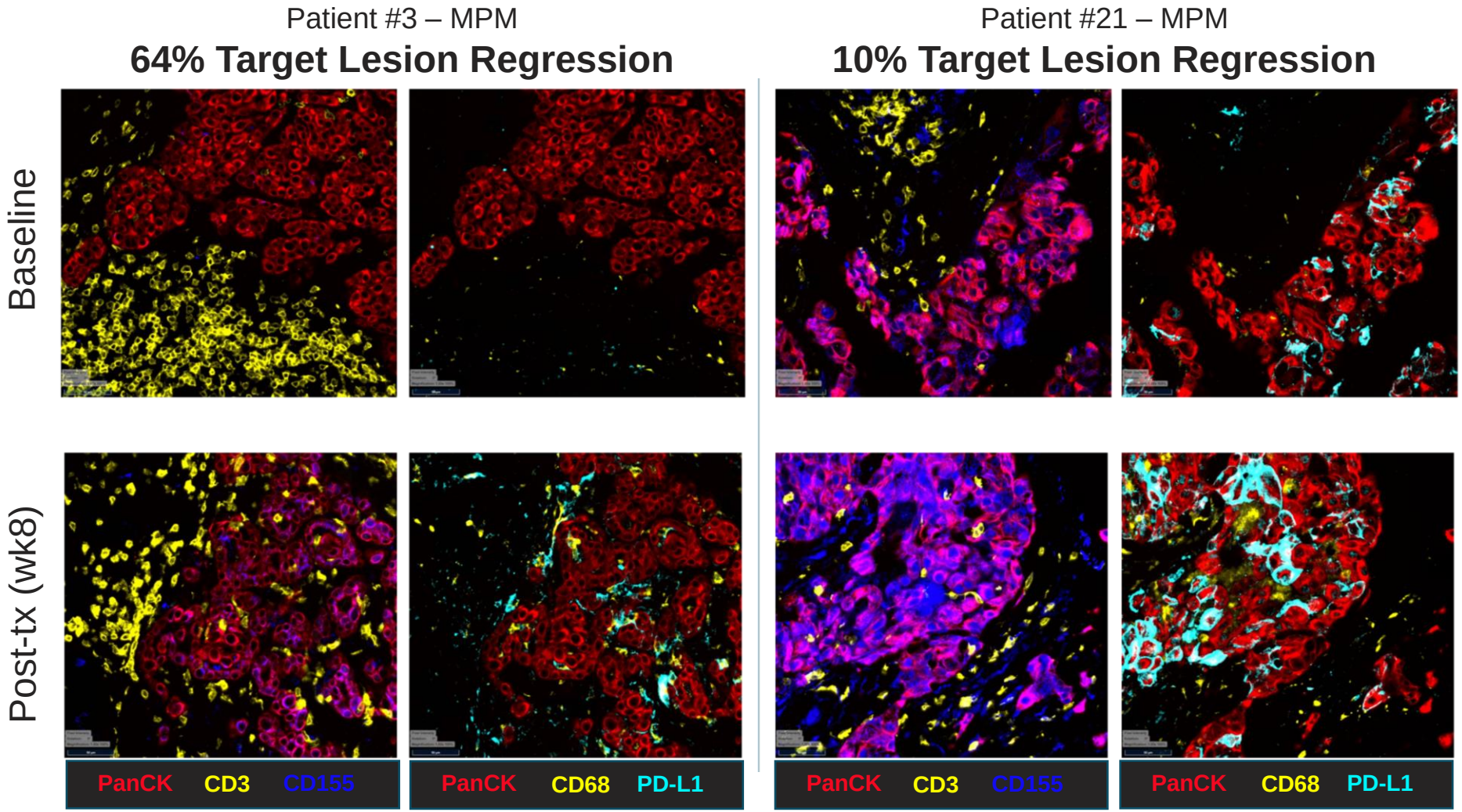
Source: CRISPR public materials, Trial: NCT04035434 (CARBON)

LD, Lymphodepletion

TCR2 THERAPEUTICS

CPIs Expected to Improve Activity of TRuC-T Cells

Immunoinhibitory Mechanisms May Play A Role in Resistance



PanCK = tumor marker; CD3 = T cell marker; CD68 = TAM marker; CD155 = TIGIT ligand; PD-L1 = PD-1 ligand

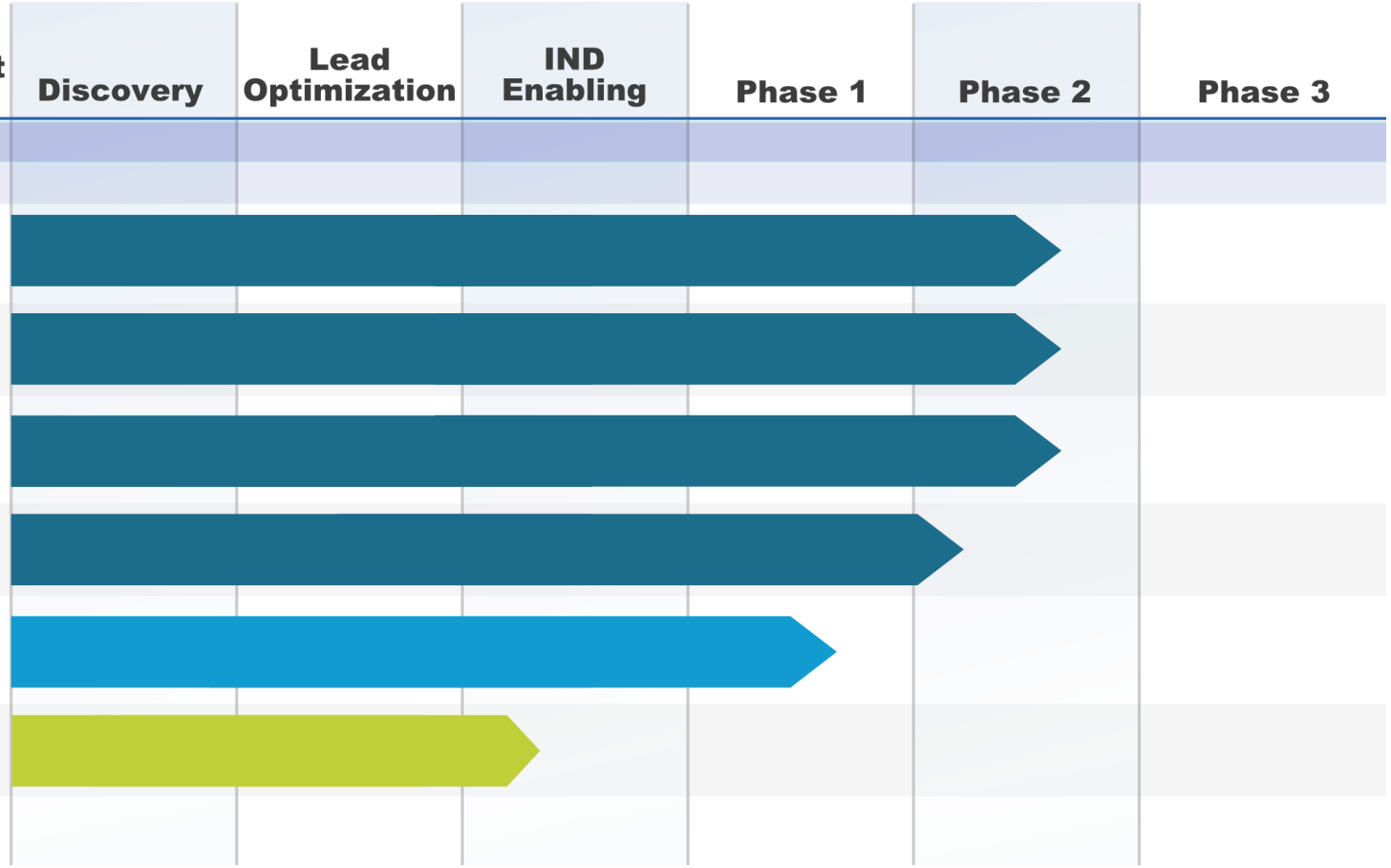
Multiparameter immunofluorescence assay performed using MultiOmxy™ (Neogenomics)

MPM, Malignant Pleural/Peritoneal Mesothelioma; CPI, Checkpoint Inhibitor

TCR2 THERAPEUTICS

Refocused Pipeline to Deliver Near-Term Clinical Data

Program	Indication(s)	Target	Enhancement / Combo
Oncology			
gavo-cel	Ovarian cancer (Treating)	MSLN	Checkpoint inhibitor
gavo-cel	MPM (Treating)	MSLN	Checkpoint inhibitor
gavo-cel	NSCLC (Enrolling)	MSLN	Checkpoint inhibitor
gavo-cel	Cholangiocarcinoma (Next wave)	MSLN	Checkpoint inhibitor
TC-510	Ovarian cancer, MPM,Pancreatic, Colorectal, TNBC	MSLN	PD-1 switch
TC-520	RCC, AML	CD70	IL-15



MSLN, Mesothelin; MPM, Malignant Pleural/Peritoneal Mesothelioma; NSCLC, Non-Small Cell Lung Cancer; TNBC, Triple Negative Breast Cancer; RCC, Renal Cell Carcinoma; AML, Acute Myeloid Leukemia

TCR2 THERAPEUTICS

Q&A