



Next-generation Cellular Therapies, T cell Engagers, and Combinations

MARCH 25–27, 2026 | TUCSON, AZ & VIRTUAL

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Society for Immunotherapy of Cancer

13347

Enhanced tumor function with IOV-5001, an autologous tumor-infiltrating lymphocytes (TIL) engineered with tissue sensing, armored membrane-tethered IL-12

Brian Gastman, MD¹, Patrick Innamarato¹, Andrew Yuhas¹, Joe Yglesias¹, Mohammed Alkhouli¹, Marcus Machin¹, Nathan Gilbert¹, Gerard Sapena¹, Jamie Blauvelt², Shari Pilon-Thomas², Sean Hall¹

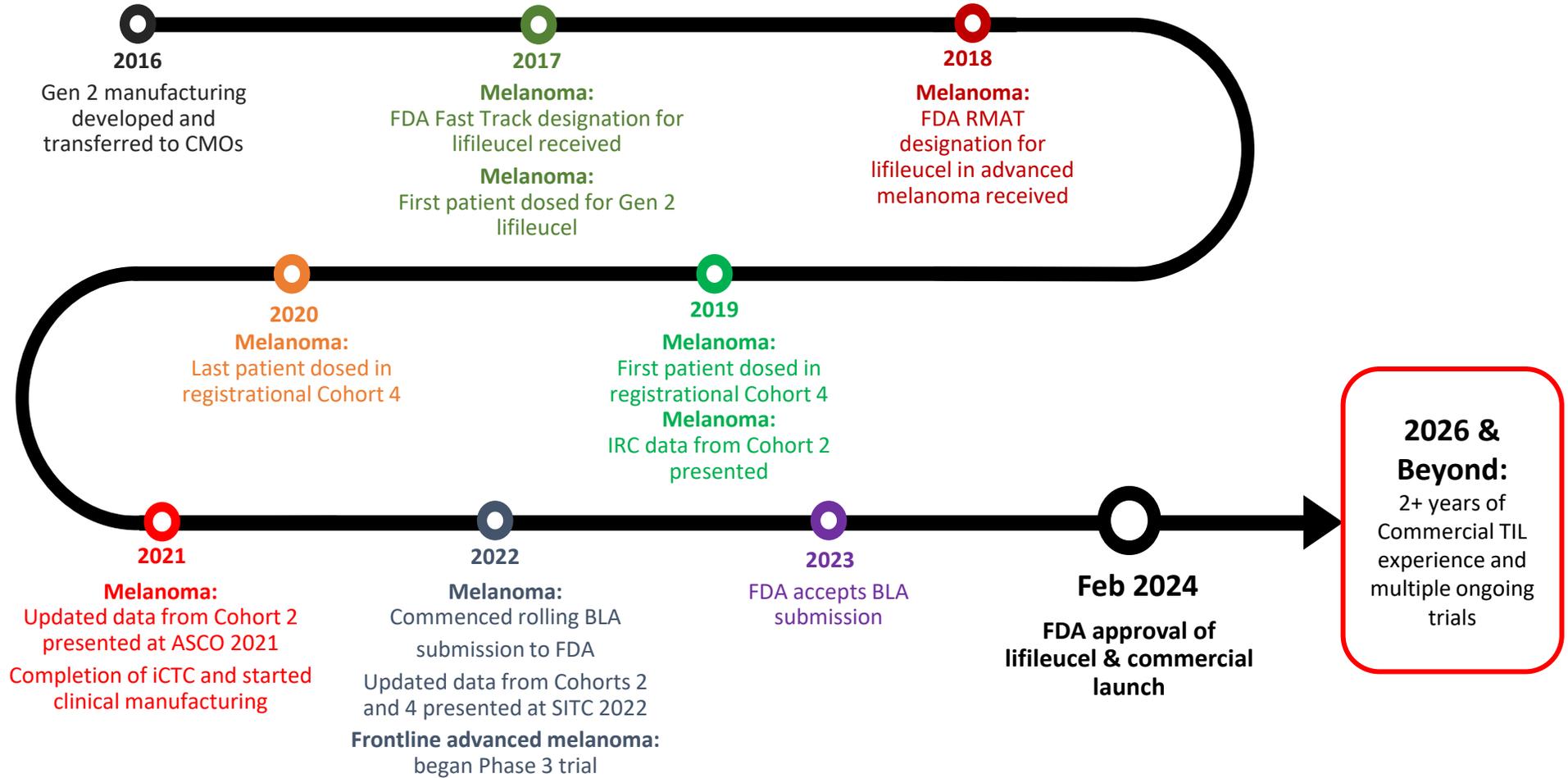
¹Iovance Biotherapeutics, Inc., San Carlos, CA, ²H Lee Moffitt Cancer Center and Research Institute, Tampa, FL

Disclosure Information

- Patrick Innamarato, Andrew Yuhas, Joe Yglesias, Mohammed Alkhouli, Marcus Machin, Nathan J. Gilbert, Gerard Sapena, Sean Hall and **Brian Gastman** are employees of Iovance Biotherapeutics, Inc., San Carlos, CA, USA, and may own stock and have no other financial relationships to disclose
- Jamie L. Blauvelt and Shari Pilon-Thomas are employees of Moffitt Cancer Center, Tampa, FL, USA
- Shari Pilon-Thomas has received ad hoc consulting fees from Morphogenesis Inc., and Iovance Biotherapeutics and serves as an advisor for KSQ Therapeutics and Chronara Biosciences

Metastatic Melanoma: Pathway to “Approval” for ACT of TIL

2016–2024:
 lovance
 Biotherapeutics
 Pioneering TIL &
 Advancing TIL in the
 Clinic



ASCO, American Society of Clinical Oncology; BLA, biologics license application; CMO, contract manufacturing organization; FDA, U.S. Food and Drug Administration; Gen, generation; GMP, good manufacturing practice; iCTC, lovance Cell Therapy Center; IRC, independent review committee; RMAT, regenerative medicine advanced therapy; SITC, Society for Immunotherapy of Cancer; TIL, tumor-infiltrating lymphocytes.

Lifileucel Addresses High Unmet Need for Patients Who Progress After Immune Checkpoint Inhibitors¹

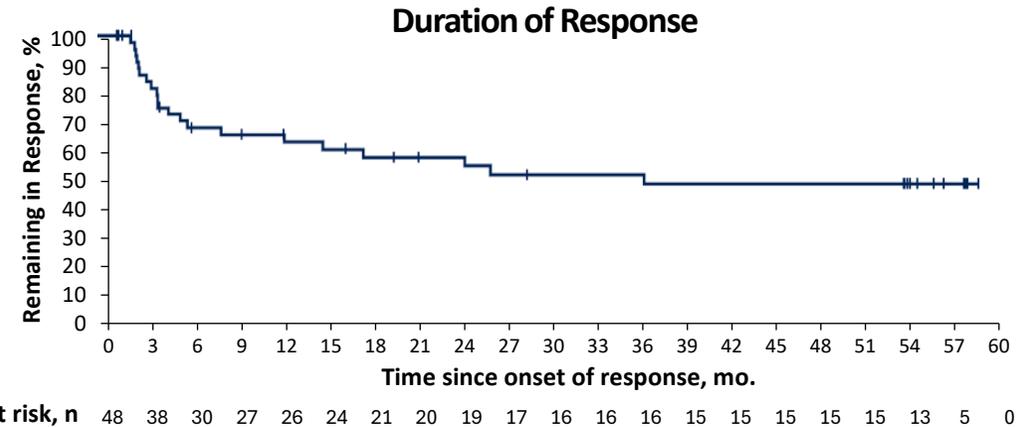
Responses at 5-year follow up

Preferred second-line+ therapy in NCCN guidelines²

ORR
31.4%

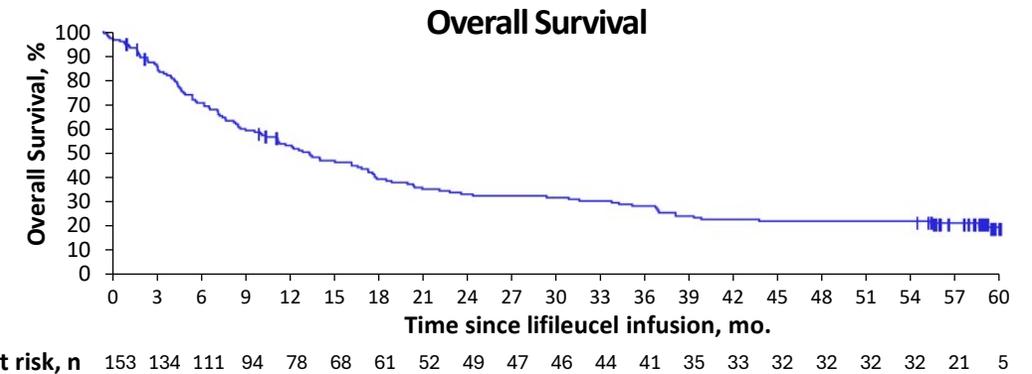
mDOR
36.5 Months

57.8 months median follow up



5 Year OS
19.7%

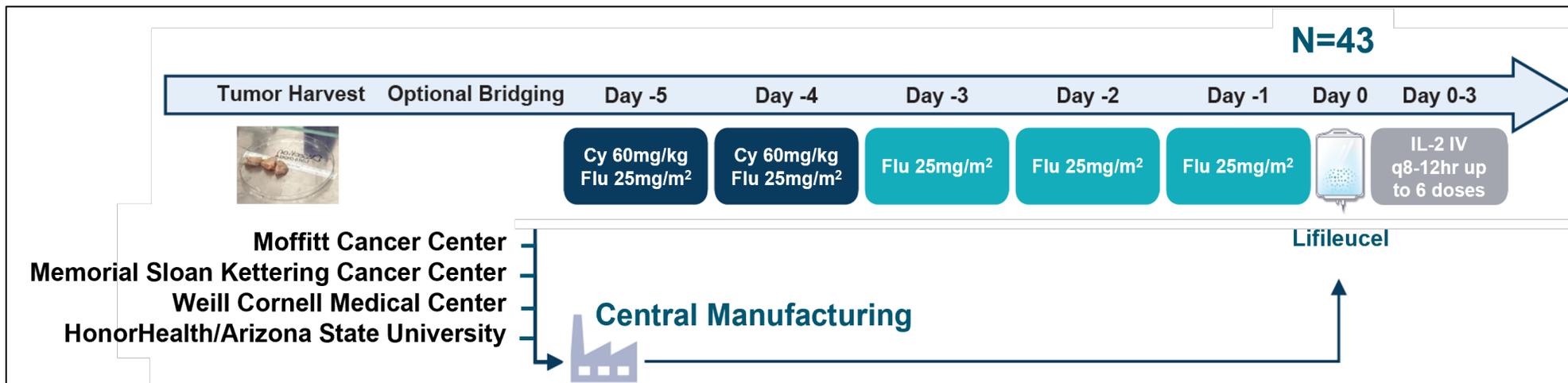
mOS
13.9 Months



mDOR, median duration of response; mOS, media overall survival; NR, not reached; ORR, objective response rate; OS, overall survival.

1. Medina et al, ASCO 2025. Pooled Analysis (n=153), Heavily Pre-Treated Patient Population 2. National Comprehensive Cancer Network® Guidelines, Melanoma: Cutaneous, Version 2.24

Real-World Evidence*



Eligibility Criteria

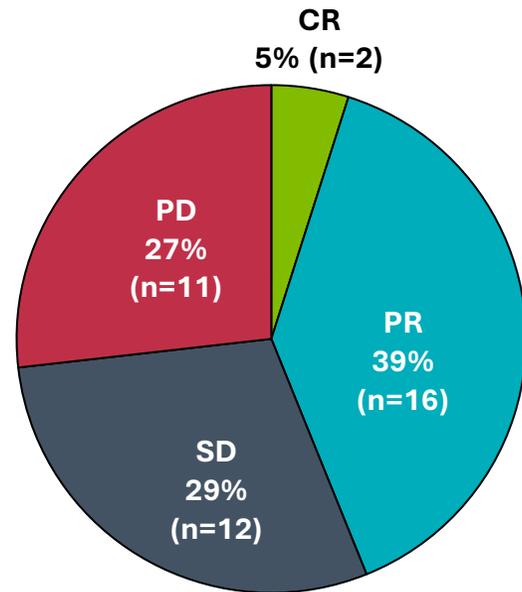
- Age ≥18 years
- Advanced melanoma
- PD-1-resistant after lifileucel approval^a
- Prior ICI therapy
- ± BRAF/MEK inhibitors (*BRAF* V600–mutant)
- Cell product manufactured per QC standards
- ≥2 clinical and/or radiographic assessments

- **Primary endpoint:** Physician-assessed ORR across centers
- **Secondary endpoints:** PFS and OS
- **Safety:** Preliminary evaluation via voluntary adverse event reporting
- **Study period:** May 16, 2024 – May 13, 2025

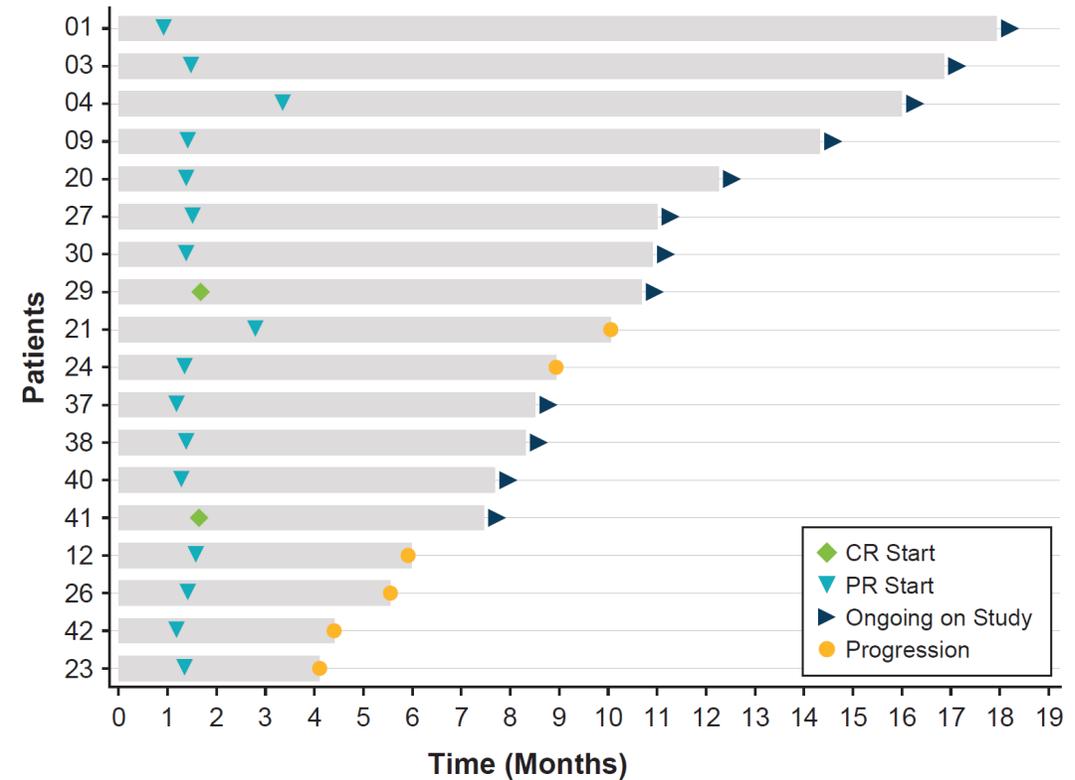
* Data presented at ASTCT 2026; Dose and schedule modifications of lymphodepletion were allowed according to institutional practices. ^aVaries by institution.

Cy, cyclophosphamide; BRAF (or *BRAF*), B-Raf proto-oncogene, serine/threonine kinase; Flu, fludarabine; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; MEK, Mitogen-activated protein kinase; ORR, objective response rate; OS, overall survival; PD-1=programmed cell death protein 1; PFS, progression-free survival; Q8-12hr, every 8 to 12 hours; QC, quality control.

Clinical Activity of Lfileucel in Advanced Melanoma*



ORR: 44% (n=18) | DCR: 73% (n=30)

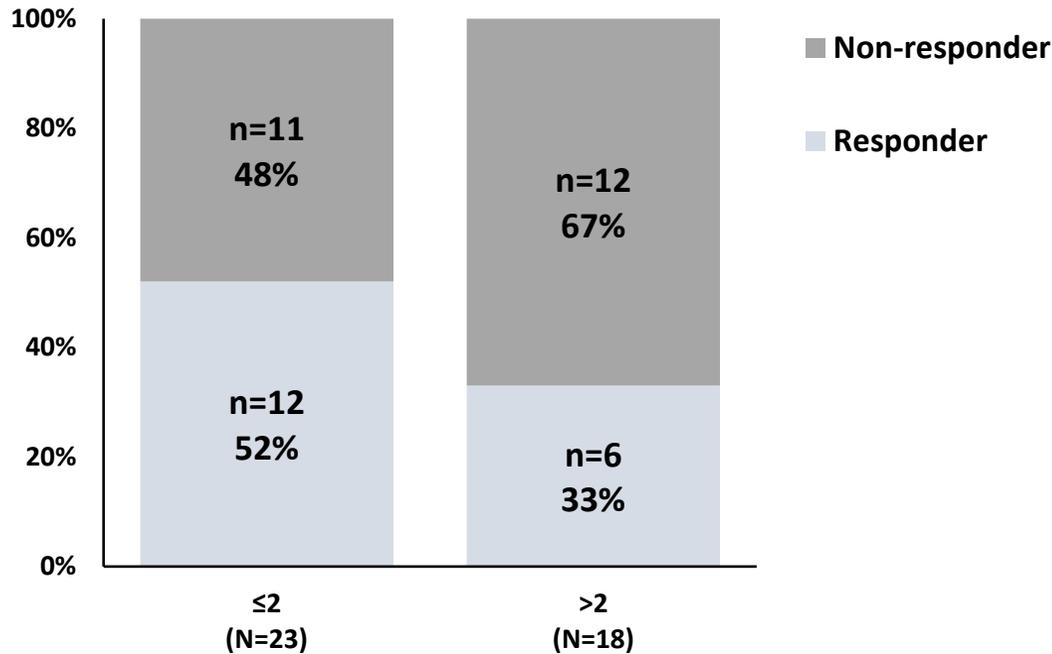


- Most responses were observed at the first radiologic assessment, with 12 ongoing during follow-up^a

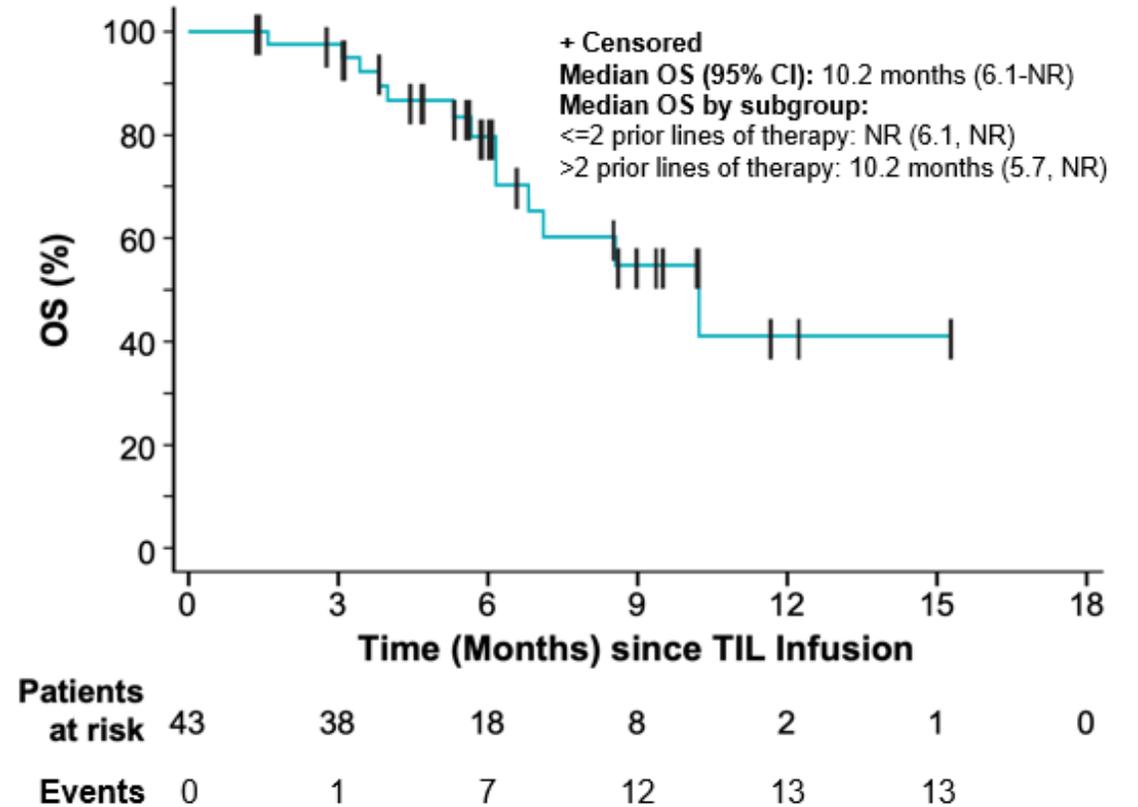
* Data presented at ASTCT 2026^a Median follow up time = 6 months. ORR was calculated based on patients with measurable lesions after tumor harvest (n=41). Swimlane plot depicts all patients with confirmed responses. CR, complete response; DCR, disease control rate; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

Survival Following Lfileucel Therapy – Preliminary Evaluation*

Prior Lines of Therapy



Overall Survival



* Data presented at ASTCT 2026 ; NR, not reached; OS, overall survival; PFS, progression-free survival.

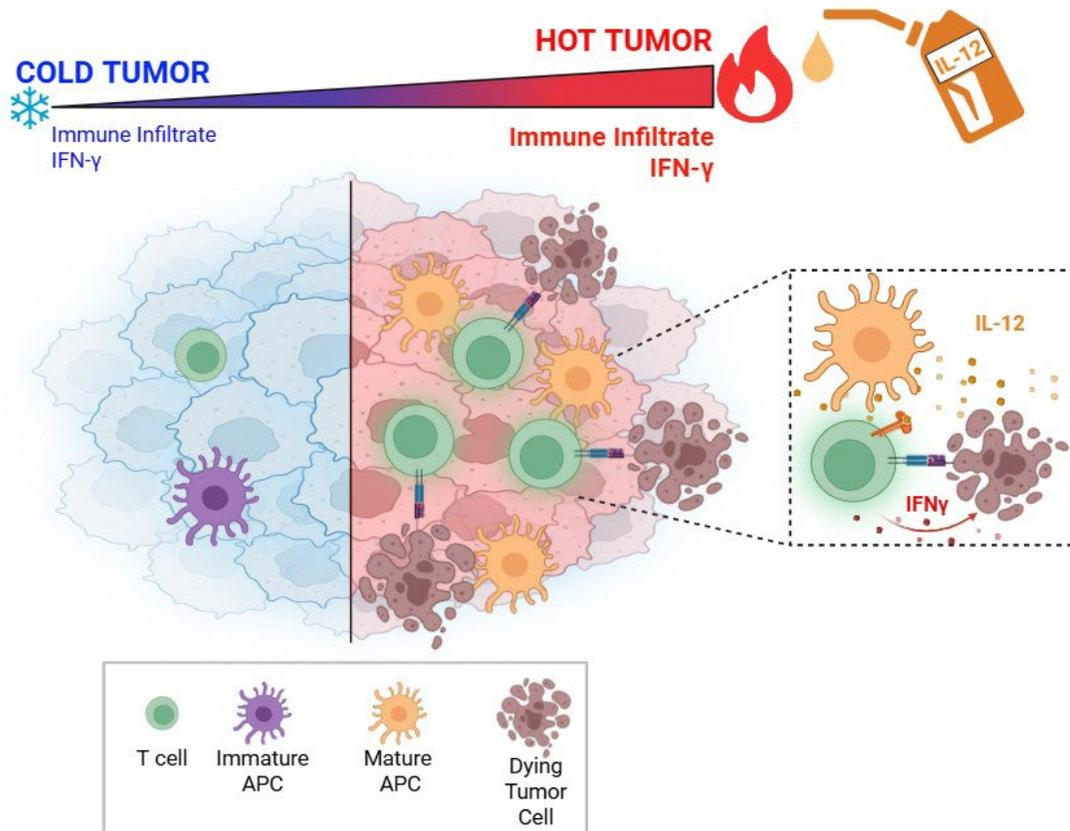
Iovance Solid Tumor Portfolio Highlights

	INDICATION & TREATMENT SETTING	PHASE 1	PHASE 2	PHASE 3
Lifileucel Pipeline	Lifileucel + pembrolizumab	Frontline advanced melanoma	TILVANCE-301 (FTD, Confirmatory)	
	Lifileucel	Post-chemo & anti-PD-1 advanced NSCLC	IOV-LUN-202: Cohorts 1&2 (FTD)	
	Lifileucel	Post-chemo DDLPS or UPS Sarcoma	IOV-SAR-201*	
	Lifileucel	Post-chemo & anti-PD-1 endometrial cancer	IOV-END-201: Cohorts 1&2	
Next-Generation Products	PD-1 Inactivated TIL (IOV-4001)	Post anti-PD-1 advanced melanoma	IOV-GM1-201: Cohort 1	
	PD-1 Inactivated TIL (IOV-4001)	2-4L incl. post-anti-PD-1 advanced NSCLC	IOV-GM1-201: Cohort 2	
	IL-2 analog (IOV-3001)	TIL treatment regimen	IOV-IL2-101	
	IL-12 tethered TIL (IOV-5001)	Basket trial	IOV-GE1-201*	

*Not yet enrolling.

2L, second line; 4L, fourth line; DDLPS, dedifferentiated liposarcoma; FTD, Fast Track Designation; ICI, immune checkpoint inhibitor; IL-2, interleukin-2; IL-12, interleukin-12; NSCLC, non-small cell lung cancer; PD-1, programmed cell death protein-1; TIL, tumor infiltrating lymphocytes; UPS, undifferentiated pleomorphic sarcoma.

Turning COLD Tumors HOT: IL-12 Fuels the Reprogramming of the Tumor Microenvironment to Improve Immunotherapy

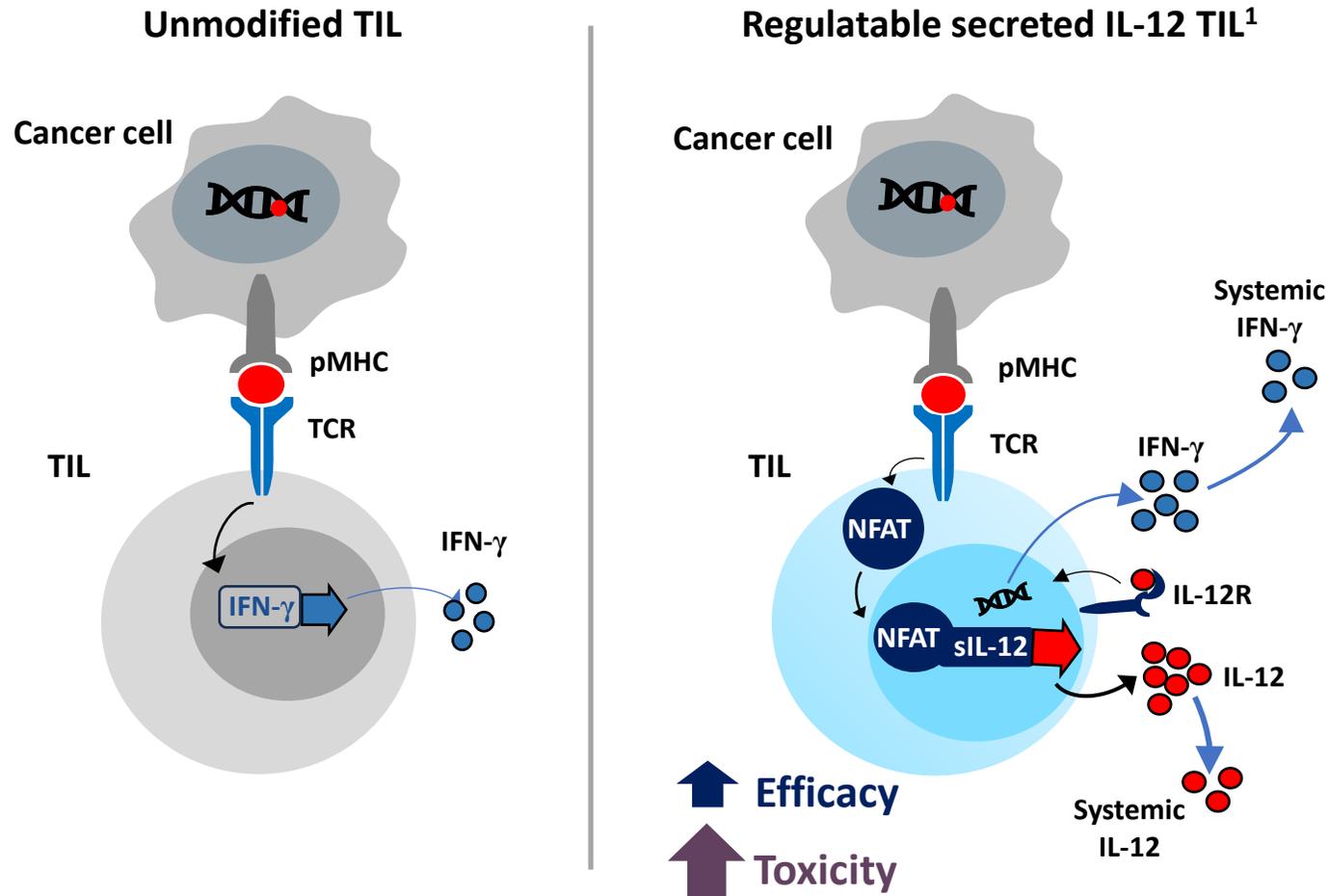


- IL-12 is a pro-inflammatory T cell- and NK cell-activating cytokine produced by APCs¹
- IL-12 induces the production of IFN- γ by IL-12R-expressing T cells and augments TH1-directed immunity¹
- IL-12 and IFN- γ together reverse dysfunctional antigen presentation & reprogram the tumor microenvironment to support anti-tumor T cell activity^{2,3}

APC, antigen presenting cell; IFN- γ , interferon gamma; IL-12, interleukin-12; IL-12R, interleukin-12 receptor; NK, natural killer cell.

1. Cheng EM, et.al, *Cancer Immunol Immunother.* 2022;71:2057-65. 2. Kerkar SP, et. al, *Mol Ther.* 2013;21:1369-77. 3. Jia Z, et.al, *Front Immunol.* 2022;13:952231.

Prior Clinical Experience: IL-12-secreting Autologous TIL Without IL-2 Enhances Clinical Efficacy in Patients with Advanced Metastatic Melanoma



- Cell dose–escalation trial of autologous TIL transduced with a gene encoding a single-chain IL-12 driven by a nuclear factor of the activated T cells promoter (NFAT)¹
- **ORR of 63%** in 16 patients was observed with inducible IL-12 secreting TIL at doses between 0.3 to 3e9 gene–modified TIL
- Associated with **severe toxicities** likely attributable to high levels of systemic IL-12 limits clinical use

IFN- γ , interferon gamma; IL-2, interleukin-2; IL-12, interleukin-12; IL-12R, interleukin 12 receptor; NFAT, nuclear factor of activated T cells; ORR, objective response rate; pMHC, peptide-major histocompatibility complex; TCR, T-cell receptor; TIL, tumor-infiltrating lymphocyte.

1. Zhang L et al, *Clin Cancer Res* 2015;21(10):2278–2288.

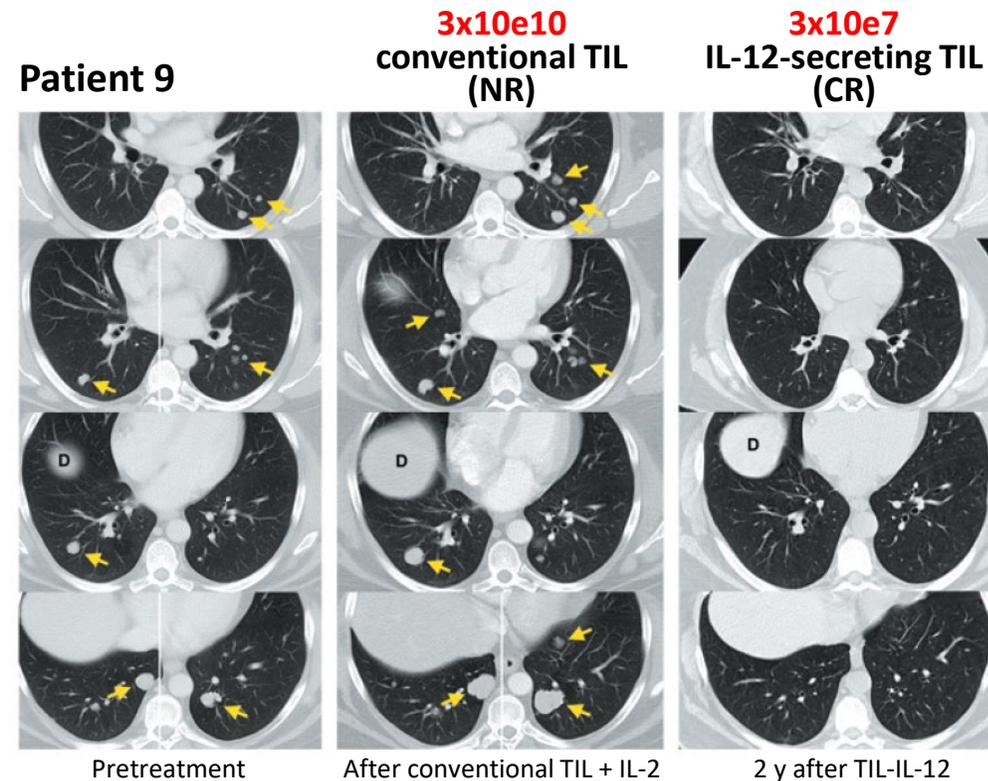
Prior Clinical Experience: IL-12-secreting Autologous TIL Without Systemic IL-2 Demonstrates Enhanced Efficacy at Lower Cell Doses than Conventional TIL¹

ORR of 63% in 16 patients was observed after infusion with IL-12-secreting TIL at doses between 0.3 to 3e9 cells

Table 1. Patient demographics treatment and response

Patient	Age/gender	Sites of disease	Prior treatment	Infusion cell number ×10 ⁹	Transduction efficiency (%)	Infusion IL12 Td cell number ×10 ⁹	Response (mo)
1	56 F	lu, sc, ln	IL2, surgery	0.001	3	0.00003	NR
2	47 M	lu, li, ln	IL2, IMTOX	0.003	21	0.00063	NR
3	30 M	lu, sc, ln	IL2, YT	0.01	35	0.0035	NR
4	50 M	lu, ln, bo	IL2	0.01	2	0.0002	NR
5	20 F	sp, ad, ki, lu, li, sc, ln	YT, ipi	0.01	3	0.0003	NR
6	42 M	lu, sc	IL2	0.01	7	0.0007	NR
7	40 M	ln, sc	IL2	0.01	5	0.0005	NR
8	48 M	lu, ln	IL2	0.01	52	0.0052	NR;
9	47 M	lu, ln	YT	0.03	6	0.0018	CR (38+)
10	60 M	lu, ad	IL2, ipi	0.01	29	0.0029	NR
11	61 M	ln, lu, sc	IL2	0.03	31	0.0093	NR
12	63 M	liver, sc	IL2	0.03	24	0.0072	NR
13	64 M	neck, lu	IL2	0.03	38	0.0114	NR
14	41 F	R toe, lu, sc, ln	IL2	0.03	2	0.0006	NR
15	34 F	li, panc, ln	IL2	0.1	17	0.017	NR
16	63 F	sc, ln, li	Surgery, xrt, IL2	0.1	2	0.002	NR
17	50 M	sp, panc, lu, li, brain, sc	IL2	0.1	32	0.0032	NR
18	63 M	ln, lu	IL2	0.3	16	0.048	PR (4)
19	45 M	sc, ln, brain	IFN, surgery, IL2, TIL	0.3	14	0.042	PR (6)
20	60 F	lu, ln	IFN, xrt, IL2	0.3	12	0.036	PR (21)
21	58 M	sc, ln	YT	1	17	0.17	PR (27+)
22	30 F	ln, lu, brain	Surgery, IFN, xrt, IL2	1	16	0.16	NR
23	59 M	sc, ln	Surgery, MART-F5	1	4	0.04	NR
24	62 F	lu, thigh	Surgery, IL2	3	4	0.12	PR (11)
25	65 M	sc, ln, adrenal	IL2, ipi	3	15	0.45	PR (7)
26	67 M	sc, ln, lu, li, adrenal	Surgery, IL2, ipi, Bor/Sor	1.1	8	0.088	NR
27	38 M	ln, sc	xrt	3	10	0.3	CR (21)
28	58 F	sc, kidney, lu, ln	Surgery	3	14	0.42	PR (4)
29	51 M	sc, bo, spine, lu, ln	IFN, IL2	1	10	0.1	NR
30	61 M	ln, li	Surgery, MART F-5 adj trial +IL2	1	6	0.06	PR (5)
31	65 M	lu, brain, sc	Surgery	1	3	0.03	NR
32	23 M	lu, brain	Surgery	1	4	0.04	PR (12+)
33	36 M	li, ln	Surgery, xrt, IFN, IL2, VFN, anti-PD-1	1	4	0.04	NR

Abbreviations: abd, abdominal; bilat, bilateral; Bor, Bortezomib; F, female; IMTOX, anti-CD25 immunotoxin; ipi, ipilimumab; L, left; li, liver; ln, lymph node; lu, lung; M, male; MART-F5; NR, no response; PR, partial response; R, right; sc, subcutaneous; Sor, sorafenib; T-cell receptor-engineered cells; VFB, vemurafenib; xrt, radiation; YT, short-term cultured TIL.



Adapted from Zhang L, Rosenberg SA, et al, *Clin Cancer Res* 2015;21(10):2278–2288.

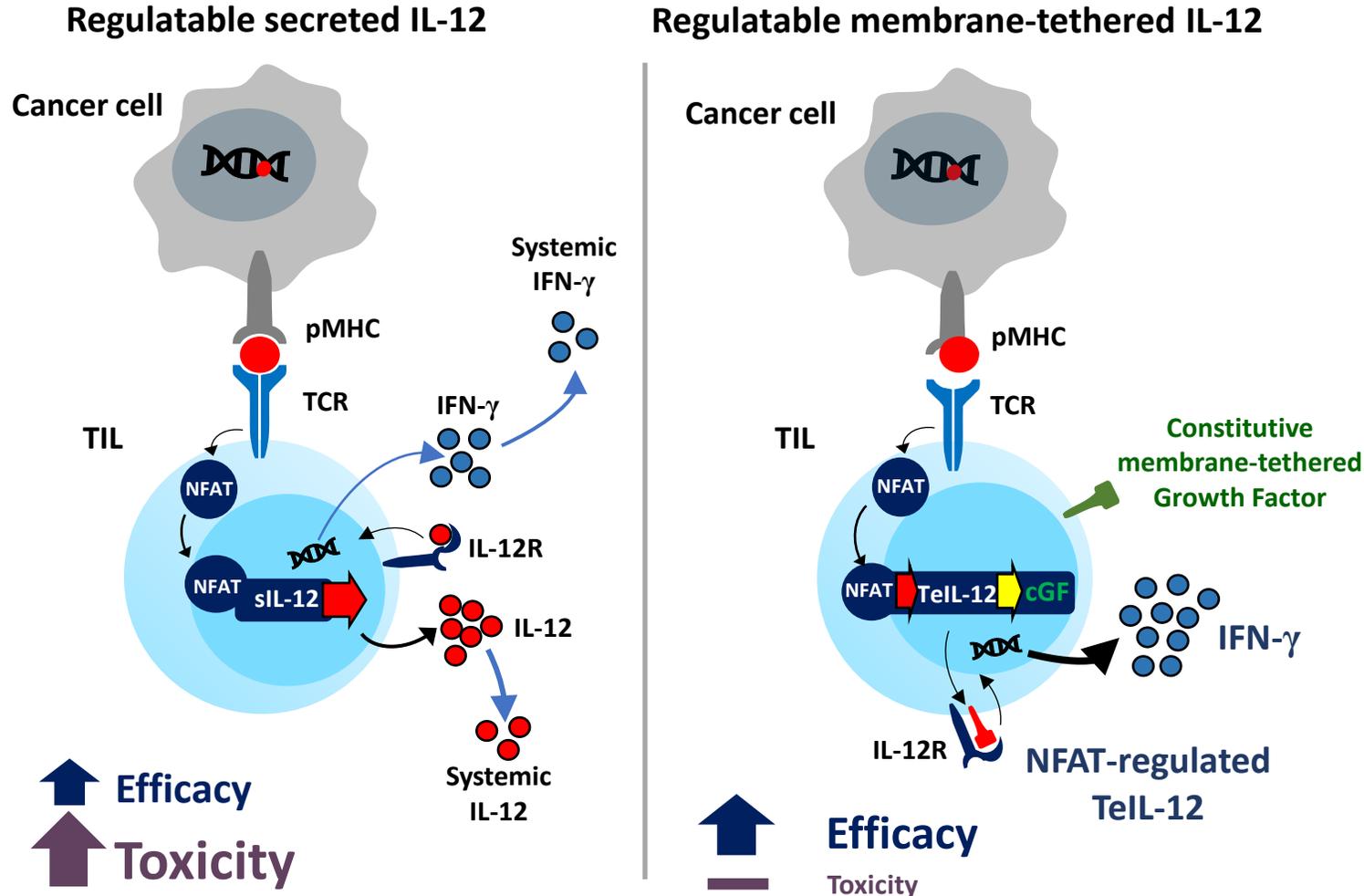
Complete tumor regression after administration of IL-12 secreting TIL (without IL-2), in a patient that previously progressed after conventional TIL (with IL-2)

IL-2, interleukin-2; IL-12, interleukin-12; ORR, objective response rate; TIL, tumor-infiltrating lymphocyte.

1. Zhang L et al, *Clin Cancer Res* 2015;21(10):2278–2288.

IOV-5001 Is an Autologous TIL Product Genetically Engineered to Express Regulatable Membrane-tethered IL-12 (TelL-12)

IOV-5001



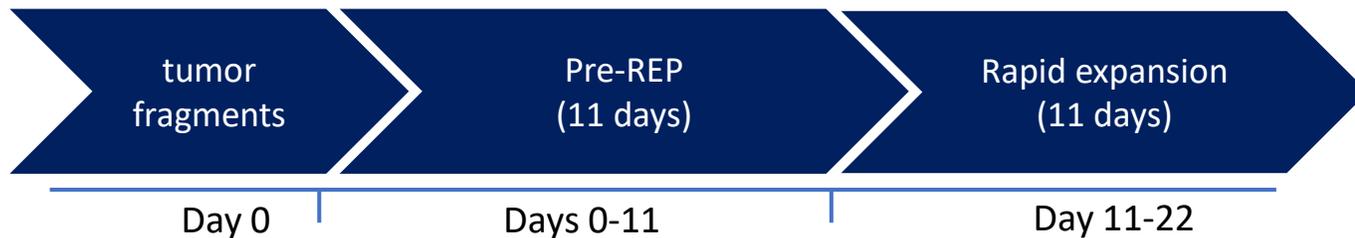
- Tethering IL-12 to the cell membrane can improve safety by avoiding systemic release of IL-12¹
- Enhanced efficacy observed with infusion of lower cell numbers
- May support expansion into less T cell infiltrated tumors

cGF, Constitutive membrane-tethered Growth Factor; IFN-γ, interferon gamma; IL-12, interleukin-12; IL-12R, interleukin-12 receptor; NFAT=nuclear factor of activated T cells; TCR=T-cell receptor therapy; pMHC, peptide-major histocompatibility complex; TelL-12, membrane-tethered IL-12; TIL, tumor-infiltrating lymphocyte.

1. Zhang L, et al. *J Immunother Cancer*. 2020.

Generation of IOV-5001 for Nonclinical Studies

Process to manufacture conventional Gen 2 TIL



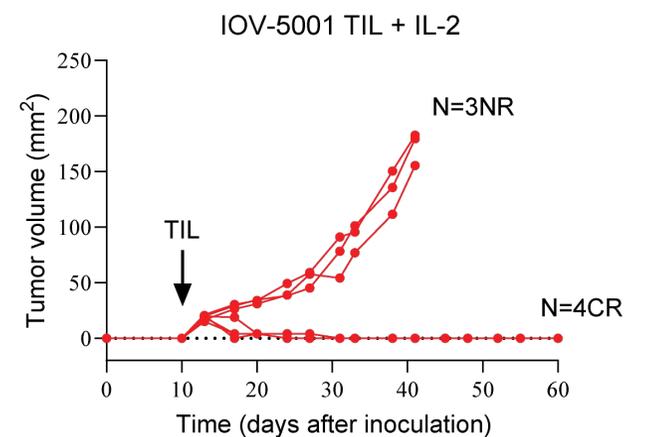
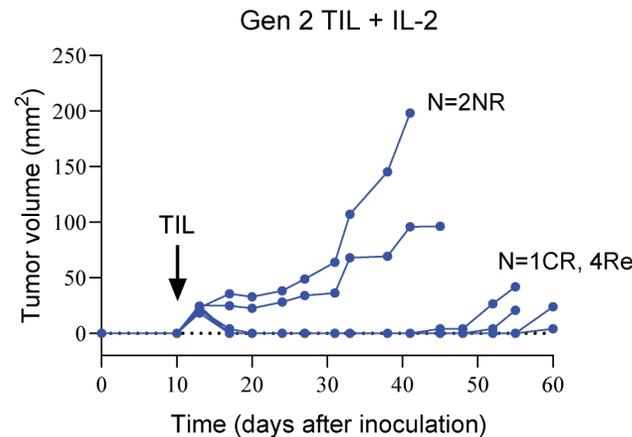
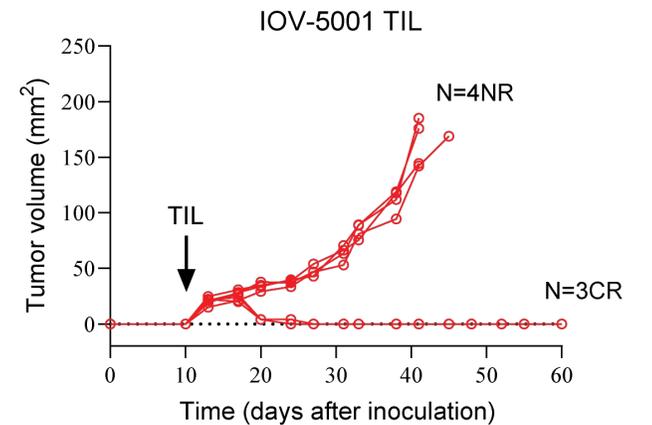
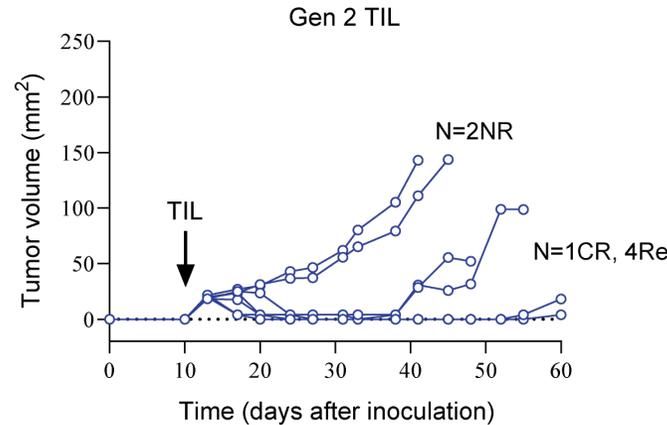
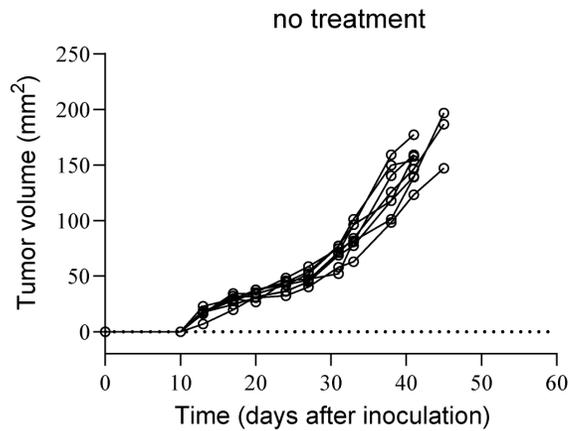
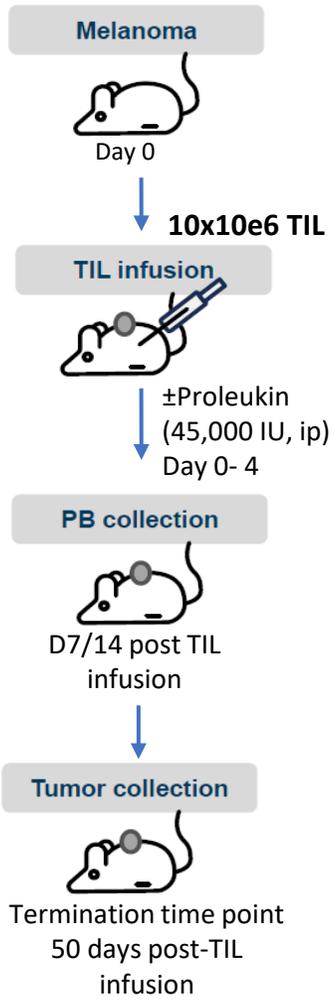
Process to manufacture IOV-5001 TIL



Dual sense lentiviral vector. Inducible *TelL-12* is under 6 NFAT-driven promoters, and constitutive cytokine expression is under the EF-1 α promoter.
 EF-1 α , elongation factor 1 α ; Gen, generation; LTR, long-terminal repeat; NFAT, nuclear factor of activated T cells; pre-REP=pre-rapid expansion protocol; *TelL-12*, membrane-tethered NFAT–interleukin-12.

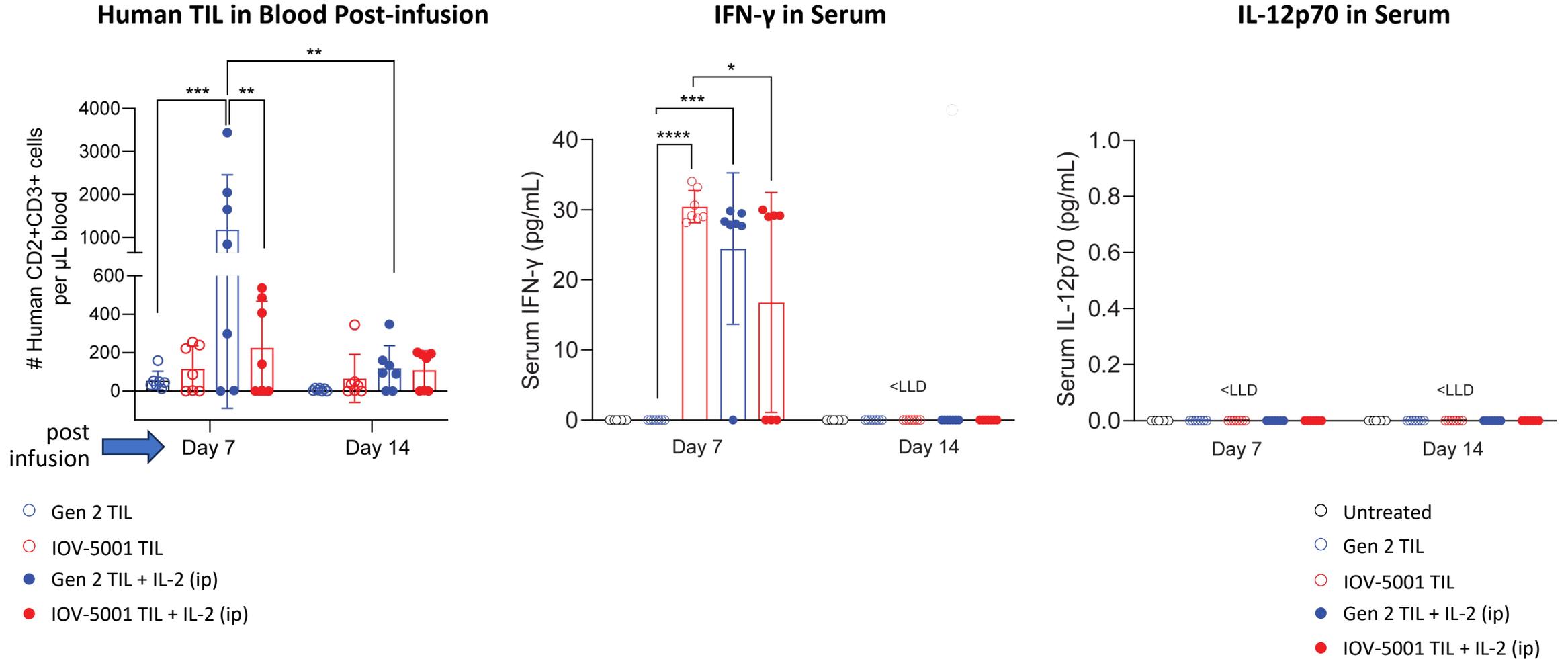
Durable Anti-tumor Activity of IOV-5001 TIL Irrespective of Exogenous IL-2 Support

No evidence of tumor relapse in IOV-5001 treated mice



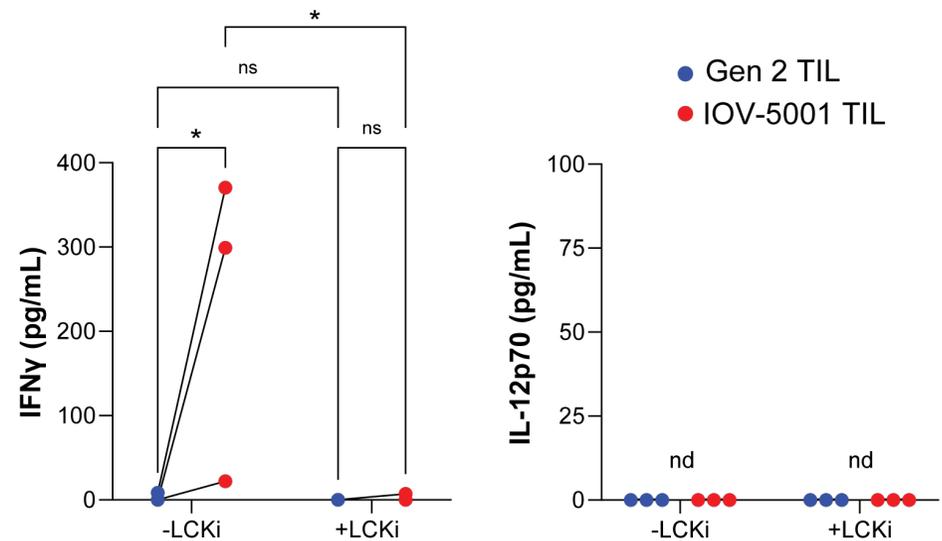
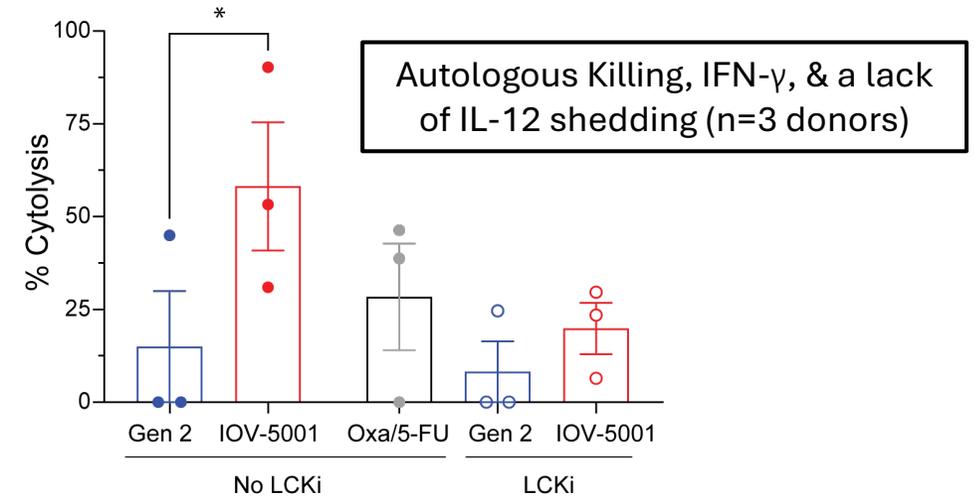
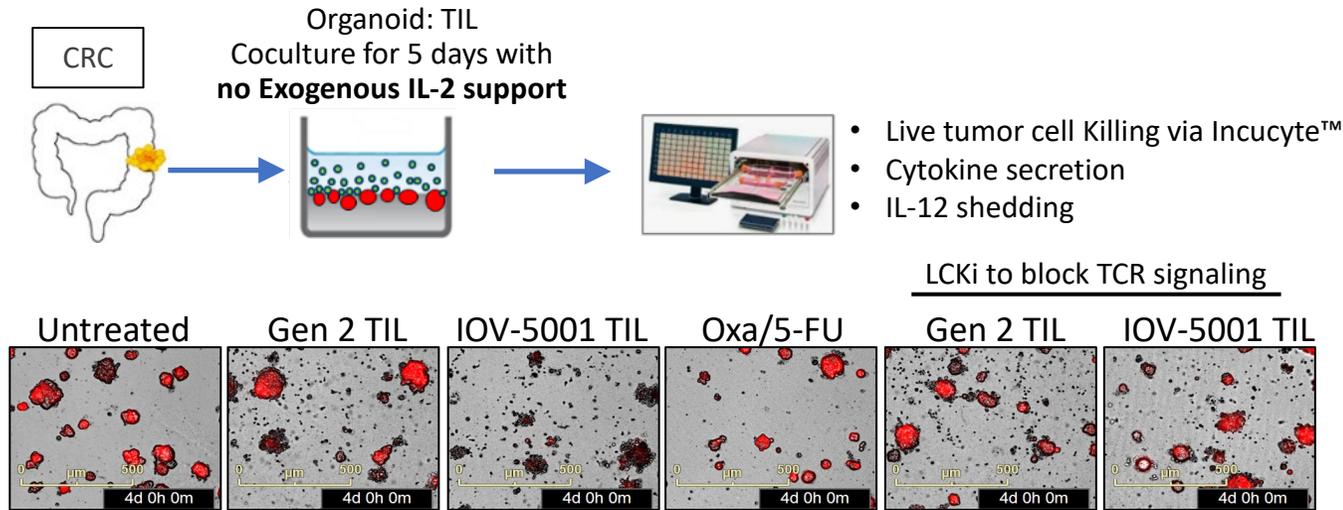
CR, complete response; D, day; Gen, generation; IL-2, interleukin-2; ip, intraperitoneal; IU, international unit; square millimeter; NR, no response; PB, peripheral blood; Re, relapse; TIL, tumor-infiltrating lymphocyte.

Detection of TIL in Blood of Mice Infused with IOV-5001 without Systemic Release of IL-12



CD2, cluster of differentiation 2; CD3, cluster of differentiation 3; Gen, generation; IFN-γ, interferon gamma; IL-12, interleukin-12; ip, intraperitoneal; pg/mL, picograms per milliliter; TIL, tumor-infiltrating lymphocyte; μL, microliter.

IOV-5001 TIL Demonstrate Enhanced Killing of Tumor Organoids Without Exogenous IL-2 Support and No Shedding of IL-12



Conclusions

- IOV-5001, an autologous TIL engineered with NFAT-inducible (tissue sensing, armored) TeIL-12 confers durable antitumor activity in the absence of exogenous IL-2
- The tight regulation of IL-12 and elimination of shedding highlights a key safety profile of IOV-5001
- Lower TVC for efficacy provides an opportunity to expand into indications that have lower T cell infiltration (e.g. colder tumors), which historically did not have access to TIL therapy
- A Phase 1/2 study assessing IOV-5001 in patients with metastatic solid cancers is planned
 - Solid Cancers lead to 90% of all cancer deaths and many, remain incurable

Acknowledgments

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- Colleagues at Iovance Biotherapeutics