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LAG-3 IMMUNOTHERAPY

Unlocking the power of the immune system to fight cancer and autoimmune disease

Forward-Looking Statements

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Immutep Highlights

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Leader in LAG-3 immunotherapy

LAG-3 pure play with three clinical-stage assets and two preclinical programs designed to fight cancer & autoimmune diseases.

First-in-Class Lead Candidate

Eftilagimod alpha (efti), a unique immune system activator, has compelling data with good safety across several clinical trials.*

Validation through partnerships

Multiple partnerships and collaborations with large pharma.

MERCK
Merck KGaA
Darmstadt, Germany
GSK
EDC
NOVARTIS
LabCorp

Global presence; strong IP/balance sheet

Global presence and strong IP across diversified LAG-3 portfolio. Well-funded with cash runway to early 2026.

Large opportunity & multiple catalysts ahead

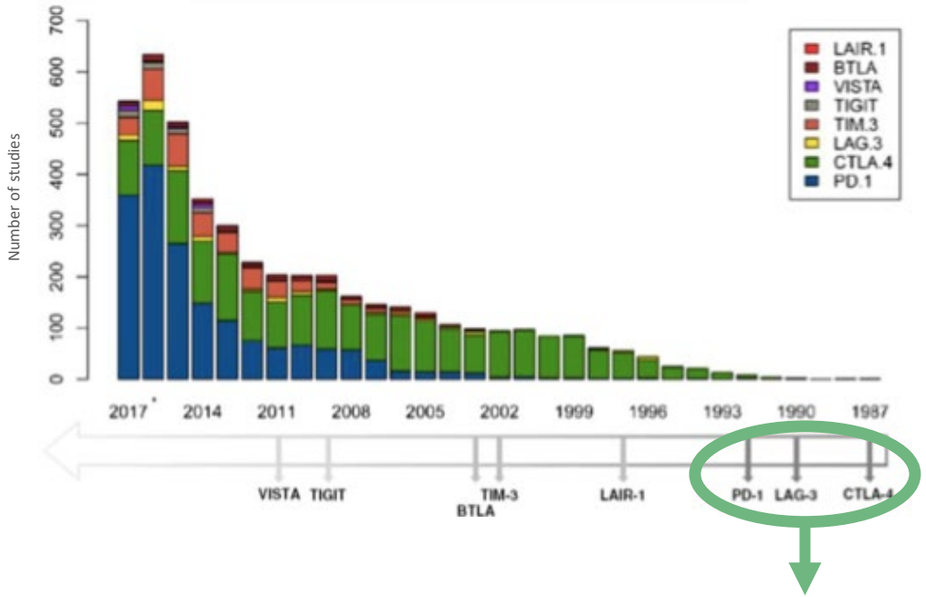
Later-stage clinical programs are in large addressable markets (e.g., lung, breast, and head & neck cancer**). Multiple data readouts in ‘24.

* (1) Combining the antigen-presenting cell activator eftilagimod alpha (soluble LAG-3) and pembrolizumab: overall survival data from the 1st line non-small cell lung cancer (NSCLC) cohort of TACTI-002 – ESMO 2023; (2) Biomarker and multivariate analyses results from AIPAC: A phase IIb study comparing efti to placebo in combination with weekly paclitaxel in HR+ HER2- metastatic breast carcinoma. ESMO - May 2022; (3) Results from a Phase II study of efti and pembrolizumab in patients with PD-L1 unselected metastatic 2nd line head and neck squamous cell carcinoma (HNSCC) SITC 2021.

**Global market estimates for NSCLC, HNSCC, and MBC are $24BB (current), $3.5BB (by 2025) and $12.7BB (by 2024), respectively, with NSCLC expected to double to $48 billion by 2031, based on intelligence data from GlobalData and Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023).

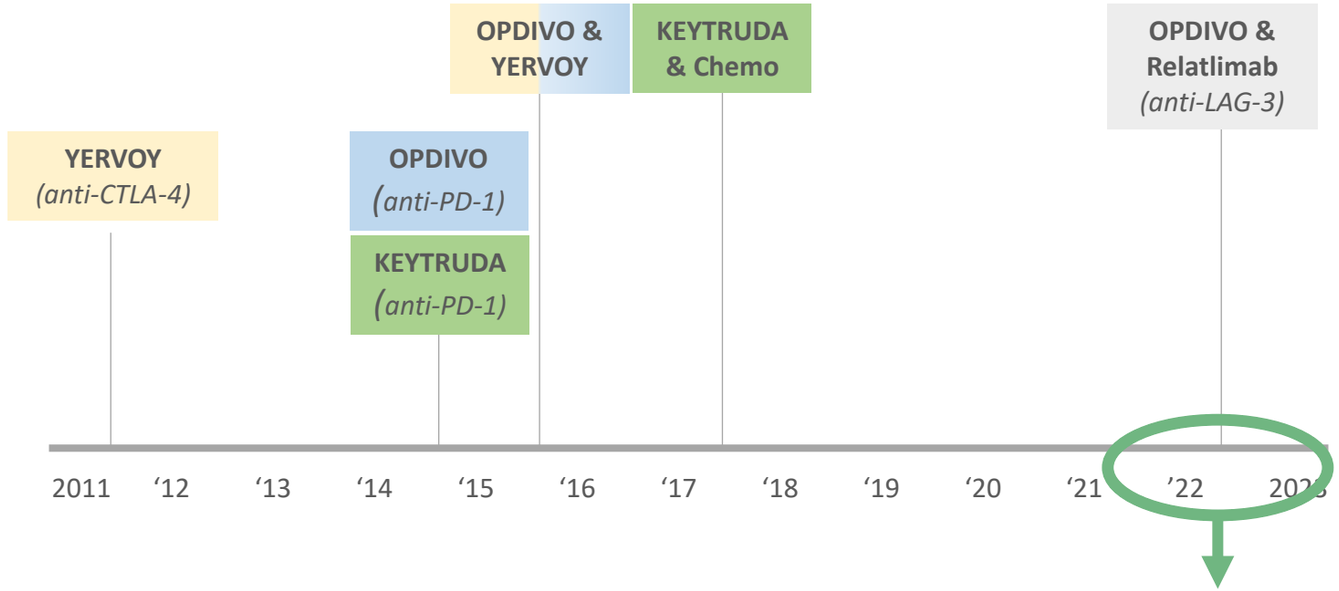
LAG-3 Newest Entrant to Immuno-Oncology (IO) Landscape

Immune Checkpoint Discovery and Clinical Studies*



LAG-3 discovered in 1990 by Immutep's Chief Scientific Officer, Dr. Frédéric Triebel

Regulatory Approval Timeline of Immuno-Oncology (IO) Therapies**

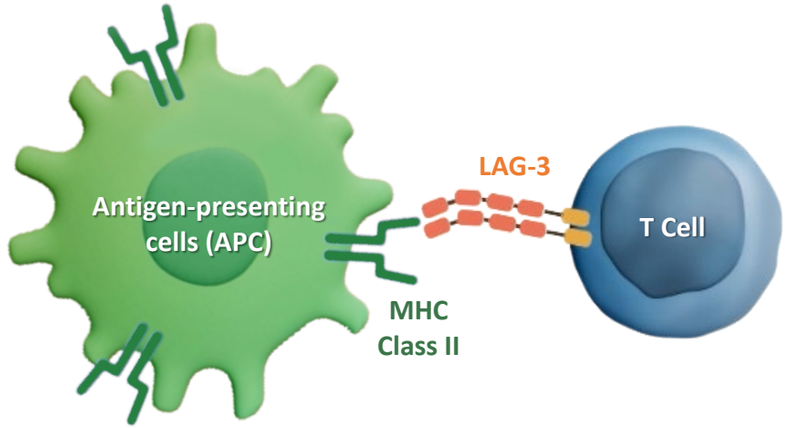


The immune system's ability to fight cancer has led to regulatory approval of IO therapies targeting the immune checkpoints **CTLA-4**, **PD-1**, and most recently **LAG-3**

*Checkpoint Inhibitors: Applications for Autoimmunity, Springer, September 2017 Current Allergy and Asthma Reports 17(10) DOI:10.1007/s11882-017-0740-z. ** YERVOY (ipilimumab), OPDIVO (nivolumab), KEYTRUDA (pembrolizumab), OPDUALAG (nivolumab + relatlimab)

Pioneering LAG-3 Immunotherapy Portfolio

Immutep has multiple first-in-class therapeutics designed around the interaction of **MHC Class II molecules** on antigen-presenting cells (APC) and **LAG-3** on T-cells to fight cancer & autoimmune disease



Targeting MHC Class II on APCs#	Targeting LAG-3 on T cells			
Efti Soluble LAG-3 fusion protein	**LAG525*** Blocking LAG-3 antibody	Anti-LAG-3 small molecule	**GSK'781*** Depleting LAG-3 antibody	**IMP761** Agonist LAG-3 antibody
	Oncology Immune Stimulation		**Autoimmune Disease** Immune Suppression	

MHC Class II = Major Histocompatibility Complex Class II. * LAG525 (leramilimab) is out-licensed to Novartis and GSK'781 is out-licensed to GSK. The clinical-stage asset GSK'781 is being transitioned back to Immutep as the licensing agreement has been terminated with an effective date of 30 May 2024.

Deep LAG-3 Pipeline in Oncology & Autoimmune Diseases

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	Program	Indication	Preclinical	Phase I	Phase II	Late Stage*	Collaborations	Commercial Rights
ONCOLOGY	**Eftilagimod Alpha** Soluble LAG-3 Protein & MHC Class II agonist	1L Head & Neck Squamous Cell Carcinoma (HNSCC)	TACTI-003 | Efti+Pembrolizumab [a]				MERCK	immutep Global Rights ex-China
		1L Non-Small Cell Lung Cancer (NSCLC), 2L HNSCC, PD-X Refractory 2L NSCLC	TACTI-002 | Efti+Pembrolizumab [a]				MERCK	
		1L Non-Squamous NSCLC	INSIGHT-003 | Efti+Pembro+Chemo [§]					
		Urothelial Cancer	INSIGHT-005 | Efti+Avelumab [§, b]				Merck KGaA Darmstadt, Germany	
		Soft Tissue Sarcoma	EFTISARC-NEO | Efti+Pembro+Radiotherapy [§]				Narodowy Instytut Onkologii	
		HR+/HER2- Metastatic Breast Cancer & TNBC	AIPAC-003 | Efti+Paclitaxel					
		Metastatic Breast Cancer & Solid Tumors	Efti+Paclitaxel and Efti+Pembrolizumab [#]				EOC	EOC Efti China Rights
	Anti-LAG-3 Small Molecule	Undisclosed					CARDIFF UNIVERSITY	immutep Global Rights
	LAG525 Anti-LAG-3 Antibody	Solid Tumors & Blood Cancer					NOVARTIS	NOVARTIS Global Rights
		Triple Negative Breast Cancer						
		Melanoma						
		Solid Tumors						
		Triple Negative Breast Cancer						
AUTOIMMUNE DISEASE	**GSK'781** Depleting LAG-3 Antibody	Ulcerative Colitis					GSK	GSK Global Rights
		Psoriasis						
		Healthy Subjects						
	IMP761 Agonist LAG-3 Antibody	Undisclosed						immutep Global Rights

Information in pipeline chart current as of February 2024. For EOC's China rights, Immutep may receive undisclosed milestones plus royalties; LAG525 - ClinicalTrials.gov (for Novartis' global rights, Immutep may receive milestones plus royalties); GSK2831781 - ClinicalTrials.gov, Phase II in Ulcerative Colitis discontinued. The clinical-stage asset GSK'781 is being transitioned back to Immutep as the licensing agreement has been terminated with an effective date of 30 May 2024. * Late stage refers to active Phase IIb clinical trials or more clinically advanced clinical trials; # Conducted by EOC in China. Immutep has no control over either the trials. § Investigator Initiated Trials controlled by lead investigator & therefore Immutep has no control over this clinical trial; [a] In combination with KEYTRUDA®; [b] In combination with BAVENCIO®.

Efti

A proprietary soluble LAG-3 protein and
first-in-class MHC Class II agonist

Efti: A Soluble LAG-3 'Key' to Stimulate Immune System via MHC II

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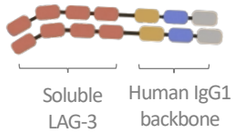
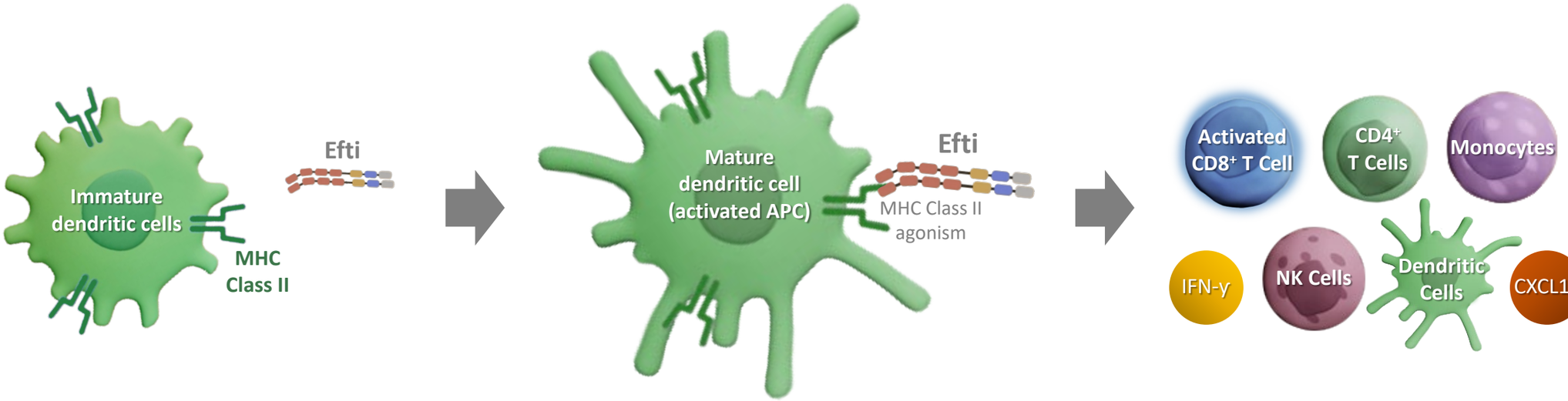
Eftilagimod alpha (efti)

A first-in-class soluble LAG-3 fusion protein with high affinity for a subset of MHC Class II molecules on antigen-presenting cells (APCs)





Efti's unique activation of APCs through MHC Class II agonism drives a broad, sustained adaptive/innate immune response to fight cancer*

* In clinical trials, including monotherapy and in combination with anti-PD-(L)1 therapies and with chemotherapy, efti has led to significant and sustained increases in anti-tumor cells and chemokines / cytokines including those listed in the graphic.
MHC Class II = Major Histocompatibility Complex Class II. APC = Antigen-Presenting Cell.

Systemic Immune Effect Leading to Positive Clinical Outcomes

Encouraging data from efti in combination with IO or chemotherapy across multiple oncology indications

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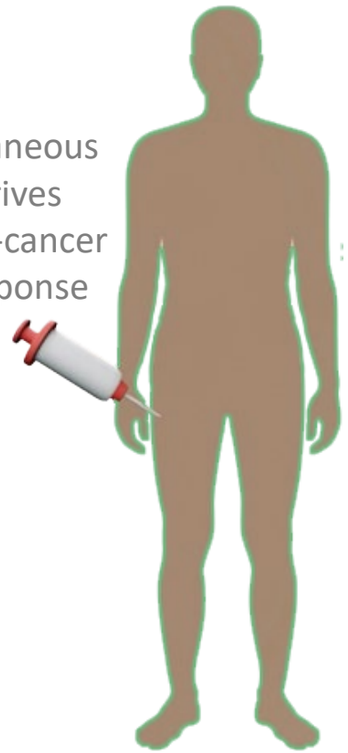
Efti's subcutaneous delivery drives systemic anti-cancer immune response



First Line Metastatic Non-Small Cell Lung Cancer
Doubling of overall survival and response rates of anti-PD-1 (KEYTRUDA®) monotherapy

Second Line Head & Neck Squamous Cell Carcinoma
Doubling responses of anti-PD-1 (KEYTRUDA®) monotherapy and 8X increase in complete responses

Metastatic Melanoma
Disappearance of all target tumor lesions for patients with suboptimal response to anti-PD-1 (KEYTRUDA®)

Advanced Solid Tumors (gastric, cervical, etc.)
Durable responses in immuno-oncology insensitive indications with anti-PD-L1 (BAVENCIO®)

Metastatic HR+/HER-2 Negative Breast Cancer
Improved overall survival vs SOC chemotherapy with significant increases in pre-specified subgroups

Efti + Anti-PD-1 Therapy
Efti + Anti-PD-L1 Therapy
Efti + Chemotherapy

* Based upon clinical data from TACTI-002, INSIGHT-004, TACTI-mel and AIPAC trials.

Differentiated Approach in Oncology

Efti has complementary action with immune checkpoint inhibitors (ICIs) like anti-PD-(L)1 therapy

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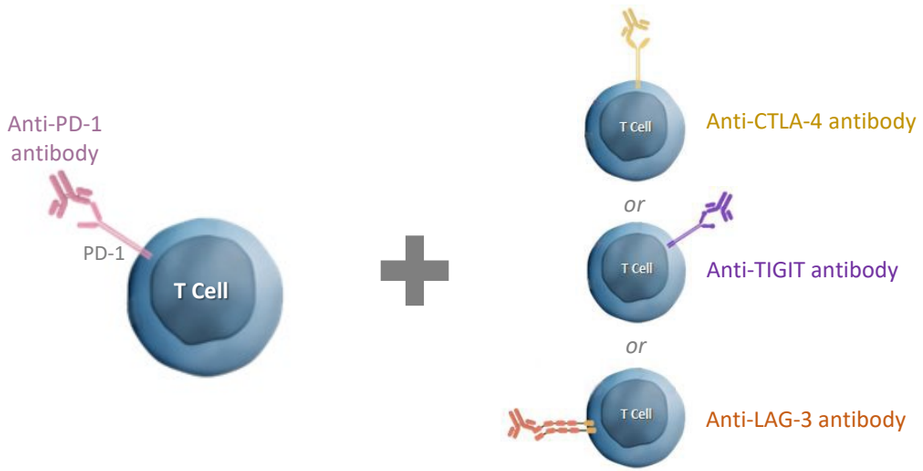
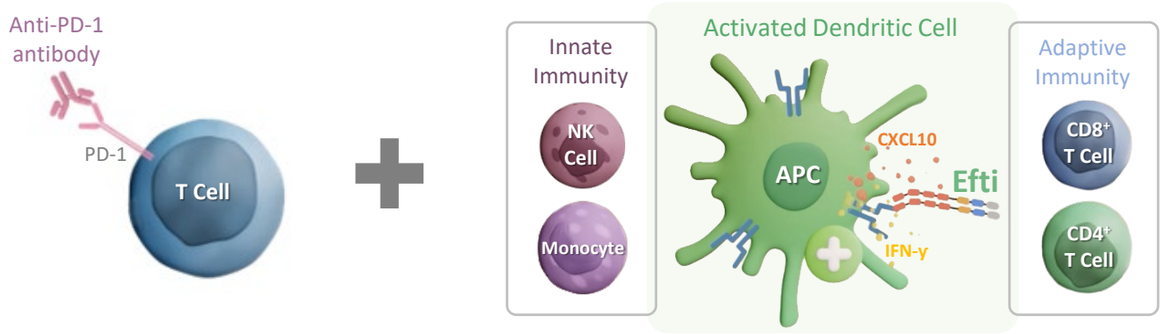
Many ICI combinations with anti-PD-(L)1 therapy focus on T cells alone and just target different immune checkpoints on these T cells



- Efficacy has been mostly limited to “hot” tumors (e.g. high PD-L1 expression) where anti-PD-(L)1 monotherapy is already effective
- Toxicity increases for IO-IO combinations that block two immune checkpoints versus one checkpoint on these T cells[1,2]

Efti’s unique activation of dendritic cells, which engages the adaptive & innate immune system, complements anti-PD-(L)1 therapy that targets T cells



- Efficacy seen across “hot”, “tepid”, and “cold” tumors (e.g. high, low, and negative PD-L1 expression) with efti and anti-PD-(L)1
- Additionally, efti in combination with anti-PD-(L)1 has a favourable safety profile

1. Increased rate of high-grade treatment-related adverse events: 59% in patients treated with ipilimumab (anti-CTLA-4) plus nivolumab (anti-PD-1) versus 23% in patients treated with nivolumab and 28% in patients treated with ipilimumab – Larkin et. al. - Five-Year Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma, N Engl J Med 2019; 381:1535-1546 DOI 10.1056/NEJMoa1910836. 2. Grade 3 or 4 treatment-related adverse events occurred in 18.9% of patients in the relatlimab–nivolumab group and in 9.7% of patients in the nivolumab group.17.7% of patients in the relatlimab–nivolumab group discontinued treatment due to drug-related adverse events as compared to 8.9% in the nivolumab group. – Tawbi et. al. Relatlimab and Nivolumab versus Nivolumab in Untreated Advanced Melanoma, N Engl J Med 2022; 386:24-34, DOI: 10.1056/NEJMoa2109970

Substantial Commercial Opportunity in Combination with ICIs

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Encouraging Clinical Data from Efti in Combination with Anti-PD-(L)1 Therapy including KEYTRUDA® & BAVENCIO®

- **More than double Overall Survival** of KEYTRUDA® (anti-PD-1) monotherapy and well above other standard-of-care IO-IO and/or IO-chemotherapy combinations in first line non-small cell lung cancer (1L NSCLC)
- **More than double Progression Free Survival** of KEYTRUDA® monotherapy in 1L NSCLC patients across varying levels of PD-L1 expression
- **Double the Overall Response Rate** of KEYTRUDA® monotherapy in 1L NSCLC and in second line head & neck cancer (2L HNSCC) in all-comer PD-L1 trial
- **Deep, durable responses in negative & low PD-L1 expressing patients** with both KEYTRUDA® and with BAVENCIO® (anti-PD-L1) across multiple indications

KEYTRUDA® became the world's top selling drug in 2023 with sales exceeding $25 billion

Anti-PD-1**

KEYTRUDA® (pembrolizumab) Injection 100 mg
OPDIVO® (nivolumab)
LIBTAYO® (cemiplimab-rwlc) Injection 350 mg
Jemperli (dostarlimab-gxly) Injection 500 mg

$35+ Billion
in 2023 sales

Anti-PD-L1**

TECENTRIQ® atezolizumab
IMFINZI® durvalumab
BAVENCIO® avelumab Injection 20 mg/mL

$9+ Billion
in 2023 sales

* Based upon clinical data from TACTI-002, INSIGHT-004, and TACTI-mel trials. Source of sales figures: 1. Bloomberg and company reports; Currency: USD. 2023 sales of approved anti-PD-1 therapies include pembrolizumab (KEYTRUDA®) ~$25 billion, nivolumab (OPDIVO®) ~$9 billion, cemiplimab (LIBTAYO®) ~$918 million, dostarlimab (JEMPERLI®) ~$175 million. Sales of approved anti-PD-L1 therapies include atezolizumab (TECENTRIQ®) ~$4.2 billion, avelumab (BAVENCIO®) ~$961 million, durvalumab (IMFINZI®). ~$4.2 billion

Late-Stage Pipeline Addressing Large Markets with Unmet Needs

Efti's three late-stage oncology programs are focused on: Lung, Head and Neck, and Breast Cancer

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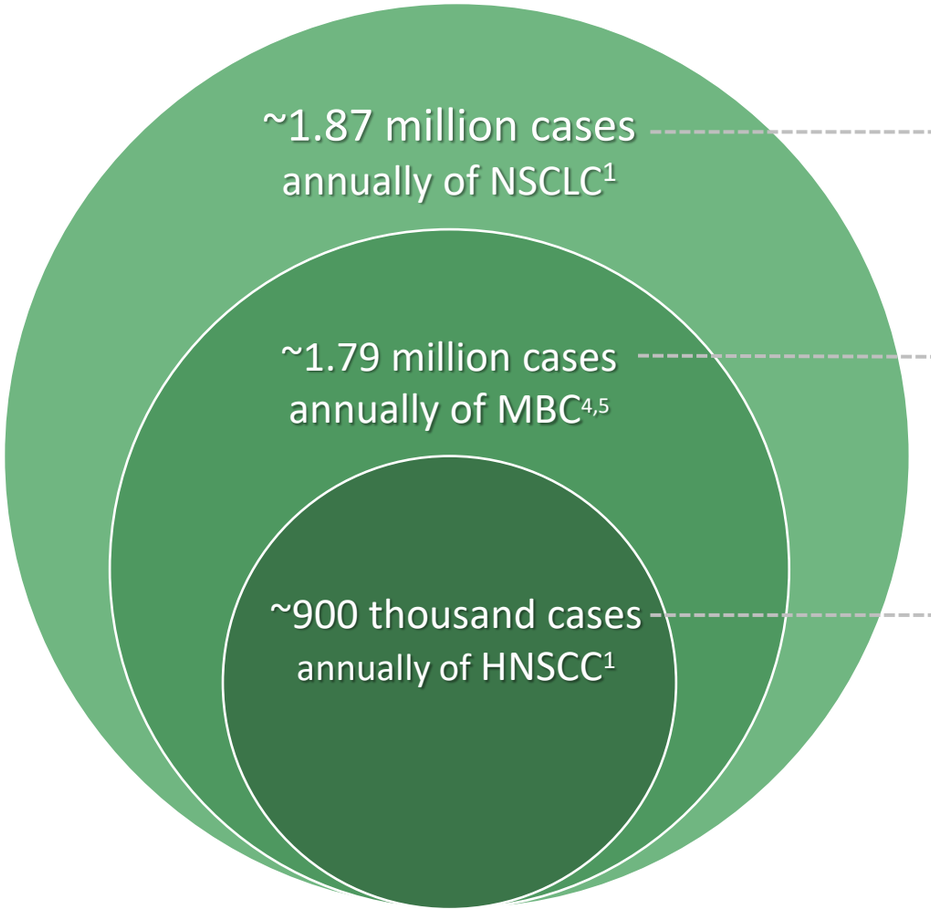

Non-small cell lung cancer (NSCLC)*
drug market to nearly double to $48 billion in 2031[2]

Metastatic breast cancer (MBC)
market to reach $12.7 billion by 2024[6]

Head and neck squamous cell carcinoma (HNSCC)*
market projected to reach $3.5 billion by 2025[3]

*Efti has FDA Fast Track designation in 1L NSCLC and 1L HNSCC

1. Global Cancer Observatory. International Agency for Research on Cancer. World Health Organization. 2. Nature Reviews Drug Discovery 22, 264-265 (2023) doi: https://doi.org/10.1038/d41573-023-00017-9
3. GlobalData. 4. Cancer Stat Facts: Female Breast Cancer Subtypes - NCI SEER. 5. World Health Organization; Breast Cancer Fact Sheet. 6. Estimation of Datamonitor Healthcare, Informa Pharma Intelligence for US, Jap, EU

Efti + Anti-PD-1 in First Line Non-Small Cell Lung Cancer (NSCLC)

ASCO 2022 - Dr. Enriqueta Felip presenting 1L NSCLC data from TACTI-002/KN-798 in Oral Presentation

SITC 2022 - Dr. Wade Iams presenting 1L NSCLC data from TACTI-002/KN-798 in Late Breaking Abstract Oral Presentation

ESMO 2023 - Dr. Enric Carcereny presenting Overall Survival data in 1L NSCLC from TACTI-002/KN-798

Non-Small Cell Lung Cancer (NSCLC) Overview

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Lung cancer is the leading cause of cancer death and 80-85% of the ~2.2 million cases each year are NSCLC[1]

Immune checkpoint inhibitors (ICI) have revolutionized NSCLC treatment yet ~80% patients don't respond to monotherapy

ICI + chemotherapy or ICI + ICI combinations have limited durability and/or higher toxicity & discontinuation rates

Despite treatment advances, Overall Survival is still under 2 years for most NSCLC patients[2]

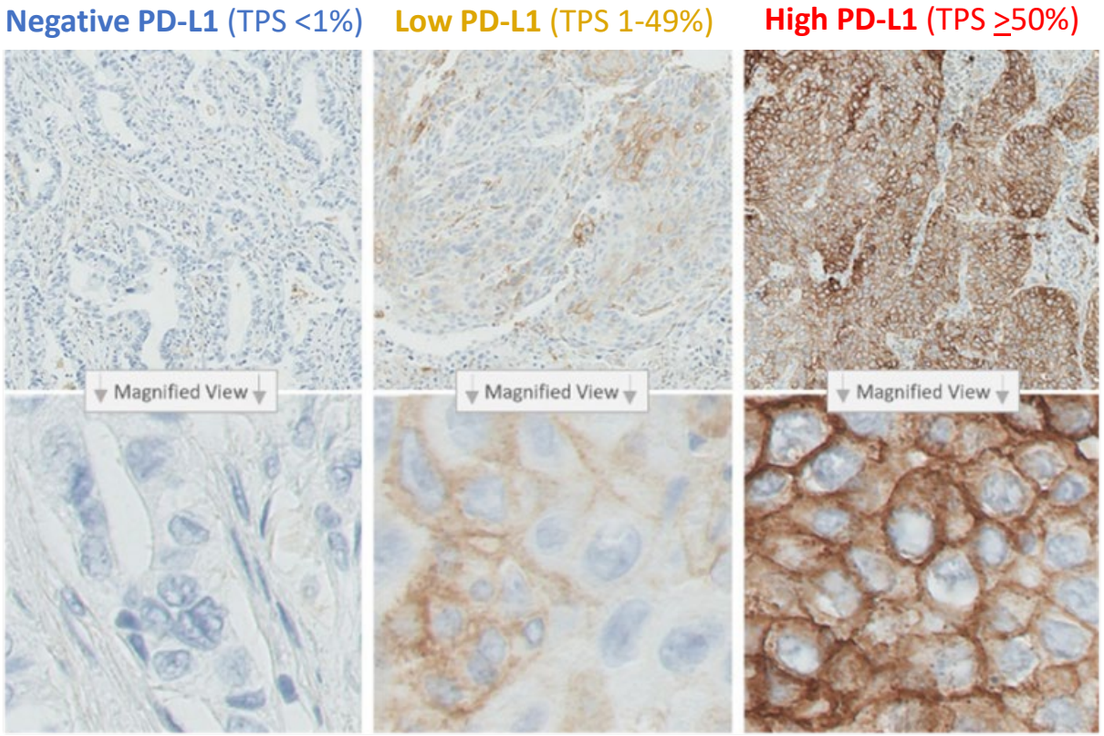
$48 Billion
Major Market Therapeutic Sales in 2031[3]

$24 Billion
Major Market Therapeutic Sales in 2021[3]

1. Calculated from Global Cancer Observatory (WHO), 2020 data & American Cancer Society, About Lung Cancer; 2.Tang S et al. Immune Checkpoint Inhibitors in Non-Small Cell Lung Cancer: Progress, Challenges, and Prospects. Cells. 2022 Jan 19;11(3):320. doi: 10.3390/cells11030320; 3. Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023) doi: https://doi.org/10.1038/d41573-023-00017-9.

PD-L1 Expression Levels and Why They Matter in 1L NSCLC

- PD-L1 expression as measured by Tumor Proportion Score (TPS) is an FDA approved predictive biomarker in 1L NSCLC for ICIs including anti-PD-(L)1 therapy
- Patients are grouped by high (TPS ≥50%), low (TPS 1-49%), and negative (TPS <1%) PD-L1 expression
- Generally, high expressors (who have a strong preexisting local anti-tumor T cell response) respond best, low expressors respond sub-optimally, and negative expressors have negligible responses to ICI therapies
- The mixed clinical responses to anti-PD-(L)1 therapy across these three PD-L1 expression levels are reflected in the regulatory landscape of approved chemotherapy-free ICI therapies (as shown in the graphic to the right)



Approved Chemotherapy-free ICI Therapies in 1L NSCLC by PD-L1 Expression*

Negative PD-L1 (TPS <1%)	Low PD-L1 (TPS 1-49%)	High PD-L1 (TPS ≥50%)
None approved in Europe or the US for patients with negative PD-L1 expression	**None approved** in Europe, and **two approved**** in the US for patients with low PD-L1 expression	**Three approved** in both Europe and the US for patients with high PD-L1 expression

Image from Garon et al. Pembrolizumab for the treatment of non-small-cell lung cancer. N Engl J Med. 2015;372:2018–28. PD-L1 staining is shown by the presence of the brown chromogen. Expression of PD-L1 by tumor cells at baseline is known to be correlated with the level of IFN-gamma producing activated T cells at the tumor site, and is reflective of a strong pre-existing tumor-specific T cell response. * For patients with high PD-L1 expression, KEYTRUDA (anti-PD-1), TECENTRIQ (anti-PD-L1), and OPDIVO combined with YERVOY (anti-PD-1 + anti-CTLA4) are approved in US and Europe. For patients with low PD-L1 expression, KEYTRUDA as well as OPDIVO combined with YERVOY are approved in the US. ** Only OPDIVO combined with YERVOY is a NCCN Category 1 treatment option in the US.

TACTI-002 / KN-798 Trial Overview and Baseline Characteristics

Part A: Large Phase II trial (N=114) in metastatic 1st Line non-small cell lung cancer (1L NSCLC)

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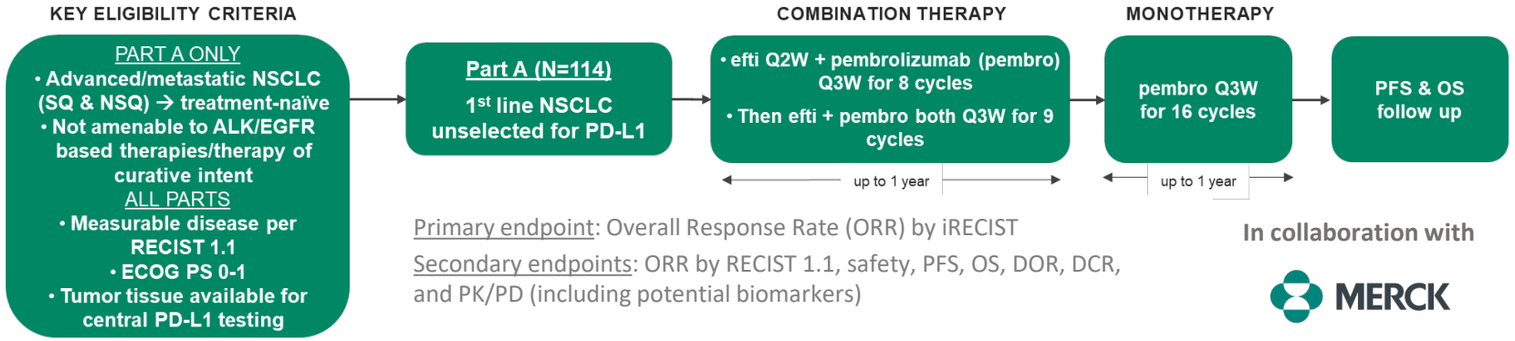
TACTI-002 (Part A) in 1L NSCLC

- Phase II, open label, Simon's two stage design
- Six countries (US, UK, ES, PL, UA, AU)
- 114 patients enrolled across 18 sites

PD-L1 Expression in TACTI-002

- TACTI-002 enrolled 1L NSCLC patients regardless of PD-L1 expression
- ~75% patients have PD-L1 TPS <50%, with ~35% having negative expression (TPS <1%)
- ~25% patients have high PD-L1 (TPS ≥50%); this is lower proportion than would typically be expected



Primary endpoint: Overall Response Rate (ORR) by iRECIST

Secondary endpoints: ORR by RECIST 1.1, safety, PFS, OS, DOR, DCR, and PK/PD (including potential biomarkers)

In collaboration with MERCK

Baseline characteristics for TACTI-002 Part A		N=114	
Age, median (range), years		67 (44-85)	
Sex, n (%)	Female / Male	30 (26.3) / 84 (73.7)	
ECOG PS score, n (%)	0 / 1	43 (37.7) / 71 (62.3)	
Smoking status, n (%)	Current or Ex-smoker / Non-smoker	108 (94.7) / 6 (5.3)	
Histology, n (%)	Squamous / Non-squamous / Unknown	40 (35.1) / 72 (63.2) / 2 (1.8)	
Metastatic disease, n (%)	Yes / No	113 (99.1) / 1 (0.9)	
PD-L1 expression TPS, n (%)		*Central only* [1]	*Central + local* [2]
	< 1%	32 (35.6)	37 (34.3)
	1-49%	38 (42.2)	42 (38.9)
	≥ 50%	20 (22.2)	29 (26.9)
Previous therapy, n (%)	Radiotherapy	38 (33.3)	
	Surgery	23 (20.2)	
	Systemic therapy for non-metastatic disease	26 (22.8)	

Patients were recruited according to Simon's optimal two-stage design: during the first stage, 17 pts were recruited; second stage recruitment (n=19) was opened only after the number of responses was above 4. An extension stage (n=78) could be added if there were above 12 responses. In total, 114 pts were enrolled.

[1] N=90; Central assessment of PD-L1 TPS using Dako IHC 22C3 pharmDx. [2] N=108; Central + local assessment. For 18 patients, local assessment used predominantly Dako IHC 22C3 pharmDx due to non-evaluable central assessment results.

Strong Efficacy Data across all PD-L1 Expression Levels in 1L NSCLC

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Tumor Response by PD-L1 Expression Level[1]

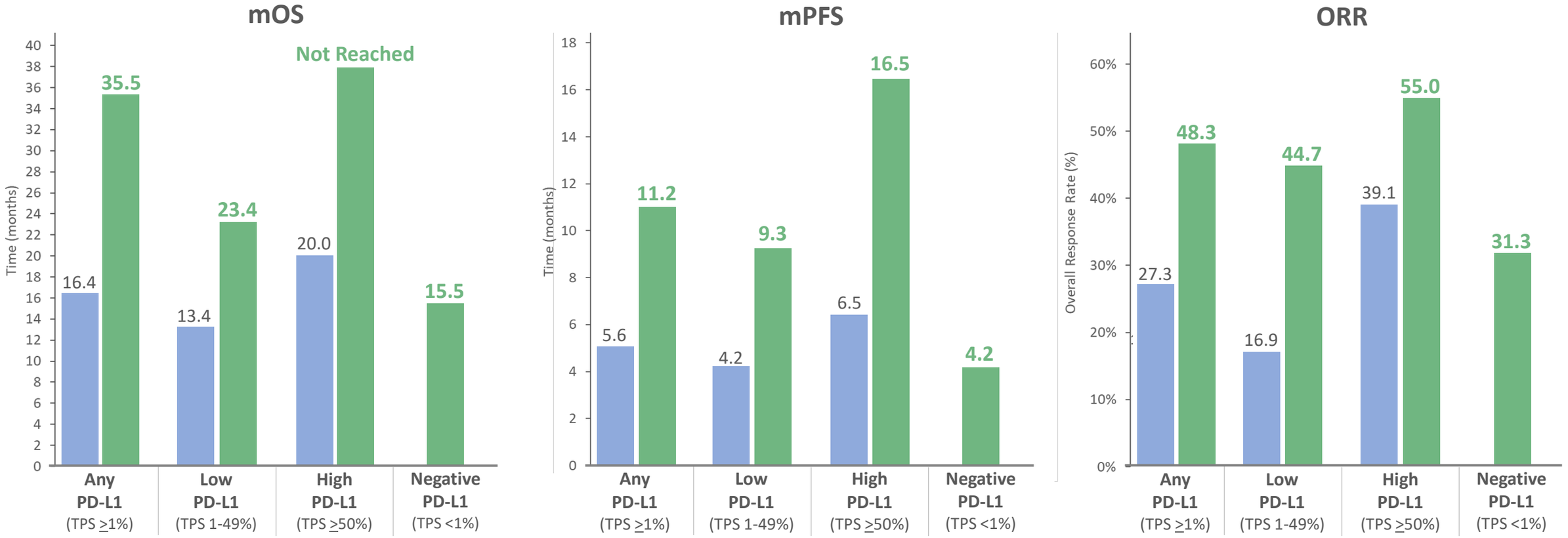
	All-Comer	Negative PD-L1	Low PD-L1	High PD-L1	Any PD-L1
	TPS 0-100% N=114	TPS <1% N=32	TPS 1-49% N=38	TPS ≥50% N=20	TPS ≥1% N=58
ORR[2,3,4]	40.4%	31.3%	44.7%	55.0%	48.3%
mPFS[2], months	6.6	4.2	9.3	16.5	11.2
mDoR[2], months	21.6	20.7	NR	18.7	24.2
mOS, months	**20.2**	**15.5**	**23.4**	**Not Reached**	**35.5**

ORR – Overall Response Rate
mPFS – median Progression Free Survival
mDOR – median Duration of Response
mOS – median Overall Survival

- Strong efficacy across all patients, including negative & low expressors (~75% of patients in TACTI-002), differentiates efti with anti-PD-1 from other chemotherapy-free IO combinations in 1L NSCLC
- Excellent Overall Survival, the gold standard benchmark in oncology
- Exceptional durability and quality of responses with favorable safety profile
- Results offer compelling evidence of efti's unique stimulation of patients' immune systems and the positive impact that has in fighting cancer

Data cut-off date: August 15, 2023. Median follow-up 25.1 months. [1] N=90; Central assessment of PD-L1 TPS using Dako IHC 22C3 pharmDx; [2] iRECIST; [3] unconfirmed; [4] calculated using Clopper Pearson method; NR: not reached.
Note: results for PD-L1 central + local (N=108) were as follows (<1% / 1-49% / ≥50% / ≥1%): mOS, mo: 14.4 / 23.4 / 38.8 / 35.5; mPFS[2]: 4.2 / 8.3 / 16.3 / 9.8; mDoR[2]: 20.7 / 21.6 / 18.7 / 21.6.

Benchmarking to Pembrolizumab (KEYTRUDA®) Monotherapy



Robust median overall survival (mOS), median progression free survival (mPFS), and response rates (ORR) from efti plus pembrolizumab

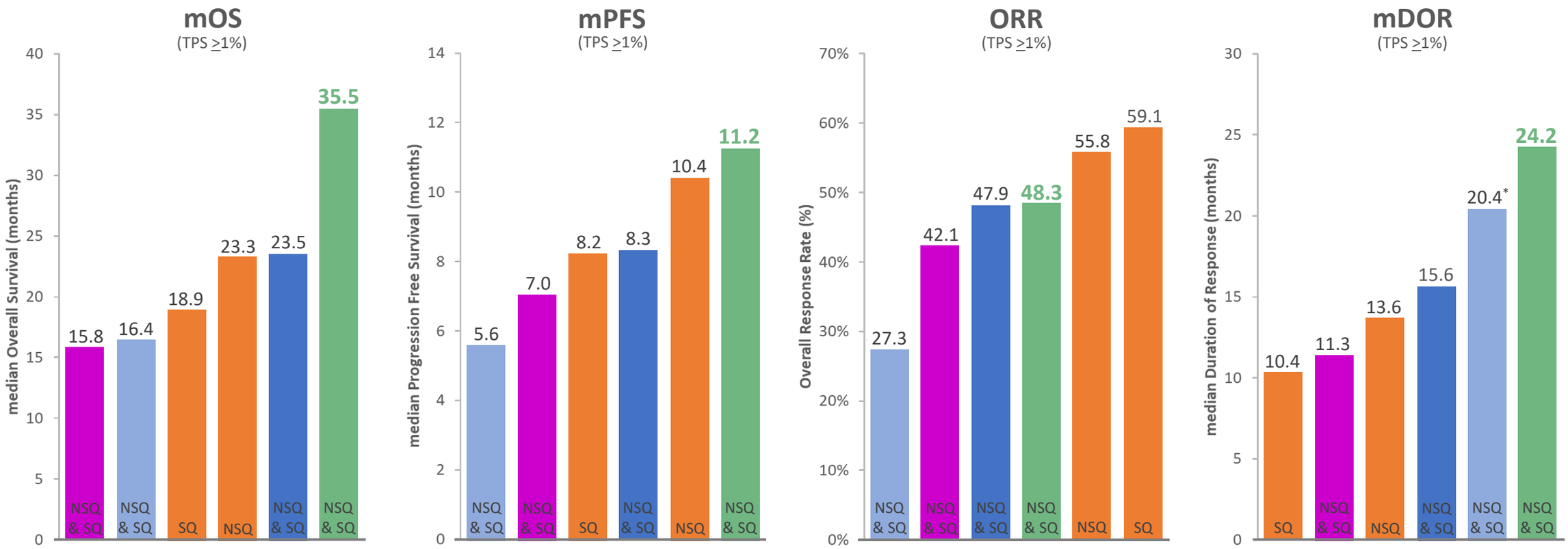
Strength of efti plus pembrolizumab in TPS 1-49% contributes significantly to TPS ≥1% results, unlike other IO + anti-PD-1 combinations

OS/PFS/ORR in negative PD-L1 (TPS <1%) patients compares well to pembrolizumab monotherapy in low PD-L1 (TPS 1-49%) patients

Pembrolizumab monotherapy data from publications/EPAR asessment report of KN-042 registrational trial. Comparison of data is from different clinical trials. Given the lack of historical results in negative PD-L1 expressing 1L NSCLC patients who received pembrolizumab monotherapy in KN-042 and other trials, the chart only has data from patients in TACTI-002 with negative PD-L1 expression. In TPS ≥1%, TACTI-002 has 66% patients with TPS 1-49% and 34% with TPS ≥50%, which compares to KN-042 with ~53% patients with PD-L1 and ~47% patients with PD-L1 TPS ≥50%.

Benchmarking Efficacy to Standard-of-Care in PD-L1 TPS ≥1%

Chemo-free efti + anti-PD-1 data compares favorably to SOC chemo-free IO-IO & IO-chemo combinations



Chemotherapy-Free IO Therapies#

- Efti + pembrolizumab
- Pembrolizumab monotherapy

IO-Chemotherapy or IO-IO-Chemotherapy Therapies

- Pembrolizumab + doublet chemo
- Cemiplimab + doublet chemo
- Nivolumab + Ipilimumab + doublet chemo

NSQ = Non-squamous NSCLC / SQ = Squamous NSCLC.

Data for standard-of-care therapies taken from publications/EPAR assessment report of respective registrational trials (e.g., KN-042, KN-189, KN-407, CM-9LA, EMPOWER-Lung 3), and comparison of data is from different clinical trials. *Pembro monotherapy DOR of 20.4 months based on similar 2-year median follow up as compared to TACTI-002 Phase II median follow-up of 25.1 months. # In the TPS ≥1% patient population TACTI-002 has 66% patients with TPS 1-49% and 34% with TPS ≥50%, which compares to KN-042 with ~53% patients with PD-L1 1-49% and ~47% patients with PD-L1 TPS ≥50%.

Benchmarking to Chemo-Free Therapies in Low PD-L1 (TPS 1-49%)

Efti + pembro results in low & negative PD-L1 patients compare favorably to other therapies in low PD-L1

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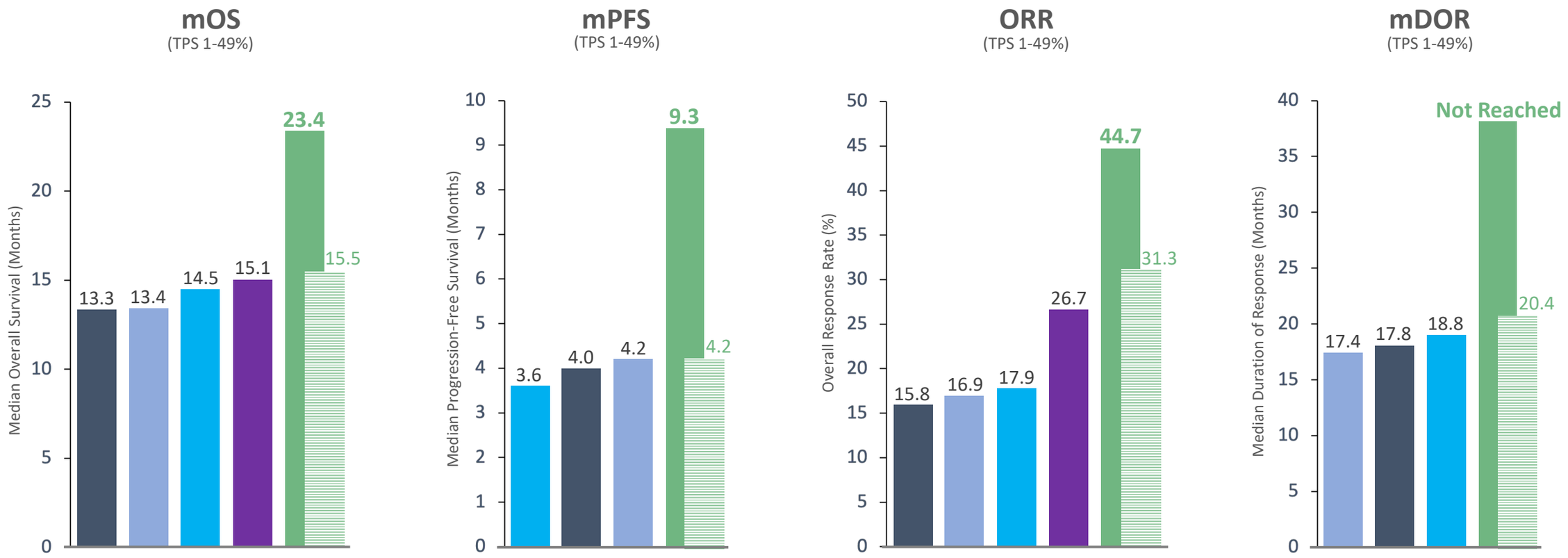


Chemotherapy-Free IO Therapies

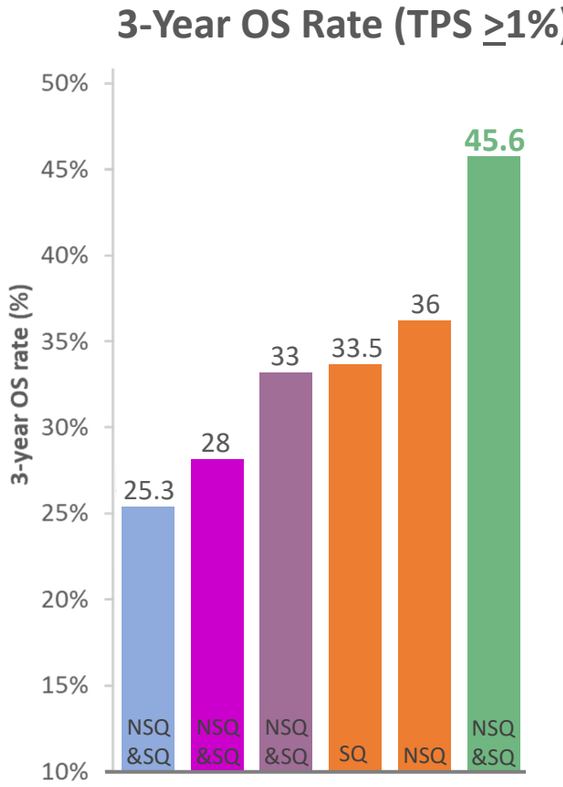
- Pembrolizumab monotherapy
- Atezolizumab monotherapy
- Atezolizumab + Tiragolumab (anti-PD-L1) (anti-TIGIT)

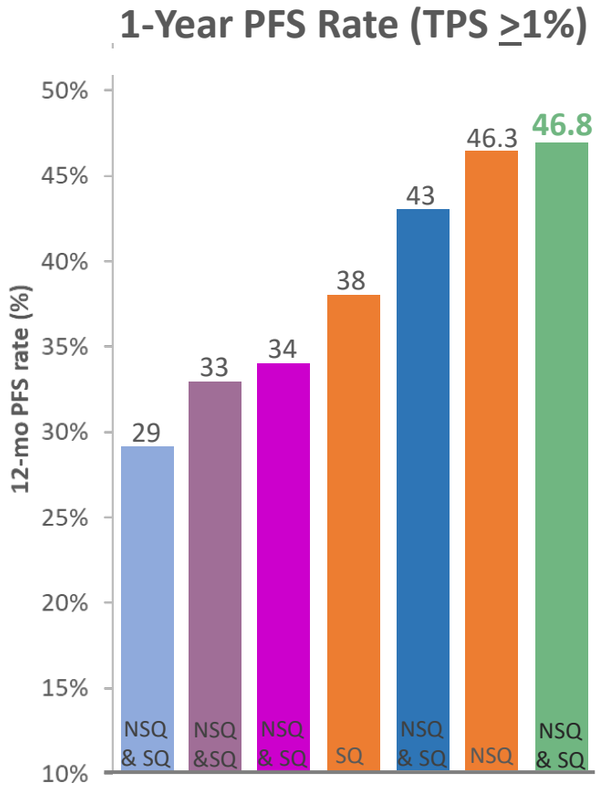
- Efti + Pembrolizumab
- Efti + Pembrolizumab in negative PD-L1 (TPS <1%)*
- Nivolumab + Ipilimumab (anti-PD-1) (anti-CTLA-4)

Note: negative PD-L1 expressing patients typically have negligible responses to ICI therapies and are not expected to perform as well as low PD- L1 expressing patients.

Pembrolizumab monotherapy data from publications/EPAR asessment report of KN-042 registrational trial, Atezolizumab and Tiragolumab + Atezolizumab data from CITYSCAPE Phase II trial. Ipilimumab + Nivolumab from CM-227 registrational trial (did not include mPFS or mDOR data), and comparison of data is from different clinical trials.

Exceptional Durability and Quality of Responses





Chemotherapy-free IO

- Efti + pembrolizumab
- Nivolumab + ipilimumab
- Pembrolizumab monotherapy

IO + Doublet Chemotherapy

- Pembrolizumab + doublet chemo
- Nivolumab + ipilimumab + doublet chemo
- Cemiplimab + doublet chemo

- Exceptional 3-year Overall Survival rate of 45.6%, superior to pembrolizumab monotherapy and standard-of-care chemo-free & chemo-containing regimens
- Positive 12-month PFS rate of 46.8%, superior to pembro monotherapy and inline/above chemo-containing regimens
- Efti + pembro may be in a unique position to lift the tail of the survival curve in patients that express PD-L1

NSQ = Non-squamous NSCLC and SQ = Squamous NSCLC. Data for standard-of-care therapies taken from publications of respective registrational trials (e.g., KN-042, KN-189, KN-407, CM-9LA, EMPOWER-Lung 3), and comparison of data is from different clinical trials.

Favorable Safety

Differentiated OS from **Efti + Pembrolizumab** achieved with a **favorable safety profile** given complementary IO approaches targeting two different immune cells as well as no use of chemotherapy

Therapy in 1L NSCLC TPS ≥1%	Drug-related Adverse Events Leading to Discontinuation[2]	Median Overall Survival[3]
Efti + Pembrolizumab	**9.6%**	**35.5 months**
Pembro + Doublet Chemo (NSQ)	20.5%	23.3 months
Pembro + Doublet Chemo (SQ)	16.8%	18.9 months
Ipilimumab + Nivolumab[1]	18.1%	17.1 months
Pembrolizumab monotherapy[1]	**9.9%**	16.4 months
Ipi + Nivo + 2 cycles of Doublet Chemo	22.1%	15.8 months

NSQ = Non-squamous; SQ = Squamous

1. Ipilimumab + Nivolumab approved in US for 1L NSCLC PD-L1 TPS >1% but not in EU; Pembro mono not approved in Europe for TPS 1-49%. 2. Treatment related adverse events leading to discontinuation taken from publications/EPAR assessments of respective trials (KN-042, KN-024, KN-189, KN-021, KN-407, CM-227, CM-9LA). 3. Arrow lengths are proportional representations of Overall Survival data. Data for standard-of-care therapies taken from publications of respective registrational trials (e.g., KN-042, KN-189, KN-407, CM-227, CM-9LA), and comparison of data is from different clinical trials.

Th1 Biomarker Data Linked to Improved Clinical Outcomes

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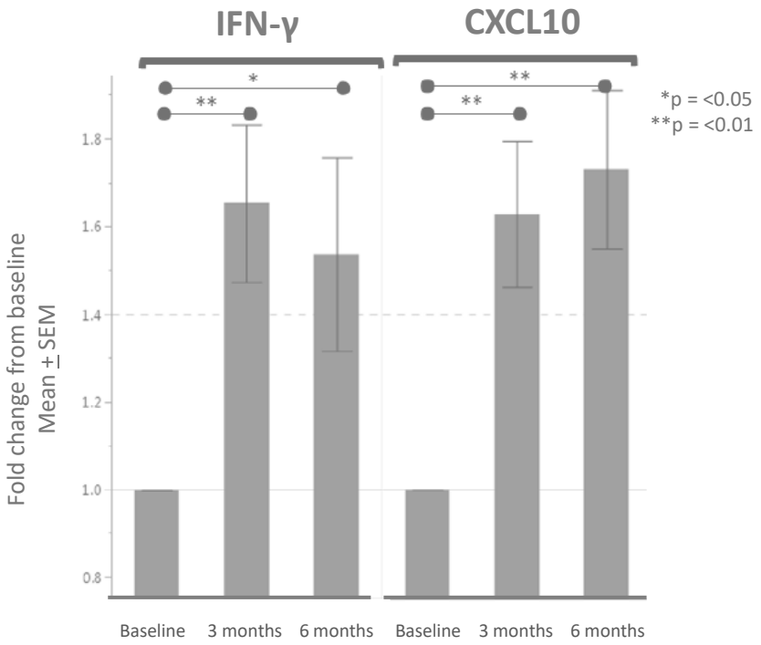
Significant, sustained increases in CXCL10 & IFN-γ in TACTI-002 Phase II trial in 1L NSCLC tied to efti's unique stimulation of immune system



* Similar increase in Th1 biomarkers also seen in randomized AIPAC Phase IIb trial in metastatic breast cancer, which combined efti solely with chemotherapy

- **IFN-γ** – After first efti dosing, 86% (6/7) of responders* showed a ≥1.4-fold change and 86% (6/7) of non-responders# had less than a 1.4-fold change.
- **CXCL10** – After first efti dosing, 100% (7/7) of responders* showed a ≥1.4-fold change and 100% (5/5) of non-responders# had less than a 1.4-fold change.

CXCL10 may be an important biomarker with anti-PD-1 therapies**

"Strategies that support effector T cell recruitment via induction of CXCL10 should be considered as a mechanism-based intervention to expand immunotherapy efficacy." [1]

Journal for ImmunoTherapy of Cancer

"…Chemokines CXCL9/10 are indispensable for robust responses to immune checkpoint inhibitors (anti-PD-1 and anti-CTLA-4)…" [2]

CLINICAL CANCER RESEARCH

"CXCL9 and CXCL10 bring the heat to tumors" [3]

Science Immunology

"Circulating CXCL10 at baseline appeared to be a robust predictor of response." [4]

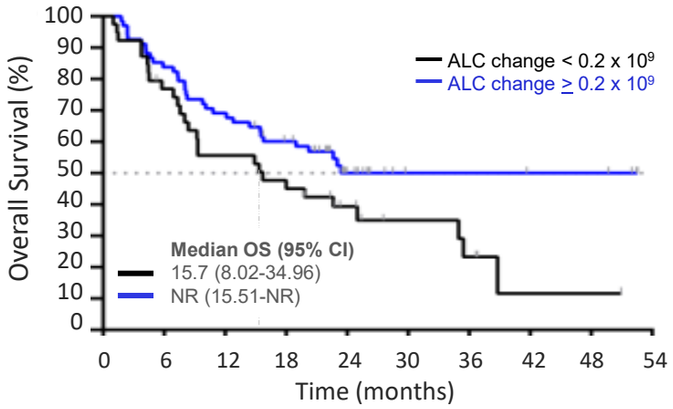
Journal for ImmunoTherapy of Cancer

Data from Immutep's SITC 2023 presentation. *Responders: CR=Complete Response, PR=Partial Response. #Non-responders: SD=Stable Disease, PD=Progressive Disease, NE=Non-Evaluable, NA=Not Available **1. Immune cell and tumor cell-derived CXCL10 is indicative of immunotherapy response in metastatic melanoma. Reschke R, Yu J, Flood BA, et al., *J Immunother Cancer 2021*; 9:e003521. doi:10.1136/ jitc-2021-003521; 2. Macrophage-Derived CXCL9 and CXCL10 Are Required for Antitumor Immune Responses Following Immune Checkpoint Blockade, House et al., *Clin Cancer Res (2020)* 26 (2): 487–504. https://doi.org/10.1158/1078-0432.CCR-19-1868; 3. CXCL9 & CXCL10 bring the heat to tumors, Reschke et al., *Sci Immunol. 2022* Jul 22;7(73):eabq6509. 4. Phase II study of pembrolizumab in refractory esophageal cancer with correlates of response and survival, de Klerk et al., *J Immunother Cancer. 2021;* 9(9)

ALC Biomarker Data Links Efti to Improved Overall Survival

1L Non-Small Cell Lung Cancer - TACTI-002 Phase II

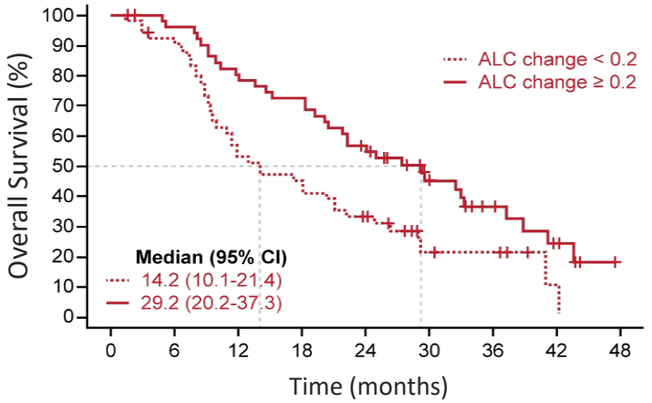
Efti + Pembrolizumab (anti-PD-1)



>30 months OS gain
P value = 0.029

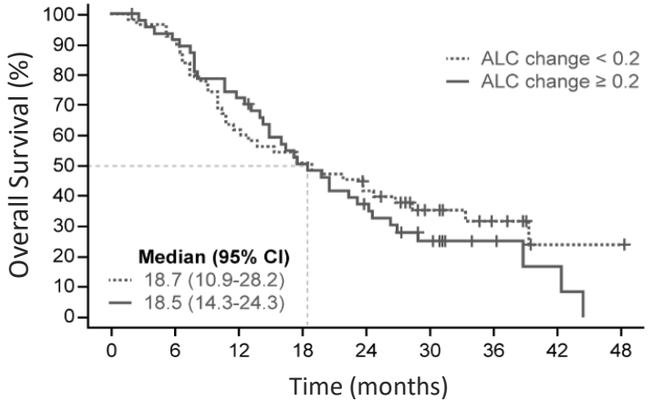
Metastatic Breast Cancer - AIPAC Randomized, Double-Blind Phase IIb

Efti + Paclitaxel (chemotherapy)



15 months OS gain
P value = 0.003

Placebo + Paclitaxel



No OS gain
P value = 0.246

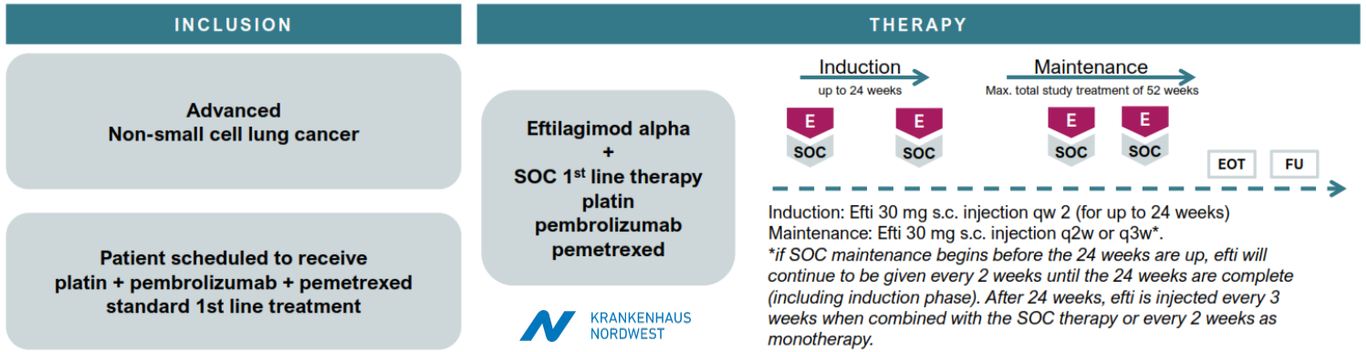
In trials combining efti with anti-PD-1 therapy (TACTI-002) and efti with chemotherapy (AIPAC), an early increase in ALC* is significantly associated with improved Overall Survival (OS). This is not seen in the control arm of the double-blind randomized AIPAC Phase IIb trial, suggesting efti is leading to an effective immune response including a large increase in activated anti-cancer cells.

* Within first 9 weeks (before 4th cycle)

INSIGHT-003: IO-IO-Chemo Combination Trial in 1L NSCLC

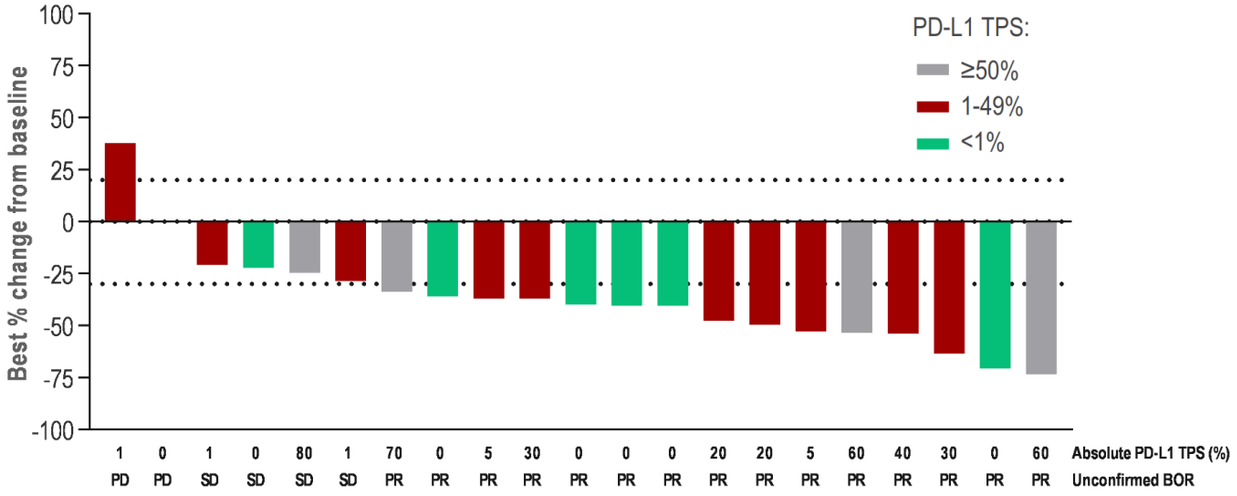
Promising initial efficacy & safety from first-in-human study evaluating efti + anti-PD-1 + doublet chemo

INSIGHT-003 - Investigator-initiated study in first line non-squamous NSCLC

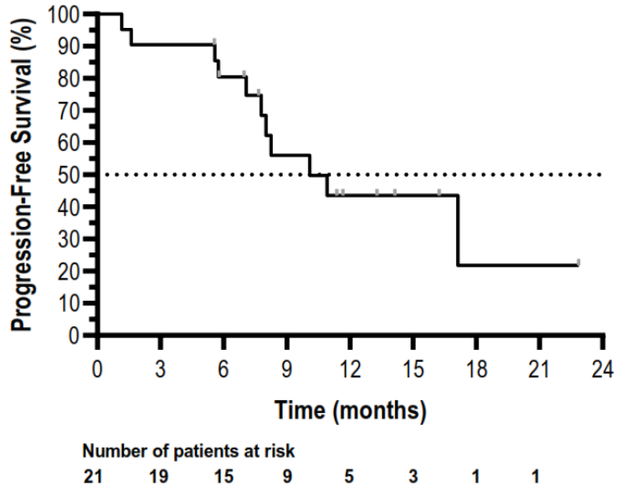


- Triple combination well tolerated and appears safe
- At data cut-off, unconfirmed ORR of 71.4% (confirmed ORR of 66.7%)
- mPFS of 10.1 months and mOS was not reached in ITT population (median follow up 12.4 months)

Best Overall Response by PD-L1 Status



Progression-Free Survival



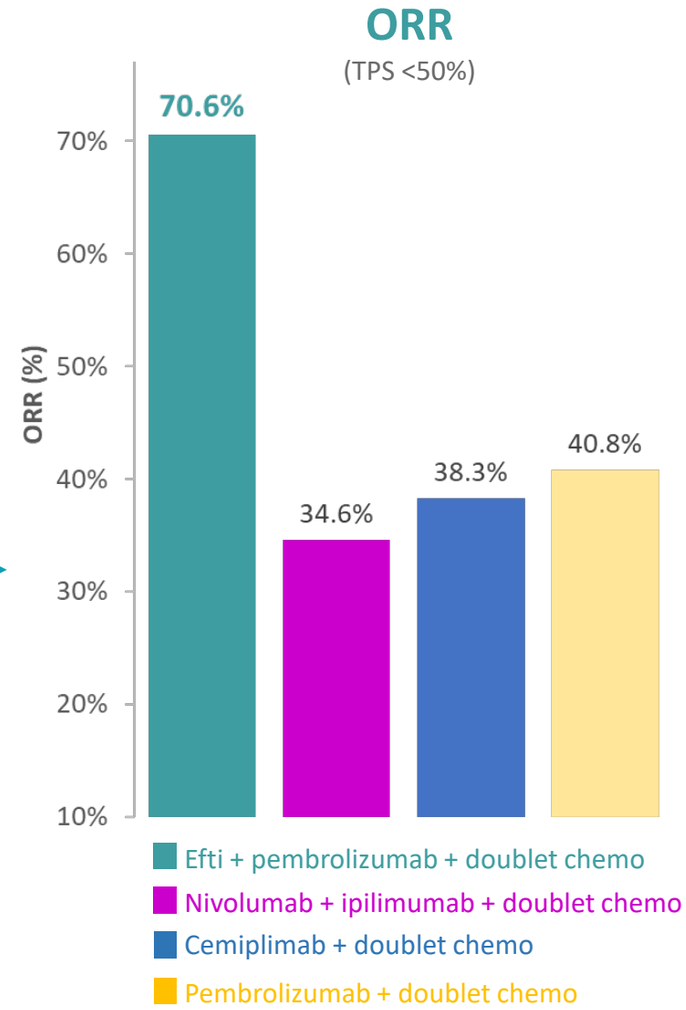
Source: ESMO 2023 Poster (#1042P) – A Atmaca et al., INSIGHT 003 evaluating feasibility of eftilagimod alpha (soluble LAG-3) combined with 1st line chemo-immunotherapy in metastatic non-small cell lung cancer (NSCLC) adenocarcinomas – a multicenter early phase trial.

Efti + Anti-PD-1 + Chemotherapy versus SoC in PD-L1 TPS <50%

Tumor Response	PD-L1 expression level (TPS)			
	<1%, N=7	1-49%, N=10	≥50%, N=4	<50%, N=17
ORR* unconfirmed, n (%)	5 (71.4)	7 (70.0)	3 (75.0)	12 (70.6)
ORR* confirmed, n (%)	5 (71.4)	6 (60.0)	3 (75.0)	11 (64.7)
mPFS*, months (% events)	10.1 (42.9)	10.9 (60.0)	7.1 (50.0)	10.9 (52.9)
mOS, months (% events)	17.4 (28.6)	NR (10)	NR (25)	NR (17.6)

* Per RECIST 1.1.

INSIGHT-003 data compares favorably to registrational trials of standard-of-care anti-PD-1 and chemotherapy combinations, including ORR between 34.6% to 40.8%, in the same PD-L1 TPS <50% patient population.[1,2]



Source: ESMO 2023 Poster (#1042P) – A Atmaca et al., INSIGHT 003 evaluating feasibility of eftilagimod alpha (soluble LAG-3) combined with 1st line chemo-immunotherapy in metastatic non-small cell lung cancer (NSCLC) adenocarcinomas – a multicenter early phase trial.

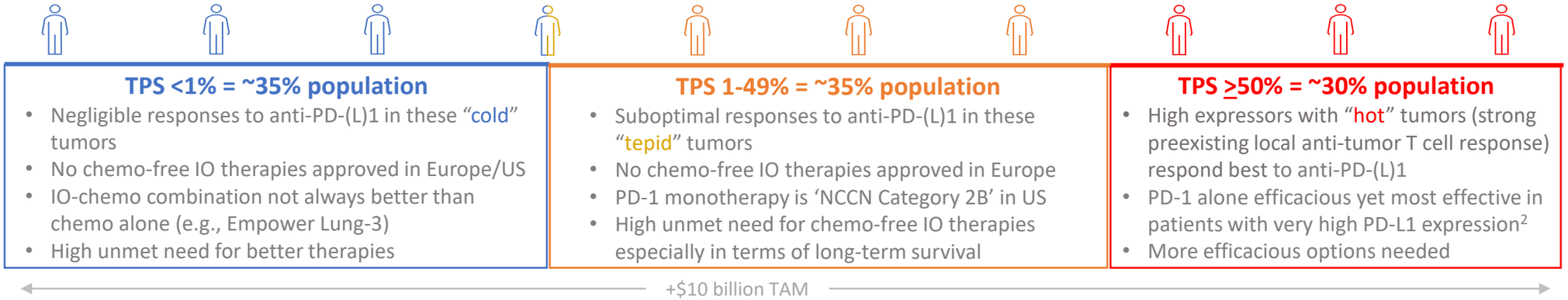
1. Journal of Clinical Oncology 2020 38:14, 1505-1517, Updated Analysis From KEYNOTE-189: Pembrolizumab or Placebo Plus Pemetrexed and Platinum for Previously Untreated Metastatic Nonsquamous Non–Small-Cell Lung Cancer; EMPOWER-Lung 3: EPAR Assessment Report MA/CHMP/118736/2023 of 23 February 2023; CheckMate 9LA: M. Reck et al. Lancet Oncol 2021, https://doi.org/10.1016/j.esmoop.2021.100273. 2. EMPOWER-Lung 3 (Cemiplimab + doublet chemo) and CM-9LA data includes squamous patients as well. Comparison of data is from different clinical trials

Efti Uniquely Positioned in 1st line Non-Small Cell Lung Cancer

Large potential opportunity for efti with both chemo-free IO-IO and IO-IO-chemo combinations

1L NSCLC Patient Population by PD-L1 Tumor Proportion Score (TPS)[1]

PD-1 expression levels have substantial impact on clinical outcomes for anti-PD-(L)1 therapies



The strength of the clinical data presented at ESMO 2023, SITC 2022, and ASCO 2022 shows *efti has significant potential to address all PD-L1 levels*

(1) Patient population estimates by PD-L1 expression: based on publications of registrational trials KN-001, KN-189, KN-407, EMPOWER-Lung 3 and TACTI-002 all comer Phase II trial. (2) Aguilar et al. Ann. Onc. 2019, 1;30(10):1653-1659. DOI: 10.1093/annonc/mdz288
(3) Market size estimates are based on intelligence data from GlobalData and Nature Reviews Drug Discovery 22, 264-265 (23 Jan 2023) doi: https://doi.org/10.1038/d41573-023-00017-9. Note Efti + pembrolizumab has Fast Track Designation in ≥1% TPS in 1L NSCLC.

Efti + Anti-PD-1 in Head & Neck Cancer

Efti + Pembro in Head & Neck Squamous Cell Carcinoma

Strong, durable efficacy in second line HNSCC

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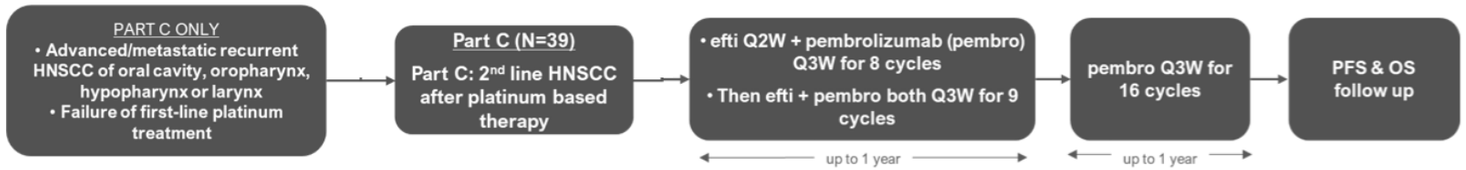
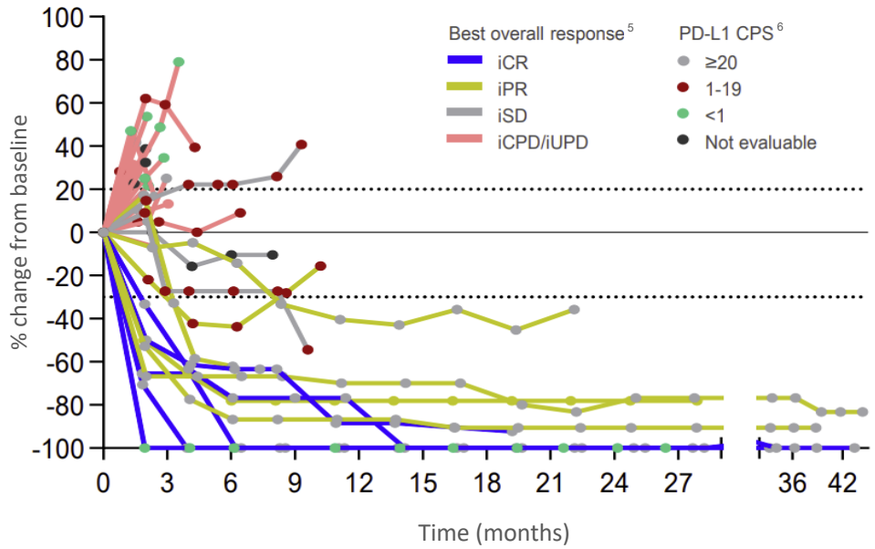
TACTI-002/KEYNOTE-798 (Part C): 2nd Line Head & Neck Squamous Cell Carcinoma (2L HNSCC)

TACTI-002/KEYNOTE-798 Part C Trial Design



- Encouraging ORR of 29.7% in ITT population (all-comer PD-L1) and treatment well-tolerated
- Early onset of responses (median ~2 months) that were deep (13.5% CRs) and durable (median DoR not reached despite a median follow up of ~39 months)
- Promising ORR of 60%, median PFS of 13.6 months and median OS of 15.5 months in patients with CPS ≥20

	ITT N=37	CPS ≥1* N=25	CPS ≥20* N=15
ORR[2,3]	29.7%	38.5%	60.0%
mPFS[2,4], months	2.1	2.3	13.6
6-mo PFS rate	32.4%	40.0%	53.3%
mDoR[2], months	NR	NR	NR
mOS[4], months	8.7	12.6	15.5
12-mo OS rate	46.0%	52.0%	66.7%



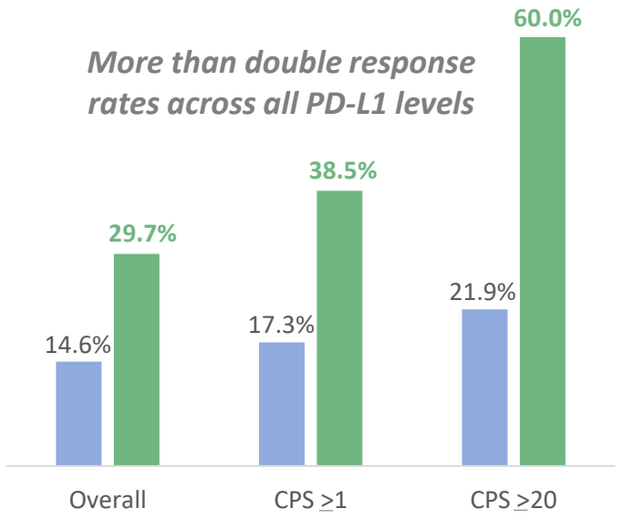
Data from Final results from TACTI-002 Part C: A Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with metastatic 2nd line head and neck squamous cell carcinoma unselected for PD-L1 – ASCO 2023. * Central assessment of PD-L1 CPS using Dako IHC 22C3 pharmDx for 32 pts. 2. By iRECIST (local assessment). 3. 95% confidence intervals calculated using Clopper-Pearson method. 4. 95% confidence intervals calculated using Kaplan Meier survival analysis method. 5. Best overall response by iRECIST (local assessment). 6. Central PD-L1 assessment with Dako kit.

Benchmarking to Pembro Monotherapy

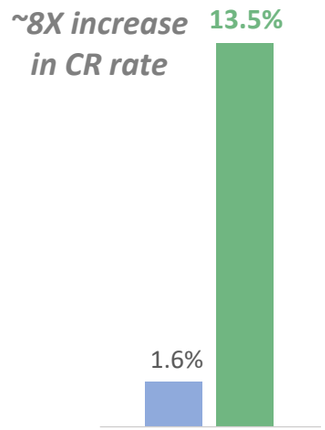
Robust ORR, CR and OS for efti + pembro vs pembro alone with favorable safety profile in 2L HNSCC

TACTI-002/KEYNOTE-798 (Part C): 2nd Line Head & Neck Squamous Cell Carcinoma (2L HNSCC)

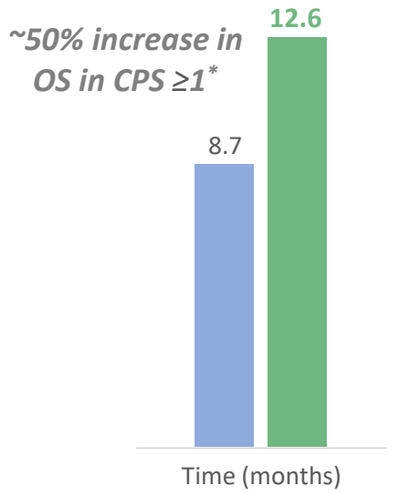
Overall Response Rate



Complete Response Rate

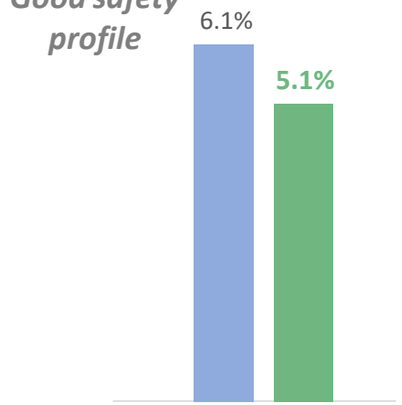


Overall Survival Rate



Discontinuation Rate

from drug-related adverse events



Efti + pembrolizumab

Pembrolizumab monotherapy#

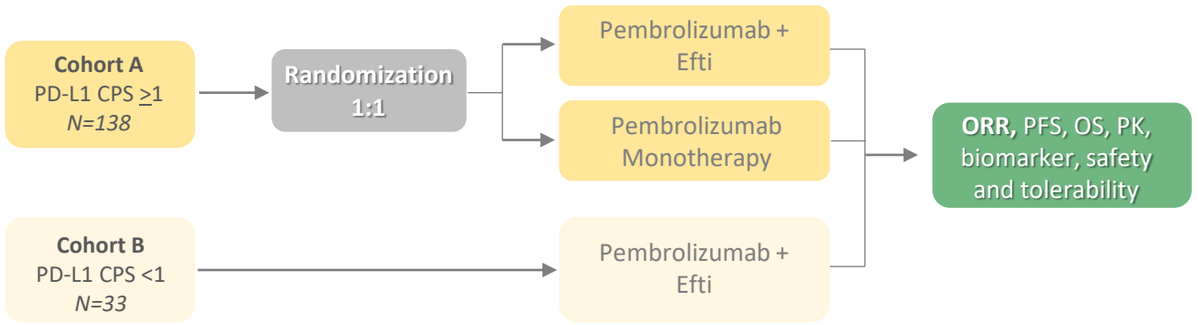
Data from Final results from TACTI-002 Part C: A Phase II study of eftilagimod alpha (soluble LAG-3 protein) and pembrolizumab in patients with metastatic 2nd line head and neck squamous cell carcinoma unselected for PD-L1 – ASCO 2023. #Data for Keytruda (pembrolizumab monotherapy or 'pembro mono') derived from KN-040 trial.

TACTI-003 - Randomised Phase IIb in First Line HNSCC

Efti + anti-PD-1 therapy has FDA Fast Track designation in first line recurrent or metastatic HNSCC

TACTI-003/KEYNOTE-PNC-34: First Line Recurrent or Metastatic Head & Neck Squamous Cell Carcinoma (1L HNSCC)

TACTI-003 / KEYNOTE-PNC-34 Trial Design



- Randomised, multicentre Phase IIb trial evaluating efti in combination with pembrolizumab (KEYTRUDA®) completed enrollment in Nov 2023
- A total of 171 patients enrolled:
  - 138 patients in 1:1 randomised Cohort A evaluating efti + KEYTRUDA® versus KEYTRUDA® monotherapy. Cohort A has patients whose tumors express PD-L1 (CPS ≥1), with CPS 1-19 and CPS ≥20 used as stratification factors. Clinical results for these three CPS groups will be evaluated.
  - 33 patients in Cohort B. This cohort includes patients with negative PD-L1 expression (CPS <1). These patients only receive efti plus KEYTRUDA® because anti-PD-1 monotherapy is ineffective in CPS <1.
- Expect to report first data in H1 CY2024

Pembrolizumab monotherapy approved for 1st line HNSCC patients whose tumors express PD-L1 (CPS ≥1) and pembrolizumab with chemo approved for 1st line HNSCC in all-comer PD-L1 population. FDA approval based on KN-048.
Immutep conducts this clinical trial and has a clinical trial collaboration and supply agreement with Merck & Co., Inc., Kenilworth, NJ, USA (known as MSD outside the US and Canada).

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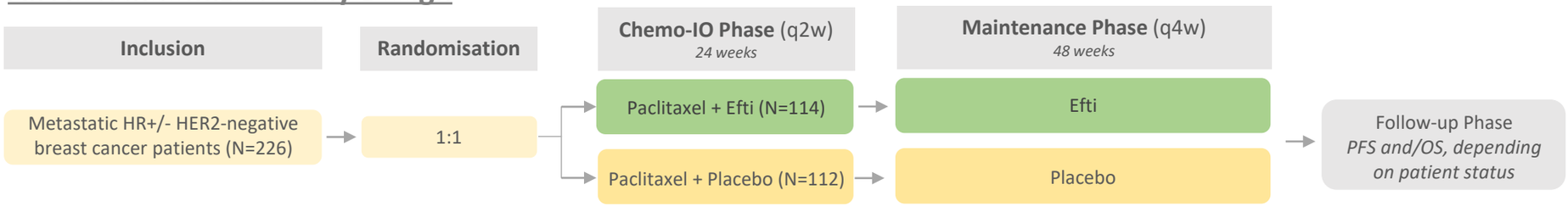
Efti + Chemotherapy in Metastatic Breast Cancer

Efti + Chemo in Randomized Phase IIb in Metastatic Breast Cancer

Broad anti-cancer immune response generated from efti in combination with paclitaxel

AIPAC: **A**ctive **I**mmunotherapy and **PAC**litaxel - Double blind, 1:1 randomized Phase IIb trial with 226 patients evaluating efti + paclitaxel (N=114) and paclitaxel + placebo (N=112)

AIPAC Randomized Study Design



AIPAC was conducted in 34 sites across: Belgium, France, Hungary, Poland, Netherlands, United Kingdom, and Germany

Pharmacodynamic Analysis of Efti with Chemotherapy:

Significant increase in adaptive/innate immune response observed in AIPAC*

Activated CD8+ T Cells	Effector Memory CD8+ T Cells	Activated CD4+ T Cells	Peripheral Dendritic Cells	Myeloid Dendritic Cells	Monocytes	NK Cells	Absolute Lymphocytes	Interferon-gamma	CXCL10
✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

* Biomarker and multivariate analyses results from AIPAC: A phase IIb study comparing eftilagimod alpha (a soluble LAG-3 protein) to placebo in combination with weekly paclitaxel in HR + HER2 - metastatic breast carcinoma – ESMO Breast 2022; Combination of paclitaxel and a LAG-3 fusion protein (eftilagimod alpha), as a first-line chemoimmunotherapy in patients with metastatic breast carcinoma (MBC): Final results from the run-in phase of a placebo-controlled randomized phase II – ASCO 2018

Fold Change of Key Biomarkers Compared to Baseline in AIPAC

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ESMO BREAST CANCER
Onsite and Online Congress
BERLIN GERMANY
3-5 MAY 2022
Abstract #171P

Biomarker	Treatment	Fold change mean ± SEM Median (25%Q-75%Q) [Min-Max]	P-value (2-sided rank-sum Wilcoxon test)
Monocytes	efti (n=42)	**5.81** ±1.49 **2.07** (1.40-5.16) [0.63-56.00]	0.025
	placebo (n=34)	**2.29** ±0.44 **1.47** (1.21-2.23) [0.09-13.57]	
Activated CD4 T cells	efti (n=45)	**2.17** ±0.23 **1.56** (1.07-3.14) [0.42-7.13]	0.206
	placebo (n=35)	**1.54** ±0.13 **1.31** (1.05-1.84) [0.26-4.14]	
Activated CD8 T cells	efti (n=42)	**2.54** ±0.35 **1.76** (1.10-3.25) [0.35-10.75]	0.027
	placebo (n=34)	**1.86** ±0.40 **1.17** (0.79-1.67) [0.20-13.14]	
CXCL10	efti (n=32)	**2.78** ±0.30 **2.39** (1.36-3.93) [0.67-7.25]	0.006
	placebo (n=22)	**1.56** ±0.18 **1.40** (0.86-2.18) [0.35-3.17]	

- Efti with paclitaxel significantly increases primary target cells (monocytes), secondary target cells (CD4* & CD8 T cells), and the chemokine CXCL10, which were not observed in the placebo group
- Absolute lymphocyte count (ALC) showed early and sustainable increase within the efti arm
- Increases in ALC, IFN-γ, and CXCL10 have also occurred in TACTI-002 Phase II clinical trial of efti in combination with anti-PD-1 therapy and no chemotherapy

Biomarker and multivariate analyses results from AIPAC: A phase IIb study comparing eftilagimod alpha (a soluble LAG-3 protein) to placebo in combination with weekly paclitaxel in HR + HER2 - metastatic breast carcinoma – ESMO Breast 2022
* Increase in CD4 not statistically significant

Substantial Increase in CD8+ T Cells Correlated to Stronger OS

Immune system stimulation & synergies with chemotherapy led to encouraging efficacy/safety

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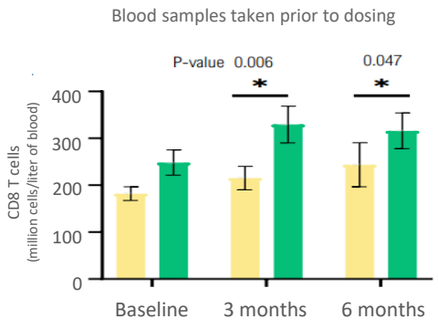
SITC 2021 WASHINGTON, D.C. NOV. 10–14 Join us in person or virtually

Late Breaking Abstract (#948)
Final Results from AIPAC

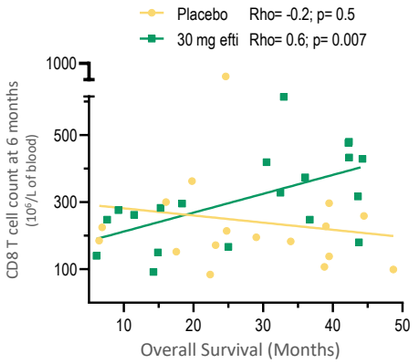
	Paclitaxel N=112	Efti + paclitaxel N=114	*Differential*
Overall Response Rate	38.4%	48.3%	*+9.9%*
Disease Control Rate	75.9%	85.1%	*+9.2%*
Median Overall Survival (mOS)	17.5 months	20.4 months	*+2.9 months*
mOS in Pre-Specified Subgroups			
Low Monocytes, <0.25/nl	12.9 months	32.5 months	*+19.6 months, P=0.008*
Under 65 Years	14.8 months	22.3 months	*+7.5 months, P=0.017*
Luminal B	12.6 months	16.8 months	*+4.2 months, P=0.049*

Effects were significant and clinically-meaningful in these pre-specified groups

CD8⁺ T cell count increased significantly

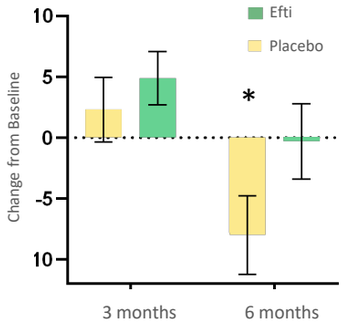


Significant correlation between OS & Cytotoxic CD8⁺ T cell count



Sustained Quality of Life (QoL)

vs significant decline in placebo grp*



Final results from AIPAC: A phase IIb trial comparing eftilagimod alpha (soluble LAG-3 protein) in combination with weekly paclitaxel in HR+ HER2- MBC - SITC 2021
*Quality of Life (QoL) as measured by Global Health Status / QoL QLQC30-B23

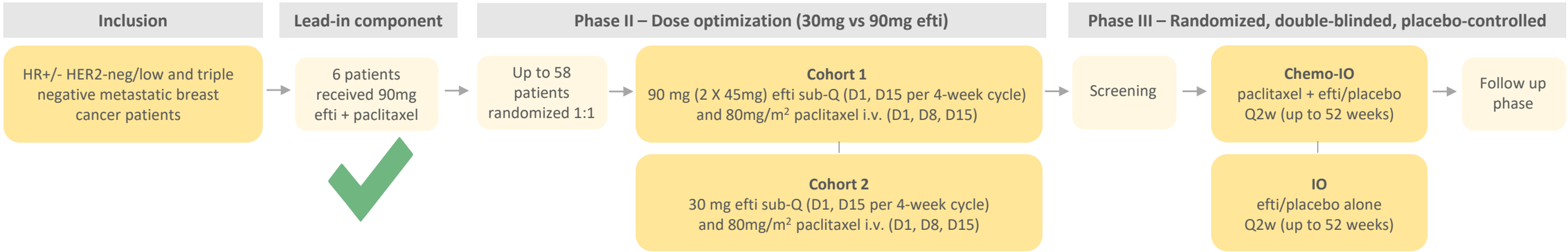
AIPAC-003 Phase II/III Trial Underway in Metastatic Breast Cancer

AIPAC-003: **A**ctive **I**mmunotherapy (Eftilagimod Alpha) and **PAC**litaxel

AIPAC-003: Integrated Phase II/III trial in Metastatic Breast Cancer (MBC)

- Trial design incorporates feedback from FDA & EMA and provides risk-balanced approach
- Patient population: HR+/- HER2-negative/low and triple negative MBC (~78% breast cancer cases[1])
- Efti + paclitaxel administered same day and IO-chemo treatment can continue until disease progression
- **Completed safety lead-in and treatment well tolerated with encouraging initial efficacy in six MBC patients, who exhausted all endocrine therapy including CDK4/6 inhibitors, demonstrated by a 50% response rate, including one complete response, and a 100% disease control rate**
- Randomised Phase II dose optimization underway evaluating 30mg and 90mg efti

AIPAC-003 Study Design



1. Cancer Stat Facts: Female Breast Cancer Subtypes - NCI SEER, World Health Organization; Breast Cancer Fact Sheet.

Additional Oncology Indications and Studies

Efti + Anti-PD-L1 (Avelumab) in Metastatic Urothelial Cancer

INSIGHT-004 – Completed Phase I dose escalation study in advanced solid tumors*

- Efti in combination with avelumab (BAVENCIO®) safe with promising signals of efficacy in 12 patients
- 5/12 partial responses (42%) in different solid tumors**
- Encouragingly, durable responses achieved in patients with low & negative PD-L1 expression and in non-immunogenic tumors

INSIGHT-005 – Ongoing Phase I study in metastatic urothelial cancer

- Investigator-initiated study evaluating safety & efficacy of efti and avelumab (BAVENCIO®) in up to 30 patients
- Jointly funded by Immutep & Merck KGaA, Darmstadt, Germany
- Targeting area of high unmet need: patients not eligible for platinum-based chemotherapy or who are progressing during/after platinum-based chemotherapy
- Announced first patient enrolled and safely dosed in Jan 2024

Merck KGaA
Darmstadt, Germany

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KRANKENHAUS NORDWEST

*ASCO 2021: J Clin Oncol 39, 2021 (suppl 15; abstract 2518); DOI 10.1200/JCO.2021.39.15_suppl.2518. **Two PRs in Cohort 1 (6mg efti + 800mg aveumab) in patients with MSI high colorectal cancer and pleural mesothelioma, and three PRs in Cohort 2 (30mg efti + 800mg avelumab) in patients with squamous cell anal carcinoma, squamous cervical cancer carcinoma (negative PD-L1 TPS <1%) , and adenocarcinoma gastroesophageal junction (GEJ Type III).

Soft Tissue Sarcoma: Orphan Disease with High Unmet Need

Investigator-initiated trial studying novel triple combination of Efti + Radiotherapy + KEYTRUDA

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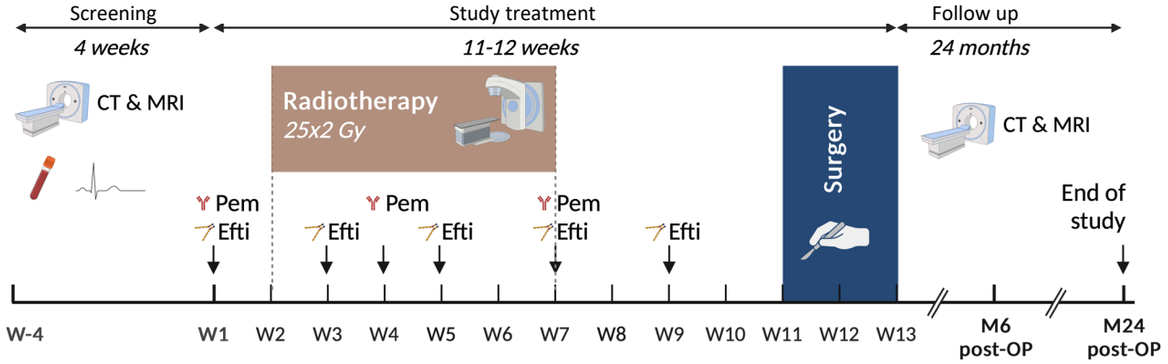
EFTISARC-NEO Trial Design*



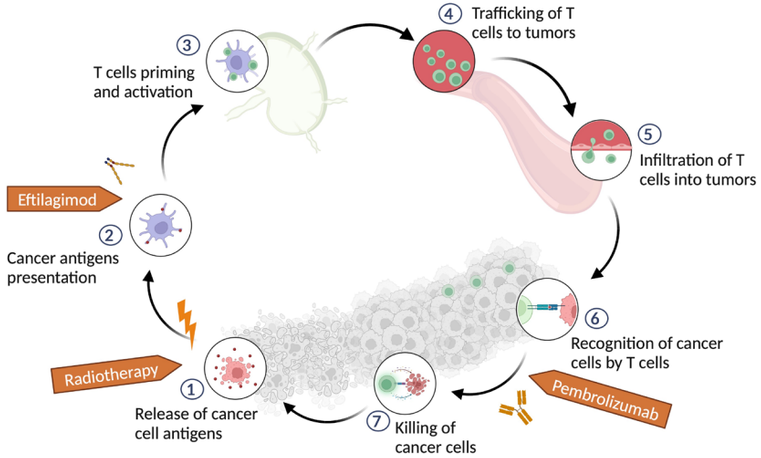
- First trial studying efti in neoadjuvant, non-metastatic cancer setting
- Importantly, study will provide access to tumor tissue prior to and after treatment, so tumor microenvironment can be assessed**
- Cost-efficient Phase II study mostly funded by grant from Polish government
- Started treating patients in July 2023; up to 40 patients will be enrolled

Rationale for triple combination based on cancer-immune cycle*

"…Given efti's synergistic effects with immune checkpoint inhibitors and its ability to arm, activate, and proliferate cytotoxic T cells with radiotherapy-induced cancer antigens, this combination has a strong foundation to drive effective immunity against soft tissue sarcoma, a rare and aggressive disease in immense need of new therapeutic approaches…"

- Dr. Paweł Sobczuk

Narodowy Instytut Onkologii
im. Marii Skłodowskiej-Curie Państwowy Instytut Badawczy



*Pembrolizumab in combination with eftilagimod alpha and radiotherapy in neoadjuvant treatment of patients with soft tissue sarcomas - EFTISARC-NEO trial – Trial in Progress Poster at ESMO 2023. ** Blood samples and tumor biopsies will be taken for translational studies.

Novel Small Molecule Anti-LAG-3 Preclinical Program

Collaboration established in 2019 combining Immutep's deep LAG-3 biology experience and expertise of world leading scientists at Cardiff University

"We are delighted to collaborate with Immutep on this important project to develop a **small molecule anti-LAG-3** treatment for cancer patients that could offer the **convenience of a tablet or capsule at a fraction of the cost of existing anti-LAG-3 candidates**."

Professor Andrew Godkin, Theme Lead in Immunology in the College of Biomedical Life Sciences, Cardiff University*

* 8 June 2021, Immutep Reveals a New anti-LAG-3 Research Program

IMP761 & Summary

Targeting Autoimmune Disease with Immune Checkpoint Agonists

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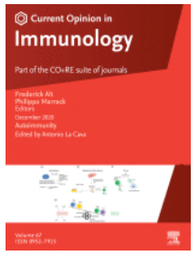


Inhibitory receptor agonists: the future of autoimmune disease therapeutics?

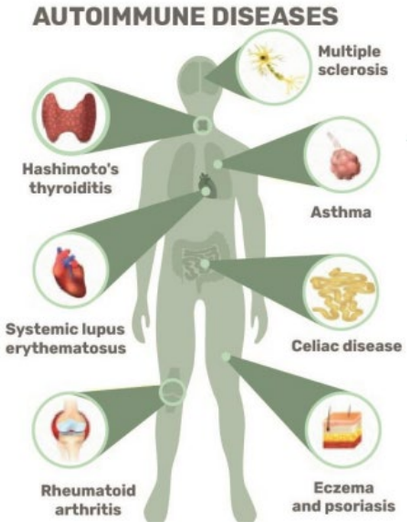
"Although critical questions remain, inhibitory receptor agonists represent an underappreciated and untapped opportunity for the treatment of autoimmune and inflammatory diseases"

From bench to bedside: targeting lymphocyte activation gene 3 as a therapeutic strategy for autoimmune diseases

"The manipulation of the LAG3 pathway can serve as a promising therapeutic strategy"

Fewer LAG-3⁺ T Cells in Relapsing-Remitting Multiple Sclerosis and Type 1 Diabetes

"These findings further support the potential clinical benefits of a LAG-3 agonist in the treatment of human autoimmunity"



Present Approaches Target the Symptoms of Autoimmune Diseases

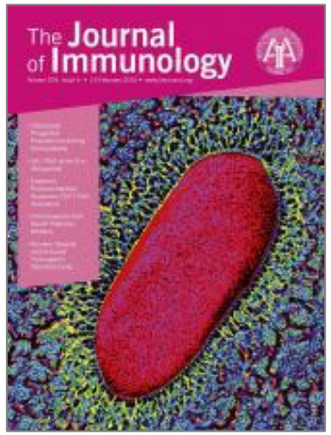
Corticosteroids, methotrexate, TNF & interleukin inhibitors (anti-TNF-α,-IL-6, -IL-17, -IL-23 mAbs)

Future Approaches Target the Causes of Autoimmune Diseases

Targeting autoimmune effector T cells with immune checkpoint (e.g. LAG-3 and PD-1) agonists

1. Grebinoski S, Vignali DA. Inhibitory receptor agonists: the future of autoimmune disease therapeutics? Curr Opin Immunol. 2020 Dec;67:1-9. doi: 10.1016/j.coi.2020.06.001. Epub 2020 Jun 30. PMID: 32619929; PMCID: PMC7744338
2. Zhou, X., Gu, Y., Wang, H. et al. From bench to bedside: targeting lymphocyte activation gene 3 as a therapeutic strategy for autoimmune diseases. Inflamm. Res. 72, 1215–1235 (2023). https://doi.org/10.1007/s00011-023-01742-y
3. Britta E. Jones, Megan D. Maerz, Henry T. Bahnson, Ashwin Somasundaram, Lucas H. McCarthy, Cate Speake, Jane H. Buckner; Fewer LAG-3+ T Cells in Relapsing-Remitting Multiple Sclerosis and Type 1 Diabetes. J Immunol 1 February 2022; 208 (3): 594–602. https://doi.org/10.4049/jimmunol.2100850

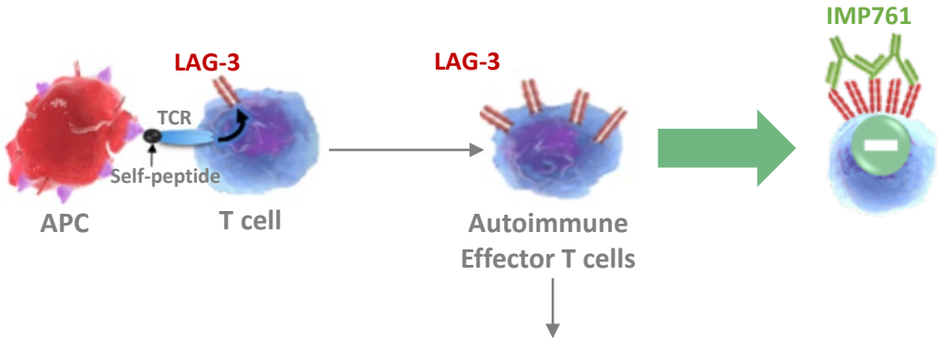
IMP761: First-in-Class LAG-3 Agonist is Potential Game-Changer



IMP761 *- A LAG-3-Specific Agonist Antibody for the Treatment of T Cell-Induced Autoimmune Diseases*

IMP761 *- Juvenile idiopathic arthritis: LAG-3 is a central immune receptor in children with oligoarticular subtypes*

IMP761 is the world's first immunosuppressive LAG-3 agonist antibody that is designed to address the underlying cause of many autoimmune diseases. This potential game-changer in the treatment landscape is expected to enter the clinic by mid-2024.



IMP761 increases natural LAG-3-mediated down-regulation of auto-reactive memory T cells (root cause of many diseases)

Epigenetic reprogramming leads to T cell helper (Th) induced Autoimmune Diseases such as Rheumatoid Arthritis (Th1), Allergic Asthma (Th2), IBS (Th17), etc.

Grebinoski S, Vignali DA. Inhibitory receptor agonists: the future of autoimmune disease therapeutics? Curr Opin Immunol. 2020 Dec;67:1-9. doi: 10.1016/j.coi.2020.06.001. Epub 2020 Jun 30. PMID: 32619929; PMCID: PMC7744338.

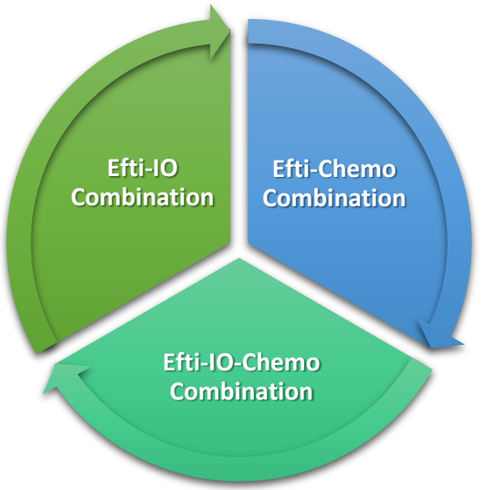
Company Highlights

Pure-play LAG-3 company with deep pipeline in oncology & autoimmune diseases:

- **Multiple LAG-3 Programs** – Three clinical-stage and two preclinical assets
- **Upcoming Milestones** – Multiple data updates from clinical programs & IMP761 expected to reach clinic in mid-2024

Lead candidate Efti addressing therapeutic gaps across the solid tumor treatment landscape:

- **First-in-class MOA** – Unique MHC Class II agonism activates innate and adaptive anti-tumor immunity
- **Activity across PD-L1 spectrum** – Activity in hot/tepid/cold tumors addressing high unmet needs
- **Consistent Outcomes** – Improved survival across multiple indications with mature data
- **Combination Flexibility** – Well-tolerated profile with standard-of-care IO and/or chemotherapy
- **Manufacturing** – Achieved 2000L commercial scale production; authorization for clinical trial use granted in Sept ‘23



Strong IP/Balance Sheet:

- **Intellectual Property** – Comprehensive IP portfolio; innovative biologics also potentially entitled to test data exclusivity (e.g., up to 12 years in US)
- **Well-Financed** – Cash balance of A$103.7 million (as of 31 December 2023); cash runway to early 2026

Board and Management

Dr Russel Howard
Non-Executive Chairman

Dr Howard has over 45 years' experience in Australian & US biotech sectors, including the Walter & Eliza Hall Institute, Schering-Plough, GSK and as Maxygen CEO. He currently is Chairman of NeuClone Pty Ltd and a former Director of Circadian Technologies Ltd.

Pete Meyers
Deputy Chairman

Mr Meyers spent 18 years in health care investment banking before taking on CFO roles in biotechnology including Eagle Pharmaceuticals, Motif BioSciences and TetraLogic Pharmaceuticals. Most recently he was CFO of Slayback Pharma, a KKR portfolio company acquired in Sept 2023.

Lis Boyce
Non-Executive Director

Ms Boyce has over 30 years' experience as a corporate lawyer and is a partner at Piper Alderman. She has a strong focus on Life Sciences and Healthcare, and is deputy chair of AusBiotech's AusMedtech Advisory Group, as well as a member of AusBiotech's State Committee for NSW.

Anne Anderson
Non-Executive Director

Ms Anderson's executive career of over 35 years spanned the global financial services and energy sectors, holding several Managing Director roles with UBS Asset Mgt, including leading its Asia Pacific Fixed Income business. She is a non-executive director of a leading Australian wealth manager, BTFM.

Marc Voigt
Executive Director & CEO

Mr Voigt has over 25 years of experience in the corporate and biotechnology sectors, including Deutsche Life Science, Revotar Biopharmaceuticals AG, Medical Enzymes AG and Allianz. He was appointed as CEO and Executive Director in July 2014. Mr Voigt is based in Berlin.

Prof. Frédéric Triebel, MD, PhD
Executive Director, CSO

Prof Triebel discovered the LAG-3 gene while working at the Gustave Roussy Institute and is a pioneer in the LAG-3 field of immuno-oncology. He was the founder of Immutep S.A., which was acquired by the Company in 2014. Based in Paris, he holds a Ph.D. in immunology (Paris University).

Deanne Miller
COO, General Counsel

Ms Miller has broad commercial experience having held legal, investment banking, regulatory compliance and tax advisory positions at RBC Investor Services, Westpac Group, Macquarie Group, the Australian Securities and Investment Commission, and KPMG.

Florian Vogl, MD, PhD
Chief Medical Officer

Dr Vogl is a board-certified MD and has over 13 years in the biopharmaceutical industry with extensive clinical development expertise in the field of oncology in the Europe and the US through roles at Cellestia Biotech, Rainier Therapeutics, Novartis and Amgen.

Christian Mueller
SVP, Strategic Development

Mr Mueller has +10 years of clinical development experience in oncology, including at Medical Enzymes AG focusing on therapeutic enzymes for cancer treatment and at Ganymed Pharmaceuticals AG developing ideal mAbs in immune oncology.

Claudia Jacoby, PhD
Director of Manufacturing

Dr Jacoby has +15 years of biotech industry experience with extensive skills in protein expression and purification as well as in analytical and preclinical development from her various positions at preclinical and clinical-stage pharmaceutical companies.

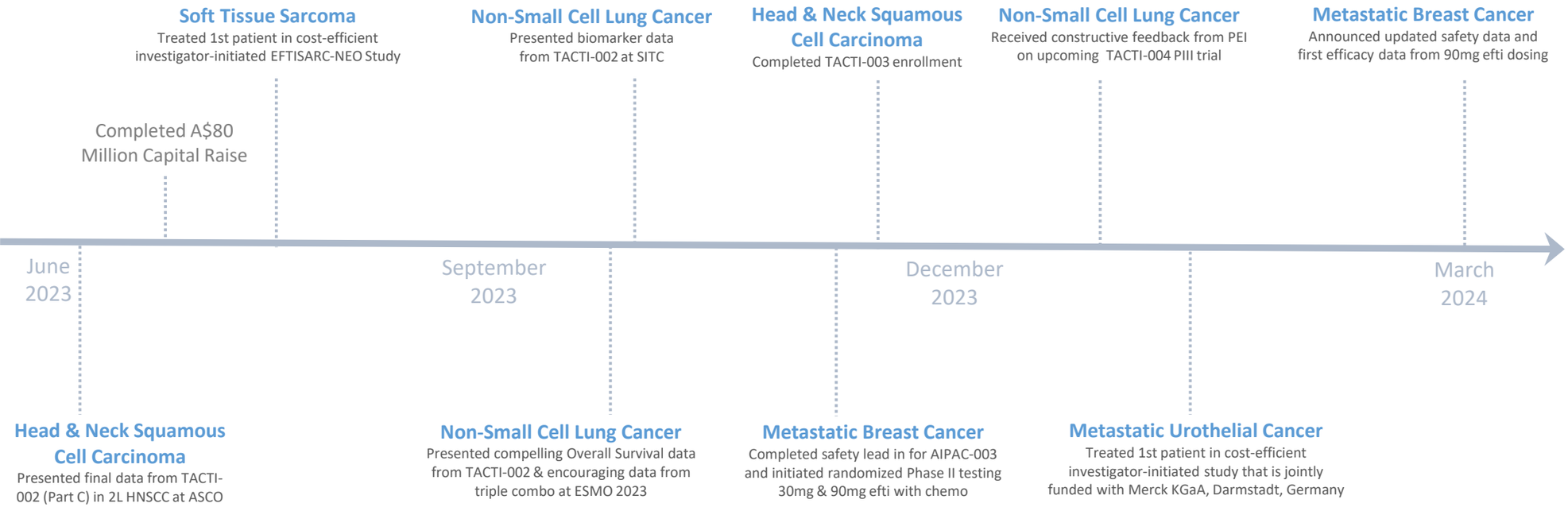
James Flinn, PhD
IP & Innovation Director

Dr Flinn is an Australian Patent Attorney with +25 years of professional experience in building and managing IP portfolios, including GSK, two US-based pharmaceutical companies, a major Australian retailer, and a Melbourne Patent Attorney firm.

David Fang
Finance Director

Joining Immutep in 2018, Mr Fang has over 12 years of accounting and auditing experience across various industries including biotechnology, manufacturing and healthcare including Group Finance Manager of Kazia Therapeutics Limited and auditor at PWC.

Recent Milestones & Looking Ahead



Strong balance sheet with A$103.7MM in cash providing runway to early 2026*

Upcoming Milestones & Catalysts

Non-Small Cell Lung Cancer
TACTI-004 trial design and preparations for study start

Head & Neck Squamous Cell Carcinoma
Data in 1H2024 from TACTI-003

Non-Small Cell Lung Cancer
Updates from triple combo INSIGHT-003 trial

Soft Tissue Sarcoma
Update from investigator-initiated EFTISARC-NEO study

Metastatic Breast Cancer
Update from AIPAC-003 study

Metastatic Urothelial Carcinoma
Update from investigator-initiated INSIGHT-005 study

Autoimmune Diseases
Continue IND-enabling studies of IMP761 and move forward to clinical development in mid-2024

Updates from partnered programs

Potential expansion of clinical trial pipeline

* As reported in Immutep Quarterly Activities report for Q2 FY2024 that ended on December 31, 2023.

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Thank You

Appendix

TACTI-mel: First-in-Man Study of Efti plus Anti-PD-1 Therapy

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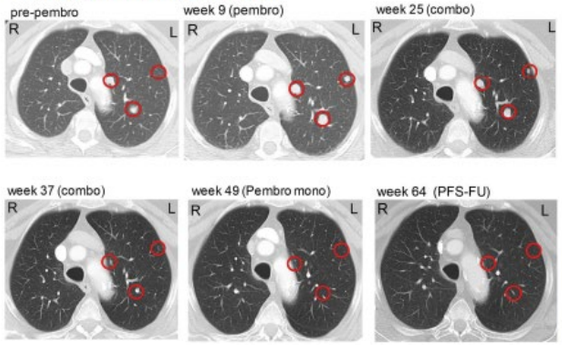
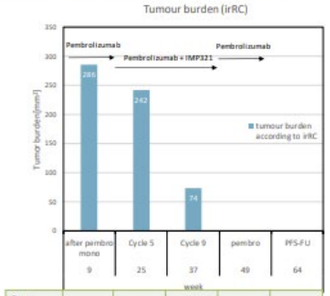
TACTI-mel evaluated efti with KEYTRUDA® (pembrolizumab) in metastatic melanoma patients with suboptimal responses or progression with KEYTRUDA monotherapy:

- Patients had very late stage of disease: 75% classified as M1c (associated with lowest probability of survival), 67% had lung metastasis, 50% had liver metastasis, 50% had elevated LDH (poor prognosis marker)
- Deep, durable responses observed with tumor shrinkage of 56% and 66% in Part A (efti 1, 6, 30mg; N=18) and Part B (efti 30mg given same day as KEYTRUDA; N=6)
- Part B (30mg; same day administration with KEYTRUDA) had 50% ORR, 66% DCR, and two-thirds of patients were progression free at six months

Patient Case #1 - Pembrolizumab + 1mg Efti (IMP321)

- Male, Caucasian, 84 years
- stage IV visceral disease (lung and thorax metastases), best response pembrolizumab monotherapy irPD
- Patient completed study, PFS-FU (incl. Pembrolizumab monotherapy) was stopped due to patient wish after week 64 → PFS censored week 64
- **Best Response: confirmed irCR**

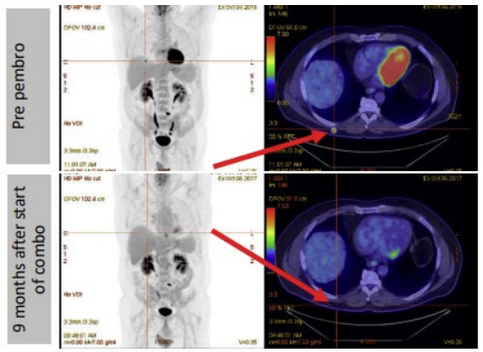




Sum Target Lesions	286 mm²	242 mm²	74 mm²	0 mm²	0 mm²
In %	100%	85%	26%	0%	0%
irRC	N/A	irSD	irPR	irCR	irCR

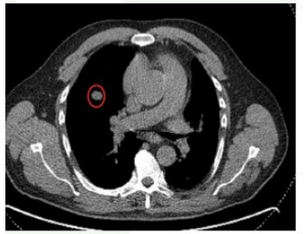
Patient Case #2 - Pembrolizumab + 6mg Efti (IMP321)

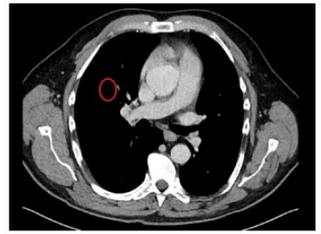
- Male, Caucasian, 54 years
- Stage IV skin/superficial disease → best response pembrolizumab monotherapy was irSD
- Target lesion: chest wall; Non-target lesion: Left common iliac LN
- Patient has completed the study treatment, PFS-FU (incl. Pembrolizumab monotherapy) ongoing → PFS 22+ months
- Complete disappearance of target lesions, lymph node normalized
- **Best Response: confirmed irPR**



Patient Case #3 - Pembrolizumab + 30mg Efti (IMP321)

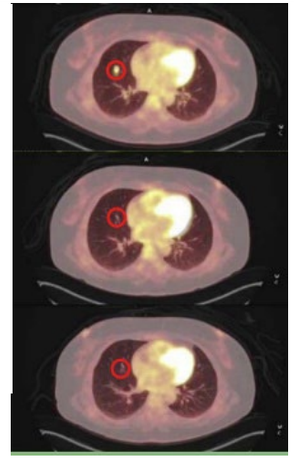
- 61-year-old male patient
- TxNxM1b at study entry in March 2018
- irPR reached by week 12 and maintained until end of study





Patient Case #4 - Pembrolizumab + 30mg Efti (IMP321)

- 46-year-old female patient
- TxNxM1c at study entry in August 2018
- Deep irPR reached by week 12 and maintained until end of study
- Residual tumor mass not metabolically active (complete metabolic response, CMR)
- PET-scans negative on two occasions, at the time of and after end of study



PET-Scans

← June 2018

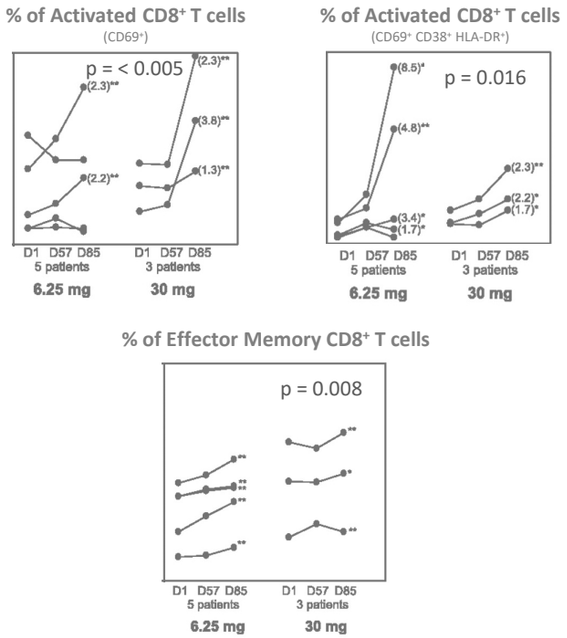
← May 2019

← Aug 2019

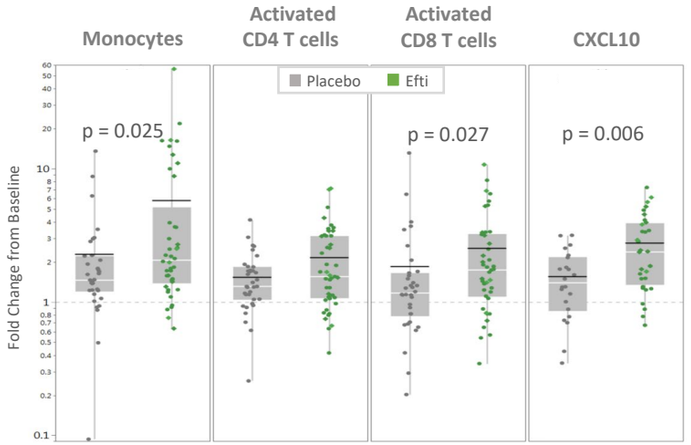
Efti Drives Adaptive & Innate Anti-Cancer Immune Response

Across multiple clinical trials, efti's activation of APCs (dendritic cells) leads to sustained increase of cytotoxic CD8+ T cells, other anti-tumor cells, as well as Interferon-gamma (IFN-γ) & CXCL10 that augment anti-cancer activity

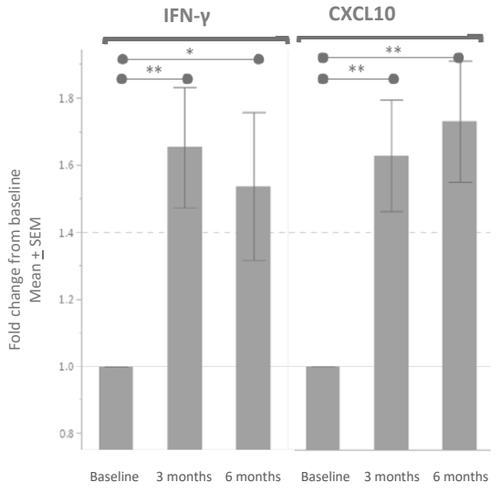
Phase I: Efti monotherapy



Phase II: Efti + paclitaxel



Phase II: Efti + pembrolizumab



*p = <0.05 **p = <0.01

Sources: (1) A Phase I Pharmacokinetic and Biological Correlative Study of IMP321, a Novel MHC Class II Agonist, in Patients with Advanced Renal Cell Carcinoma. *Clin Cancer Res (2009) 15 (19): 6225–6231*. (2) Biomarker and multivariate analyses results from AIPAC: A phase IIb study comparing eftilagimod alpha (a soluble LAG-3 protein) to placebo in combination with weekly paclitaxel in HR + HER2 - metastatic breast carcinoma – ESMO 2022. (3) Biomarker results from the 1st line non-small cell lung cancer cohort of TACTI-002: pharmacodynamic effects of combining eftilagimod alpha (soluble LAG-3) and pembrolizumab – SITC 2023