

A Global Leader in LAG-3 Therapeutics in Oncology and Autoimmune Disease

Corporate Presentation – November 2022
(ASX: IMM, NASDAQ: IMMP)

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Pioneering LAG-3 Portfolio in Oncology & Autoimmune Disease

Immutep is a pure-play LAG-3 clinical-stage company with four product candidates that address significant market opportunities in oncology & autoimmune disease

Collaborations with Industry Leaders



Merck KGaA
Darmstadt, Germany



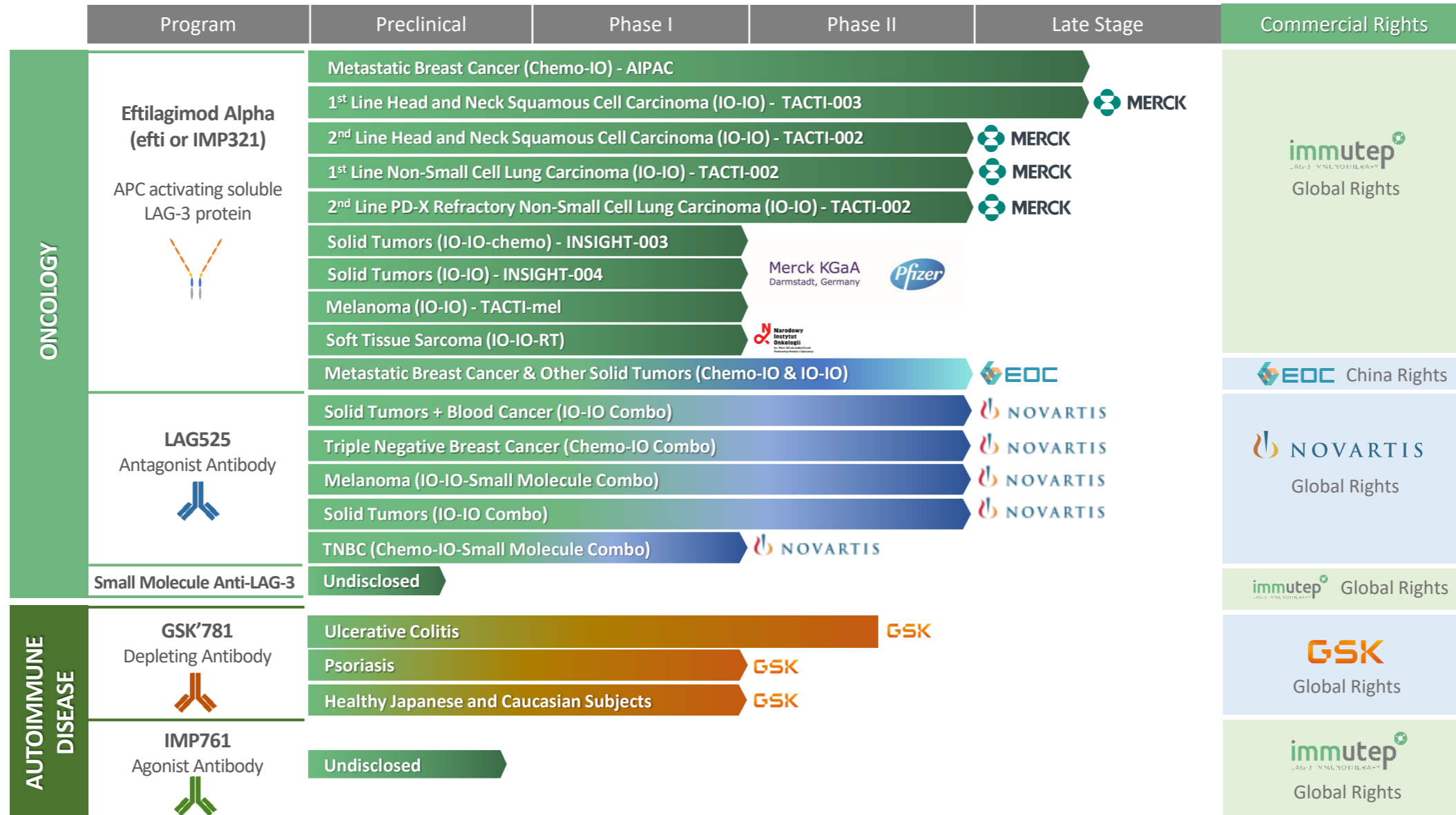
Compelling Clinical Data

Clinical trials of lead candidate eftilagimod alpha (efti) with immunotherapy & chemotherapy have shown compelling results in NSCLC, HNSCC, HR+/HER2- BC, melanoma and other solid tumors

Global Presence

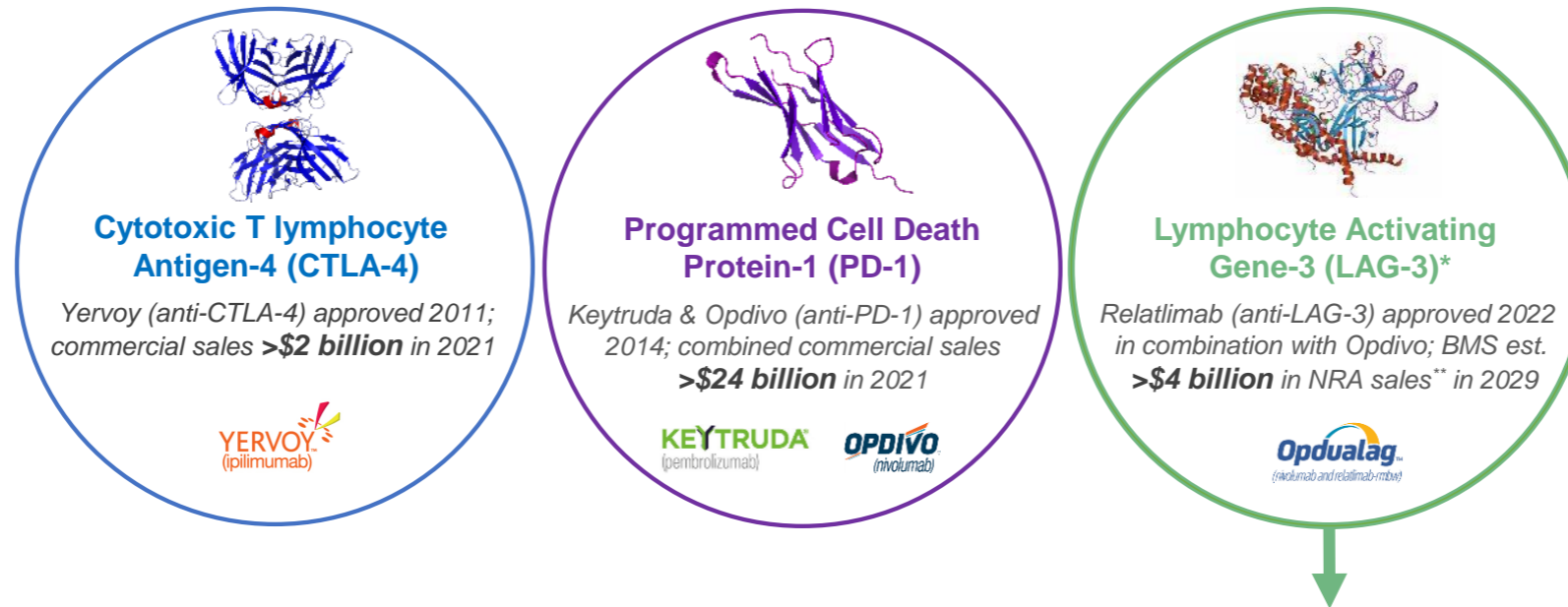


Immutep LAG-3 Pipeline



LAG-3: Approved Checkpoint with Unique Characteristics

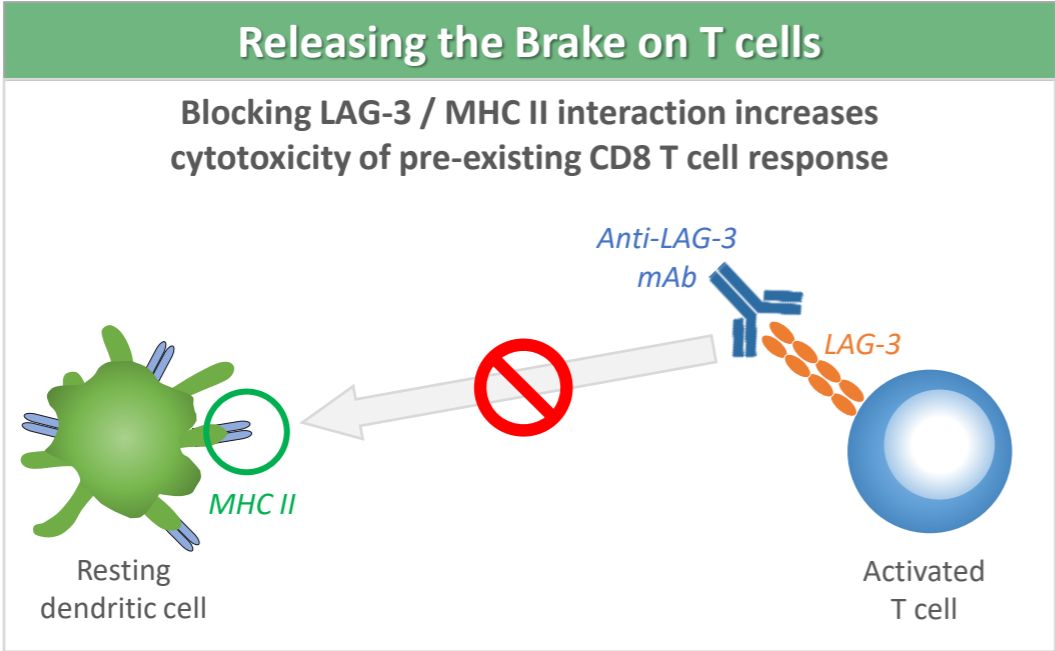
Immune system's role in controlling cancer has led to regulatory approval of immunotherapies targeting CTLA-4, PD-1, and now LAG-3 checkpoints



LAG-3 is unique in that its inhibition on T cells & activation of dendritic cells engages the adaptive & innate immune systems against cancer offering significant potential to: (1) improve responses to standard-of-care immunotherapy & chemotherapy, (2) limit emergence of resistance, (3) offer chemotherapy-free options in select indications.

LAG-3 Therapeutics for Oncology

Multiple Companies Targeting LAG-3 Inhibition



Company*	Program	Phase 1	Phase 2	Phase 3
Bristol Myers Squibb	Relatlimab	8	35	4
MERCK	Favezelimab	1	8	1
REGENERON	Fianlimab	1	1	1
NOVARTIS	Ieramilimab	1	4	
MACROGENICS	Tebotelimab	3	3	
Roche	R07247669	2	3	
Incyte	INCAGN02385	2	2	
Boehringer Ingelheim	BI754111	4	1	
Innovent	IBI110	2	1	
TESARO	TSR-033	1	1	
symphogen	SYM022	3		
F-star†	FS-118	1		

Received FDA approval in March 2022

- Immutep designed the first anti-LAG-3 antibody and licensed it to CoStim Pharmaceuticals in 2012, which was acquired by Novartis in 2014
- Novartis' anti-LAG-3 mAb, LAG525, activates effector T cells & inhibits regulatory T cells (removing two brakes on the immune system to respond to and kill cancer cells) and has been tested in multiple clinical trials combined with spartalizumab (anti-PD-1) and chemotherapy**
- IP estate for LAG525 continues to strengthen with patent grants in key markets including US, Europe, Japan and China

*Graphic adapted from Lymphocyte Activation Gene 3 in Immuno-oncology: A Soluble Protein Alternative; BioProcess International Feb 2022. Note F-star acquired by InvoX Pharma, a wholly-owned subsidiary of Sino Bioph. Ltd., Les Laboratoires Servier acquired Symphogen, and GSK acquired Tesaro;

**LAG525 - ClinicalTrials.gov (for Novartis' global rights, Immutep may receive undisclosed milestones plus royalties)

Novel Small Molecule Anti-LAG-3 Collaboration



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

"We are delighted to collaborate with Immute 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

First-in-Class Positioning in LAG-3 Oncology Landscape via Efti

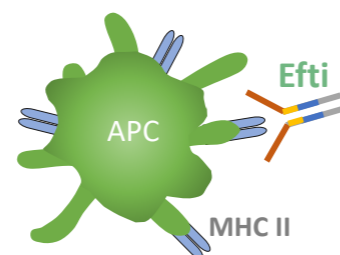
Eftilagimod alpha (Efti)



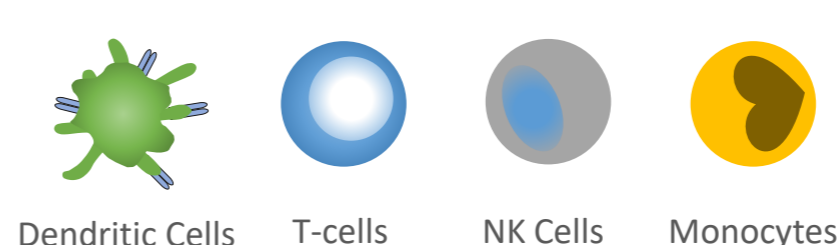
Immutep's proprietary soluble LAG-3Ig clinical candidate is a first-in-class antigen-presenting cell (APC) agonist via MHC II that capitalizes on LAG-3's unique characteristics

Pushing the Accelerator on the Immune System

APC activation with Efti



Anti-tumor immune cell activation



Broad activation of immune system

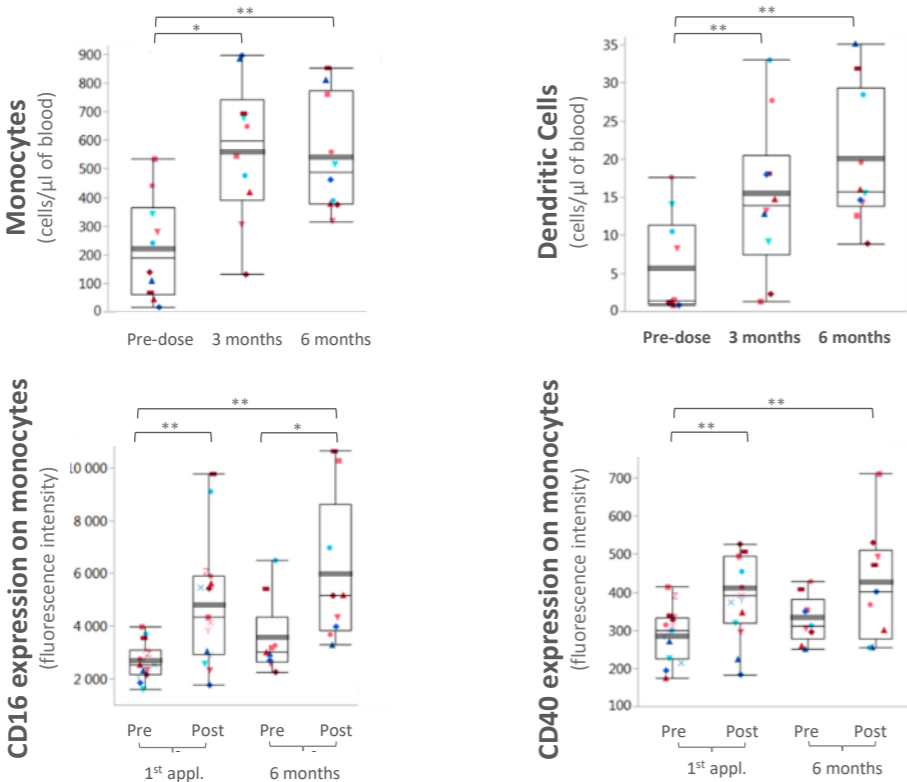
- Efti capitalizes on LAG-3's unique ability to drive adaptive & innate immune systems against cancer
- Efti has high affinity for a subset of MHC II ligand on APCs and their activation drives broad stimulation of multiple anti-tumor cells

Compelling pairing capabilities

- Excellent safety profile drives high suitability for combination partnering
- Synergistic activity & encouraging clinical results with multiple agents including anti-PD-1, anti-PD-L1, and chemotherapy
- Enhances clinical activity of anti-PD-1 across PD-L1 status, including low & negative PD-L1 tumors

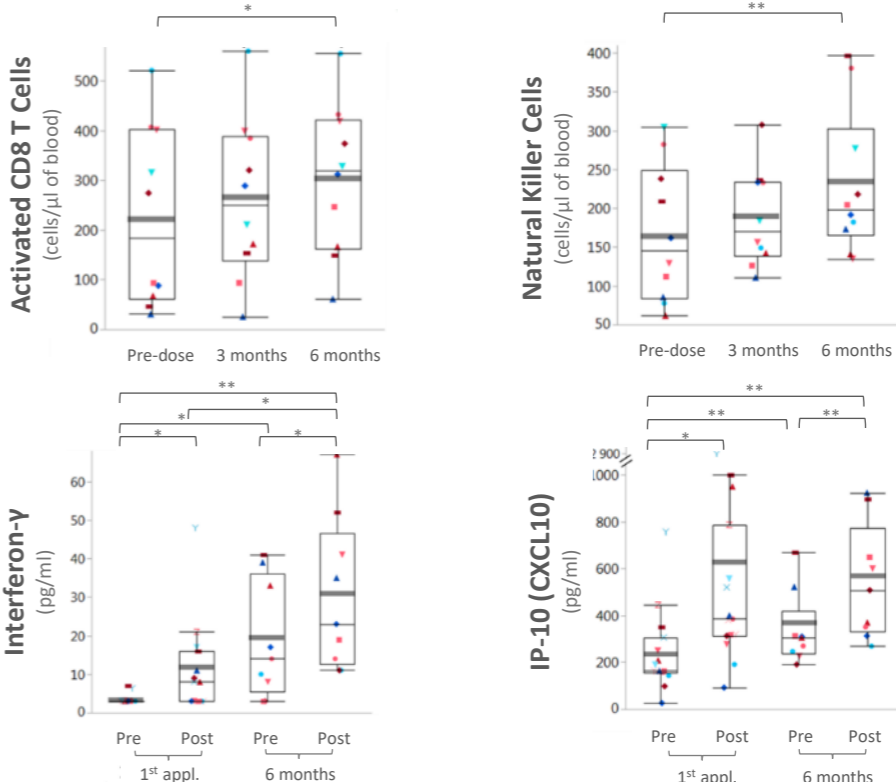
Driving Adaptive & Innate Immune Response

Efti initiates persistent increase and activation of circulating **APCs** including **monocytes** & **dendritic cells**, and drives increase in important biomarkers



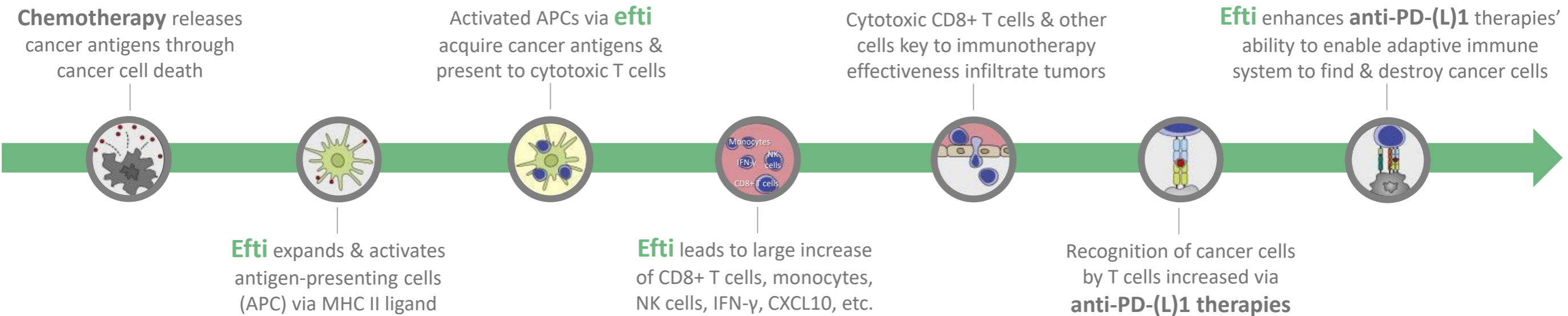
*p<0.05 **p<0.005

Efti drives sustained increase of cytotoxic **CD8 T cells** and **Natural Killer cells** as well as key Th1 biomarkers **IFN-γ** and **IP-10 (CXCL10)**



*p<0.05 **p<0.005

Synergies with Chemotherapy & IO Checkpoint Inhibitors



A Soluble Form of Lymphocyte Activation Gene-3 (IMP321/Efti) Induces Activation of a Large Range of Human Effector Cytotoxic Cells

Chrystelle Brignone, Caroline Grygar, Manon Marcu, Knut Schäkel and Frédéric Triebel
The Journal of Immunology September 15, 2007, 179 (6) 4202-4211; DOI: 10.4049/jimmunol.179.6.4202

naturemedicine

A potential biomarker for anti-PD-1 immunotherapy - A recent study identifies an immune cell type known as classical monocytes in the peripheral blood as a potential biomarker for response to anti-PD-1 immune checkpoint therapy in metastatic melanoma.

Goswami, S., Basu, S. & Sharma, P.
Nat Med 24, 123–124 (2018). <https://doi.org/10.1038/nm.4489>

ScienceImmunology

CXCL9 and CXCL10 bring the heat to tumors

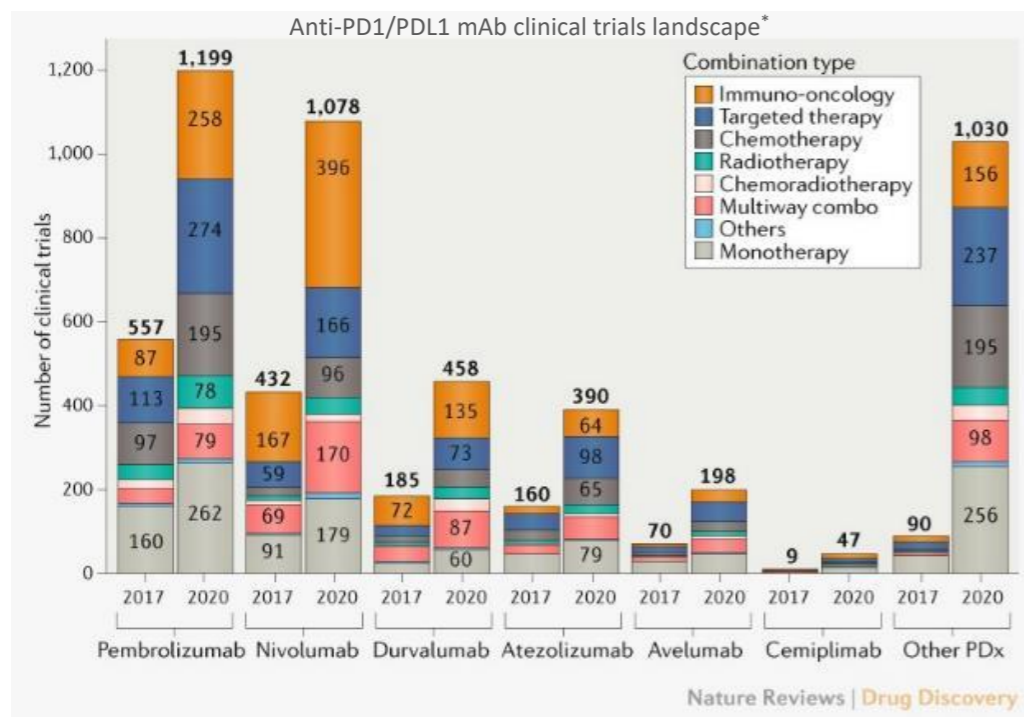
Robin Reschke, Thomas F. Gajewski
SCIENCE IMMUNOLOGY - 22 Jul 2022, Vol 7, Issue 73
DOI: 10.1126/scimmunol.abq6509



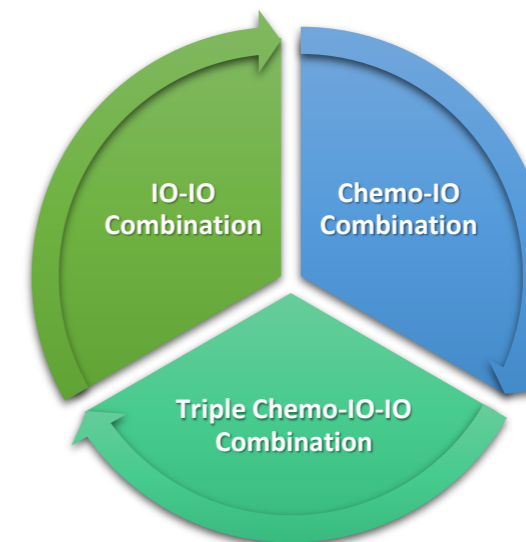
Monocyte-derived APCs are central to the response of PD1 checkpoint blockade & provide a therapeutic target for combination therapy

Schettlers STT, Rodriguez E, Kruijssen LJW, et al
Journal for ImmunoTherapy of Cancer
2020;8:e000588. doi: 10.1136/jitc-2020-000588

Pipeline in a Product with Broad Potential



Efti Clinical Trials Confirm Broad Combination Potential

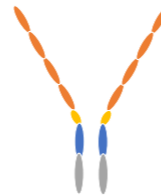


- Efti + Anti-PD-1 (pembrolizumab)**
Head & Neck Squamous Cell Carcinoma (1L & 2L),
Non-Small Cell Lung Carcinoma (1L & 2L), Sarcoma, Melanoma
- Efti + Anti-PD-L1 (avelumab)**
Solid tumors (GI, Cervical, etc.)
- Efti + Chemo (paclitaxel)**
HER2-negative/HR+ metastatic Breast Cancer
- Efti + Anti-PD-1 (pembrolizumab) + Chemo (carboplatin)**
Solid tumors

Unmet need in 1L NSCLC
as median OS still <24
months for most
patients

Low PD-L1 status
patients have poorer
responses to checkpoint
treatment
(TPS <50% = ~70% of
total population)

High discontinuation rate
due to toxicity limits DoR
of chemo and checkpoint
combinations

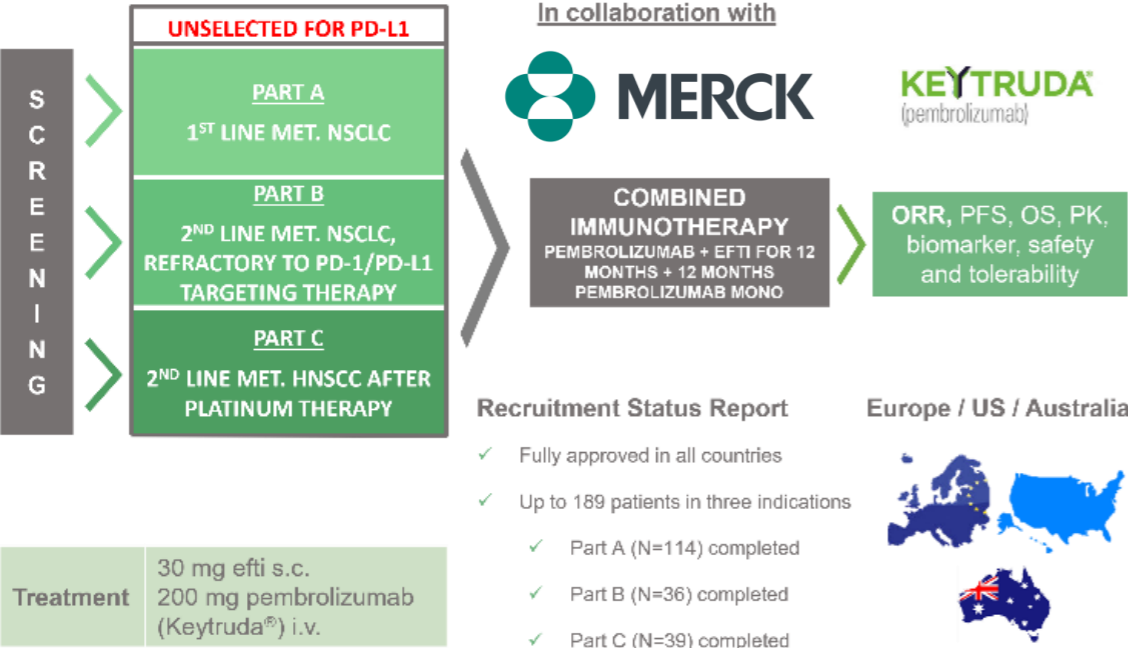


Well-tolerated treatment options that synergize with SOC and improve outcomes across PD-L1 status, including negative & low PD-L1 tumors, are necessary in frontline NSCLC. Efti in combination with anti-PD-1 immunotherapy has significant potential to fill this unmet need.

Phase II Trial Evaluating Efti + Pembro in 1L NSCLC

TACTI-002/KEYNOTE-798: 1st Line Non-Small Cell Lung Cancer (Part A)

TACTI-002: Two ACTIVE Immunotherapeutics in NSCLC & HNSCC



Baseline characteristics for PD-L1 All Comer Trial		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	106 (93.0) / 8 (7.1)
PD-L1 expression TPS ¹ , n (%)	< 1%	37 (32.5)
	1-49%	40 (35.1)
	≥ 50%	31 (27.2)
	Not evaluable	6 (5.3)
Previous therapy, n (%)	Radiotherapy	38 (33.3)
	Surgery	23 (20.2)
	Systemic therapy for non-metastatic disease	25 (21.9)

All-comer trial for patients with all levels of PD-L1 expression;
~33% & ~68% of 1L NSCLC patients in TACTI-002/KEYNOTE-798 (Part A) have PD-L1 TPS of <1% & <50%, respectively.

Encouraging Clinical Results; Primary Objective Achieved; Strong ORR/PFS Across Entire PD-L1 Spectrum vs Pembrolizumab



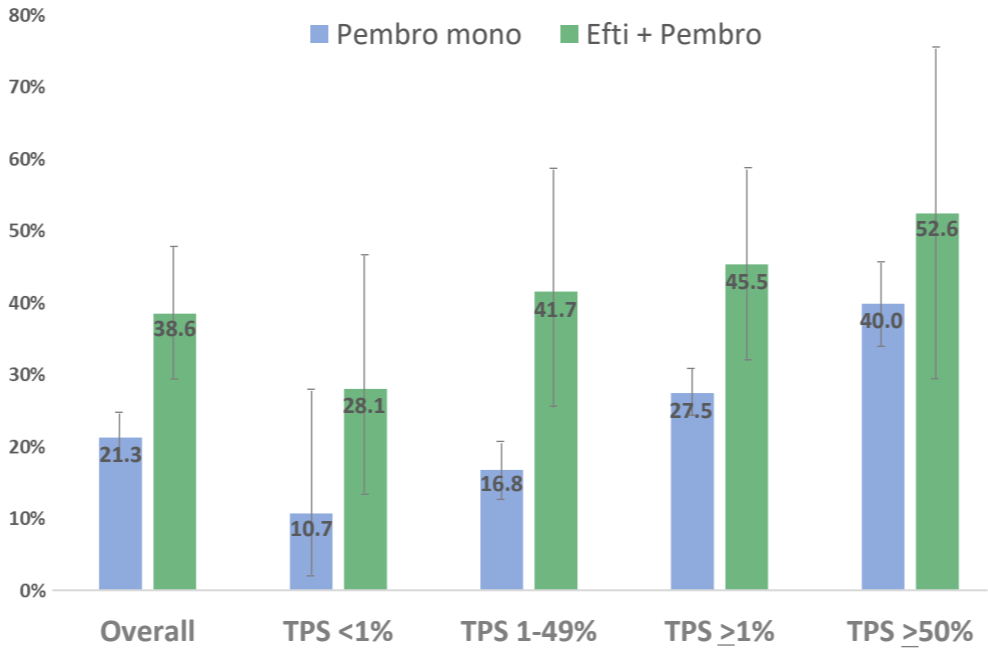
TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

Key Takeaways

- Primary objective achieved (ORR >35%)
- Superior ORR/PFS across all PD-L1 levels
- Sustained, durable responses
- Safe, well tolerated

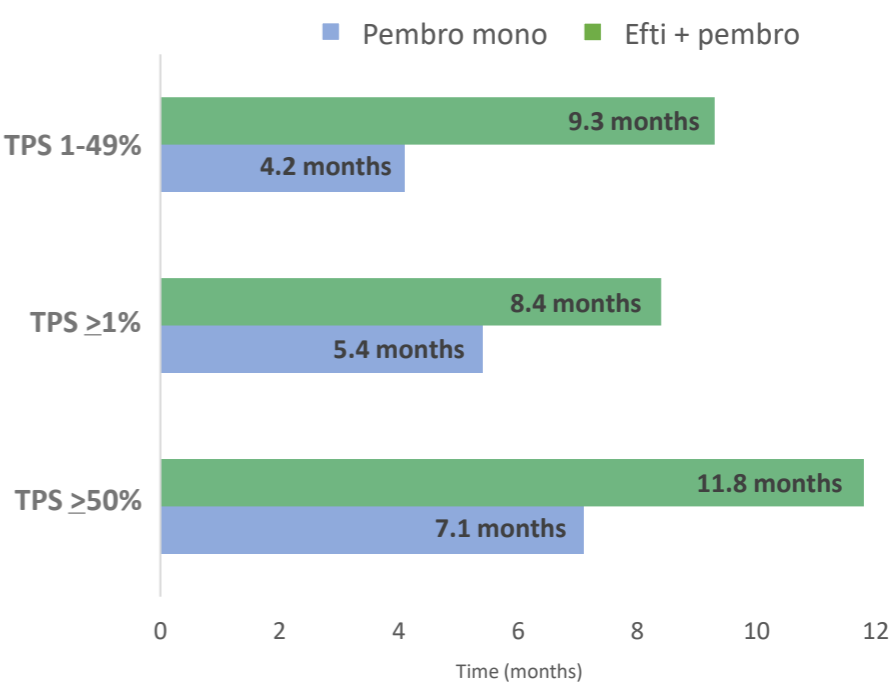
Overall Response Rate* (ORR)

(with 95% confidence intervals)



Median Progression Free Survival# (PFS)

(by PD-L1 TPS Score)

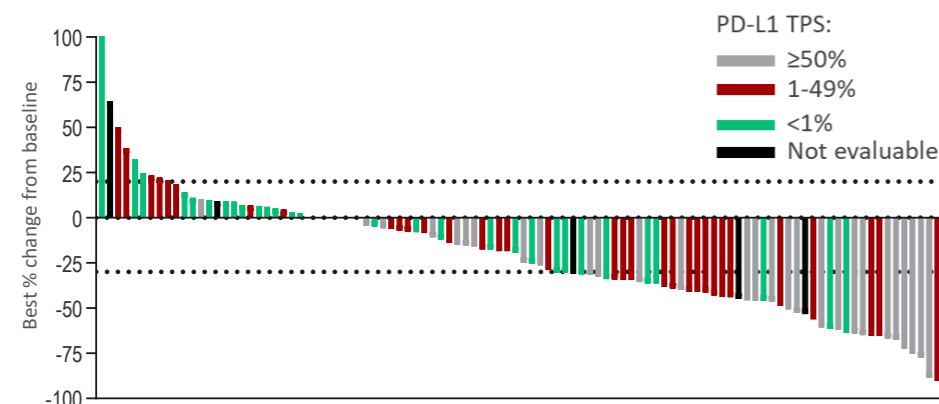


15 * Efti + Pembro ORR by iRECIST, unconfirmed, Total (N=114) and PD-L1 TPS subgroups (N=87). Data cut-off April 15, 2022. Pembrolizumab ("pembro") mono efficacy used for benchmarking for ORR: Total calculation based on KN-001; KN-042 and on adjustment for the same PD-L1 subgroup distribution as in TACTI-002. < 1 % TPS: calculation based on limited data set from KN-001 (1st & 2nd line altogether). 1-49%, ≥ 50%, and ≥ 1 % TPS based on KN-001, KN-042. # PFS by PD-L1 status (N=108) using central assessment for 87 patients. For 21 patients, local assessment used due to non-eval central assessment results. Pembro mono efficacy used for benchmarking: 1-49%, ≥ 50%, and ≥ 1 % TPS based on KN-001, KN-042. Lancet [https://doi.org/10.1016/S0140-6736\(18\)32409-7](https://doi.org/10.1016/S0140-6736(18)32409-7), Oral Presentation 2018 ASCO, EPAR assessment report, N Engl J Med 2016; 375:1823-33; KN-024 update J Clin Oncol 2019, KN-024 J Clin Oncol 2021

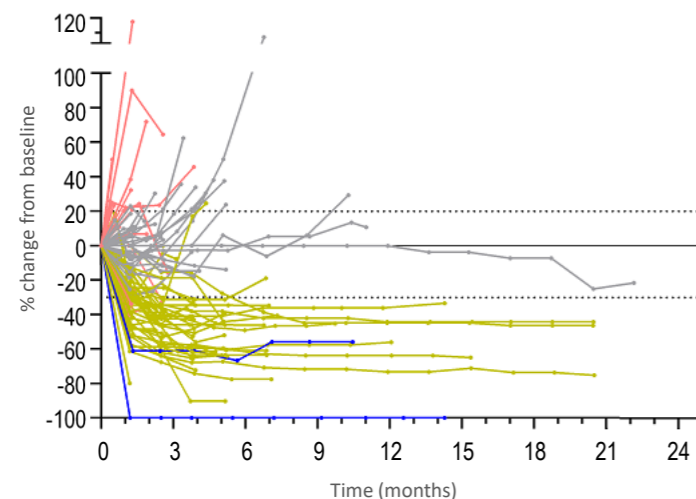
Deep and Durable Responses

TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

Tumor Burden Reduced in Majority of Patients



Change in Tumor Size Over Time



- Responses are deep & long-lasting; median DoR not yet reached
- 80% (35) of responses¹ already confirmed & 11.4% (5) pending confirmation
- 95% of patients having a response < 4 months after study start
- Only 8.6% of patients with confirmed response² progressed ≤ 6 months until data cut-off
- 66% (68) of patients with post-baseline assessment had decrease in target lesions

Benchmarking against IO & IO-Chemo Combinations

TACTI-002/KEYNOTE-798: 1L NSCLC (Part A)

	TPS	Treatment	Efficacy ⁽¹⁾		Toxicity: AEs leading to disc.
1L NSCLC	≥ 1%	Efti + Pembro	ORR 45.5%	PFS 8.4 mos	< 10%
		Pembro mono	ORR 27.5%	PFS 5.4 mos	1-14%
		Ipi + Nivo ⁽²⁾	ORR 36%	PFS 5.1 mos	18%
	1-49%	Efti + Pembro	ORR 41.7%	PFS 9.3 mos	< 10%
		Doublet Chemo + Pembro	ORR 49.2% (NSQ) & 50% (SQ)	PFS 7.2 (SQ) & 9.2 (NSQ) mos	14%
		Pembro mono	ORR 16.8%	PFS 4.1 mos	1-14%
	≥ 50%	Efti + Pembro	ORR 52.6%	PFS 11.8 mos	< 10%
		Pembro/Atezo/Libtayo mono	ORR 35-45%	PFS 7-10 mos	1-14%
	0-100%	Efti + Pembro	ORR 38.6%	PFS 6.9 mos	< 10%
		Doublet Chemo	ORR 19-30%	PFS 5-9 mos	8-22%
		Doublet Chemo + Pembro	ORR 48% (NSQ) & 63% (SQ)	PFS 6 (SQ) & 9 (NSQ) mos	14%
		Doublet Chemo + Atezo + Beva	ORR 56%	PFS 8.4 mos	33%
		Doublet Chemo + Ipi + Nivo	ORR 38%	PFS 6.7 mos	19%

- ✓ Low efficacy of anti-PD-(L)1 monotherapy for patients with TPS <50% (~70% of total population)
- ✓ Double chemo + anti-PD-(L)1 → increased ORR & OS but shorter DoR due to chemo & more toxic; Ipi & Beva combos → high burden in terms of toxicity & high number of patients discontinuing
- ✓ Efti addresses both issues as shown with TACTI-002 results; INSIGHT-003 trial also exploring efti + pembro + chemo combination

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 TACTI-002/KEYNOTE-798: 2nd Line NSCLC, PD-X Refractory (Part B)

Very difficult-to-treat patient population in 2L NSCLC:

- Confirmed progression after anti-PD-1/PD-L1 therapy
- 67% received chemo + anti-PD-1/PD-L1 in 1st line
- 75% have PD-L1 TPS of <50%

Encouraging efti + pembro clinical results:

- Median OS of 9.6 months in PD-L1 TPS of 1-49%
- Median OS not yet reached in PD-L1 TPS of >50%
- 2 confirmed & durable PRs (9+ & 23+ months)
- L-term (6+ months) disease control in 25% patients
- 36.5% patients alive at 18 months
- Combination safe & well tolerated

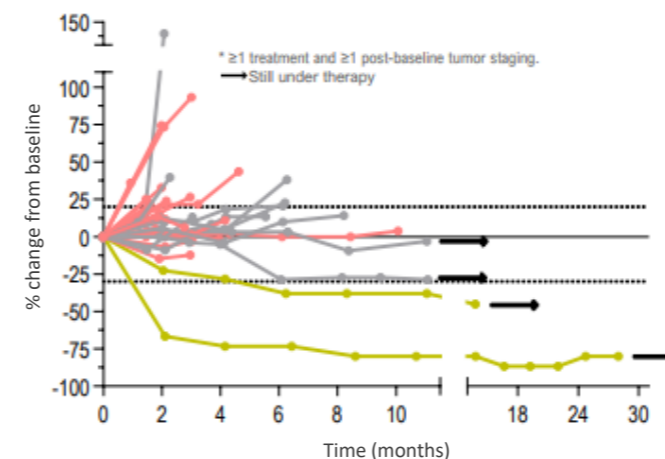
ORR, PFS and OS for ITT and PD-L1 subgroups

PD-L1 TPS	ITT (N=36)	<1% (N=13)	1-49% (N=14)	>50% (N=6)
ORR (iRECIST) %	5.6	-	-	16.7
Overall Survival				
Median, months	9.7	8.7	9.6	NR
6-month OS, %	72.2	61.5	71.4	100
12-month OS, %	43.4	46.2	32.7	66.7
18-month OS, %	36.5	46.2	16.3	NR
Progression-free Survival (iRECIST)				
Median, months	2.1	2.1	1.9	7.6
3-month OS, %	30.6	23.1	14.3	66.7
6-month OS, %	25	15.4	14.3	50

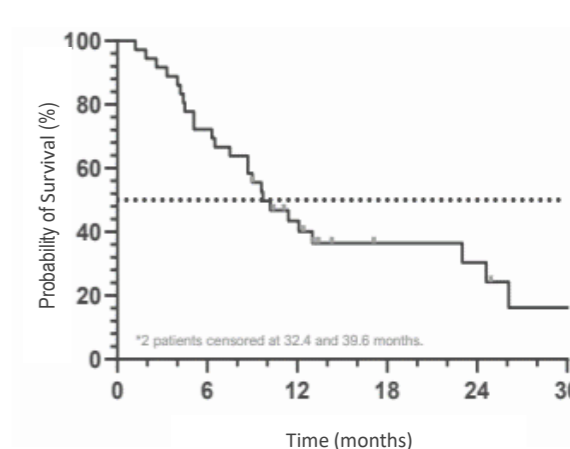
Best overall response, ITT

Tumor response* (N=36)	iRECIST (%)	RECIST 1.1 (%)
Partial Response	5.6%	5.6%
Stable Disease	30.6%	10%
Progression	61.1%	23%
Not Evaluable**	2.8%	2.8%
Overall Response Rate (ITT)	5.6%	5.6%
Disease Control Rate (ITT)	36.1%	33.3%

Spider Plot (N=34)*



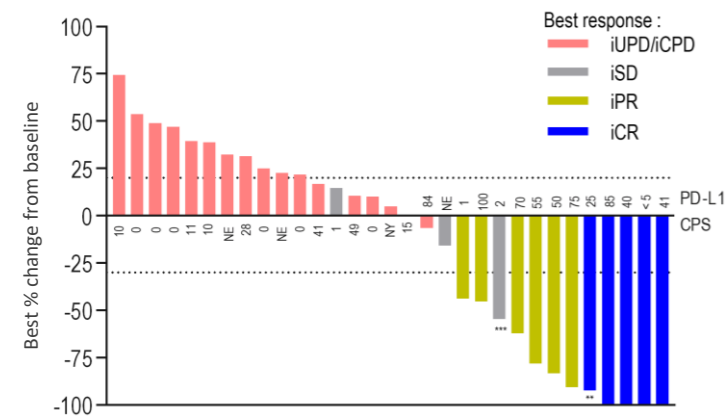
Overall survival, ITT (N=36)*



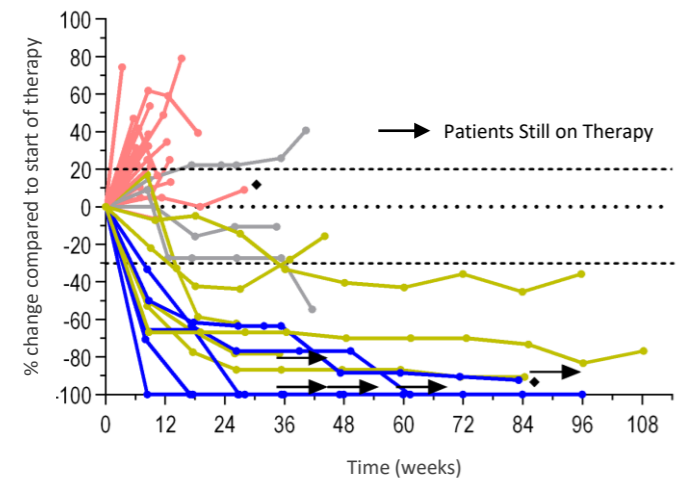
2L HNSCC: Robust ORR/CR with Long-Lasting Efficacy

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

Responses at all PD-L1 levels including 5 iCRs



Deep and durable responses



	Efti + Keytruda Combination*	Keytruda Monotherapy#
Clinical Trial & Phase	P2 (TACTI-002/KN-798)	P3 (KN-040)
Patient Number / tumor type	39 / 2L HNSCC	247 vs. 248 / 2L HNSCC
PD-L1 Status	PD-L1 All comer	PD-L1 All comer
Complete Response (CR) %	13.5%	1.6%
Partial Response (PR) %	16.2%	13%
Stable Disease (SD) %	8.1%	22.7%
ORR in evaluable patients %	35.5%	n/a
Overall Response Rate (ORR) %	29.7%	14.6%
PD-L1 CPS ≥1% group	40.7%	17.3%
PD-L1 CPS ≥20% group	64.3%	21.9%
Median PFS (months)	2.1	2.1
PD-L1 CPS ≥1% group	4.1	2.2
Median OS (months)	12.6	8.4
PD-L1 CPS ≥1% group	12.6	8.7

Eight-fold increase in CR
with efti + pembro

More than double ORR
across all PD-L1 levels
with efti + pembro

Fast Track Designation in 1L HNSCC

TACTI-003: Phase IIb in 1st Line Head and Neck Squamous Cell Carcinoma (HNSCC)

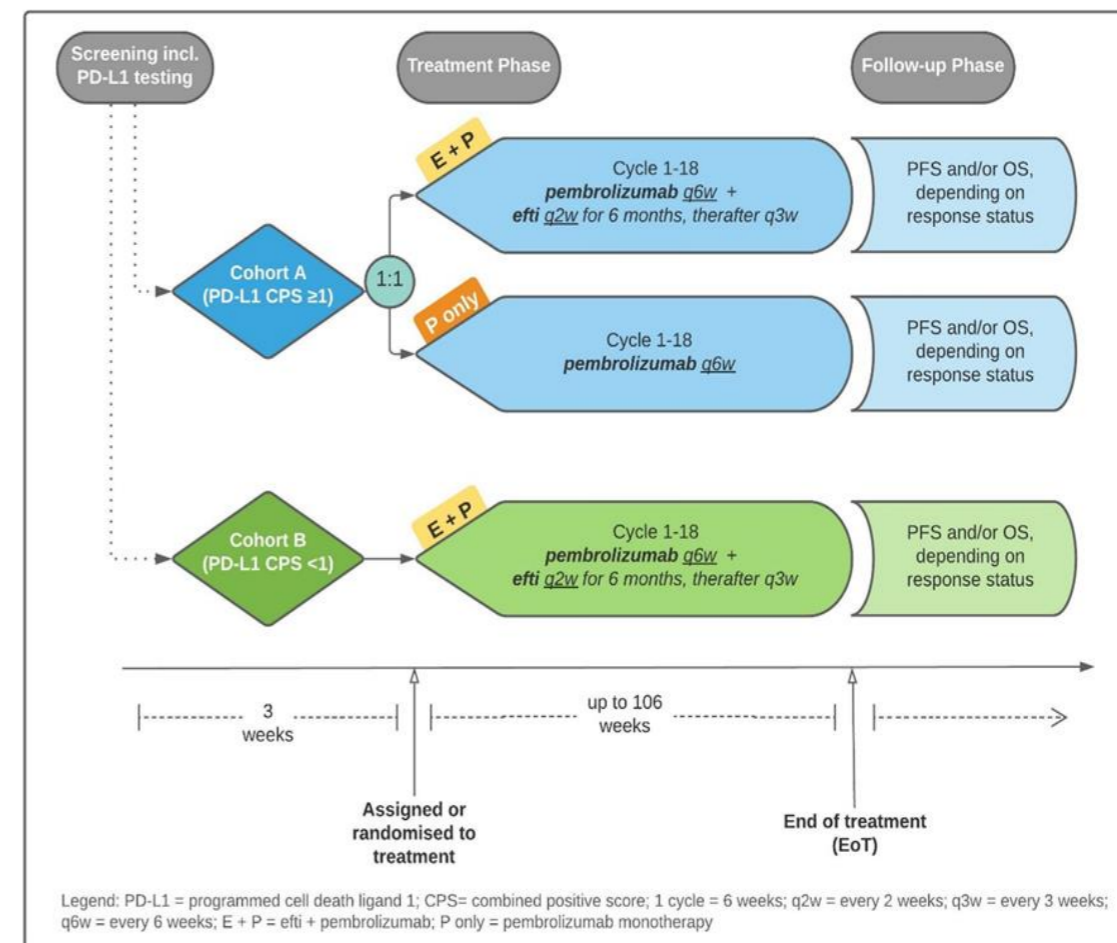


Status:

- Recruiting (~30% enrolled; recruitment accelerating as further sites have been activated*)
- **FDA Fast Track designation on strength of TACTI-002 data in 2L HNSCC**

Design:

- Randomised trial with ORR as primary endpoint
- Sites worldwide (AU, US, Europe)
- Approximately 154 patients: either to be randomised to have sufficient patients in each group or in an experimental arm



Efti + Anti-PD-L1 (Avelumab) in Advanced Solid Tumors

INSIGHT-004: Phase I in Various Advanced Solid Tumors

Merck KGaA
Darmstadt, Germany



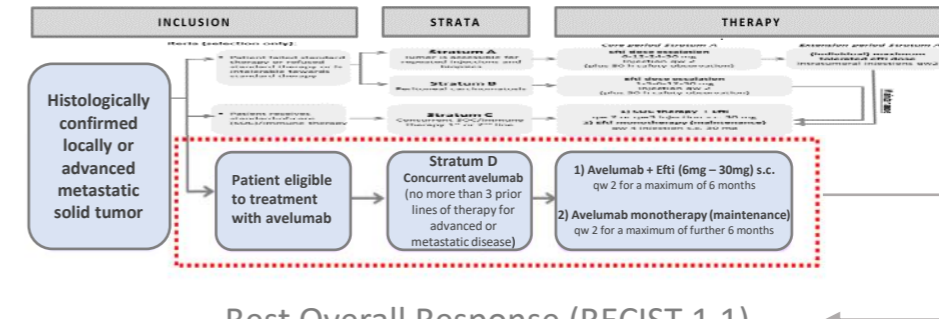
KRANKENHAUS
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Dose escalation study evaluating efti in combination with BAVENCIO (avelumab)

Key Takeaways*:

- Combination safe with promising signals of efficacy including durable responses
- 5/12 (42%) partial responses in different indications:
 - (1) 1st line MSI high colorectal cancer;
 - (2) 1st line pleural mesothelioma;
 - (3) after radio-chemo in squamous anal cell;
 - (4) pre-treated squamous cervical cancer (PD-L1 TPS < 1%) carcinoma;
 - (5) 3rd line gastroesophageal junction
- Activity also observed in pre-treated non-immunogenic tumors



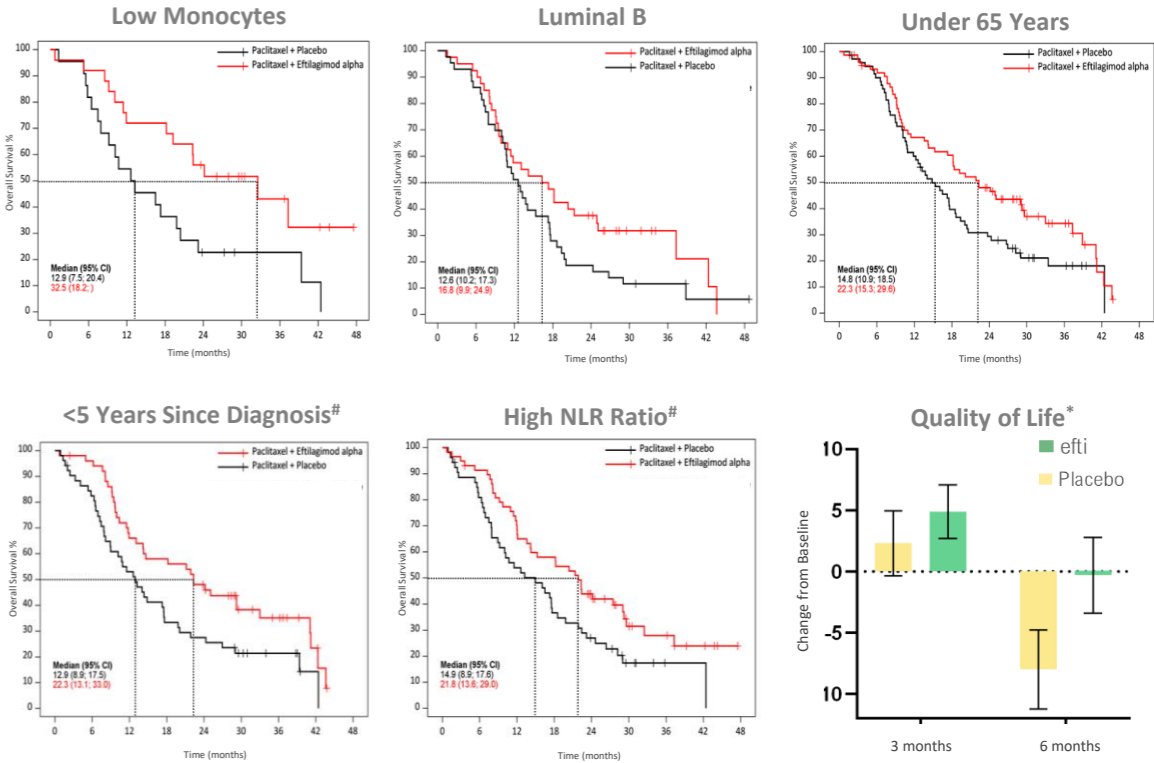
AIPAC Phase IIb: Significant OS Improvement Across Multiple Pre-Specified Subgroups with Superior QoL

AIPAC: Active Immunotherapy PAClitaxel in HER2–/ HR+ metastatic breast cancer Phase IIb Trial

AIPAC: Multicenter, placebo-controlled, double-blind, 1:1 randomized Phase IIb study; 226 patients randomized to efi (N=114) or placebo (N=112)

Subgroup Analysis	Median Overall Survival	Hazard Ratio	P-value
Low Monocytes	+19.6 months mOS	HR 0.44	p=0.008
<5 Years Since Diagnosis [#]	+9.4 months mOS	HR 0.57	p=0.008
Under 65 Years	+7.5 months mOS	HR 0.66	p=0.017
High NLR Ratio [#]	+6.9 months mOS	HR 0.61	p=0.012
Luminal B	+4.2 months mOS	HR 0.67	p=0.049
No Prior Taxanes	+4.8 months mOS	HR 0.74	p=0.076

- Efti + paclitaxel had ORR & DCR of 48.3% and 85.1% vs placebo ORR & DCR of 38.4% and 75.9%, respectively
- Efti + paclitaxel led to +2.9 month increase in median OS to 20.4 months, and +0.46 month increase in PFS to 7.12 months** (Effect on PFS observed until paclitaxel discontinued at 6 months under European trial design)

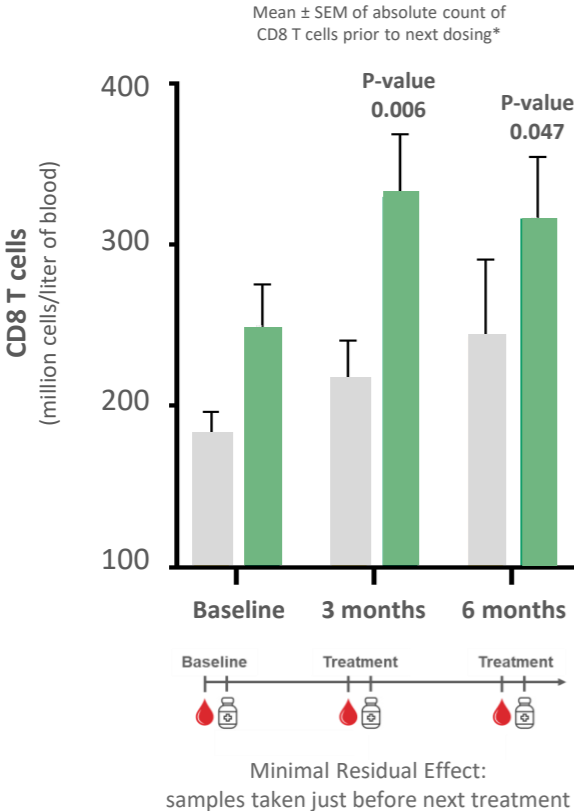


Statistically-significant OS improvement in multiple pre-specified subgroups, with no Quality of Life deterioration observed in efti group at 6 months versus significant deterioration in placebo group

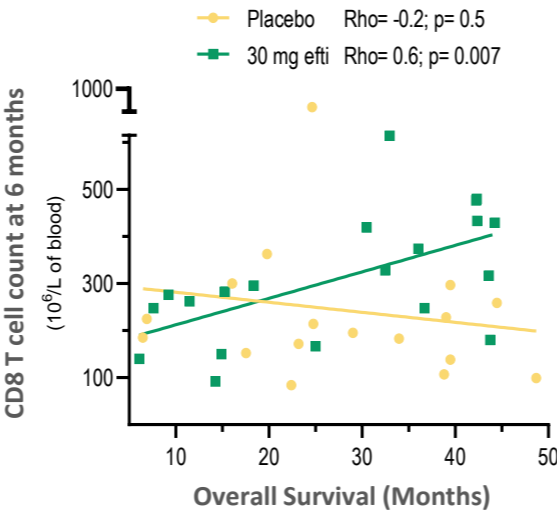
Substantial Increase in Monocytes, CXCL10, and Cytotoxic CD8⁺ T Cells Correlated to Stronger OS

AIPAC: Active Immunotherapy PAClitaxel in HER2–/ HR+ metastatic breast cancer Phase IIb Trial

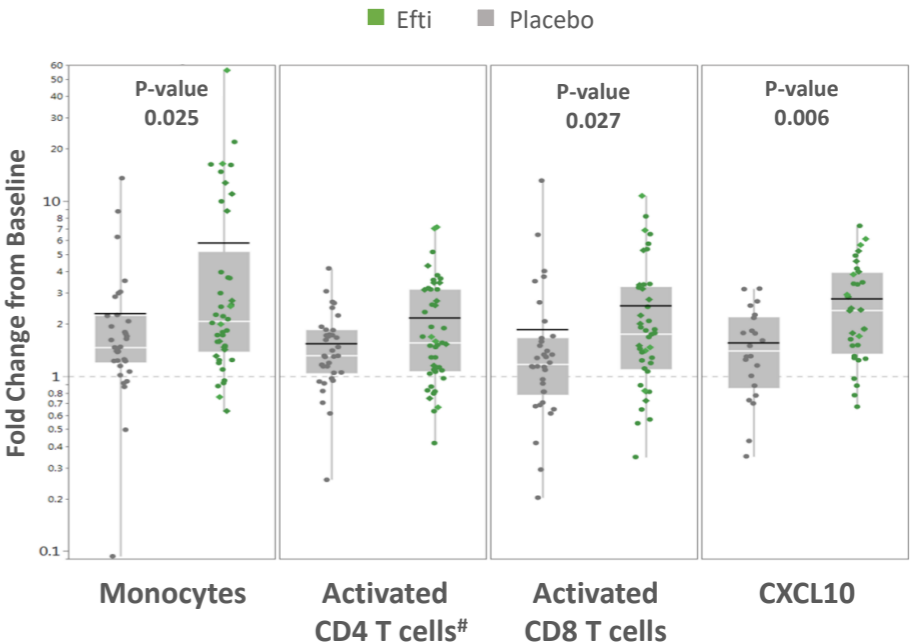
Statistically-Significant Increase of Cytotoxic CD8⁺ T Cell Count



Statistically-Significant Correlation: OS & Cytotoxic CD8⁺ T cell count



Statistically-Significant Increase in Monocytes, CD8⁺ T Cells & CXCL10



Triple IO-IO-Chemo Combination Trial

INSIGHT-003: Phase I in Solid Tumors Focusing on NSCLC Adenocarcinomas

INSIGHT-003 - Third arm (Stratum C) of ongoing Investigator-initiated study focusing on NSCLC adenocarcinomas

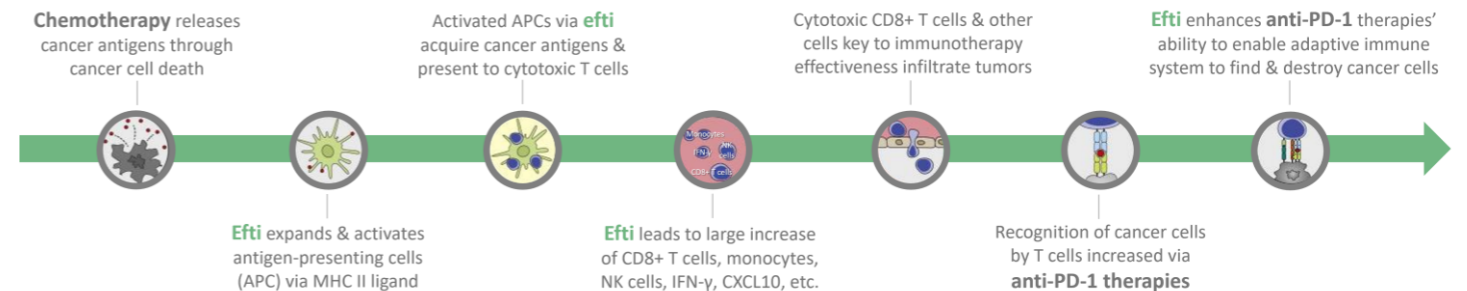
Status:

- Recruiting (over 50% enrolled*; reported good safety from initial five patients in Dec 2021)
- Initial results to be reported by year end*

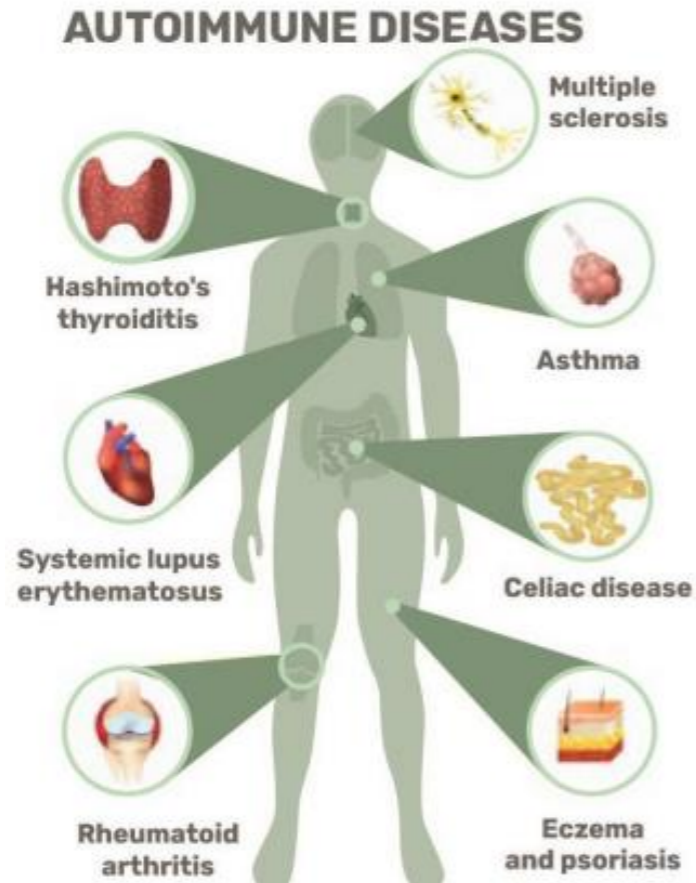
Design:

- Evaluating triple combination therapy consisting of efti in conjunction with carboplatin and anti-PD-1 therapy with solid tumors
- Trial will assess safety, tolerability and initial efficacy of the combination

Triple Combination Approach to Capitalize on Efti's Synergistic Effects with Chemotherapy & Anti-PD-1 immunotherapy



LAG-3 Therapeutics for Autoimmune Disease



Present Approaches Fight the Symptoms of Autoimmune Diseases

Treating general inflammation:

Corticoids, methotrexate, anti-TNF- α ,
-IL-6, -IL-17, -IL-23 mAbs



Future Approaches Target the Causes of Autoimmune Disease

Treating the disease process:

Targeting autoimmune memory T cells
with depleting or agonist LAG-3 antibodies

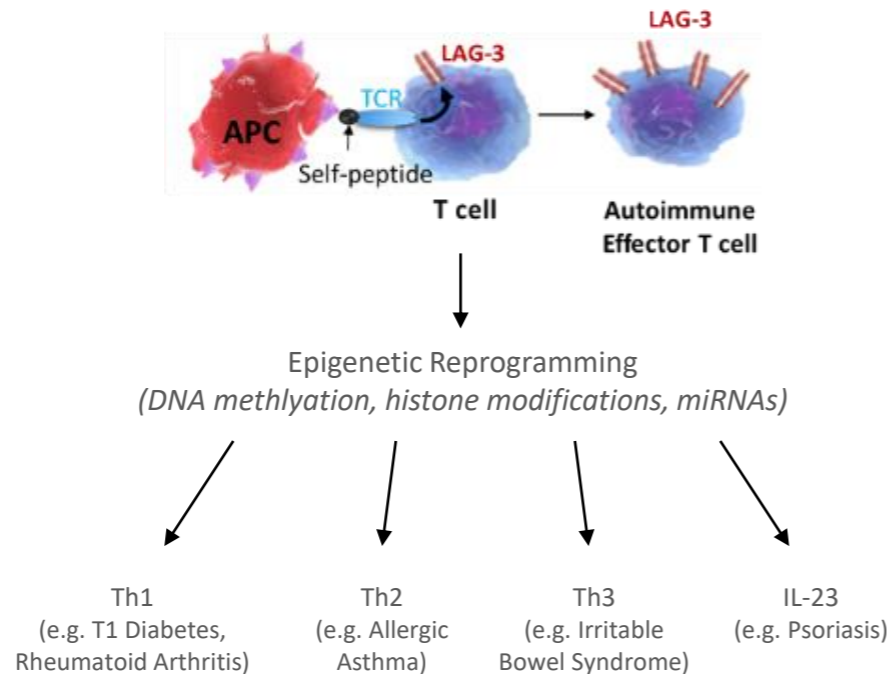
IMP761: Broad Potential Targeting Auto-Reactive Memory T Cells



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

Mathieu Angin, Chrystelle Brignone and Frédéric Triebel
J Immunol January 6, 2020, *ji1900823*

Deficiency in LAG3 Pathways Linked to Development of Autoimmune Diseases (AI)



IMP761

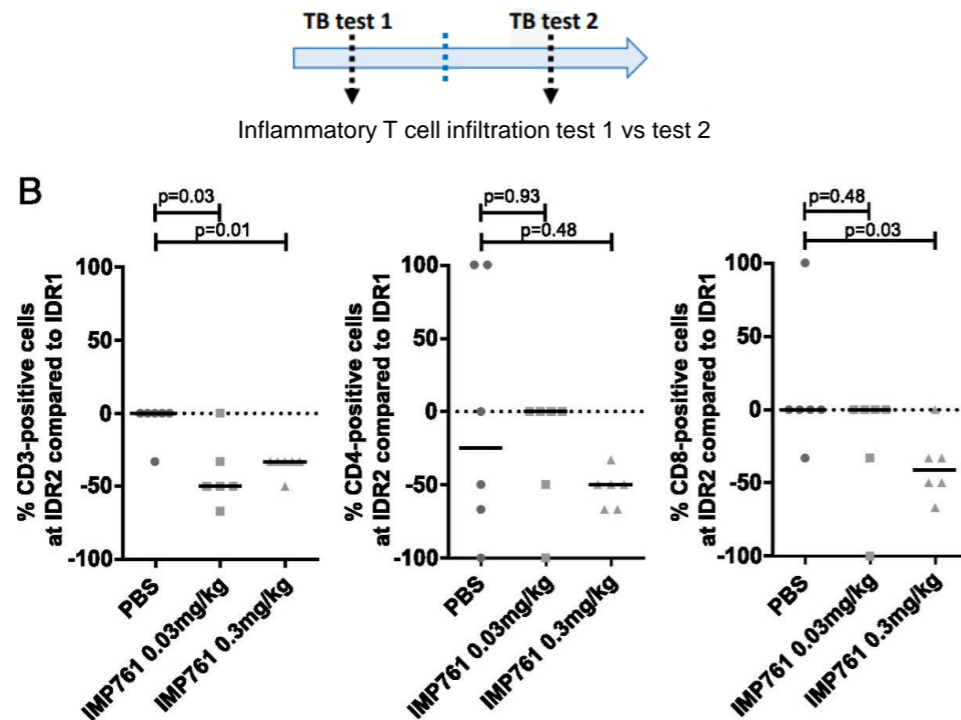
Immutep's proprietary humanized IgG4
LAG-3-specific antibody



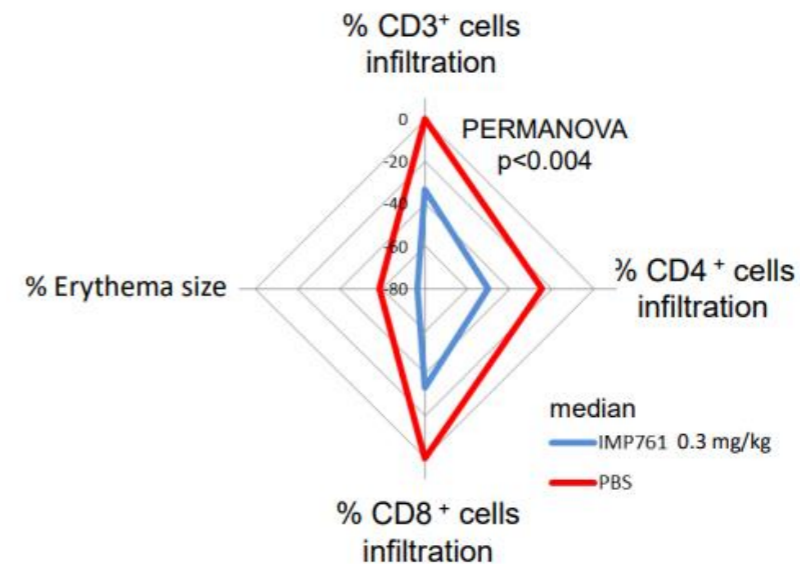
As the **first LAG-3-specific agonist** acting upstream on activated T cells, the root cause of self-Ag-specific T cell-induced disease, IMP761 is a **potential game-changer** in autoimmune diseases.

IMP761 Inhibits Inflammatory T cell Infiltration *In Vivo*

IMP761 significantly inhibits T cell infiltration of an antigen-specific intradermal reaction *in vivo* in an Ag-specific delayed-type hypersensitivity (DTH) model in non-human primate study



Percentage of CD3-, CD4-, and CD8-positive cells at IDR2 compared with IDR1 in cynomolgus macaques that received PBS control (circle) and IMP761 at 0.03 mg/kg (square) or 0.3 mg/kg (triangle).



2022 Milestones

- Year to date:
 - ✓ 1L NSCLC Oral Presentation at ASCO (TACTI-002; Part A)
 - ✓ 2L NSCLC PD-X refractory data at ELCC & WCLC 2022 (TACTI-002; Part B)
 - ✓ Fast Track Designation granted in 1L NSCLC
 - ✓ New, significant data from AIPAC study
 - ✓ IP expansion for eftilagimod alpha
- Additional clinical data updates through year end
 - New data from Phase II TACTI-002 in 1L NSCLC
 - Initial results from INSIGHT-003 (first triple-combo data)
 - Updates from randomized trial in 1L HNSCC (TACTI-003)
- Expansion of existing programs (i.e., new sarcoma trial)
- Regulatory updates
- Manufacturing scale up to 2,000L
- Updates on IMP761 & partnered programs (e.g. Novartis, GSK, EOC)

Corporate Snapshot

- Pioneering LAG-3 portfolio in oncology and autoimmune diseases with four product candidates in multiple clinical trials
- First-in-class positioning with eftilagimod alpha (efti)
- Multiple big pharma partnerships & collaborations, while retaining full control of efti (ex-China) & IMP761
- Well funded with ~A\$73.9 million* in cash
- Cash runway to early CY2024*
- Ticker symbols:
 - ✓ IMM (ASX)
 - ✓ IMMP (NASDAQ)
- Market cap ~A\$251M / \$161M US**



Thank You