



Update on New Data in First Line Treatment of Metastatic Non-Small Cell Lung Cancer Presented at ESMO Congress 2023

Global Webcast Presentation - Monday, October 23rd, at 8AM AEDT (Sunday, October 22nd, at 5PM ET)



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

Forward-Looking Statements

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Eftilagimod Alpha (efti):
A First-in-Class Soluble LAG-3 Protein and
MHC Class II Agonist

Deep Pipeline

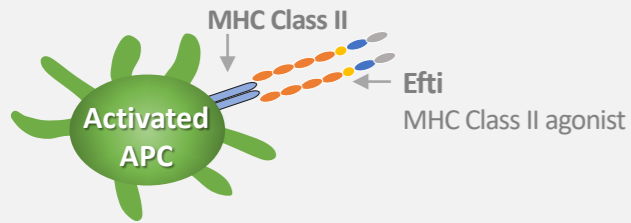
	Program	Indication	Preclinical	Phase I	Phase II	Late Stage*	Collaborations	Commercial Rights
ONCOLOGY	Eftilagimod Alpha Soluble LAG-3 Protein & MHC Class II Agonist 	1L Head & Neck Squamous Cell Carcinoma (HNSCC)	TACTI-003 Efti+Pembrolizumab ^a				  Merck KGaA Darmstadt, Germany  	 Global Rights ex-China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

Information in pipeline chart current as of May 2023; AIPAC-003 Phase II/III trial expected to begin Q1'2023. 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](#) (for GSK's global rights, Immutep may receive milestones plus royalties), Phase II in Ulcerative Colitis discontinued. * 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. ^s 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[®].

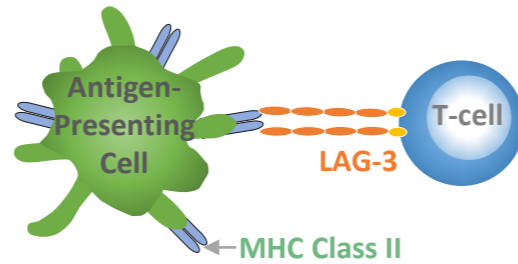
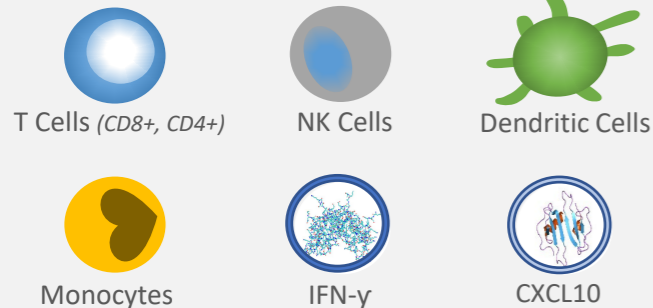
Immutep's Pioneering Immunotherapies

Only company with multiple therapeutic approaches around LAG-3 / MHC Class II interaction

Targeting MHC Class II on APCs with Soluble LAG-3 Protein (Efti)

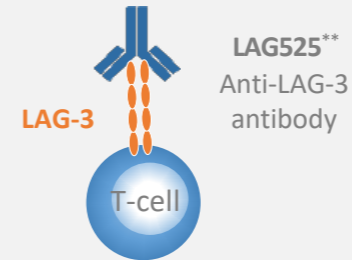


Activating APC (e.g., dendritic cells) with efti leads to a systemic anti-cancer immune response. Can work well in "hot", "tepid", and "cold" tumours.



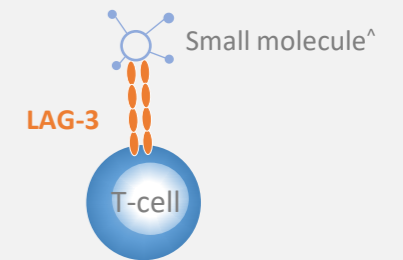
LAG-3 on T cells binds to MHC Class II molecules# on antigen-presenting cells (APC)

Targeting LAG-3 on T cells with an Antagonist Antibody



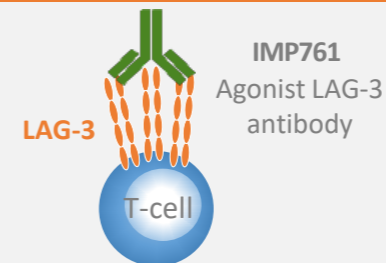
Blocking LAG-3 on T cells prevents LAG-3-mediated co-inhibitory signaling, allowing T cells to attack cancer

Targeting LAG-3 on T cells with Small Molecules



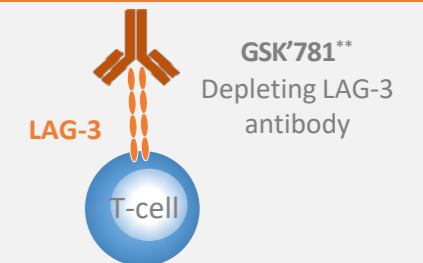
Small molecules blocking LAG-3 could offer convenience of an oral pill at a fraction of the cost of biologics

Targeting LAG-3 on T cells with an Agonist Antibody



Increasing LAG-3's natural down-regulation of auto-reactive memory T cells may address autoimmune diseases

Targeting LAG-3 on T cells with a Depleting Antibody

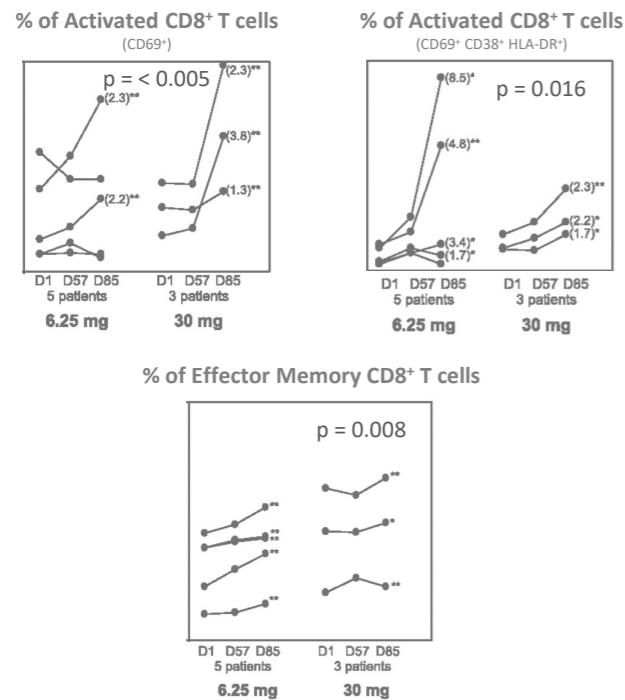


Depleting LAG-3 T cells can suppress immune system's response, enabling treatment of autoimmune diseases

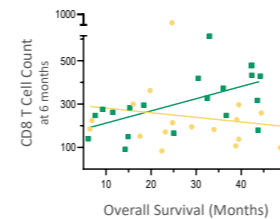
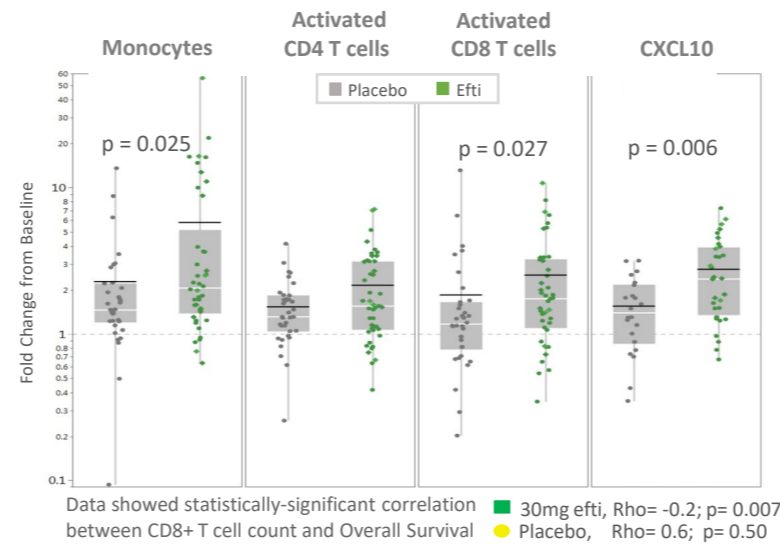
Efti Driving Adaptive & Innate Immune Response

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- γ (IFN- γ) & CXCL10 that augment anti-cancer activity

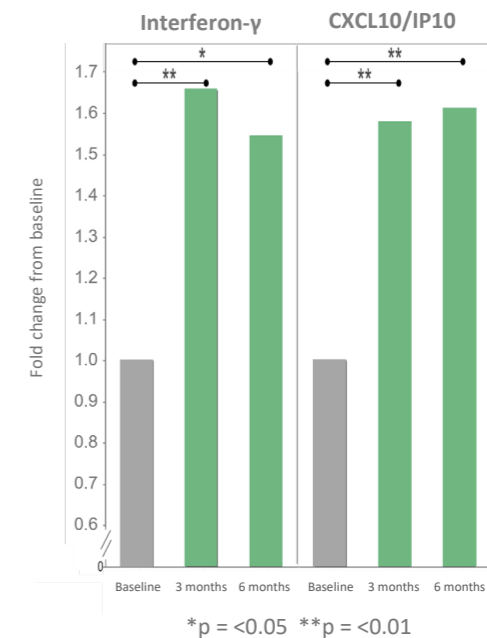
Phase I: Efti monotherapy



Phase II: Efti + paclitaxel



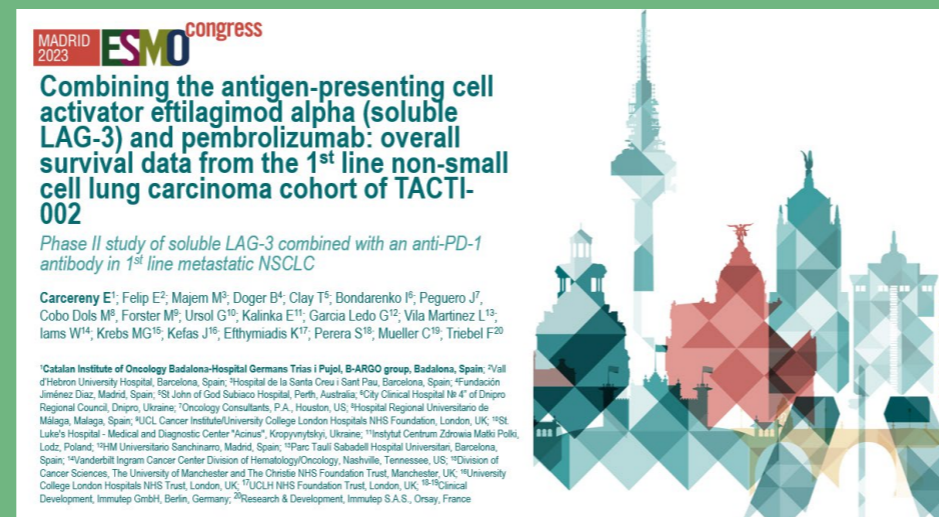
Phase II: Efti + pembrolizumab



TACTI-002 Phase II Trial – Part A

Efti + Pembrolizumab Combination in First Line Treatment of Metastatic Non-Small Cell Lung Cancer

Data Update from ESMO 2023 Mini Oral Presentation



MADRID 2023 ESMO congress

Combining the antigen-presenting cell activator eftilagimod alpha (soluble LAG-3) and pembrolizumab: overall survival data from the 1st line non-small cell lung carcinoma cohort of TACTI-002

Phase II study of soluble LAG-3 combined with an anti-PD-1 antibody in 1st line metastatic NSCLC

Carcereny E¹; Felip E²; Majem M³; Doger B⁴; Clay T⁵; Bondarenko I⁶; Peguero J⁷; Cobo Dols M⁸; Forster M⁹; Ursol G¹⁰; Kalinka E¹¹; Garcia Ledo G¹²; Vila Martinez L¹³; Iams W¹⁴; Krebs MG¹⁵; Kefas J¹⁶; Elthymiadis K¹⁷; Perera S¹⁸; Mueller C¹⁹; Triebel F²⁰

¹Catalan Institute of Oncology Badalona-Hospital Germans Trias i Pujol, B-ARGO group, Badalona, Spain; ²Vall d'Hebron University Hospital, Barcelona, Spain; ³Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; ⁴Fundación Jiménez Díaz, Madrid, Spain; ⁵St John of God Subiaco Hospital, Perth, Australia; ⁶City Clinical Hospital № 4 of Dnipro Regional Council, Dnipro, Ukraine; ⁷Oncology Consultants, P.A., Houston, US; ⁸Hospital Regional Universitario de Málaga, Málaga, Spain; ⁹UCL Cancer Institute/University College London Hospitals NHS Foundation, London, UK; ¹⁰St. Luke's Hospital - Medical and Diagnostic Center "Kosmus", Kropyvnytskyi, Ukraine; ¹¹Instytut Centrum Zdrowia Matki Polki, Lodz, Poland; ¹²HM Universitario Sanchinarro, Madrid, Spain; ¹³Parc Taulí Sabadell Hospital Universitari, Barcelona, Spain; ¹⁴Vanderbilt Ingram Cancer Center Division of Hematology/Oncology, Nashville, Tennessee, US; ¹⁵Division of Cancer Sciences, The University of Manchester and The Christie NHS Foundation Trust, Manchester, UK; ¹⁶University College London Hospitals NHS Trust, London, UK; ¹⁷UCLH NHS Foundation Trust, London, UK; ¹⁸⁻¹⁹Clinical Development, Immutep GmbH, Berlin, Germany; ²⁰Research & Development, Immutep S.A.S., Orsay, France

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)

Trial Design (Part A)

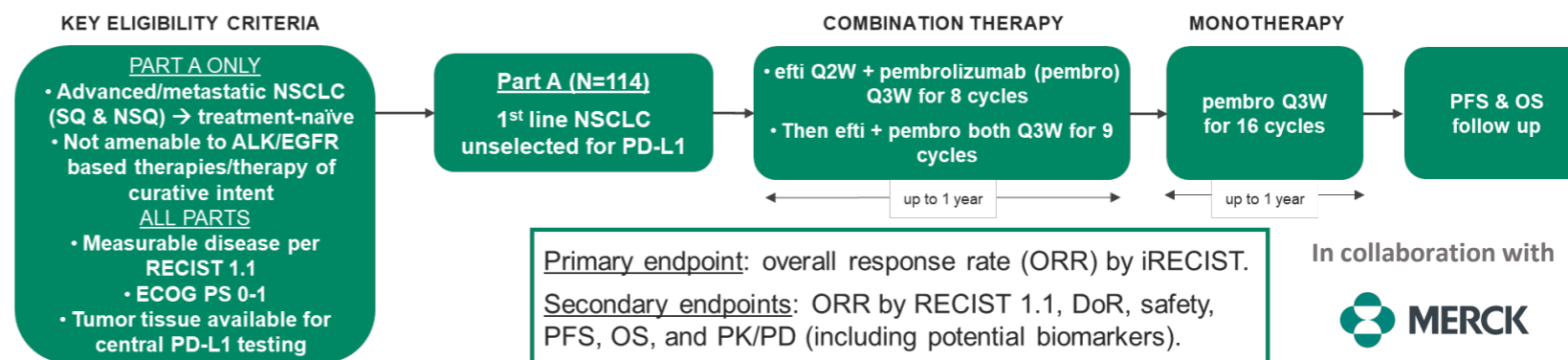
- Phase II, open label, Simon's two stage
- Six countries (US, UK, ES, PL, UA, AU)
- 18 sites
- 114 patients enrolled

Baseline characteristics

- Trial enrolled 1L NSCLC patients regardless of PD-L1 Tumor Proportion Score (TPS) expression
- ~75% of patients have PD-L1 TPS of <50%
- Lower proportion of patients with PD-L1 TPS ≥50% than would be expected

Safety

- No new safety signals compared to pembrolizumab monotherapy



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 ¹ (%)	< 1%	Central only 32 (35.6)	Central + local 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)	

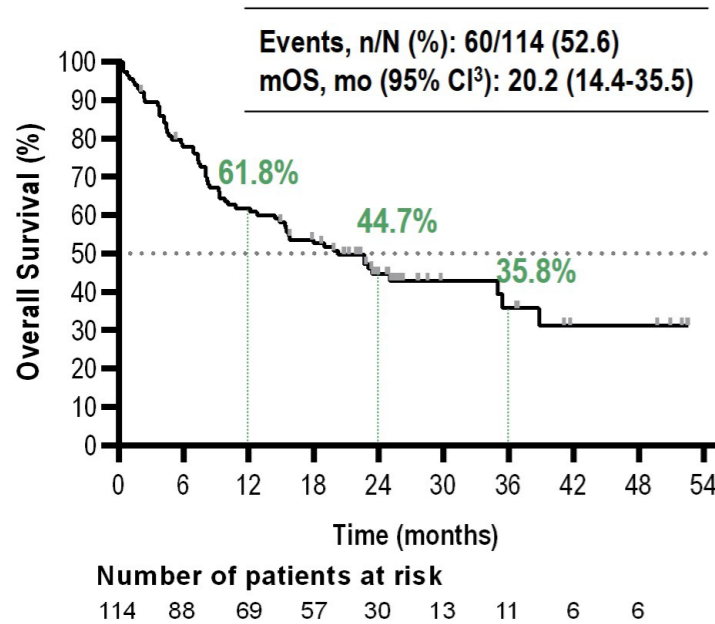
Note: Patients were recruited according to Simon's optimal two-stage design: during the first stage, 17 pts were recruited; second stage recruitment (n=19) was opened only after the number of responses was above 4. An extension stage (n=78) could be added if there were above 12 responses. In total, 114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

Key Efficacy Data in ITT Population

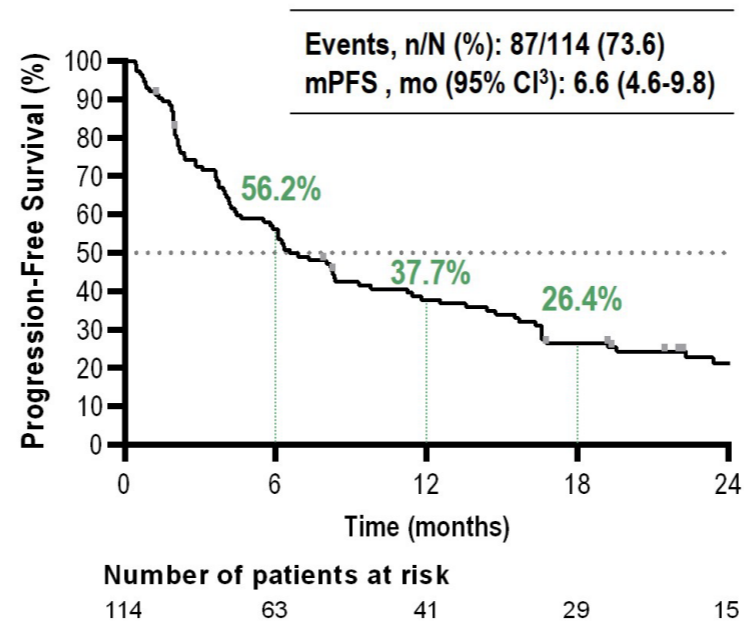
Intent-to-treat (ITT) population (N=114) includes ~75% patients with TPS <50% and ~35% with TPS <1%

- Strong response rate of 40.4%¹ [95% CI³: 31.3-50.0] in conjunction with high median DoR of 21.6 months²
- Median OS of 20.2 months (with median follow up of 25.1 months!)
- Excellent 12-month PFS (37.7%) and 36-month OS (35.8%) rates

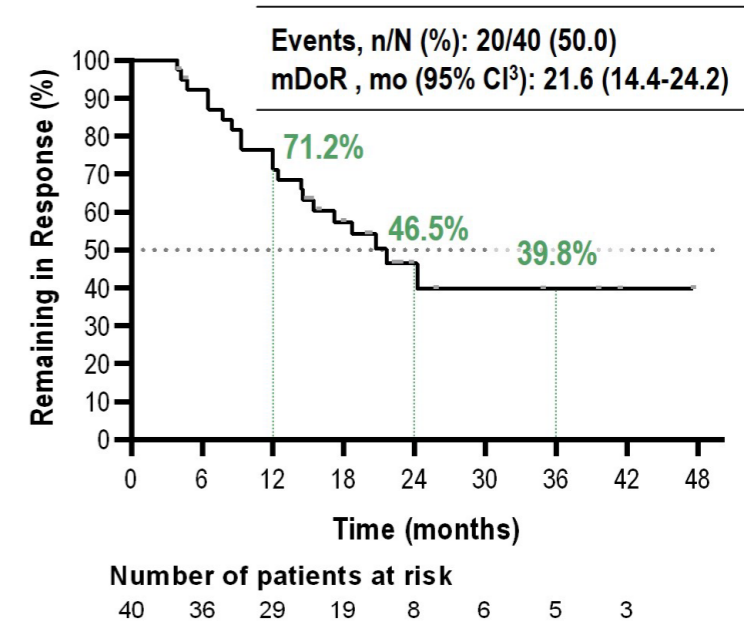
Overall Survival, ITT (N=114)



Progression Free Survival¹, ITT (N=114)



Duration of Response³, (N=40)



Excellent Survival Benefit across all PD-L1 Expression Levels

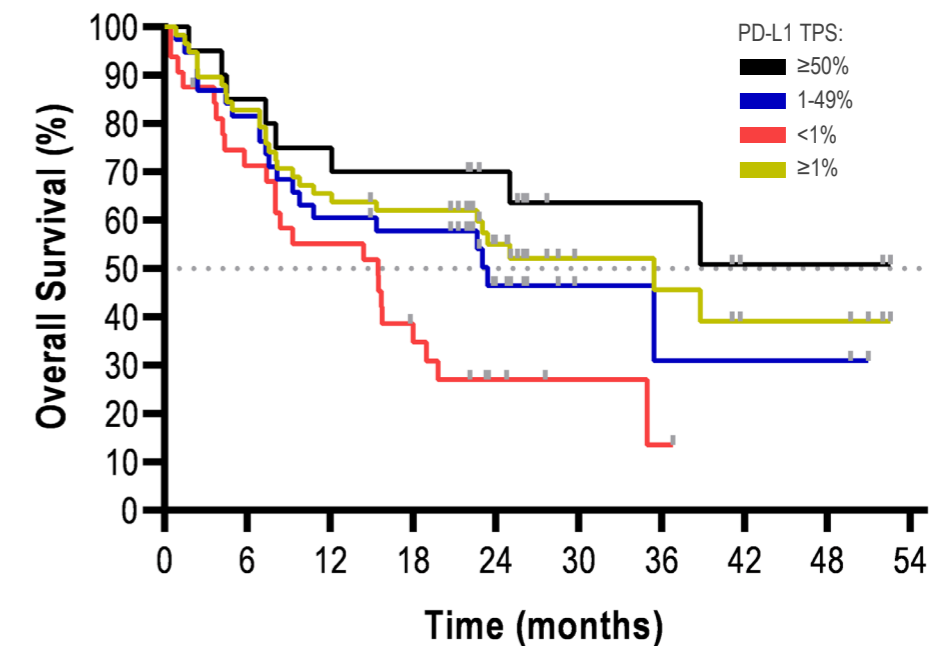
Strong efficacy with any PD-L1 (TPS \geq 1%) and PD-L1 negative (TPS <1%), low (TPS 1-49%), high (TPS \geq 50%)

Promising efficacy with strong Overall Response Rate (ORR), Progression Free Survival (PFS), Duration of Response (DOR), and Overall Survival (OS) visible across all PD-L1 TPS subgroups including negative and low expressing patients^{1,2}

Tumor Response by Central PD-L1¹, N=90

Efficacy parameter	TPS <1% n (%), N=32	TPS 1-49% n (%), N=38	TPS \geq 50% n (%), N=20	TPS \geq 1% n (%), N=58
ORR ^{2,3} , % (95% CI) ⁴	31.3 (16.1-50.0)	44.7 (28.6-61.7)	55.0 (31.5-76.9)	48.3 (35.0-61.8)
mPFS ² , months (% events)	4.2 (90.6)	9.3 (71.1)	16.5 (70.0)	11.2 (70.7)
mDoR ² , months (% events)	20.7 (57.1)	NR (35.7)	18.7 (63.6)	24.2 (48.0)
mOS, months (% events)	15.5 (71.9)	23.4 (52.6)	NR (40.0)	35.5 (48.3)

Overall Survival by central PD-L1¹

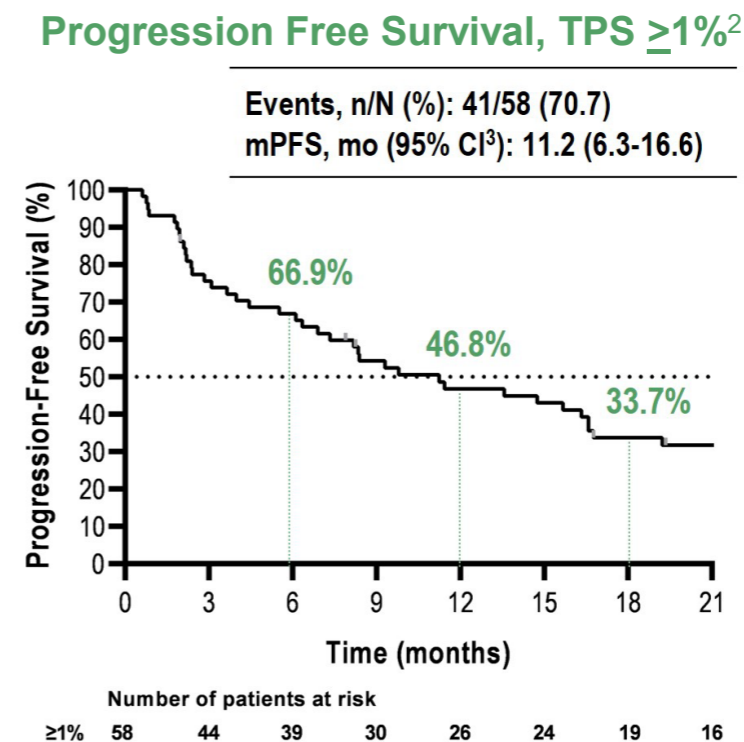
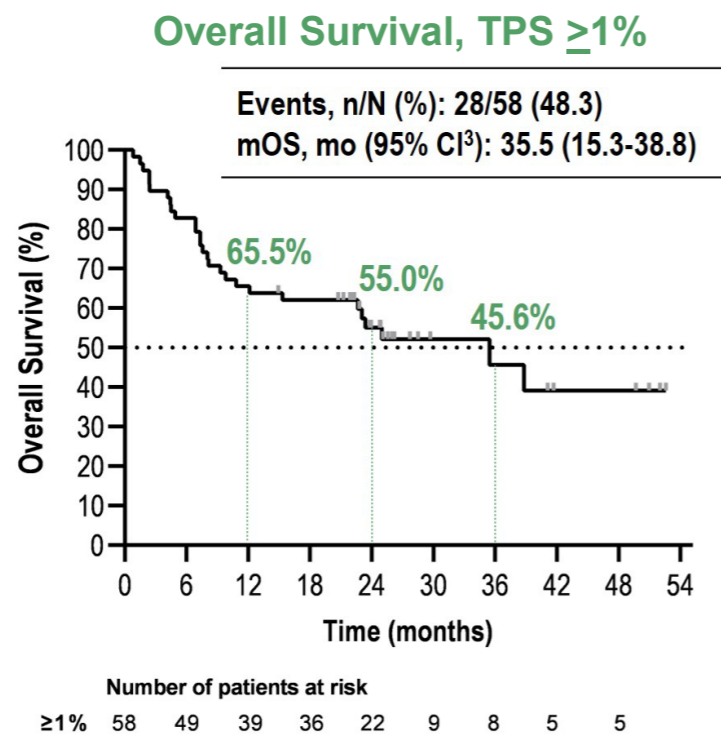


	Number of patients at risk								
	0	6	12	18	24	30	36	42	48
\geq 50%	20	18	16	15	12	7	6	3	3
1-49%	38	32	24	22	11	4	4	3	3
<1%	32	23	18	10	5	3	3		
\geq 1%	58	49	39	36	22	10	9	5	5

Significant 35.5-Month Median OS Reached in TPS $\geq 1\%$

Patients with any PD-L1 expression or TPS $\geq 1\%$ represent $\sim 65\%$ of the 1L NSCLC patient population

- Significant median OS of 35.5 months¹
- 48.3% ORR, median PFS of 11.2 months, and median DoR of 24.2 months
- 12-month PFS- and 36-month OS-rate are very promising at 46.8% and 45.6%, respectively
- Strength of data in PD-L1 TPS 1-49% (N=38, 66% of TPS $\geq 1\%$ group[#]), including 44.7% ORR, 9.3-month mPFS, mDOR not reached, and 23.4-month mOS, contributed significantly to overall results in TPS $\geq 1\%$ unlike other IO-IO combinations



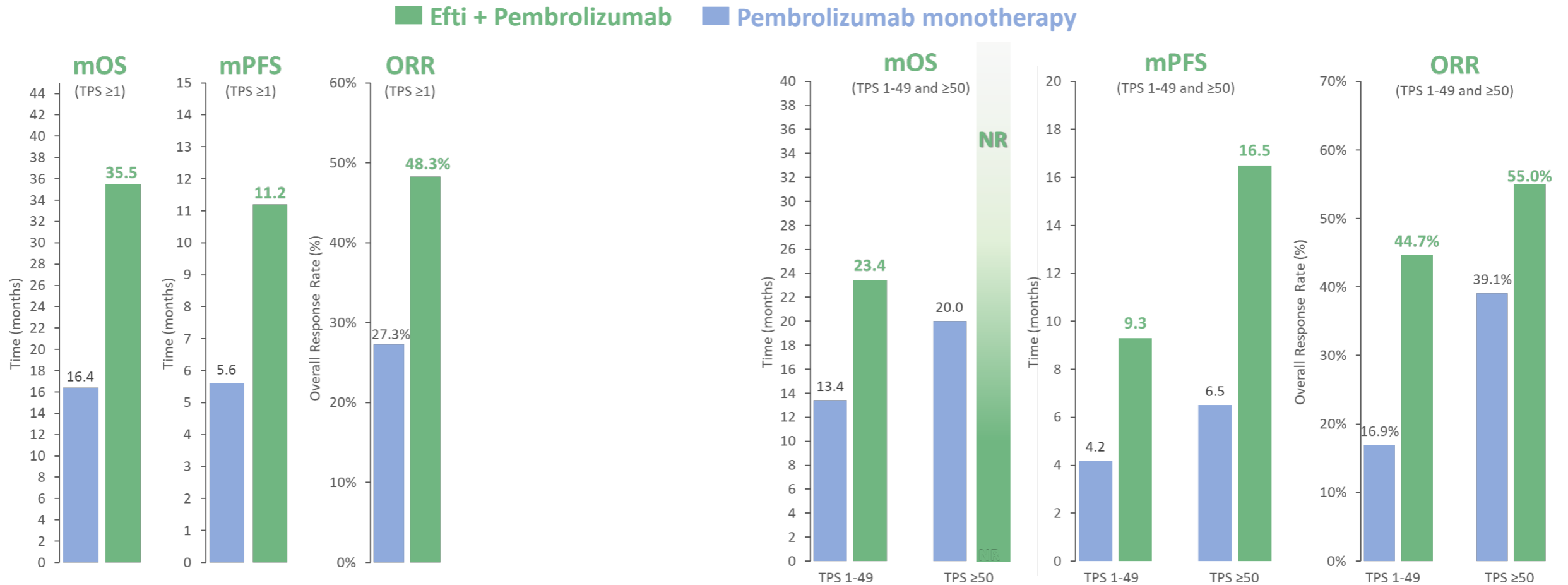
¹ The mOS in TPS $\geq 1\%$ was attained with both central assessment of PD-L1 (N=58) and in larger patient group with central + local assessment of PD-L1 (N=71). ² iRECIST and RECIST 1.1 for PFS was comparable with 61.6%, 43.7% and 32.8% at 6, 12, and 18 months, respectively, as per RECIST1.1.

³ 95% confidence intervals calculated using Clopper-Pearson method or using Kaplan-Meier survival analysis method.

[#] For reference, in TPS $\geq 1\%$, TACTI-002 has 66% patients with TPS 1-49% and 34% with TPS $\geq 50\%$, which compares to KN-042 with $\sim 53\%$ patients with PD-L1 and $\sim 47\%$ patients with PD-L1 TPS $\geq 50\%$.

Benchmarking against Pembrolizumab Monotherapy

Robust Overall Survival, Overall Response Rates, and Progression-Free Survival across all PD-L1 levels



TPS ≥1%

- Efficacy increased by 1.5- to 2-fold for all important efficacy parameters while maintaining safety and durability
- For patients with SD, BOR translates to meaningful OS
- Confidence intervals do not overlap for ORR

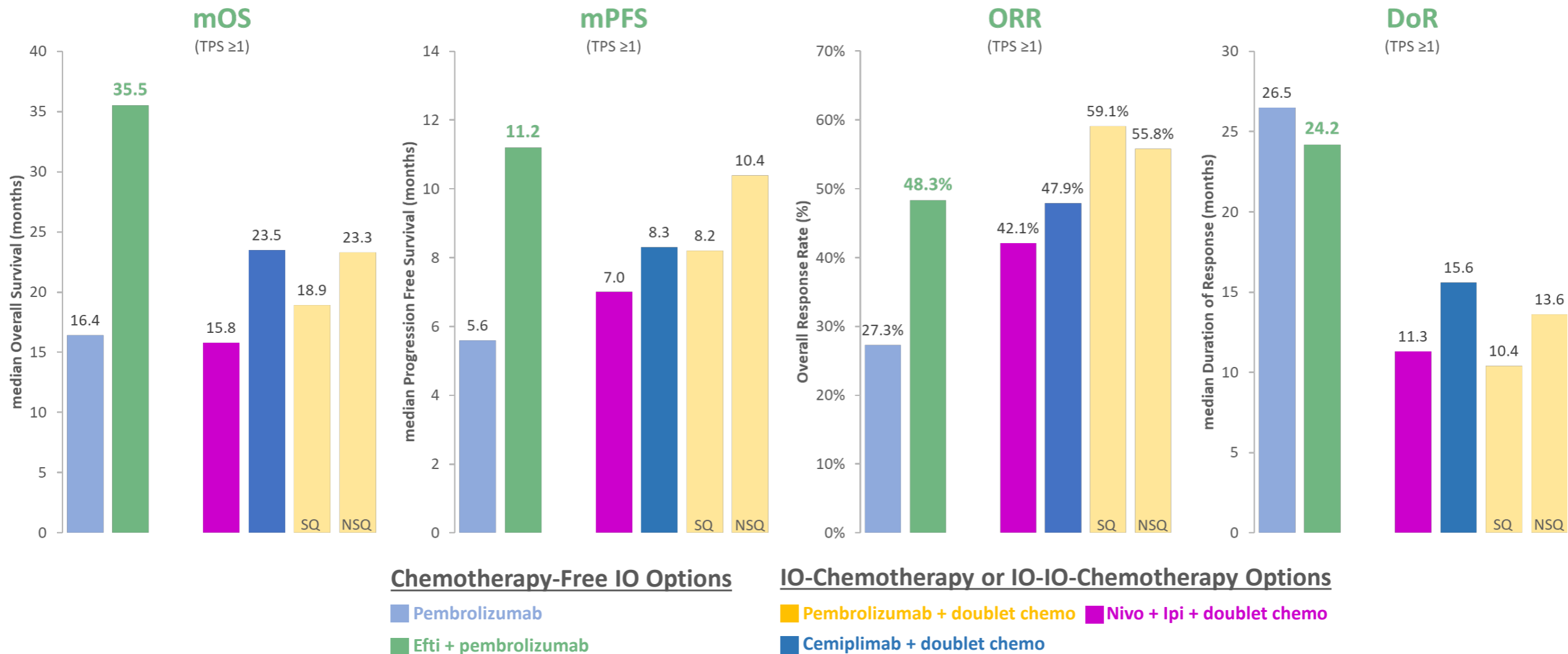
TPS 1-49% and TPS ≥50%

- In TPS 1-49%, efficacy increased by 1.5- to over 2-fold for all important efficacy parameters while maintaining safety and durability
- In TPS ≥50%, strong ORR, PFS & mOS that strengthened as not reached with August 2023 cut-off, up from 38.8 months with March 2023 cut-off

Benchmarking Efficacy to Standard-of-Care

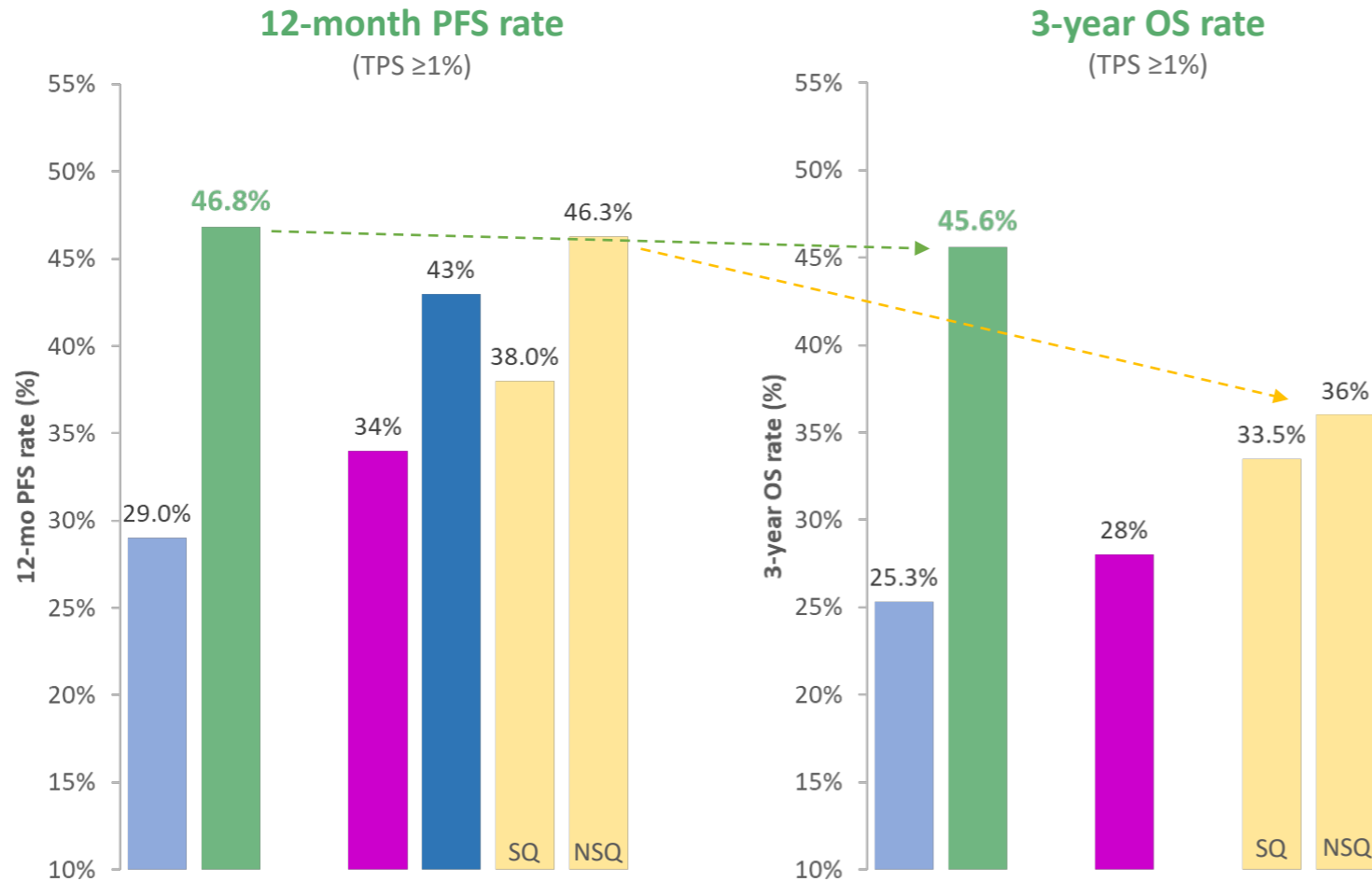
ORR, PFS, DOR and OS from Efti + Pembro as compared to Standard-of-Care therapies in PD-L1 TPS ≥1%

ORR, PFS and DoR of Efti + Pembro translates into substantially better Overall Survival



Benchmarking Long-Term Effects

Exceptional durability and quality of responses exhibited through OS and PFS rates in PD-L1 TPS ≥1%



- Efti+Pembro has a **similar 12-month PFS rate (46.8%)** compared to chemo-containing regimens and **superior 12-month PFS rate** to pembro mono
- Efti plus pembro has an **exceptional 3-year OS rate (45.6%)** higher than all chemo-containing regimens
- **12-mo PFS rate translates into 3-year OS rate for E+P unlike other approaches**

→ Efti + pembro may be in a unique position to lift the tail of the survival curve

Chemotherapy-Free IO Options

- Pembrolizumab
- Efti + pembrolizumab

IO-Chemotherapy or IO-IO-Chemotherapy Options

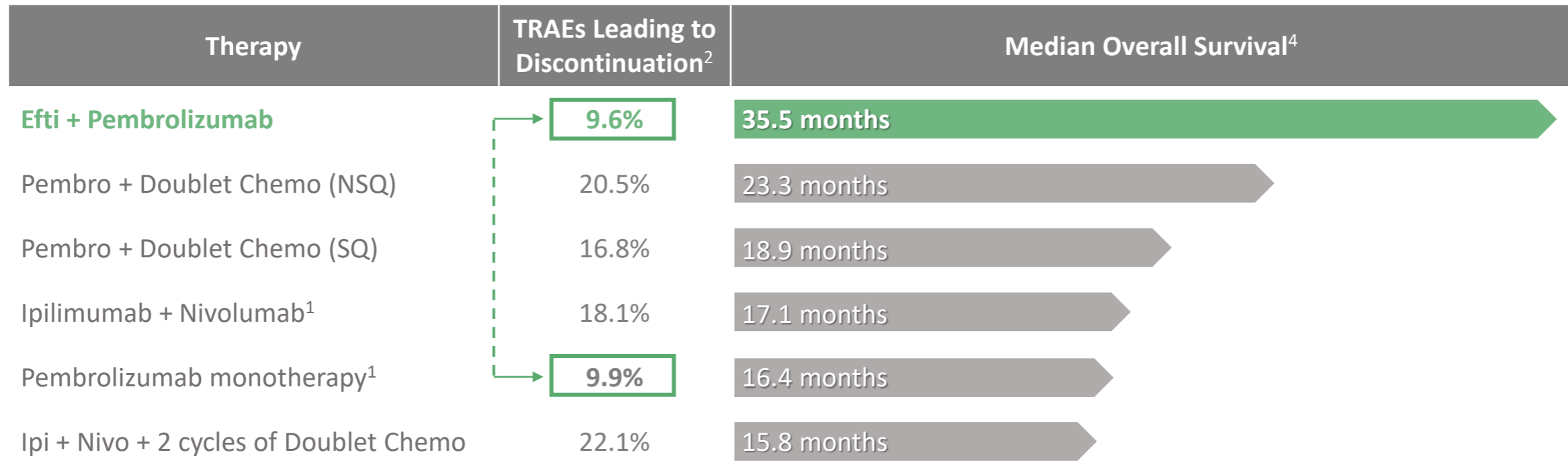
- Pembrolizumab + doublet chemo
- Nivo + Ipi + doublet chemo
- Cemiplimab + doublet chemo

Benchmarking against Standard-of-Care in 1L NSCLC

Overall survival & safety of efti + pembro vs. IO, IO-chemo, & IO-IO-chemo in patients with PD-L1 TPS $\geq 1\%$



Differentiated OS from **Efti + Pembro** that extends well beyond all standard-of-care regimens achieved with a **favorable safety profile** that is comparable to pembrolizumab monotherapy



NSQ = Non-squamous; SQ = Squamous

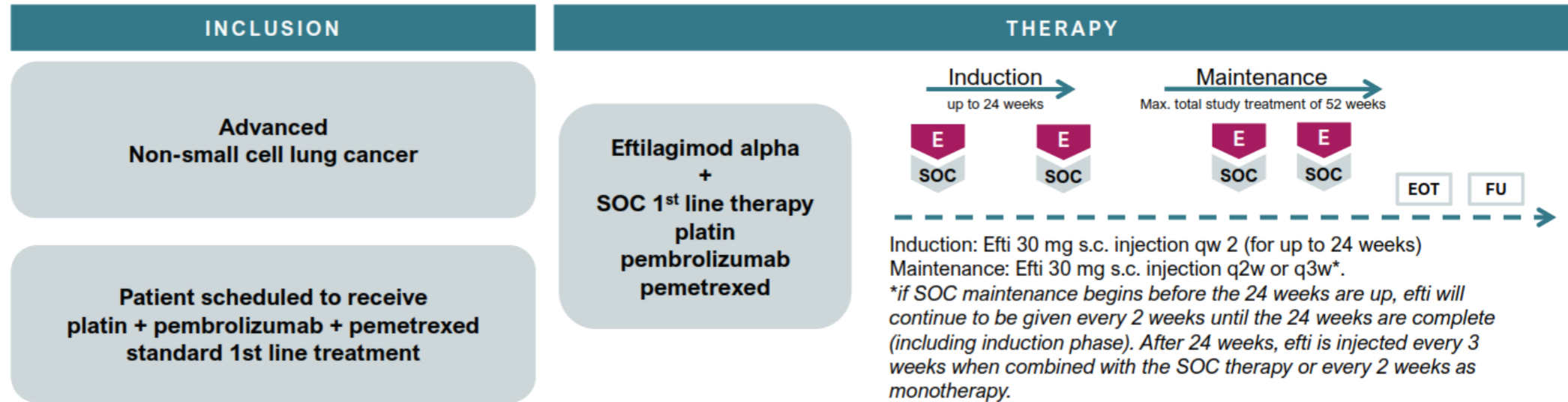
INSIGHT-003 Phase I Trial:

**Efti + Pembrolizumab + Chemotherapy
Combination in Metastatic Non-Squamous First Line NSCLC**

Data from ESMO Abstract
(Poster will be presented tomorrow)

INSIGHT-003: IO + IO + Chemo Combination Trial

INSIGHT-003 - Investigator-initiated study focusing on front line non-squamous NSCLC adenocarcinomas



Design:

- Evaluating triple combination therapy consisting of efti in conjunction with carboplatin/pemetrexed & anti-PD-1 therapy
- Study focuses on pts with TPS <50%
- Trial assessing safety, tolerability and initial efficacy

Key aspects:

- 21 pts recruited as of Jan 2023 → extension opened in summer CY'2023 and trial has already recruited six additional patients
- Strong 67% ORR and 91% DCR detailed in ESMO abstract with older cutoff date (updated data to be presented at ESMO with later cutoff date and more mature data)
- Triple combination has been well tolerated & appears to be safe. No occurrence of unacceptable toxicities

Outlook:

- ESMO poster presentation with new data will be published within ~24 hours from this webcast
- Immunetep is looking forward to have the additional patients recruited soon → expected by H1 2024
- Current IO-chemotherapy combinations generate ORR near 40% level for patients with TPS <50%. Goal is to generate a higher ORR as compared to any approved chemo+anti-PD-1 combination in this TPS <50% setting that would warrant further investigation.

Registration strategy in First Line Treatment of Metastatic Non-small Cell Lung Cancer

Multiple options moving forward for TACTI-004 in 1L NSCLC

First Line Metastatic Non-Small Cell Lung Cancer

Significant patient population whose treatment options are limited in durability & tolerability

1L NSCLC^{1,2}

- 1.87 million NSCLC diagnoses per annum –
- Most frequent cause of cancer death (18%) –
- 1.3 million patients develop metastatic disease & are eligible to receive anti-PD-(L)1 –
- Global NSCLC market is expected to nearly double to US\$48bn by 2031 with ICIs capturing half of market³ –
- 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 –

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

Patients with **low PD-L1 status** have poorer responses to checkpoint therapy (TPS <50% = **~70% patient population**)

High discontinuation rates due to toxicity **limits Duration of Response** of checkpoint & chemo combinations

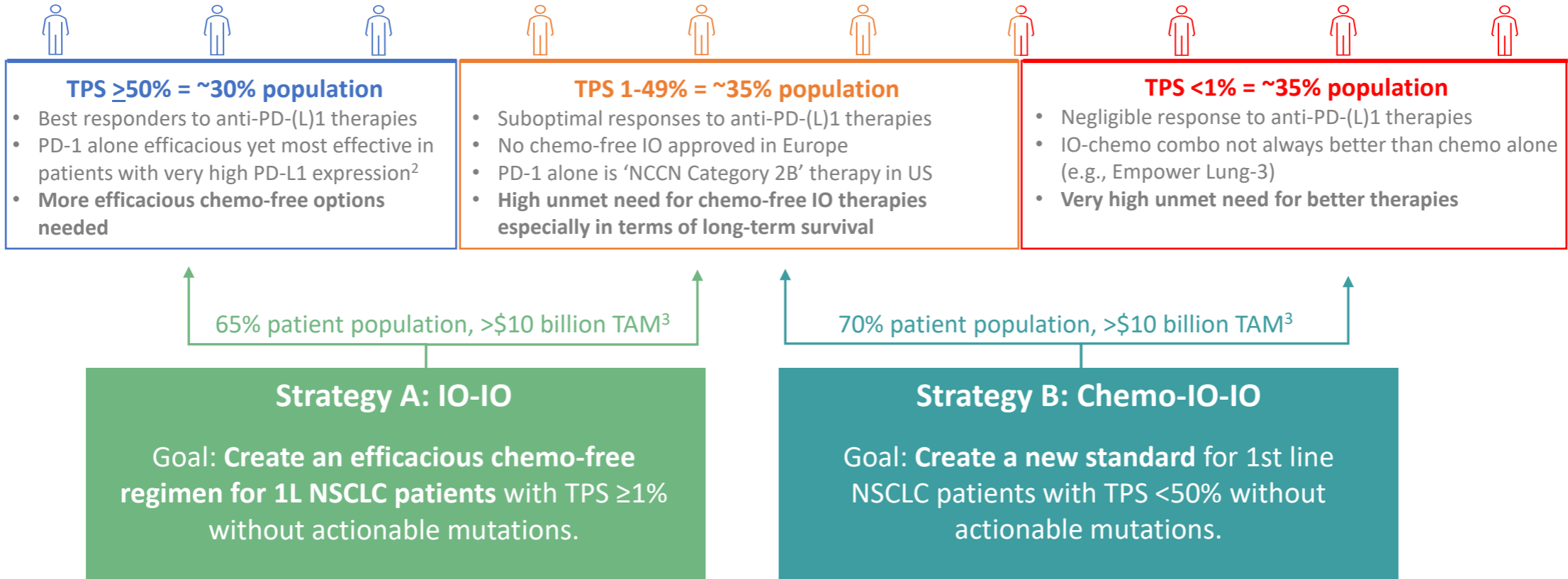
Efti Uniquely Positioned in 1st line Non-Small Cell Lung Cancer



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 come 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.

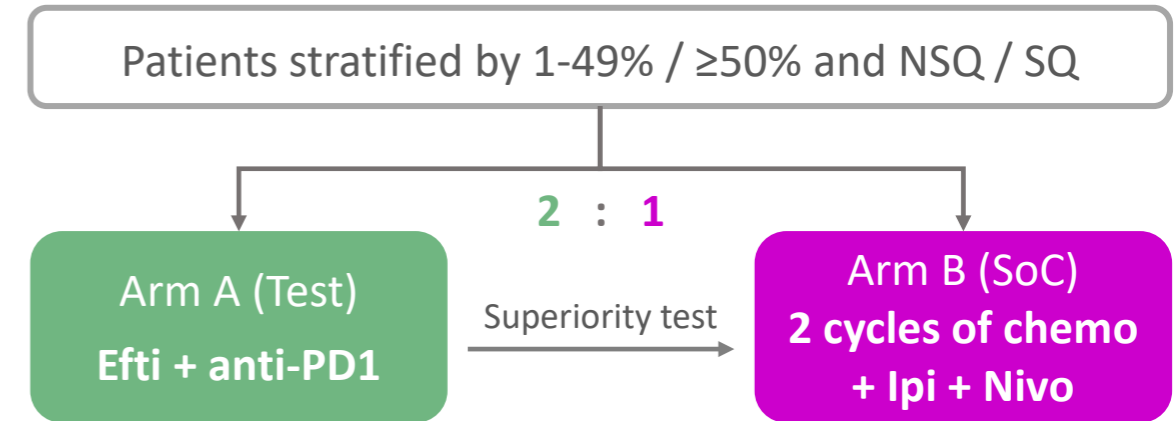
Scenarios for Phase 3 REGISTRATION Study

Strength of new data drives multiple options for chemo-free IO-IO combination with efti + anti-PD-1

General aspects

- Immunetep is preparing to conduct a Phase 3 study and has multiple options given the strength of new data presented at ESMO 2023
- Aim is to capture US and EU markets (70-80% of global 1st line NSCLC market)
- Trial design/timelines subject to Regulatory Authority interactions, Competent Authority approval, stakeholder feedback, as well as partnering discussions
- Practical implications are:
 - Choice of comparator arm: influence on sample size, feasibility, commercial aspects
 - Comparator arm should be NCCN 1 category 1 and ESMO recommended
 - Patient population: strength of the data allows for TPS $\geq 1\%$, and also for a potential focus on 1-49% or $\geq 50\%$
- Sample size & comparator arm will be based on acceptance by Competent Authorities in key global markets, including the US and Europe, and design to ensure good likelihood of success

Details for current Scenario: PD-L1 TPS $\geq 1\%$



- 2 : 1 randomized, multi-national, open label Phase 3
 - Sample size app. 630 pts
 - Primary Objective: Overall Survival
 - Other objectives: PFS, ORR, DOR, QoL, safety
 - Robust statistical assumptions with necessary power (e.g., 90%) and 2-sided alpha of e.g., 5%
 - Includes a futility analysis after ~225 patients
 - Fast Track designation
- focus of discussions with regulators and other stakeholders

Summary

Conclusion:

- Excellent overall survival data in first line treatment of metastatic non-small cell lung cancer (NSCLC) through combination of efti, our proprietary soluble LAG-3 and MHC Class II agonist, with anti-PD-1 therapy
- Strength of efficacy data (OS, ORR, PFS, DOR) across all levels of PD-L1 expression differentiates efti + anti-PD-1 from other chemotherapy-free IO-IO combinations
- Efti's complimentary mechanism-of-action through dendritic cell (APC) activation via MHC Class II agonism appears to greatly increase the # of patients who respond to anti-PD-1, including low & negative PD-L1 patients
- Initial pharmacodynamic data of efti+pembro reveals significant increase in IFN- γ & CXCL10 (Th1 biomarker) \rightarrow proof of principle

Outlook:

- Multiple development options to capture the entire NSCLC market by PD-L1 status through chemo-free IO+IO combinations in TPS $\geq 1\%$ or IO+IO+chemo combination that targets low and negative PD-L1 (TPS $< 50\%$) patients
- Planning around intelligent registrational Phase III trial is in progress and under discussion with regulators. Strength of new data drives multiple options for chemo-free IO-IO combination with efti + anti-PD-1.
- Final trial design and patient population will depend on feedback from agencies and other stakeholders

Strong Balance Sheet & Significant Milestones Ahead

Milestones Achieved in 2023:

- ✓ Strong cash position of A\$110.1m as of 30 September 2023 post A\$80m capital raise in June providing cash runway to early CY2026
- ✓ Initiated AIPAC-003 PII/PIII trial of efti + chemo in MBC
- ✓ Commenced cost-efficient investigator-initiated chemo-free EFTISARC-NEO PII study in soft tissue sarcoma
- ✓ Presented final data from TACTI-002 (Part B) in anti-PD-(L)1 refractory 2L NSCLC
- ✓ Presented final data from TACTI-002 (Part C) in 2L HNSCC
- ✓ Received regulatory approval for initiation of jointly-funded INSIGHT-005 with Merck KGaA, Darmstadt, Germany
- ✓ Compelling Overall Survival data from TACTI-002 PII in 1L NSCLC presented at ESMO Congress 2023

Upcoming Milestones:

- Data update from INSIGHT-003 PI trial (efti + anti-PD-1 + chemotherapy) in 1L NSCLC at ESMO Congress 2023
- Complete enrolment in randomised TACTI-003 Phase IIb trial with top-line results to follow
- Updates from investigator-initiated INSIGHT-005 and EFTISARC-NEO studies
- Updates on AIPAC-003 Phase II/III trial
- TACTI-004 preparations for final trial design and study start
- IND-enabling studies of IMP761
- Start of clinical development of IMP761
- Updates from partnered programs
- Updates regarding expansion of clinical trial pipeline

Thank you!