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LAG-3 IMMUNOTHERAPY

Immutep TACTI-002 and INSIGHT Clinical Results & Update Global Webcast Slides

Immutep will present these slides as part of its global webcast, as follows:

Date & Time7.30 am Australian
Eastern Daylight Time / 5.30 pm US
Eastern Daylight Time

A replay of the webcast will also be available at www.immutep.com

(ASX: IMM, NASDAQ: IMMP)

Notice: Forward Looking Statements

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LAG-3 Overview & Product Candidates

Targeting LAG-3 / MHC II may lead to multiple therapeutics in numerous indications

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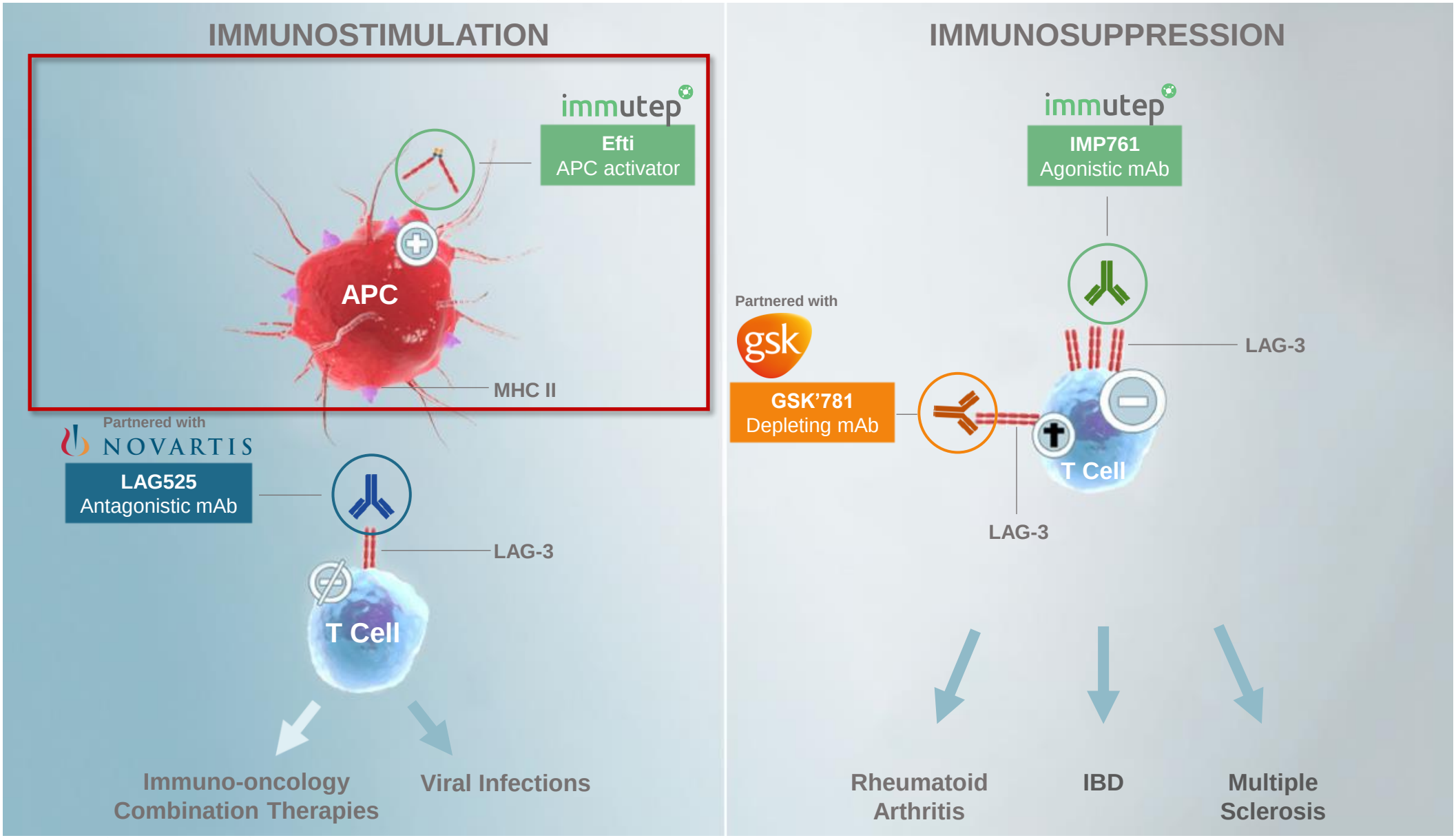
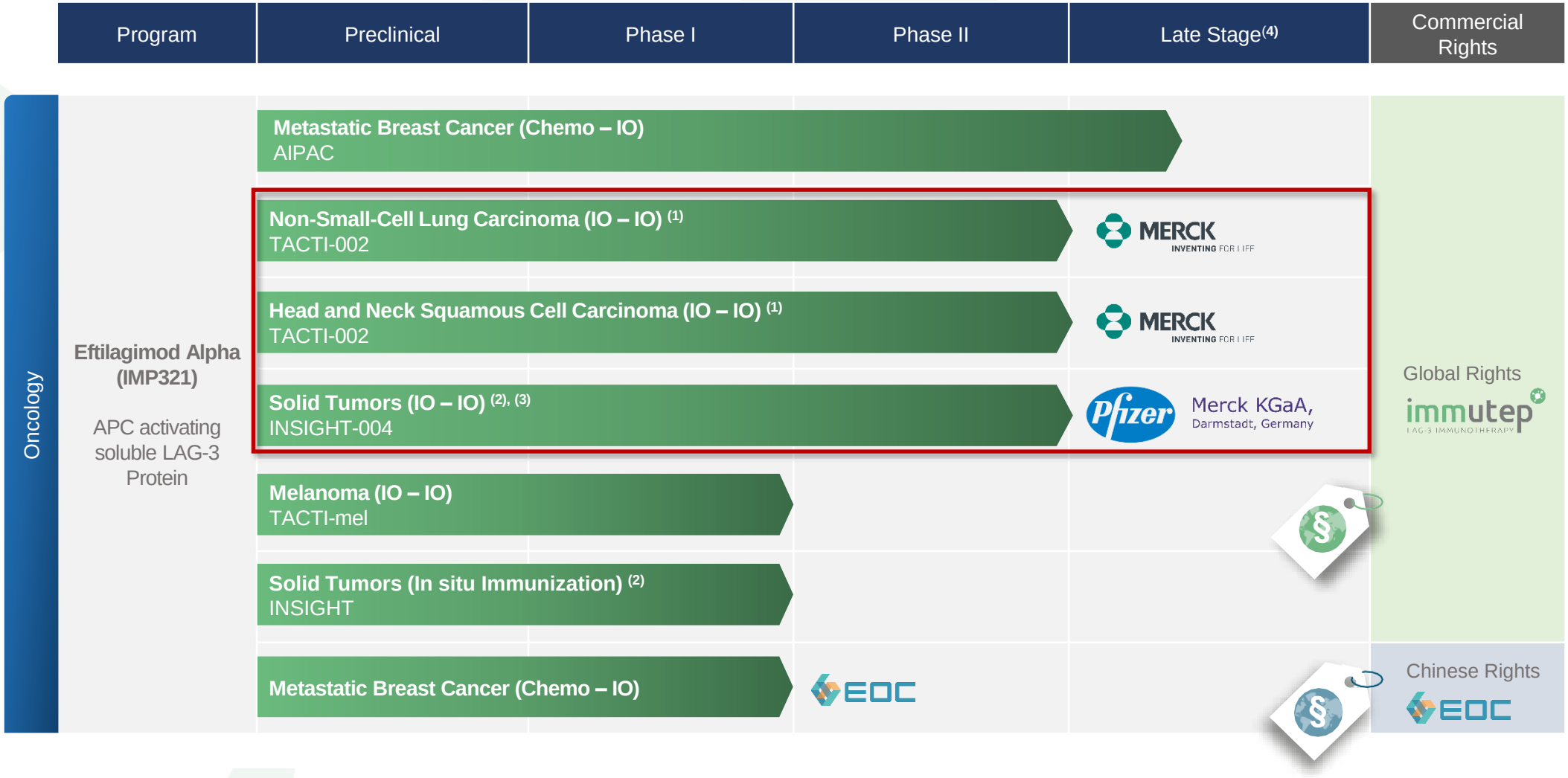


Eftilagimod Alpha (efti or IMP321)

Immutep Controlled Immuno-Oncology Pipeline*



Notes:

* Information in pipeline chart current as at May 2020

(1) In combination with KEYTRUDA® (pembrolizumab) in non-small cell lung carcinoma ("NSCLC") or head and neck carcinoma ("HNSCC")

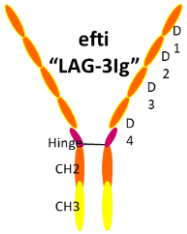
(2) INSIGHT Investigator Initiated Trial ("IIT") is controlled by lead investigator and therefore Immutep has no control over this clinical trial

(3) In combination with BAVENCIO® (avelumab)

(4) Late stage refers to Phase IIb clinical trials or more clinically advanced clinical trials

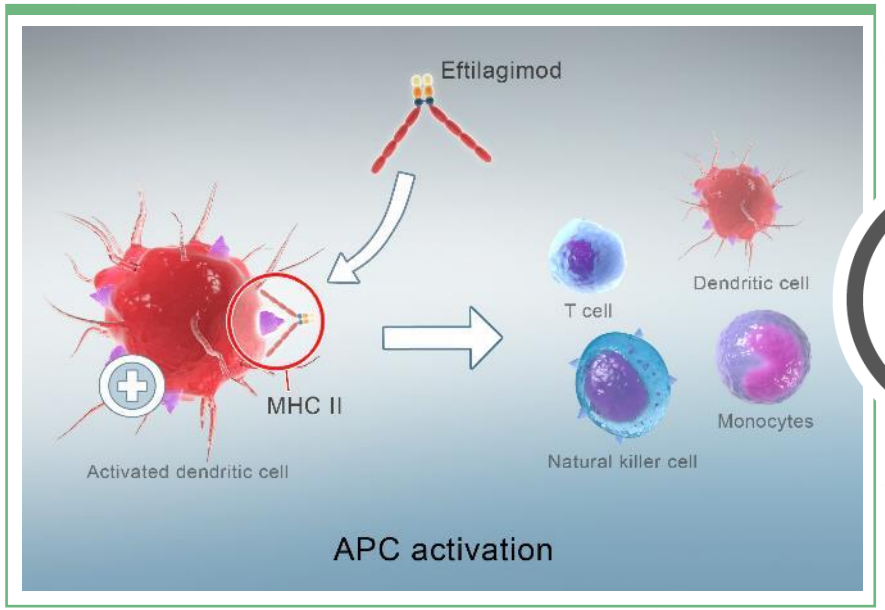
(5) EOC Pharma is the sponsor of the EOC 202 clinical trial which is being conducted in the People's Republic of China

Efti: an innovative LAG-3 I-O product candidate



- Efti is a soluble LAG-3 protein targeting a subset of MHC class II on APC
- Potentially synergistic with other therapeutic agents, e.g. I-O agents or chemotherapies

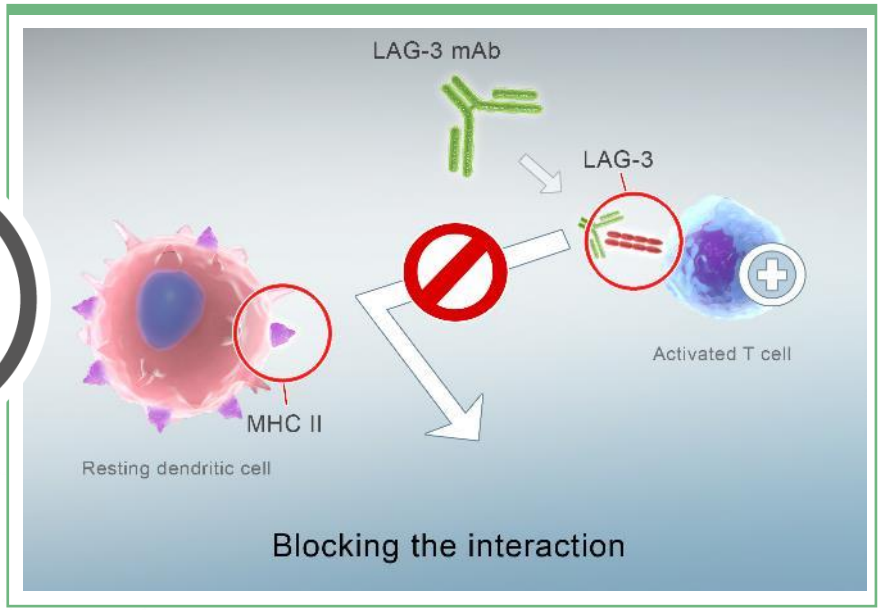
"PUSHING THE ACCELERATOR ON IMMUNE RESPONSES"



Efti is an **MHC II agonist:**
APC activator

- boost and sustain the $CD8^+$ T cell responses
- activate multiple immune cell subsets

"RELEASING THE BRAKE ON THE T CELL"

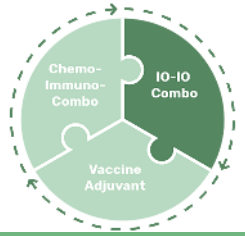


LAG-3 antagonist, or blocking, antibodies:
Immune checkpoint inhibitor

- increase cytotoxicity of the pre-existing CD8 T cell response

Combining efti and anti-PD-L1 avelumab

INSIGHT-004



Efti Clinical Development
INSIGHT-004 (Phase I)

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INSIGHT-004: dose escalation of efti in combination with avelumab

Dose escalation, solid tumors, 2 cohorts of 6 patients each → efti + avelumab (Bavenico®) for 6 months + 6 months avelumab monotherapy → Phase I, monocenter DE, open label, IIT → **RP2D, Safety,** ORR, PFS, PK, PD

Patient Population	Solid tumors after failure of standard therapy
Treatment	6 / 30 mg efti s.c. 800 mg avelumab i.v. Both every 2 weeks

Status Report

- ✓ 1 site in Germany
- ✓ Protocol approved by CA / EC
- ✓ Recruitment completed in April 2020
- ✓ No dose limiting toxicity

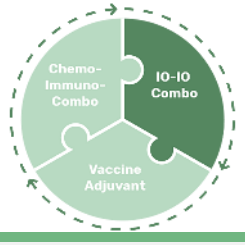
In collaboration with:

Pfizer

Merck KGaA, Darmstadt, Germany I.K.F.

Key features: safety with a PD-L1 antagonist avelumab

Notes:
R2PD – recommended phase 2 dose, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics



Efti Clinical Development
INSIGHT-004 – initial results

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- Patients were/are treated for different tumor indications, but majority for cancers of the gastrointestinal tract.
- In colorectal (CRC)- gastric (GC) and gastroesophageal junction (GEJ) adenocarcinoma usually only a small proportion of patients – around 5%[3] – benefit from immunotherapy. Patients with proficient MMR (pMMR) or with microsatellite stable (MSS) typically do not benefit[1; 2].

Key findings

- No DLTs and no new safety signals with standard dose of avelumab
- 4/12 (33 %) patients with partial responses (3/12 pts not yet staged) in:
  - 1st line MSI high colorectal cancer
  - 1st line pleural mesothelioma
  - After radiochemo in squamous anal cell carcinoma
  - 3rd line gastroesophageal junction

- Efti plus avelumab is safe and well tolerated
- Encouraging single cases in non ICI sensitive cancers

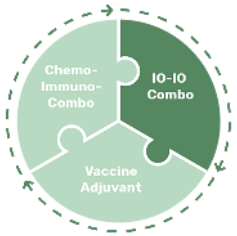
Immunotherapy in gastrointestinal malignancies[1;2;3]

Historical comparisons in metastatic colorectal cancer	ORR in MSS mCRC
anti-PD-1 monotherapy (pembr or nivo or atezo)	~0% - 2%
anti-PD-1 + anti-CTLA-4	~7% – 11%
Radiotherapy + ipi + nivo	~15%
Historical comparisons in gastric and gastroesophageal junction adenocarcinoma	**ORR in unselected GC/GEJ**
anti-PD-1/PD-L1 monotherapy (Pembro or Nivo or Avelumab) in 2nd/3rd line	~5% - 15%

Notes:
(1) N Huyghe et al.: Immunotherapy with immune checkpoint inhibitors in colorectal cancer: what is the future beyond deficient mismatch-repair tumours? Gastroenterology Report, 8(1), 2020, 11–24.
(2) A Zayac, K Almhanna: Esophageal, gastric cancer and immunotherapy: small steps in the right direction? Transl Gastroenterol Hepatol 2020;5:9
(3) J Tintelnot, A Stein: Immunotherapy in colorectal cancer: Available clinical evidence, challenges and novel approaches. World J Gastroenterol 2019 August 7; 25(29): 3920-3928

Combining efti and anti-PD-1 pembrolizumab

TACTI-002



Efti: Clinical Development TACTI-002 (Phase II)

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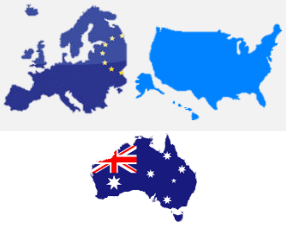
Trial Design + Introduction

- ***Phase II, multi-national, open label, Simon`s 2 stage design; PD-L1 all comer***
- ***In collaboration with Merck Sharp & Dohme (MSD)***



Eligibility

- Available tumor tissue
- ECOG 0-1
- Adequate organ functions
- **PD-L1 all comer**

Part A:
1st line met. NSCLC

Part B:
2nd line met. NSCLC, refractory for PD-1/PD-L1

Part C:
2nd line met. HNSCC after platinum

30 mg efti SC
+
200 mg pembrolizumab IV

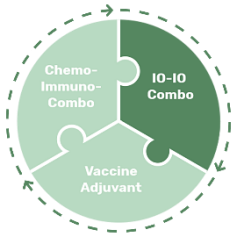
Up to 12 months then pembrolizumab alone for another 12 months

Primary: ORR (iRECIST)

Secondary: PFS, OS, PK, biomarker, PD, safety and tolerability

Study – Part	Stage 1 (N) Actual/target	Stage 2 (N) target
Part A	17/17	17/19
Part B	19/23	13 (not yet opened)
Part C	18/18	6/19

Notes:
NSCLC – non-small-cell lung cancer, HNSCC – head and neck squamous cell cancer, ORR – overall response rate, PFS – progression free survival, OS – overall survival, PK –pharmacokinetics, PD-X – any PD-1 or PD-L1 treatment



Efti: Clinical Development TACTI-002 – Safety

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Efti has a favourable safety profile in combination with pembrolizumab

Summary TACTI-002 (N=76 in total)

- No (0%) treatment related death
- 3 (3.9 %) treatment related adverse events leading to permanent discontinuation
- 31 pts (40.8%) had ≥ 1 adverse events ≥ grade 3
- No new safety signals of this combination identified until cut-off

Regimen[2]	Treatment related adverse events leading to discontinuation	Treatment related adverse events leading to death
Double Chemo	8-22%	1-6%
Ipi + Nivo	20%	< 2%
Chemo + Pembro	23-33%	3-8%
Pembro alone	10-15%	< 2%
Efti plus pembro	4%	0%

Notes:

(1) Preliminary data, cut-off 30-Apr 2020

(2) Source: Calculated from corresponding publications e.g.: Checkmate-227; Keynote-40/189/407/48;

NSCLC - Introduction

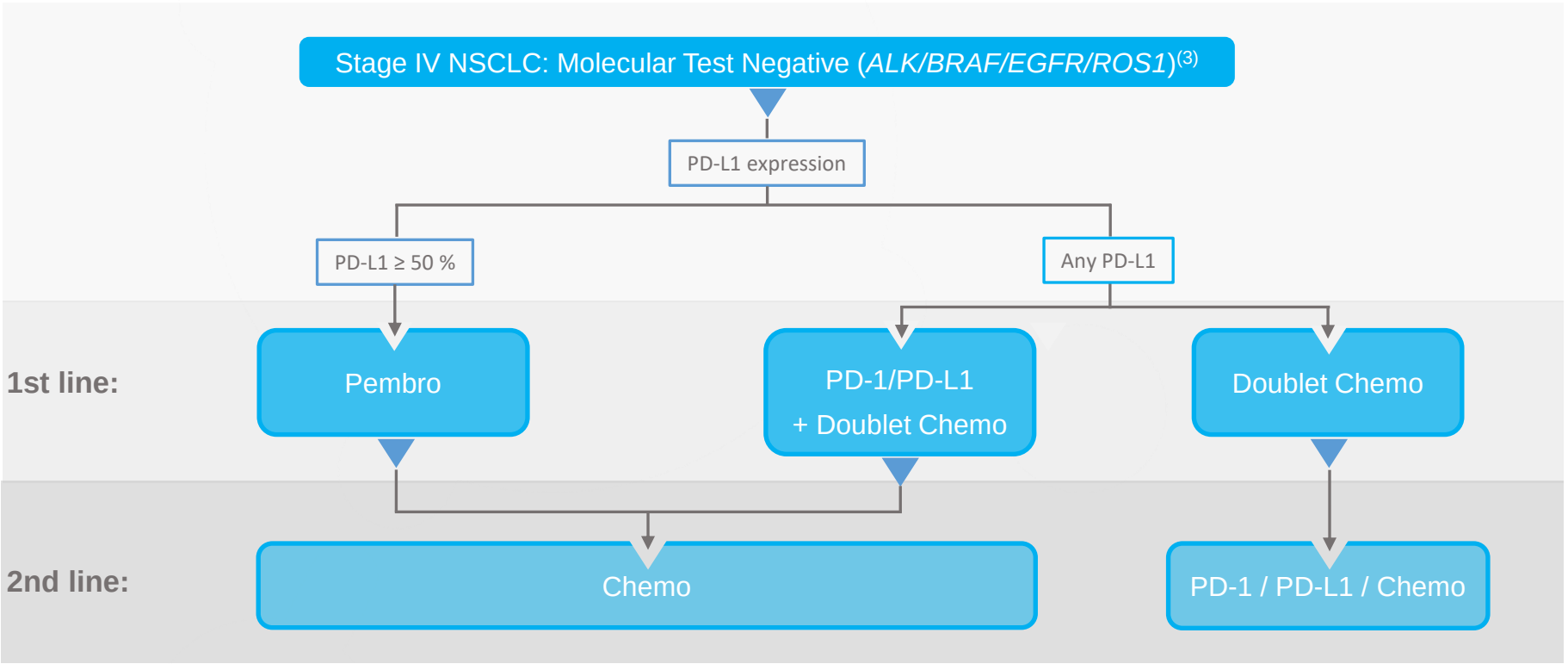
High unmet medical need for well tolerated and efficacious treatment options

Epidemiology[1]:

- 1,800,000 NSCLC diagnoses per annum worldwide growing by 1.5 % p.a.
- Approximately 1,300,000 develop metastatic disease and are eligible to receive anti-PD-1/PD-L1

Unmet need:

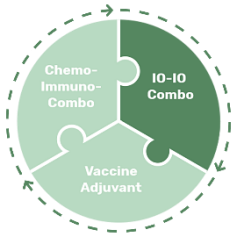
- Modest efficacy of anti PD-1/PD-L1 for pts with <50% PD-L1 **(~70% of total population)**
- Toxicity for patients / costs for health care systems of doublet chemo + PD-1/PD-L1 tremendous



US$33.9 billion

estimated market size by 2026[2]

Notes
(1) Calculated from Global Cancer Observatory (WHO), 2018 data
(2) Informa Pharma Intelligence Report 2018 for US, Japan and EU5
(3) Based on ESMO Guidelines



Efti: Clinical Development
TACTI-002 - 1st line NSCLC (part A, stage 1)

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Baseline Characteristics

- ***PD-L1 distribution as expected (~70% with < 50% PD-L1 expression) → PD-L1 all comer trial***
- ***Patients are typical NSCLC 1st line pts***

Baseline Parameters (n=17)	N (%)
Median age, yrs (range)	65 (53 – 76)
Sex Female Male	 6 (35.3) 11 (64.7)
ECOG 0 1	 12 (70.6) 5 (29.4)
Smoking status Never Current / former	 1 (5.9) 16 (94.1)
Histology Squamous Non-squamous	 10 (58.8) 7 (41.2)
Location of disease at study entry Lung Bone	 8 (47.1) 5 (29.4)

Central assessment of tumor cell PD-L1 expression (done post enrollment)		
PD-L1 (n=13)(2)	N (%)	Historical(3) Distribution
< 1%	3 (23%)	35%
1-49%	6 (46%)	35%
≥ 50%	4 (31%)	30%

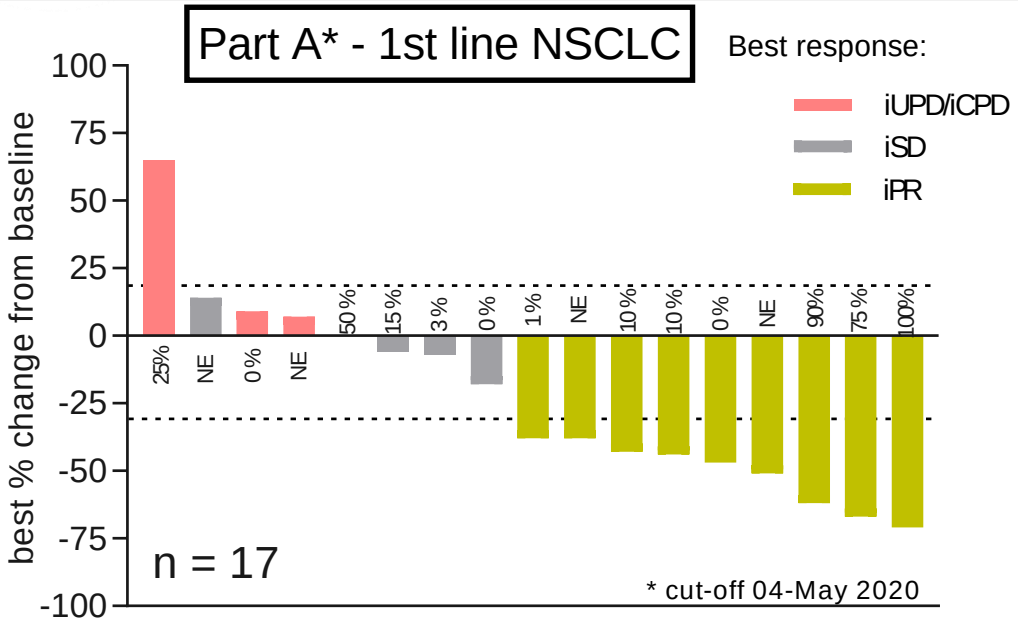
Notes:
(1) Preliminary data, cut-off May 04, 2020
(2) % in reference to evaluable samples; 4 specimens not evaluable by central lab using standard IHC kit
(3) Garon et al N Engl J Med 2015;372:2018-28

Efti: Clinical Development
TACTI-002 - 1st line NSCLC (part A, stage 1)(1)

Responses and Waterfall plot

- ***52.9 % iORR acc. to iRECIST in this PD-L1 all comer trial***
- ***Responses in all PD-L1 subgroups***

Tumor response - iBOR as per iRECIST	N (%) Total (N=17)
Complete Response (iCR)	0 (0.0)
Partial Response (iPR)	9 (52.9)
Stable Disease (iSD)	5 (29.4)
Progressive Disease (iPD)	3 (17.7)
Objective Response Rate (iORR)	**9 (52.9)**
Disease Control Rate (iDCR)	**14 (82.4)**



- Responses in all PD-L1 subgroups
- 6/9 iPR confirmed
- 12/17 (71 %) patients with target lesion decrease
- 5 / 7 iPR with NSQ; 4 / 10 with SQ

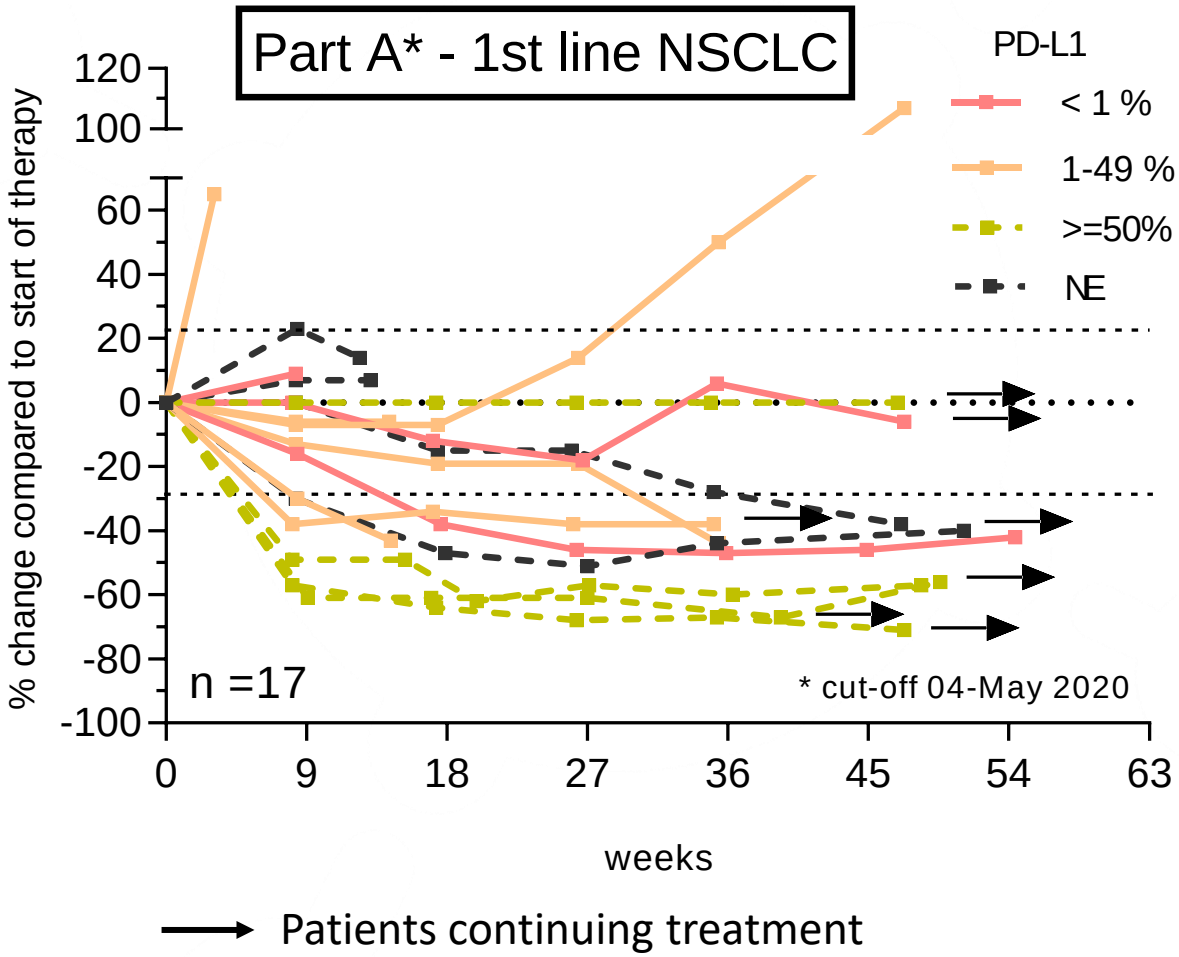
Patients by PD-L1 category	No. of Responses	No of pts
Low (< 1%)	1	3
Medium (1 - 49%)	3	6
High (≥ 50%)	3	4
Not evaluable	2	4
Overall	**9**	17

Notes:
(1) Preliminary data, cut-off 04-May 2020

Efti: Clinical Development
TACTI-002 - 1st line NSCLC (part A, stage 1)(1)

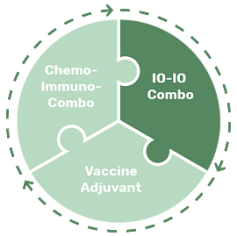
Spider plot

➢ *At data cut-off(1) 7 pts (41 %) still under treatment → estimated median PFS of 9+ months*



- 2 late responders at 8 / 11 months!
- 7 pts still under therapy → estimated median PFS of 9+ months

Notes:
(1) Preliminary data, cut-off 04 May 2020



Positioning of efti in 1st line NSCLC

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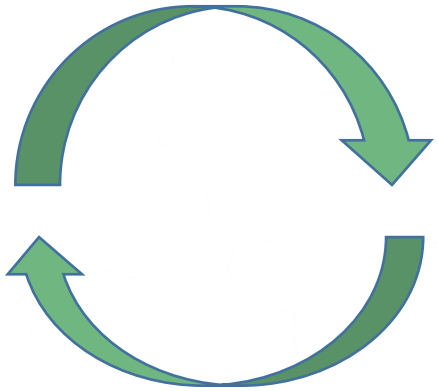
Selected SoCs 1st line NSCLC

Regimen	ORR[1,2]	Median DoR (months)	Median PFS (months)[1,2]	Median OS (months) [1,2]	Main downside/limitations[1,2]
Double Chemo	20-30%	4.9 - 7.7	5 - 6.5	10.7 - 13.9	Toxicity + low efficacy
Ipi + Nivo	33%	23.2 (>1%)	TBD	17.1	Toxicity, costs, low efficacy
Chemo + Pembro	48%	8 - 11.2	8.8	22.0	Costs, shorter DOR compared to IO alone, toxicity, nothing for 2nd line
Pembro alone[3]	~20% (~17% in 1-49%)	20.2 (>1%)	~5-6	~16	low efficacy for < 50 % PD-L1 expression

→ High unmet medical need in 1st line

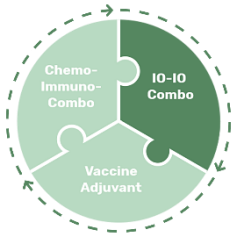
Efti + pembro (stage 1, Part A): 53% iORR PD-L1 all-comer + median PFS expected 9+ mts



✓ Higher ORR/PFS compared to Pembro alone without additional toxicity

Efti could address unmet needs in 1st line NSCLC and be a key differentiator for any anti-PD-1/PD-L1 therapy

(1) Internal evaluation;
(2) ESMO 2019: available from https://www.esmo.org/newsroom/press-office/esmo-congress-immunotherapy-chemotherapy-nsclc-checkmate227-peters
(3) Internal calculation based on published data: Garon et al, N Engl J Med 2015; 372:2018-2028 available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1501824



HNSCC Introduction

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High unmet medical need for well tolerated and efficacious treatment options

Epidemiology:

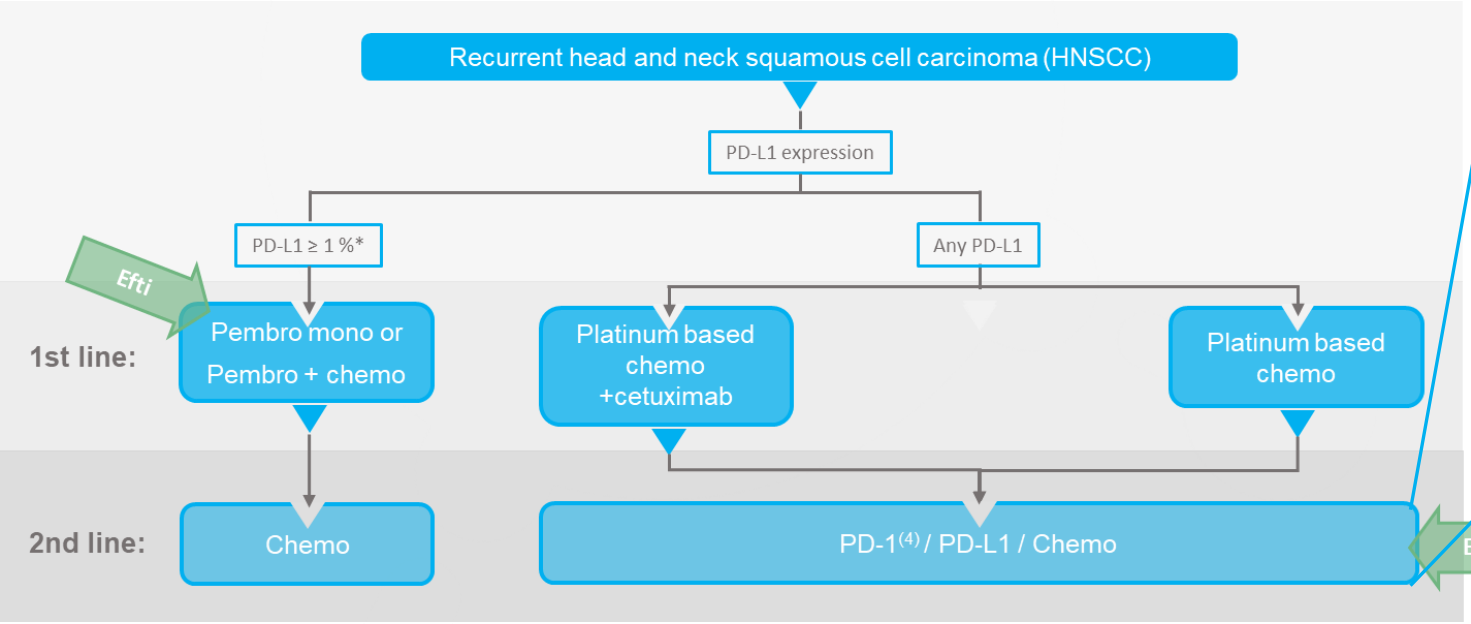
- More than 585,000 HNSCC diagnoses per annum worldwide(1)
- Approximately 350,000 develop metastatic disease and are eligible to receive anti-PD-1 monotherapy or in combination with chemotherapy

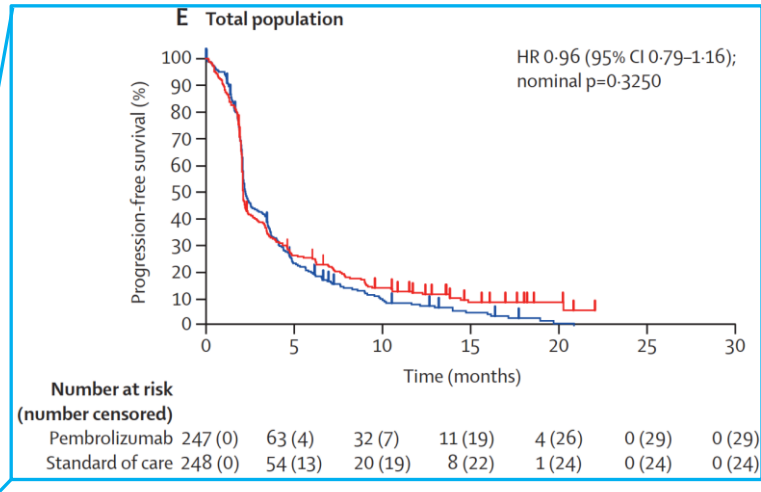
Unmet need:

- ORR of 10-18 % and median PFS in 2nd line regardless of therapy ~ 2 months

US$ 2.8 billion

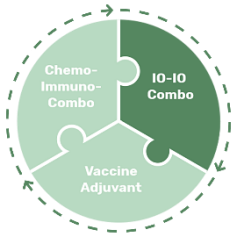
Estimated market size by 2026(3)





* - approval for Pebmro plus chemo in 1st line regardless of PD-L1 expression by FDA

(1) F Bray et al.: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA CANCER J CLIN 2018;68:394–424
(2) Athanassios Argiris et al.: Evidence-Based Treatment Options in Recurrent and/or Metastatic Squamous Cell Carcinoma of the Head and Neck. Front. Oncol., 09 May 2017 | https://doi.org/10.3389/fonc.2017.00072
(3) Estimation of Datamonitor Healthcare, Informa Pharma Intelligence for US, JP, EU (5): Head and neck cancer Forecast, December 2017 available from https://pharmastore.informa.com/product/head-and-neck-cancer/
(4) FDA and EMA approval differences. Pembrolizumab approval by the European Medicines Agency is for patients whose tumours express PD-L1 with a ≥ 50% TPS, which differs from FDA approval.
(5) Kaplan-Meyer curve was sourced from EEW Cohen et al. KEYNOTE-040, The Lancet 2018, http://dx.doi.org/10.1016/S0140-6736(18)31999-8



Efti: Clinical Development
TACTI-002 – 2nd line HNSCC (part C, stage 1)(1)

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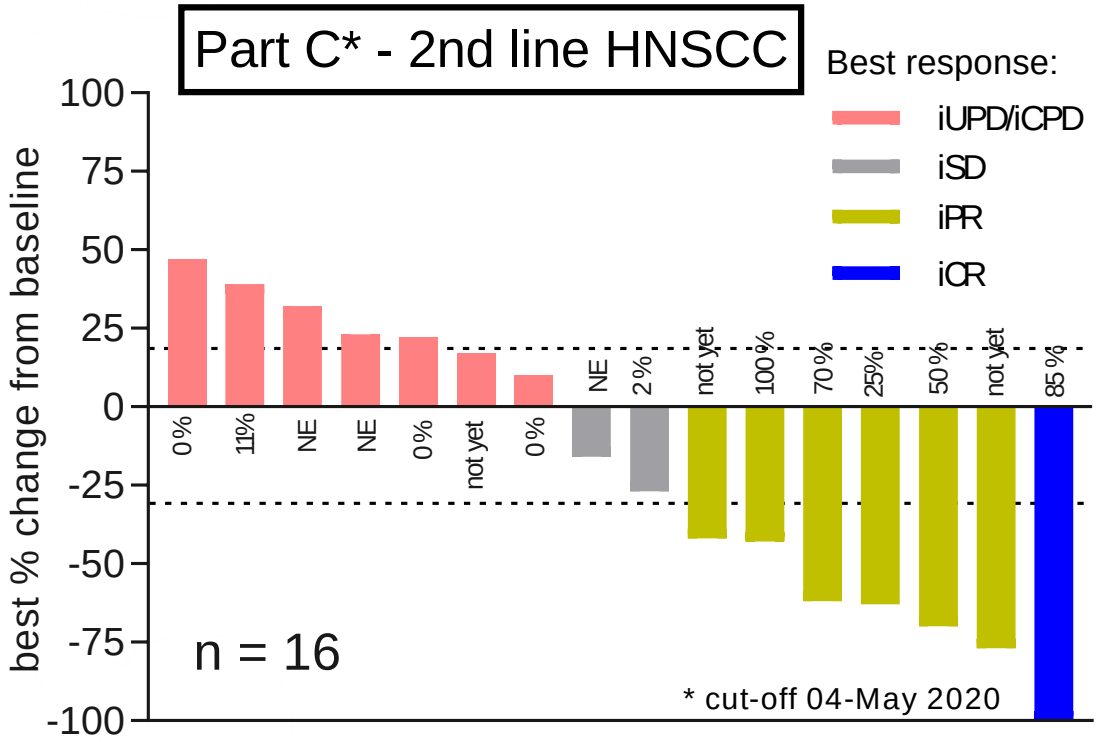
Responses and Waterfall plot

➢ ***Initial iORR of 38.9 % in this PD-L1 all comer HNSCC 2nd line patients***

- Median Age of 66, mostly male (94 %)
- ECOG 1 in 47 %
- All pre-treated with platinum-based therapy
- Different subtypes

Tumor response - iBOR as per iRECIST	N (%) Total (N=18)
Complete Response (iCR)	1 (5.6)
Partial Response (iPR)	6 (33.3)
Stable Disease (iSD)	2 (11.1)
Progressive Disease (iPD)	7 (38.9)
Not evaluable*	2 (11.1)
Objective Response Rate (iORR)	**7 (38.9)**
Disease Control Rate (iDCR)	**9 (50.0)**

* - dropped out prior to first restaging



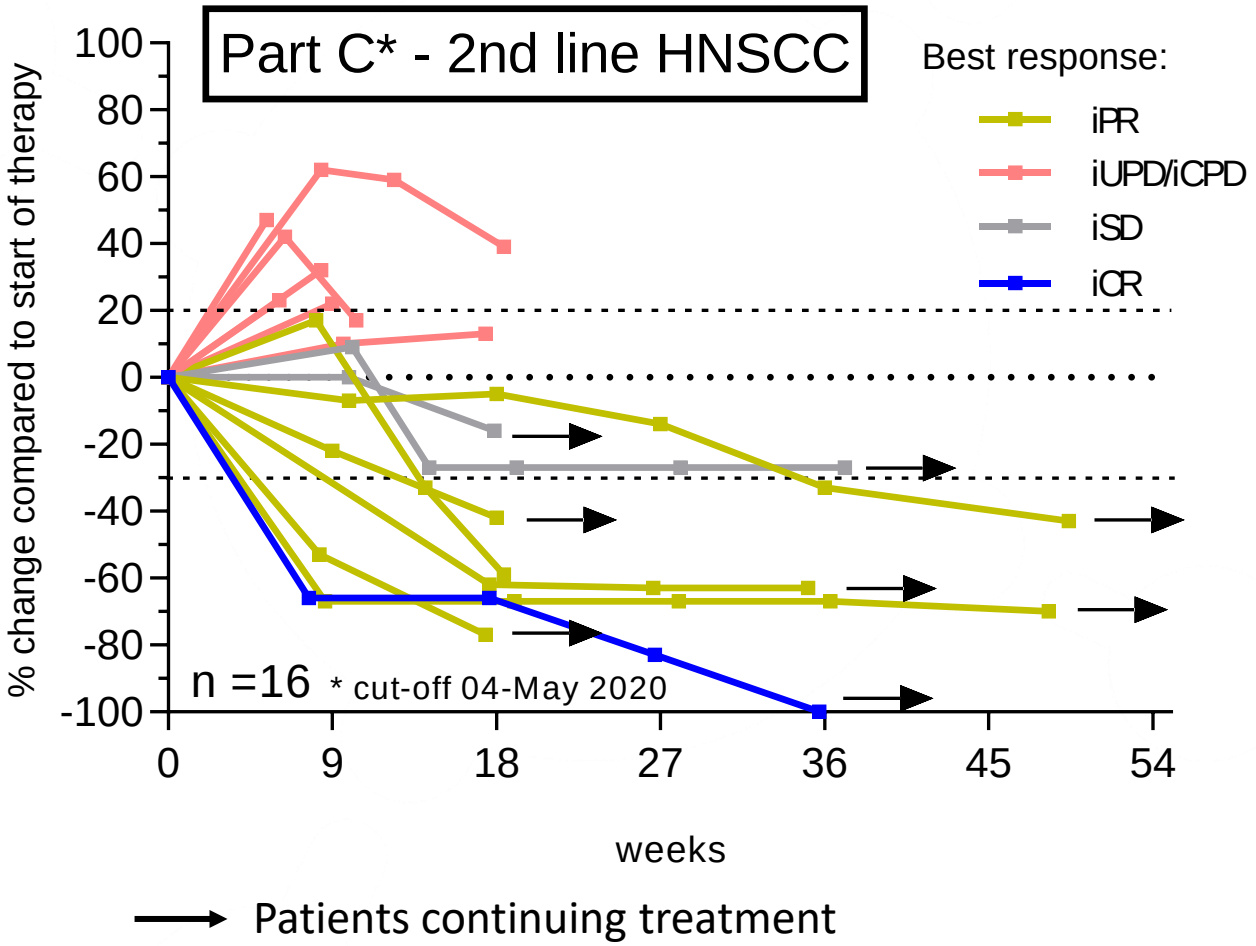
- 5/7 responses confirmed already
- 1 iCR

Note:
(1) Preliminary data, cut-off 04 May 2020

Efti: Clinical Development
TACTI-002 – 2nd line HNSCC (part C, stage 1)

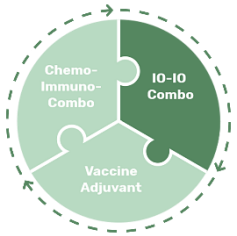
Spider plot

➢ *At cut-off 8 pts (44 %) still under therapy - HNSCC 2nd line patients*



- 1 iPR after pseudoprogression
- 1 iCR
- Responses getting deeper over time

Note:
(1) Preliminary data, cut-off 04 May 2020



Positioning of efti on 2nd line HNSCC

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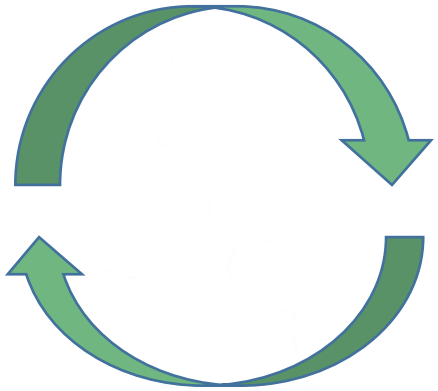
Current SoC 2nd line HNSCC

Regimen	ORR[1;3]	Median DoR (months)	Median PFS (months)[1, 3]	PFS rate at 3 / 6 months[2]	Median OS (months)[1]	Main downside/limitations[1,2,3]
Chemo	10.1%	5.0	2.3	45% / 20%	6.9	Not effective in >> 50% of patients
Pembro	14.6%	18.4	2.1	40% / 25%	8.4	Not effective in >> 50% of patients
Pembro ≥ 1% CPS	17.3%	18.4 (vs 9.6)	2.3	45% / 30%	8.7	Not effective in >> 50% of patients
Nivo	13.3%	9.7	2.0	37% / 21%	7.7	Not effective in >> 50% of patients

→ High unmet medical need in 2nd line HNSCC

Efti + pembro (stage 1, Part C): 39% iORR in PD-L1 all-comer incl. 1 iCR (6 %); 50 % DCR



✓ Higher ORR compared to Pembro alone without additional toxicity

Efti could adress unmet medical needs in 2nd line HNSCC offering a potential pathway to early regulatory interactions (registration)

(1) Keynote-040 results: available from https://www.esmo.org/newsroom/press-office/KEYNOTE-040-Evaluates-Pembrolizumab-in-Head-and-Neck-Cancer
(2) Internal calculations based on the published results of the Keynote-040 clinical trial (internal calculation done in 2019)
(3) RL Ferris et al.: Nivolumab for Recurrent Squamous-Cell Carcinoma of the Head and Neck. N Engl J Med 2016;375:1856-67.

Case Study:
Pembro FDA approval in 2nd line HNSCC in 2016

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Accelerated approval based on non-randomized phase II trials with ORR as primary endpoint

Based on: **KEYNOTE-012:**

- non-randomized, open-label, multi-cohort phase 1b study
- Primary EP:
  - ORR: 16% (95% CI: 11, 22), according to RECIST 1.1 assessed by BICR. (N=174)
  - Median PFS: 2.1 months
  - DoR*: median DoR not reached (range from 2.4+ to 27.7+ months), with 23 patients > 6 months

Supported by **KEYNOTE-055 (N=171)** interim data:

- open-label, non-randomized, Phase 2 (50 patients with >6 months of follow-up)
  - ORR: 18% acc. to RECIST 1.1
  - DoR*: estimated median of 6.9 months (range 3.0–8.31 months)

FDA condition: **KEYNOTE-040** required → failed to show significant improvement in median OS but label was not changed

* - The difference in the estimated median DoR between KEYNOTE-055 and KEYNOTE-012 may be attributable to the difference in duration of follow-up between the trials, with a maximum follow-up duration of 8.3 months for KEYNOTE-055 versus 30 months in KEYNOTE-012

Based on: E Larkins et al.: FDA Approval Summary: Pembrolizumab for the Treatment of Recurrent or Metastatic Head and Neck Squamous Cell Carcinoma with Disease Progression on or After Platinum-Containing Chemotherapy. The Oncologist 2017, 22:873-878.
Approval of the European Medicines Agency was based on Phase III KEYNOTE-40 trial

Summary and Outlook

Summary
Experience efti plus anti-PD-1/PD-L1

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✓ In total experience with 2 drugs (pembrolizumab, avelumab) in 4 different trials (6+ different indications) in up to ∑ 145 pts

Trial / Indication	TACTI-002			TACTI-mel metastatic melanoma	INSIGHT-004 Advanced solid tumors
	Part A 1st line NSCLC	Part B 2nd line NSCLC	Part C 2nd line HNSCC		
Details Indication	PD-L1 all comer; PD-X naive; SQ+NSQ	PD-L1 all comer; PD-X refractory	PD-L1 all comer; PD-X naive	PD-L1 all comer; partly with suboptimal response to pembro alone	PD-L1 all comer
No of pts	N=36 (Stage 1: 17/17; Stage 2: 17/19)	N=36 (Stage 1: 19/23; Stage 2: 0/13; not yet opened)	N=37 (Stage 1: 18/18; Stage 2: 6/19)	N=24 (Part A: 18; Part B: 6)	N=12
Highlights(1)	PD-L1 all comer; 53% iORR; median PFS 9+ months; responses, excellent safety	Not yet	PD-L1 all comer; 39% iORR incl. 5% iCR	1 CR after PD on pembrolizumab 58% ORR*; 58% progression free at 6 months	4 PRs in partly ICI insensitive indications
Historical comparison(2)	Pembro mono: ~20% ORR; 5-6 months median PFS	./.	Pembro mono: 15-18% ORR in > 1 % PD-L1	21-33% ORR; 34-46% progression free at 6 months	./.

Notes:

(1) Preliminary data, cut-off May 2020 (TACTI-002); October 2019 (TACTI-mel); Presented at ASCO 2020 Virtual in May 2020 (INSIGHT);

(2) Keynote-040 results: available from https://www.esmo.org/newsroom/press-office/KEYNOTE-040-Evaluates-Pembrolizumab-in-Head-and-Neck-Cancer and Internal calculation based on published data: Garon et al, N Engl J Med 2015; 372:2018-2028 available from: https://www.nejm.org/doi/full/10.1056/NEJMoa1501824 and other corresponding clinical trials.

*C1D1 exploratory analysis

What could be next?

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Landscape

eftilagimod alpha (MHC class II agonist)

- ✓ Results from TACTI-002 (in 2 indications) are very encouraging compared to what has been published so far
- ✓ Immutep with its two different IO product candidates (one outlicensed to Novartis) is well positioned to potentially become "the next big thing" in oncology

Other agonists

TLR agonists: Limited mostly to i.t. administration, some encouraging results in combination with anti-PD-1

CD40 agonists: Early results in combination with anti-PD-1 look encouraging → PII ongoing (Apexigen Inc)

ICOS agonists: 26 % ORR in ≥2nd line HNSCC with pembro in phase I → ongoing phase II/III by GSK

Other antagonists

LAG-3 antagonists: BMS, Novartis and others have different large programs

TIGIT antagonists: Interesting data of tigarolumab (plus Atezolizumab) in 1st line NSCLC in phase II → ORR of 31 % in PD-L1 all comer → ongoing phase III by Roche

Notes:
Current as of May 2020 based on clinicaltrials.gov
GSK ICOS results: https://www.gsk.com/en-gb/media/press-releases/gsk-presents-new-data-showing-promising-anti-tumour-activity-with-gsk3359609-an-icos-receptor-agonist-in-combination-with-pembrolizumab-in-head-and-neck-squamous-cell-carcinoma-hnscc/
Roche TIGIT results: https://www.roche.com/media/releases/med-cor-2020-05-14.htm

2020 & 2021 Outlook* and News Flow

Upcoming in 2020:

- **NSCLC 1st line** - more data from Stages 1 and 2 from TACTI-002 throughout 2020
- **HNSCC 2nd line** - initial data from Stages 1 and 2 from TACTI-002 throughout 2020
- **NSCLC 2nd line** - initial data from Stage 1 from TACTI-002 throughout 2020
- **MBC** - Overall Survival data from AIPAC: End of 2020
- **Combination with avelumab** - initial data from Phase I trial throughout 2020
- Regulatory progress
- Progress from partnered programs

Expected in 2021:

- Final data from **TACTI-002** part A and C
- Final data from **INSIGHT-004**
- Ongoing regulatory engagement
- Updates from IMP761
- Progress from partnered programs

*The actual timing of future data readouts may differ from expected timing shown above. These dates are provided on a calendar year basis.

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Thank you!