ESMO IO Congress 2017, Geneva

Roche Analyst Call

Thursday, 7 December 2017

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Introduction

Karl Mahler
Head of Investor Relations

Agenda

Welcome
Karl Mahler, Head of Investor Relations

IMpower150: Phase 3 results of carboplatin + paclitaxel +/- Avastin, with or without Tecentriq in 1L non-squamous metastatic NSCLC
Alan Sandler, M.D., Global Development Team Leader Tecentriq Lung

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Tecentriq program overview: Focusing on novel combination approaches
Sushil Patel, Ph.D., Global Product Strategy Tecentriq, Lifecycle Leader

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Q&A
Karl Mahler, Head of Investor Relations

Emerging insights from IMpower150

IMpower150 Phase 3

- ✔ First Ph3 using CIT chemo combo ± Avastin to show statistically significant and clinically meaningful PFS benefit in 1L non-sq NSCLC
- ✔ Tecentriq + Avastin + chemo combo shows benefit in all patients, regardless of :
  - PD-L1 expression / Teff signature
  - EGFR or ALK genetic alterations
  - Liver metastases
- ✔ Tecentriq + Avastin + chemo combo well tolerated, consistent with known safety risks

Open questions for the industry

Translatability of data from small studies to outcomes of definitive Ph3 studies

Efficacy of CIT agents across histologies (non-sq, sq, SCLC)

Efficacy of CIT agents dependent on chemo backbones

Tecentriq + Avastin + chemo combo has the potential to set a new standard of care

NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; non-sq=non-squamous; sq=squamous; PFS=progression-free survival; OS=overall survival

IMpower150: Phase 3 results of carboplatin + paclitaxel +/- Avastin, with or without Tecentriq in 1L non-squamous metastatic NSCLC

Alan Sandler, M.D.
Global Development Team Leader Tecentriq Lung

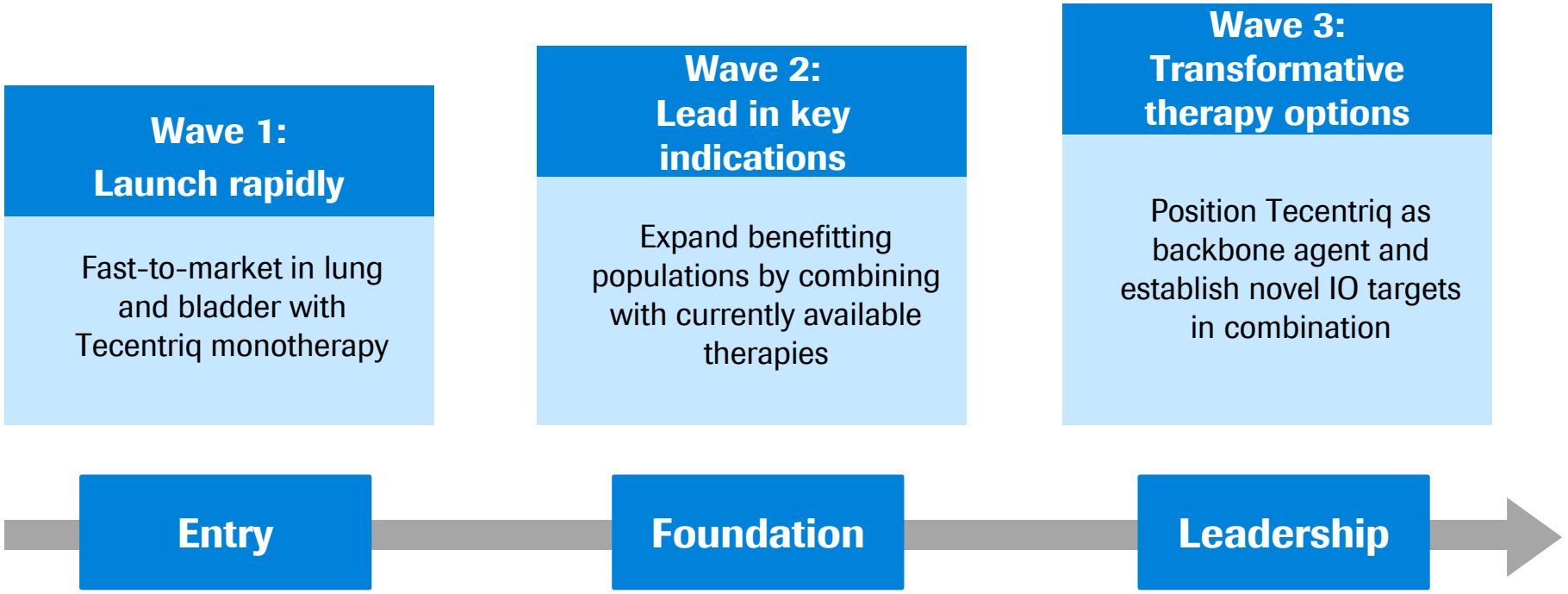
See Dr. Martin Reck presentation, ESMO IO 2017

Tecentriq program overview: Focusing on novel combination approaches

Sushil Patel
Global Product Strategy Tecentriq, Lifecycle Leader

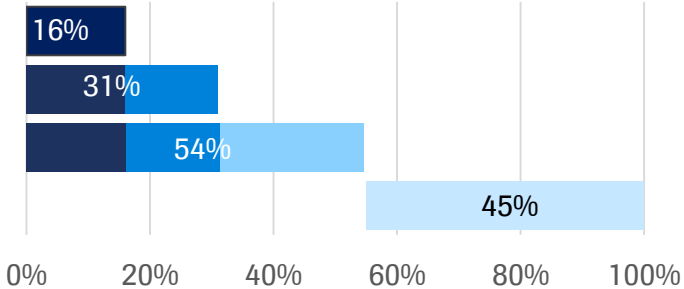
Tecentriq: Vision & strategy

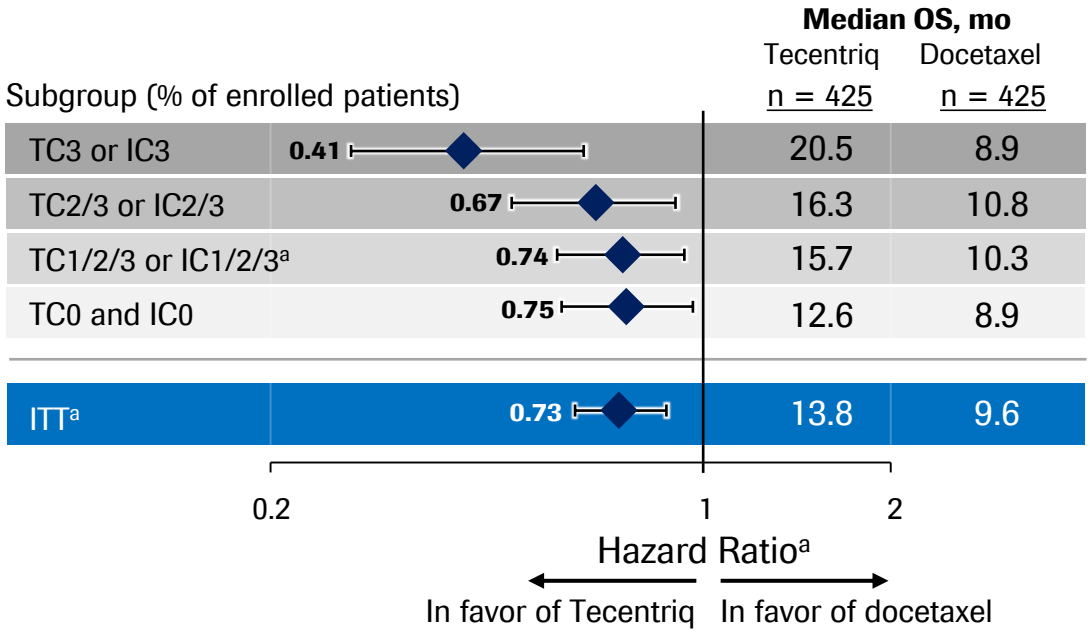
Shaping the treatment landscape long term



Wave 1: Ph3 OAK study shows OS benefit of Tecentriq monotherapy in all 2L+ NSCLC patients[1]

On-study prevalence: OS by PD-L1 expression





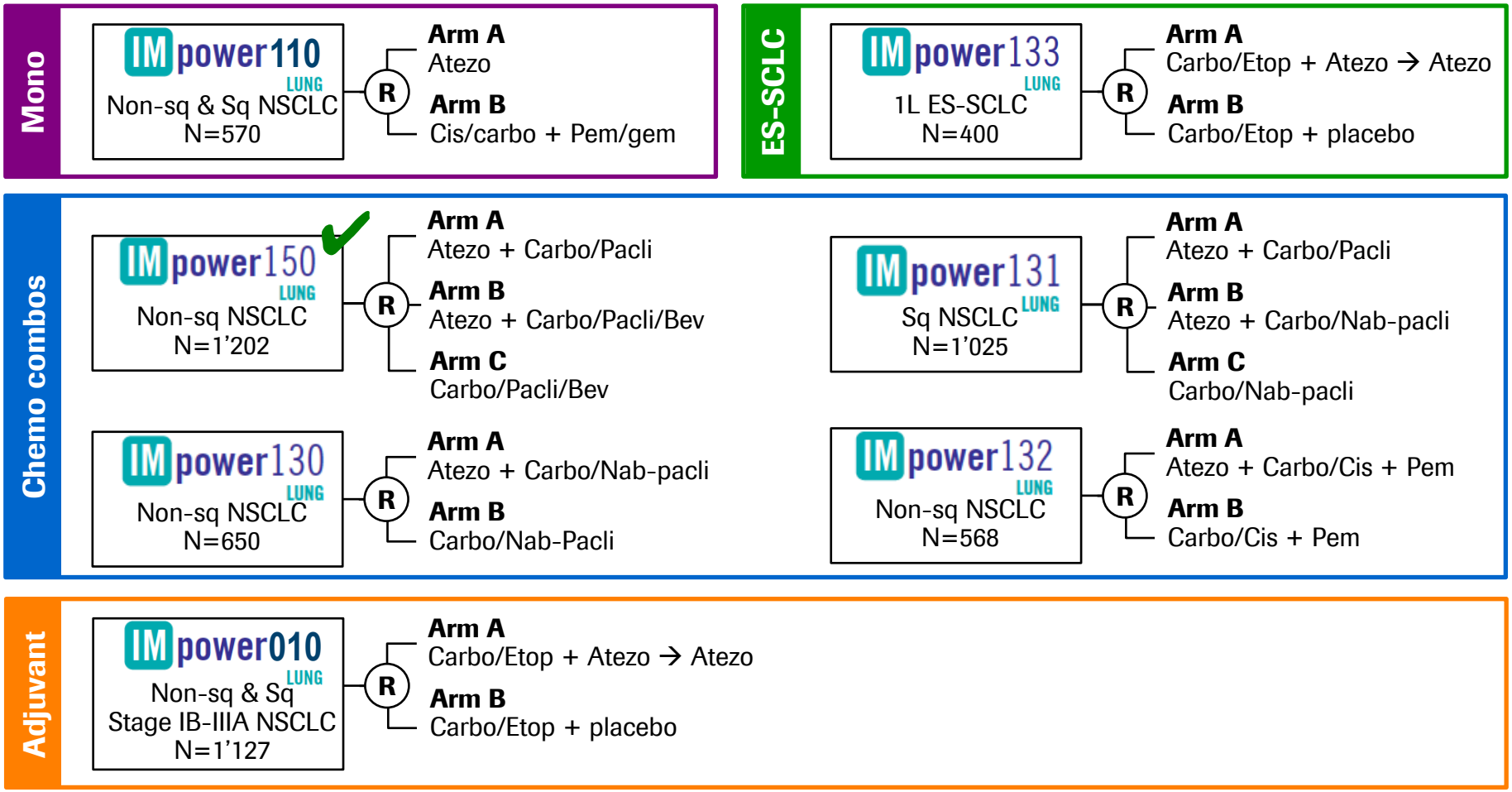
Ph3 OAK data:

- Approved for all-comers
- First CIT agent to be efficacious irrespective of PD-L1 status, including low/no PD-L1 expression
- Efficacy in important sub-groups, such as never smokers and patients with brain metastases
- Active in squamous and non-squamous histologies

[1]Barlesi et al., ESMO 2016
[a]Stratified HR for ITT and TC1/2/3 or IC1/2/3. Unstratified HR for subgroups.

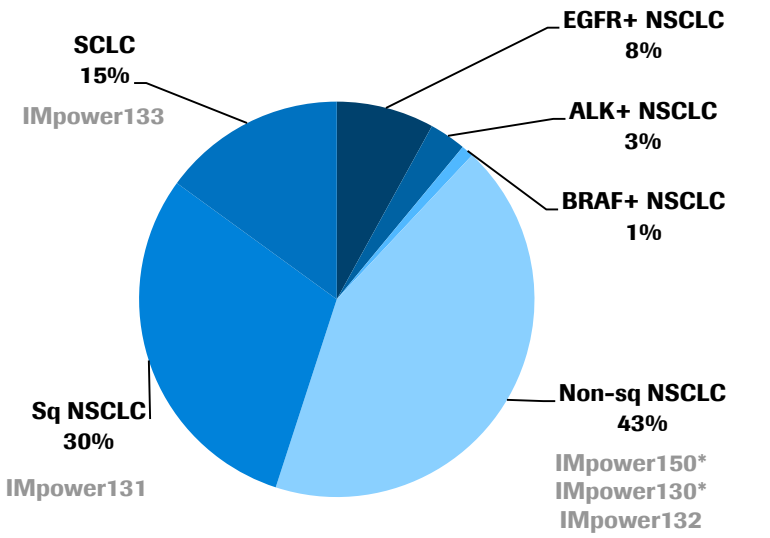
Tecentriq Ph3 program in 1L & early lung cancer

Wave 2 combo studies to read out

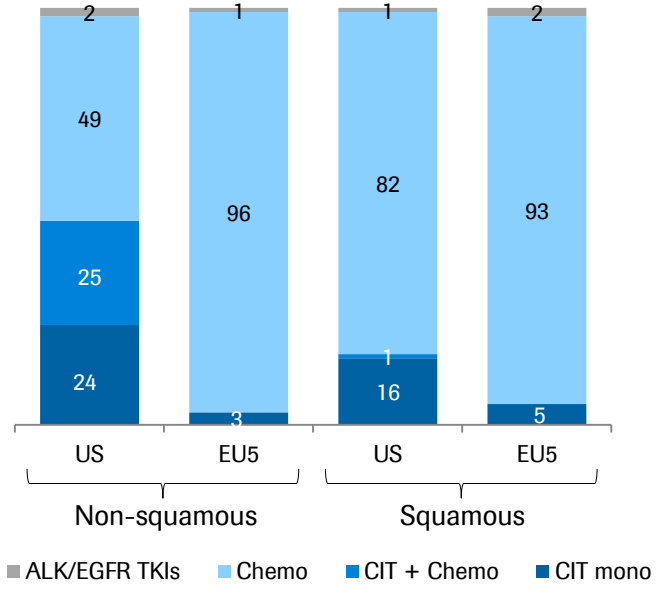


1L NSCLC: Not one disease

Histology-based subtypes



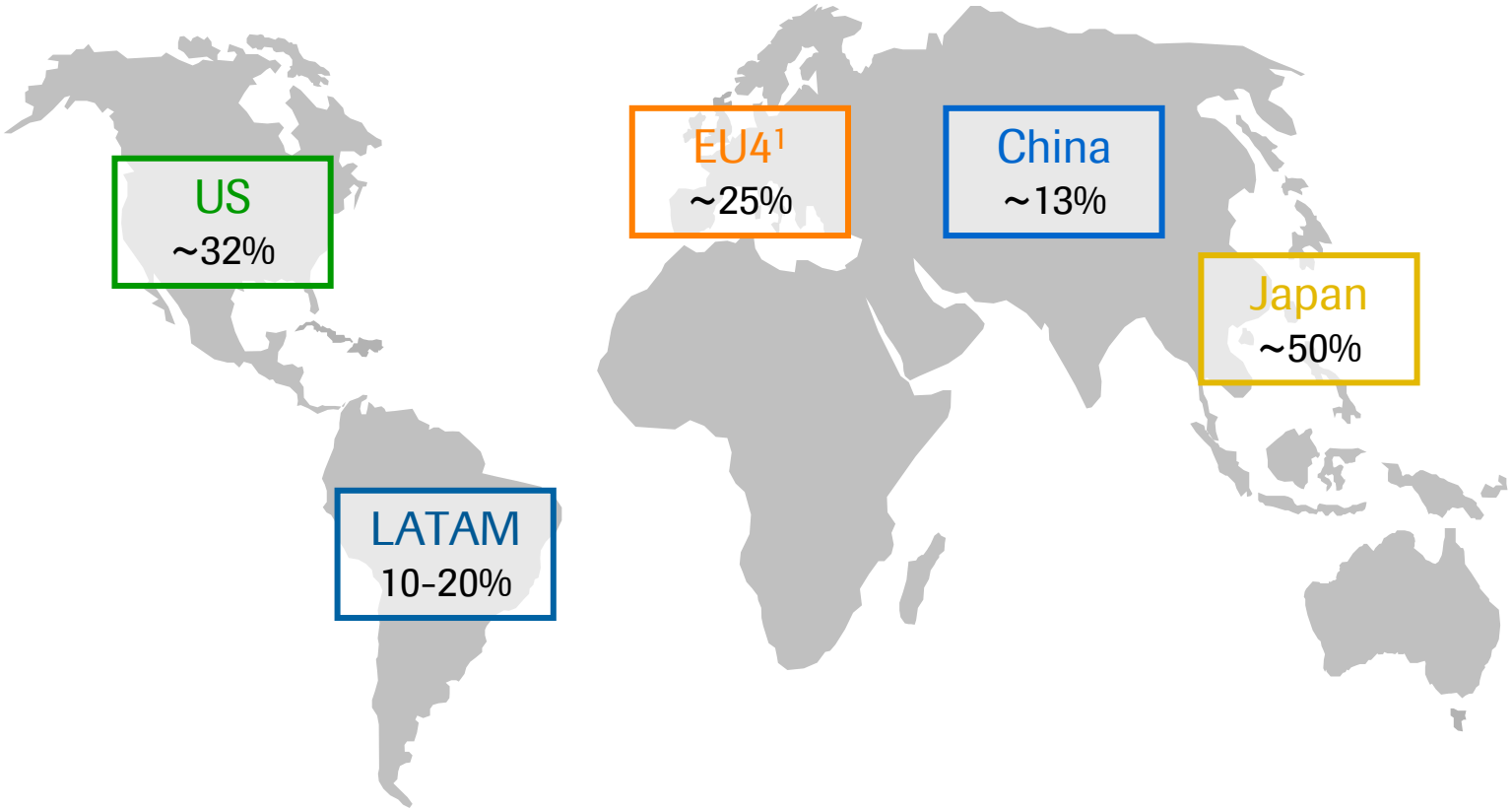
Current market share of treatment options**



Tecentriq's Ph3 program in 1L lung cancer addresses all market segments and chemo backbones

*Primary analysis population excludes patients with tumors harboring actionable mutations, EGFR and ALK, (=ITT-WT). Secondary endpoints include PFS and OS in ITT, regardless EGFR/ALK status. **1L EGFR mut- / Alk mut- NSCLC (all PD-L1 expressions) by histology.
NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous; TKI=tyrosine kinase inhibitor; CIT=cancer immunotherapies

Avastin: A standard of care in non-sq 1L NSCLC



Global Avastin shares remain significant, including key markets like US and Germany

EGFR-/ALK- platinum treated 1L NSCLC; [1]Avastin not reimbursed in UK
NSCLC=non-small cell lung cancer; Non-sq=non-squamous

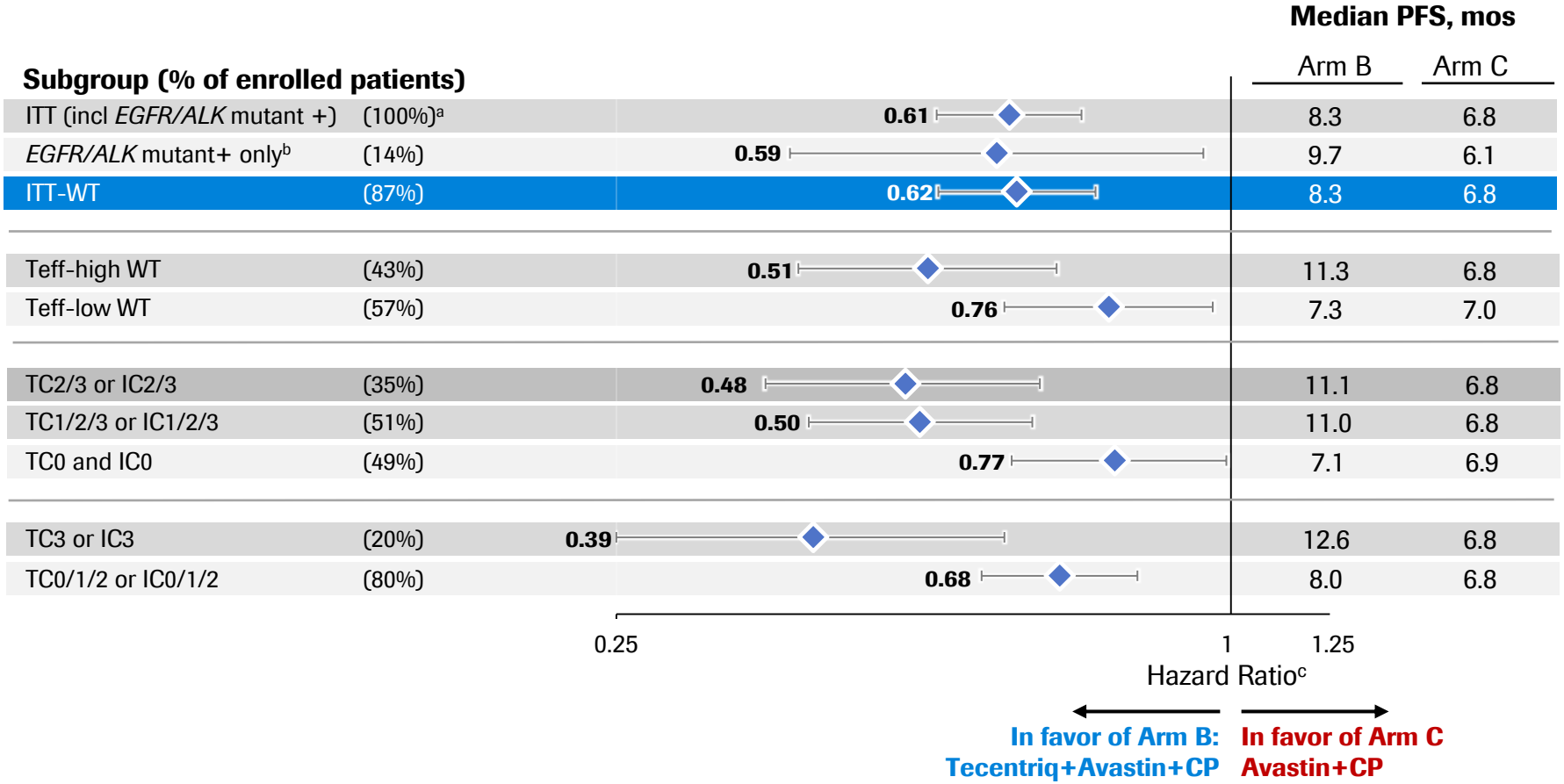
IMpower150: PFS statistically significant & clinically meaningfull in both ITT-WT and Teff-WT

	E4599[1]	IMpower150[2]	
Regimen	Avastin+CP vs. CP	Arm B vs C (Tecentriq+Avastin+CP vs. Avastin+CP)	
Population	1L AC	1L ITT-WT	1L T_{eff}-high WT
Phase	Phase 3 N=878	Phase 3 N=692	Phase 3 N=284
ORR	35% vs. 15%	64% vs 48%	69% vs 54%
mOS (mos)	12.3 vs. 10.3 HR 0.79, p=0.003	19.2 vs 14.4 HR 0.775*, p=0.0262	--
mPFS (mos)	6.2 vs. 4.5 HR 0.66, p<0.001	8.3 vs 6.8 HR 0.617, p<0.0001	11.3 vs 6.8 HR 0.505, p<0.0001
Landmark PFS @ 1yr	18% vs 8.5%**	37% vs 18%	46% vs 18%

Tecentriq adds additional benefit to Avastin + chemo backbone, preliminary OS shows numerical improvement

[1]Sandler A, et al., NEJM 2006, 355(24):2542-50; [2]Reck M, et al. ESMO IO 2017
*OS data are preliminary. Mature OS expected in H1 2018. **taken from KM curve
IMpower150: Investigator-assessed, data cutoff: September 15, 2017; CP=carboplatin and paclitaxel

IMpower150: PFS benefit in ITT and subgroups



Tecentriq + Avastin + chemo combo adds benefit in all pre-defined biomarker subgroups

M. Reck et al., ESMO 2017

IC=tumour-infiltrating immune cells; TC=tumour cells; Teff=T-effector (as defined by expression of *PD-L1, CXCL9* and *IFNγ*); CP=carboplatin and paclitaxel

[a]ITT, *EGFR/ALK* mutants, and ITT-WT % prevalence out of ITT (N=800); Teff % prevalence out of those tested in ITT-WT (N=658); PD-L1 IHC % prevalence out of ITT-WT (N=692). [b]Patients with a sensitising *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [c]Stratified HRs for ITT, ITT-WT and Teff-high WT populations; unstratified HRs for all other subgroups. Data cutoff: September 15, 2017

IMpower150: Some preliminary assessments on Arm A vs C

	ITT-WT
Regimen	Arm A vs C (Tecentriq+CP vs. Avastin+CP)
PFS HR[a]	0.936
ORR,[b] %	49% vs 48%
OS HR[a]	0.884

- Neither PFS nor OS formally tested (only when B vs C shows significant OS improvement in ITT-WT)
- Tecentriq in combination with chemotherapy well tolerated and consistent with known risks
- Preliminary data suggest that Tecentriq plus chemo look at least as good as the control (E4599); while PFS benefit of Tecentriq over the control (Avastin) is unlikely to change in IMpower150, preliminary OS data indicate the possibility of OS benefit in final data read out
- Formal assessment only in 1H 2018 post final look

M. Reck et al., ESMO 2017
[a]Stratified HR; N=348 (Arm A) and N=336 (ArmB); [b]N=347 (Arm A) and N=331 (Arm C).
Data cutoff: September 15, 2017

Tecentriq key read outs through 2019

Potentially first-to-market in 1L SCLC and sq NSCLC

	2017	2018	2019
NSCLC	**IMpower150** ✔ 1L Non-sq NSCLC PFS	**IMpower150** 1L Non-sq NSCLC OS	**KEYNOTE-189** 1L Non-sq NSCLC PFS/OS	**CheckMate 568** 1L NSCLC OS
	MYSTIC ✖ 1L NSCLC Dx+ PFS	**IMpower130** 1L Non-sq NSCLC PFS/OS	**KEYNOTE-407** 1L Sq NSCLC PFS	**CheckMate 9LA** 1L NSCLC OS
	CheckMate 227 1L NSCLC PFS	**IMpower131** 1L Sq NSCLC PFS/OS	**KEYNOTE-042** 1L NSCLC Dx+ OS	**POSEIDON** 1L NSCLC PFS
	PACIFIC ✔ STAGE III UNRES NSCLC	**IMpower132** 1L Non-sq NSCLC PFS/OS	**CheckMate 227** 1L NSCLC OS	
			MYSTIC 1L NSCLC OS	
SCLC		**IMpower133** 1L ES-SCLC PFS/OS	**CheckMate 451** 1L SCLC (Maintenance only)	
			CheckMate 331 2L SCLC OS	

Roche combo
Chemo combo
CTLA4 combo

Note: Outcome studies are event driven, timelines may change. Timelines based on publicly available disclosures.
NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous

Going beyond lung cancer: Multiple Wave 2 Tecentriq read outs to come

Readouts until Q2 2018

	Potential	Indication	Study
Lung 	Most comprehensive lung cancer program addressing all common backbones and histologies	1L non-sq NSCL, sq NSCLC, SCLC	IMpower130 IMpower131 IMpower132
GU 	Among the leaders in renal cancer	1L RCC	IMmotion151
Breast 	First-in-class in triple negative breast cancer	1L TNBC	IMpassion130
CRC 	First-in-class in colorectal cancer	2/3L CRC	IMblaze370

New insights on fundamental questions:

Indications, combos (±chemo, ±targeted therapy), biomarkers, endpoints (OS, PFS)

Note: Outcome studies are event driven, timelines may change.
NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; Non-sq=non-squamous; Sq=squamous; RCC=renal cancer; TNBC=triple negative breast cancer; CRC=colorectal cancer

Wave 3: Adding novel CIT targets to Tecentriq

Improving clinical outcomes through combinations

Agent	Target	Phase	Indication	Data
CD20 TDB + Tecentriq	CD20/CD3	Ph 1b	r/r FL, DLBCL, MCL	2018
CEA-TCB + Tecentriq	CEA/CD3	Ph 1b	Solid tumors	2018
emactuzumab + Tecentriq	CSF-R1	Ph 1b	Solid tumors	2018
selicrelumab + Tecentriq	CD40	Ph 1b	Solid tumors	2018
aTIGIT + Tecentriq	TIGIT	Ph 1b	Solid tumors	2018
aCEA-IL2v + Tecentriq	CEA	Ph 1b	Solid tumors	2018/2019
aFAP-IL2v + Tecentriq	FAP	Ph 1b	1L RCC	2019
Personalized cancer vaccine + Tecentriq	Personalized	FPI expected Q1 2018	Solid tumors	TBD

TDB=T cell dependent bispecific; TCB=T cell bispecific; FPI=first patient in

Conclusions from IMpower150
Providing a potential new standard of care

- First Ph3 immunotherapy-based chemo combo study to demonstrate statistically significant and clinically meaningful improvement in PFS in all-comer 1L non-sq NSCLC
- PFS per IRF is consistent with PFS per INV
- PFS benefit in Arm B vs C was observed in key subgroups, including patients with
  - Sensitizing *EGFR* or *ALK* genetic alterations
  - Teff-low tumors
  - PD-L1-negative tumors
  - Liver metastases
- Tecentriq in combination with chemotherapy and Avastin was well tolerated and its safety profile is consistent with known safety risks
- OS has numerical improvement in Arm B vs C, but data are not fully matured; next interim analysis for all arms is anticipated in 1H 2018

NSCLC=non-small cell lung cancer; Non-sq=non-squamous; Teff=T effector gene signature (*PD-L1, IFNγ, CXCL9*); PFS=progression-free survival; OS=overall survival; IRF=independent review facility; INV=investogator

Doing now what patients need next