
Roche

54th ASCO Annual Meeting, Chicago

Roche Analyst Event

Monday, 4 June 2018

Agenda

Welcome
Karl Mahler, Head of Investor Relations

Highlights in cancer immunotherapy
Alan Sandler, Global Head Lung Cancer Franchise

Biomarkers in the era of cancer immunotherapy
Priti S. Hegde, Ph.D., Oncology Biomarker Development

Highlights late stage portfolio outside cancer immunotherapy
Sandra Horning, M.D., Chief Medical Officer and Head Global Product Development

Oncology strategy update
Daniel O'Day, CEO Roche Pharmaceuticals

Q&A

Welcome

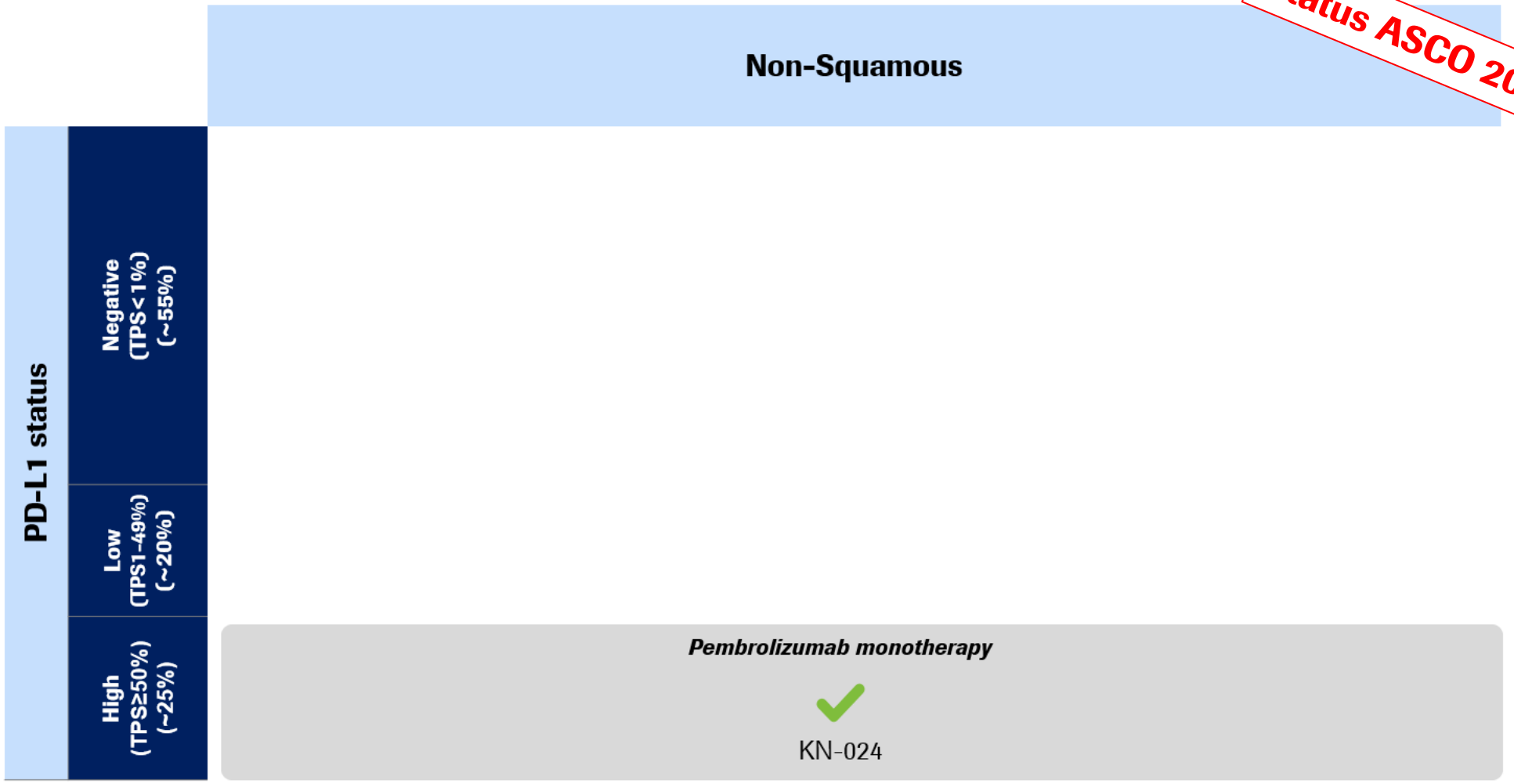
Karl Mahler

Head of Investor Relations

1L non-sq NSCLC evolving options

Roche

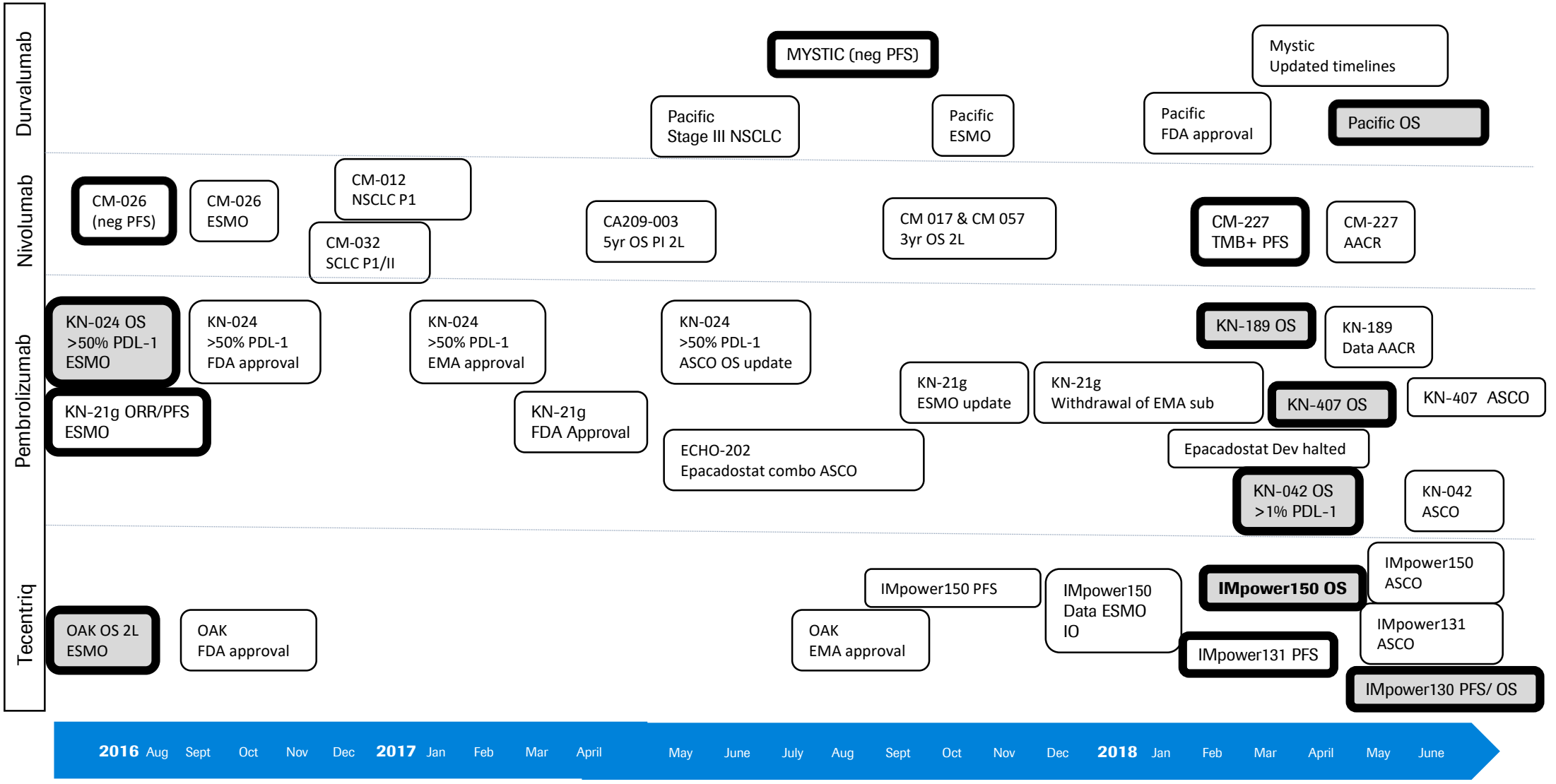
Status ASCO 2016



Illustrative

✔ = Positive data

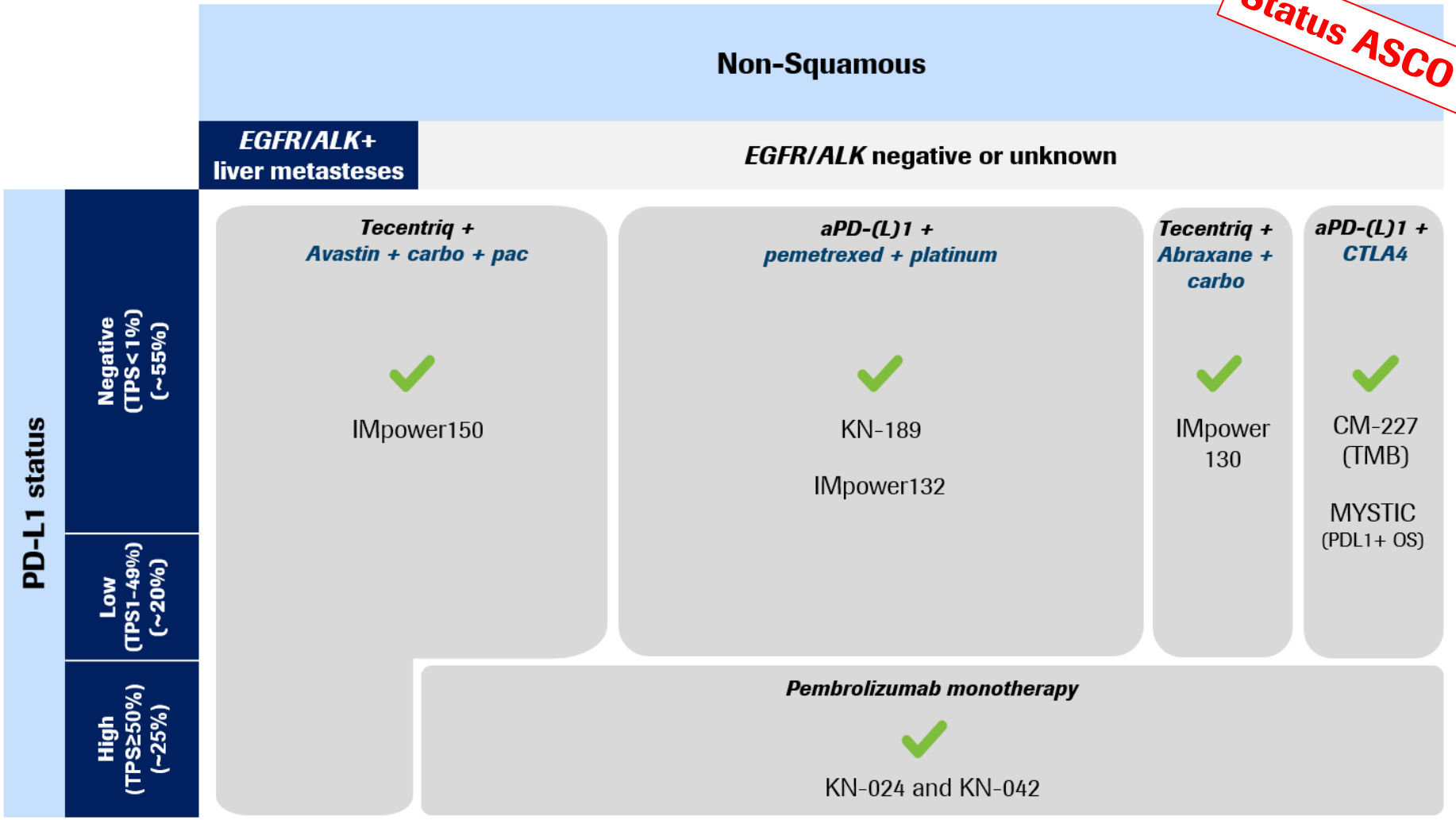
Crowded news flow in the CIT lung cancer space



Key trial readouts highlighted

1L non-sq NSCLC evolving options – Complexity increases

Status ASCO 2018



Illustrative

✔ = Positive data

Highlights in cancer immunotherapy

Alan Sandler, M.D.
Global Head Lung Cancer Franchise

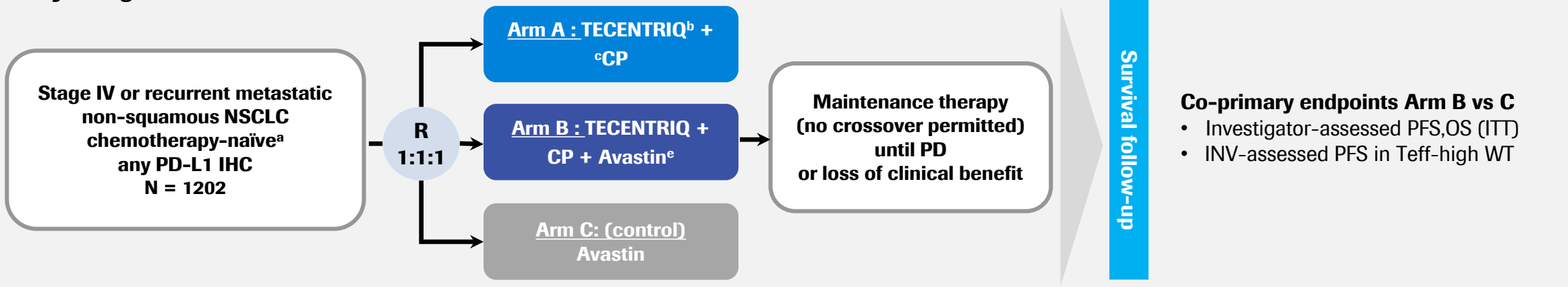
IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

IMpower131: Tecentriq + chemo in 1L sq NSCLC

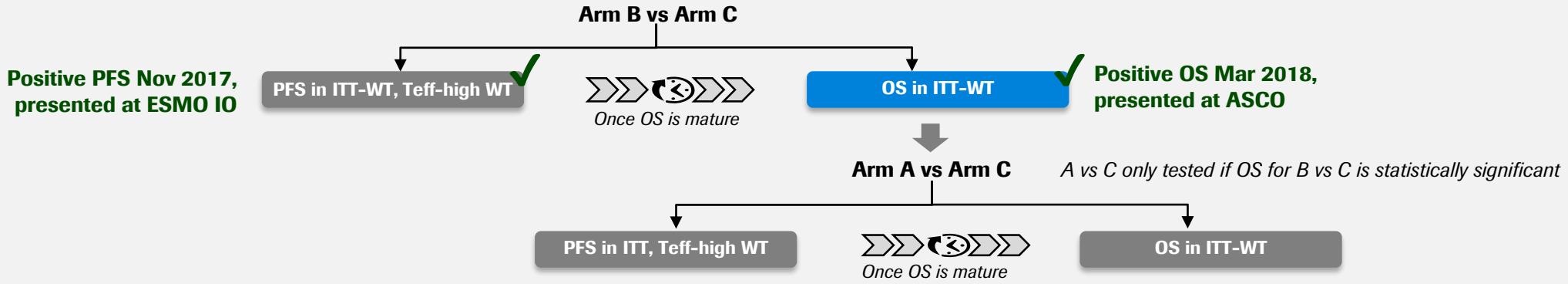
GO30140: Tecentriq + Avastin in 1L HCC

IMpower150 study design

Study design



Statistical testing hierarchy

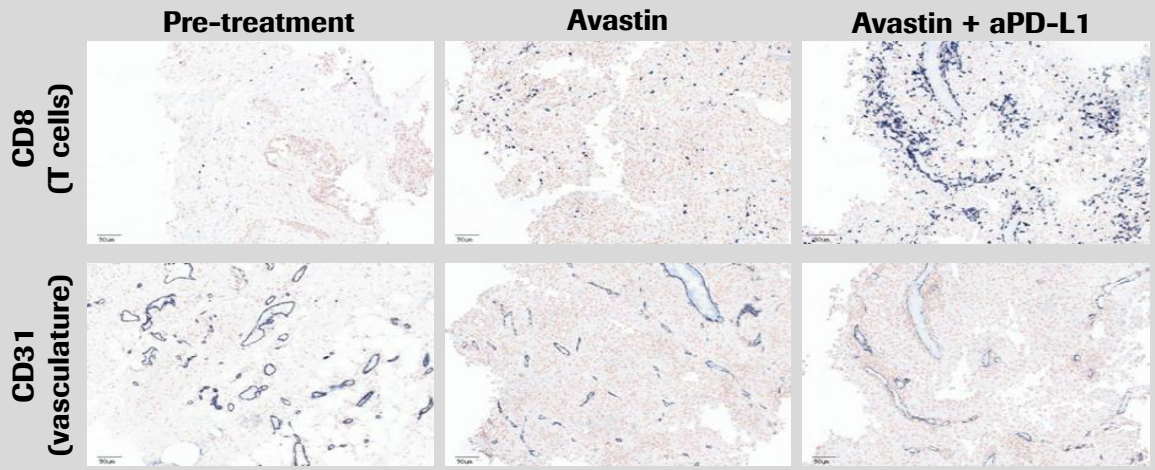


[a] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies.
[b] Tecentriq: 1200 mg IV q3w. [C] CP carboplatin: AUC 6 IV q3w; paclitaxel: 200 mg/m^2 IV q3w. [e] Bevacizumab: 15 mg/kg IV q3w. ITT-WT refers to patients without EGFR or ALK genetic alterations.

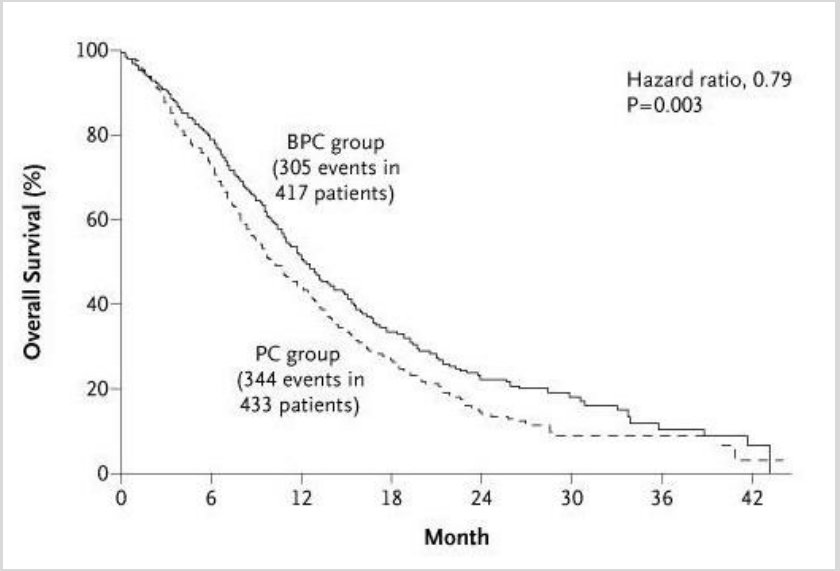
Combination with Avastin

Increased T cell infiltration and clinical activity

On-treatment biopsies show increased infiltrate and reduction in tumor vasculature



E4599 in 1L NSCLC: OS benefit with Avastin + CP versus CP

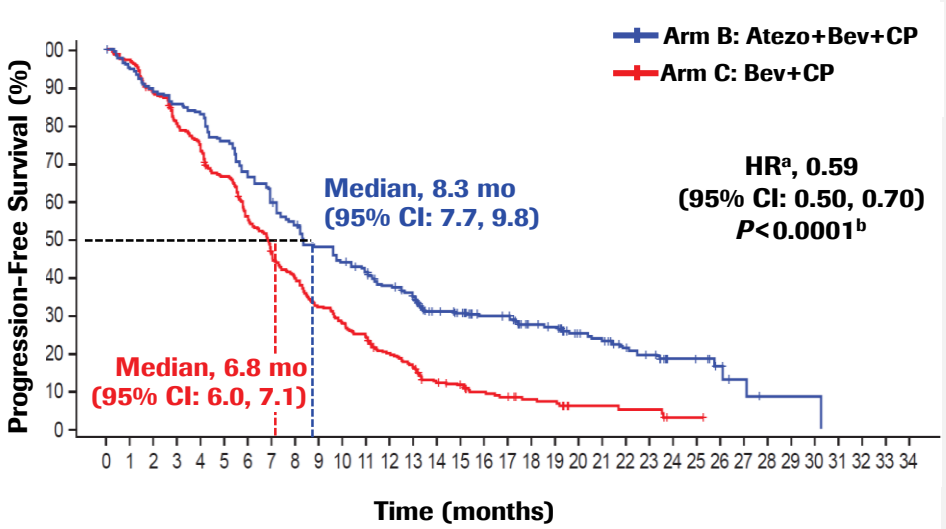


Understanding the immune modulatory properties of a-VEGF have guided the regimens for IMpower150, IMmotion151 and IMbrave150

Sznol *et al.* ASCO GU 2015; Sandler A et al. N Engl J Med 2006;355:2542-2550; IMpower150, IMmotion151, IMbrave150 refer to ongoing Ph3 studies in 1L NSCLC, 1L RCC, 1L HCC
CP = carboplatin

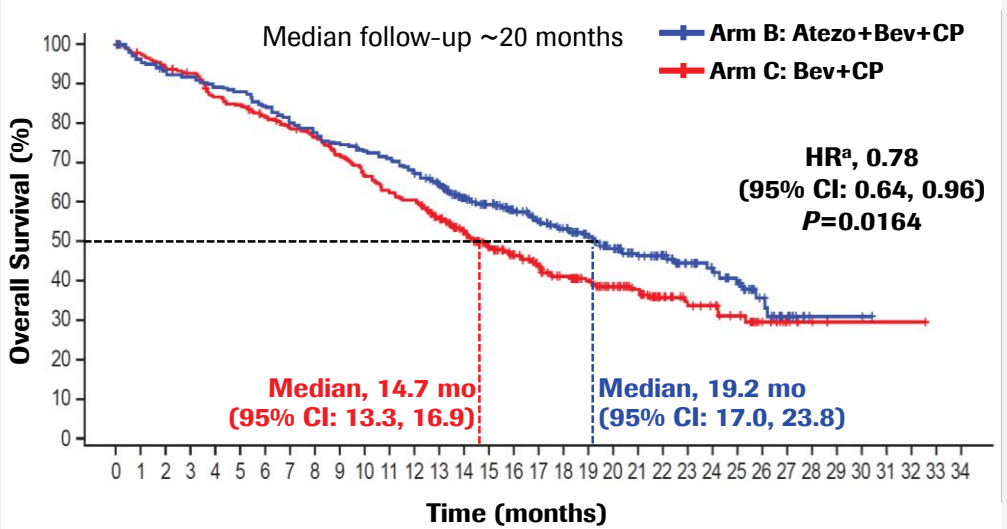
IMpower150: Co-primary PFS and OS endpoints met in ITT-WT (Arm B vs C)

PFS for Tecentriq + Avastin + chemo improved with additional follow-up



Landmark PFS, %	Arm B	Arm C
12-month	38%	20%
18-month	27%	8%

Statistically significant and clinically meaningful OS for Tecentriq + Avastin + chemo vs Avastin + chemo

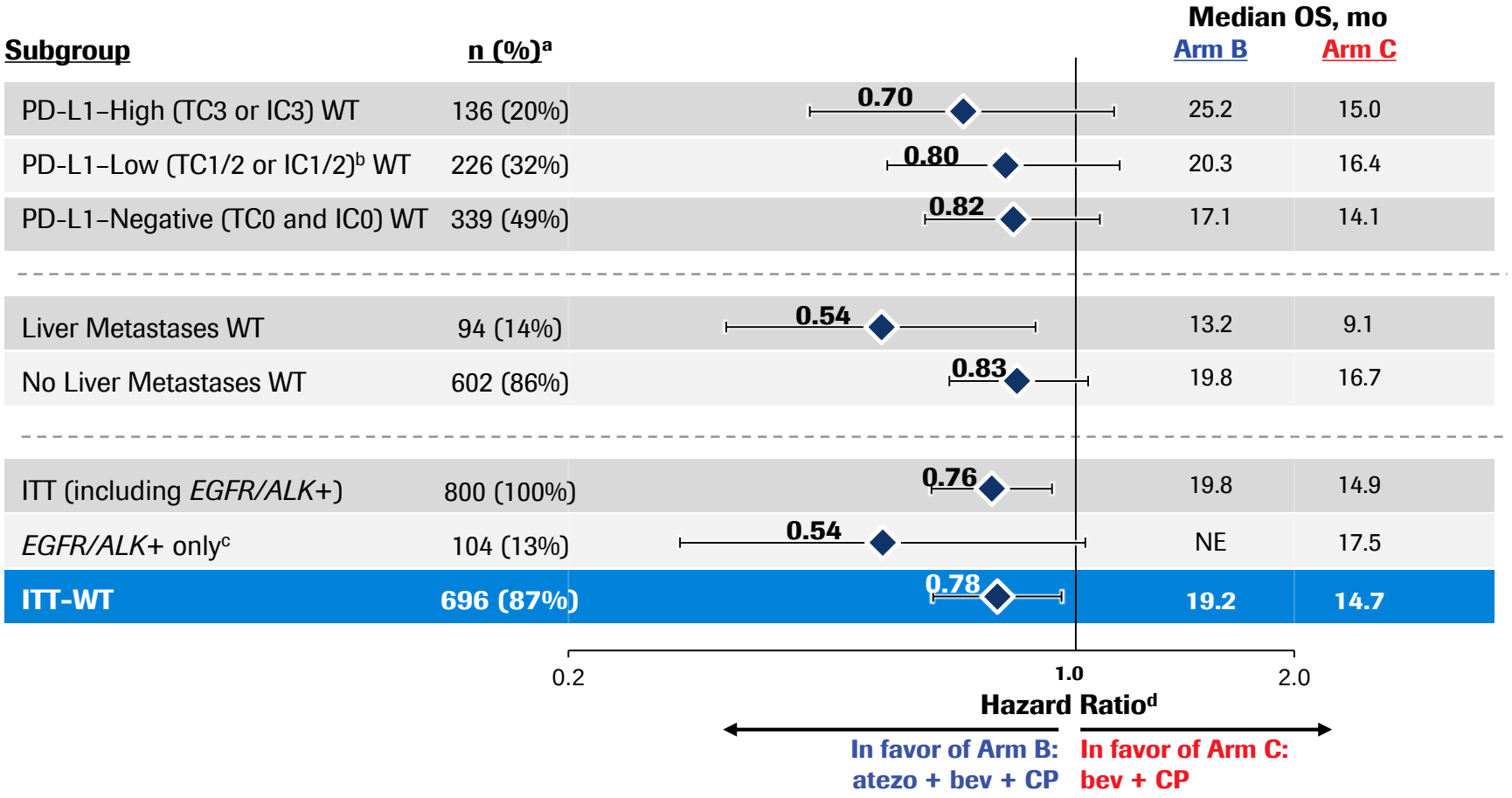


Landmark OS, %	Arm B	Arm C
18-month	43%	34%

Arm A vs C: Positive trend toward OS benefit with Tecentriq + chemo vs Avastin + chemo; final OS analysis expected in 2019

[a]Stratified HR. [b]For descriptive purposes only. Data cutoff: January 22, 2018. Minimum follow-up: 13.5 months

Meaningful OS in key subgroups (Arm B vs C)

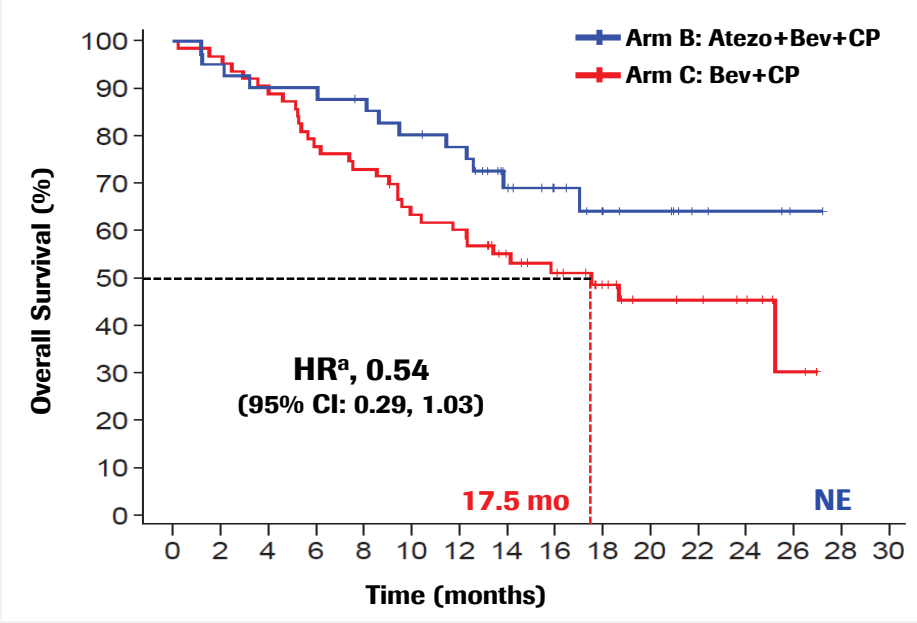


OS benefit with Tecentriq + Avastin + chemo observed across all subgroups, including patients with sensitizing EGFR or ALK genomic rearrangements, liver metastases at baseline and PD-L1 expression subgroups

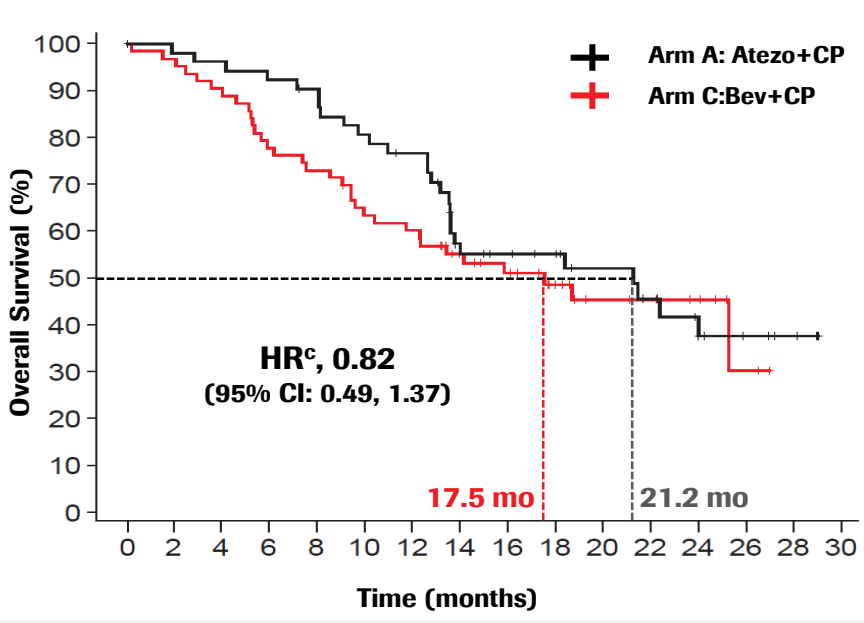
[a] Prevalence % for PD-L1 IHC and liver metastases subgroups out of ITT-WT (n=696); prevalence of ITT, *EGFR/ALK*+, and ITT-WT out of ITT (n=800). [b] Mutually exclusive subgroup that excludes TC3 or IC3 patients from the TC1/2/3 or IC1/2/3 subgroup. [c] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [d] Stratified HR for ITT-WT; unstratified HR for all other subgroups. Data cutoff: January 22, 2018

Addition of Avastin to Tecentriq and chemo prolongs survival of *EGFR/ALK*+ patients

Arm B vs Arm C



Arm A vs Arm C



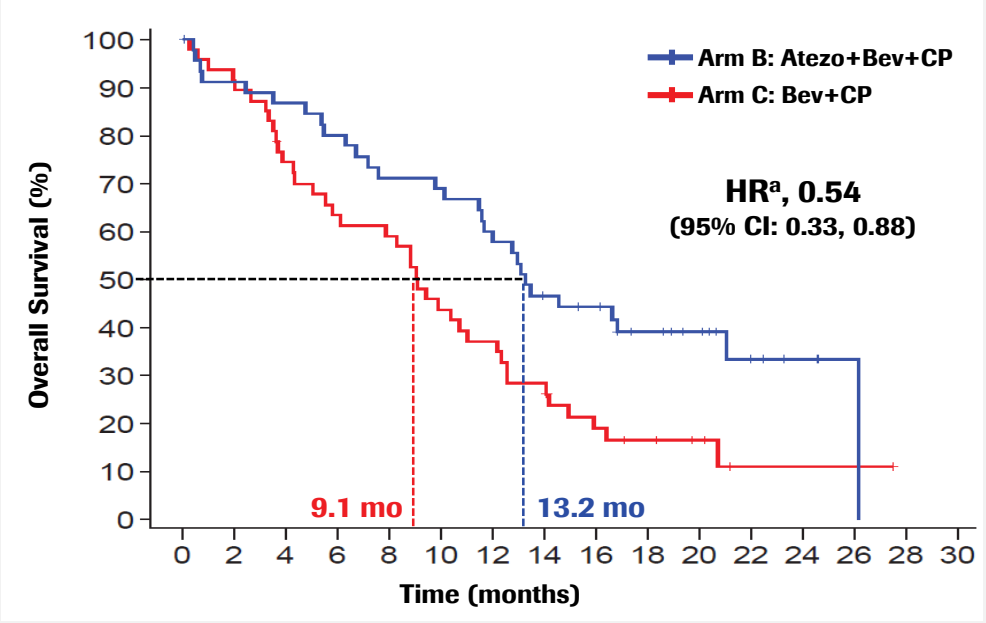
Addition of Avastin to Tecentriq and chemo led to clinical benefit in patients with EGFR/ALK genomic alterations supporting previous reports of Avastin efficacy in these patients[1]

Data cutoff: January 22, 2018

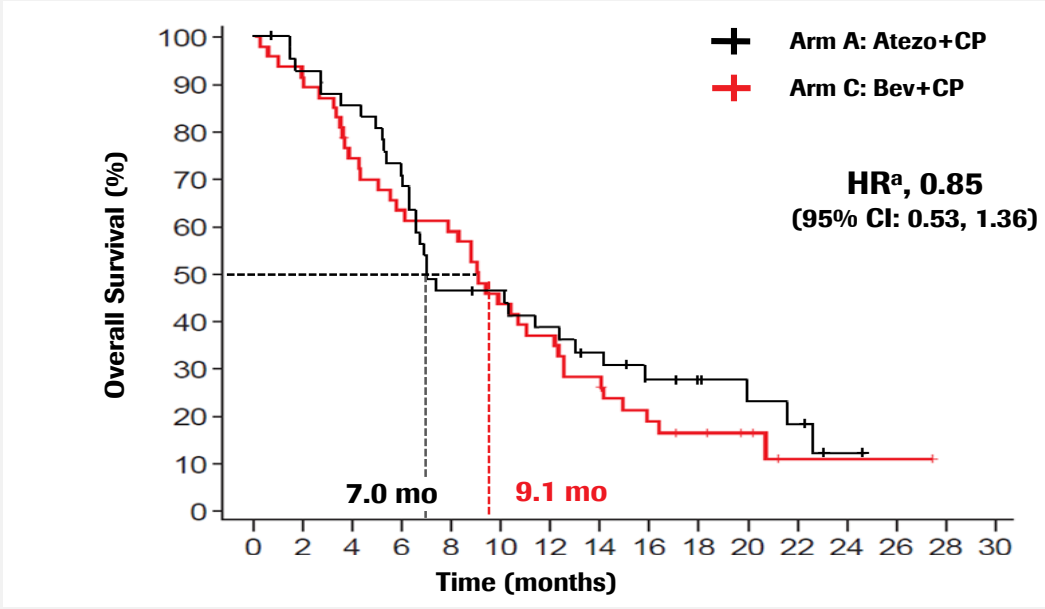
[a] Unstratified HR. [b] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [1] Seto T, et al. Lancet Oncol, 2014. 2. Sandler A, et al. N Engl J Med, 2006

Addition of Avastin to Tecentriq and chemo prolongs survival of patients with liver metastases

Arm B vs Arm C



Arm A vs Arm C



Adding Avastin to Tecentriq and chemo led to clinical benefit in patients with liver metastases supporting previous reports of Avastin efficacy in these patients[1]

Data cutoff: January 22, 2018

[a] Unstratified HR. [b] Patients with a sensitizing *EGFR* mutation or *ALK* translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [1] Sandler A et al. N Engl J Med 2006;355:2542-2550

IMpower150 conclusions

- Co-primary PFS and OS endpoints met with a statistically significant and clinically meaningful PFS and OS benefit for Tecentriq + Avastin + chemo (Arm B) vs Avastin + chemo (Arm C) in 1L non-squamous NSCLC
- OS benefit with Tecentriq + Avastin + chemo observed across all subgroups, including PD-L1 expression subgroups, patients with sensitizing EGFR or ALK genomic rearrangements, and patients with liver metastases at baseline
  - Supports previous reports of Avastin efficacy in these patient populations[1,2]
- Tecentriq in combination with chemo ± Avastin continued to be well tolerated and its safety profile was consistent with the known safety risks of the individual therapies

Tecentriq + Avastin + chemo combination provides a new treatment option for key patient populations with EGFR or ALK genomic rearrangements, and liver metastases

1. Seto T, et al. Lancet Oncol, 2014. 2. Sandler A, et al. N Engl J Med, 2006

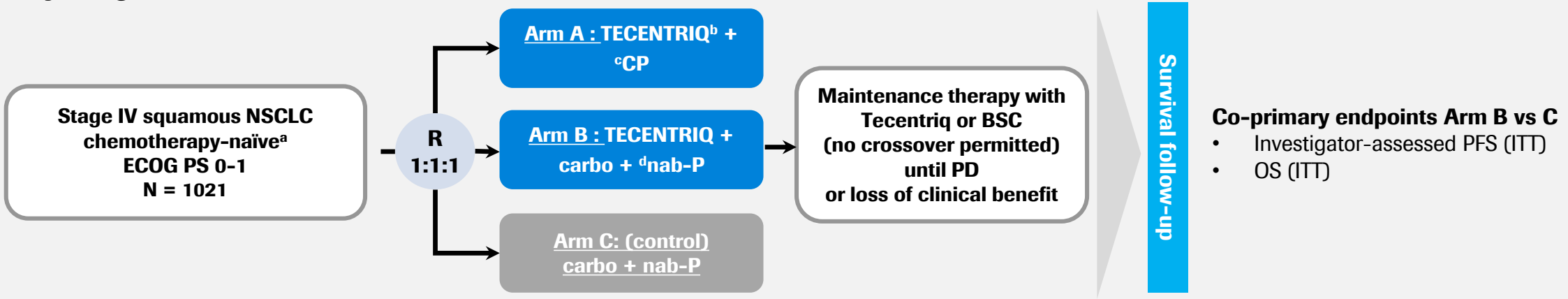
IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

IMpower131: Tecentriq + chemo in 1L sq NSCLC

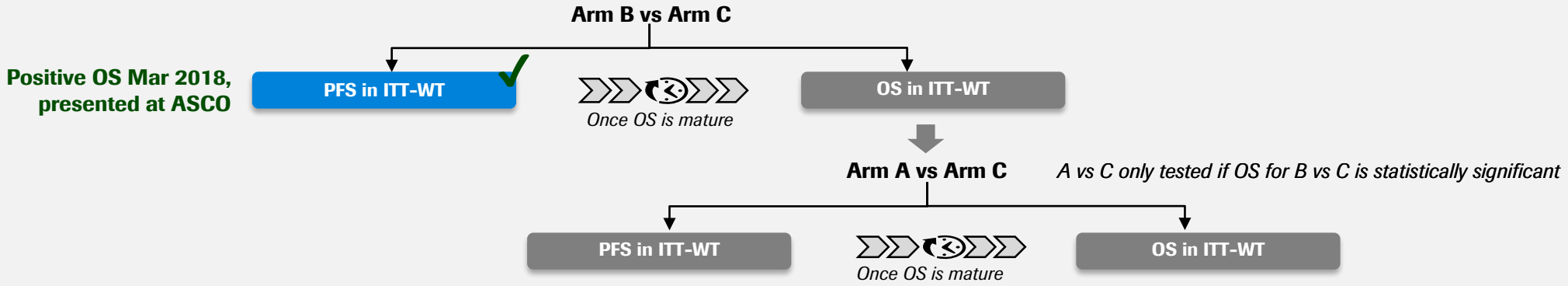
GO30140: Tecentriq + Avastin in 1L HCC

IMpower131 study design

Study design



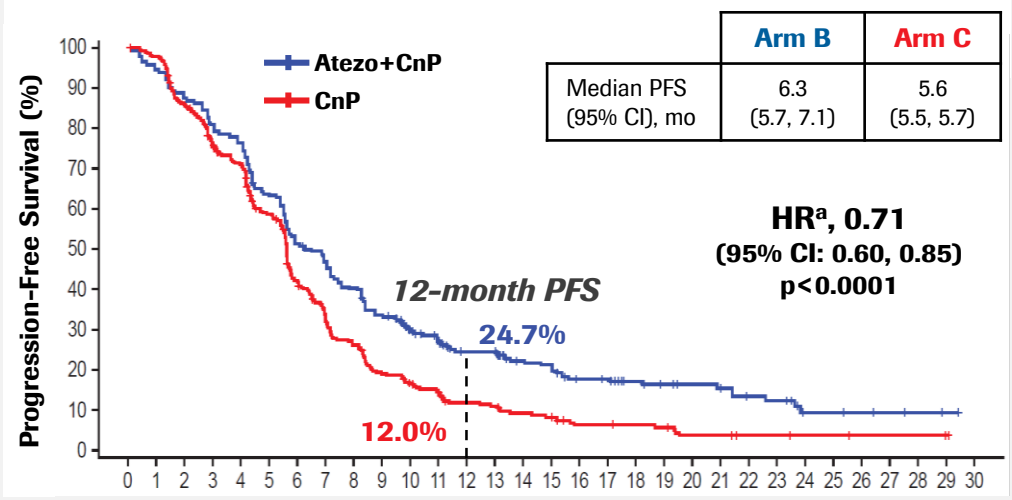
Statistical testing hierarchy



[a]ITT population includes patients with EGFR mutations and ALK translocations; patients with a sensitizing EGFR mutation or ALK translocation must have disease progression or intolerance of treatment with one or more approved targeted therapies. [b] Tecentriq: 1200 mg IV q3w. [c] CP: carboplatin AUC 6 IV q3w; paclitaxel 200 mg/m2 IV q3w. [d] nab-P: nab-paclitaxel 100 mg/m2 IV qw

PFS and subgroups in ITT (Arm B vs Arm C)

INV-assessed PFS – ITT



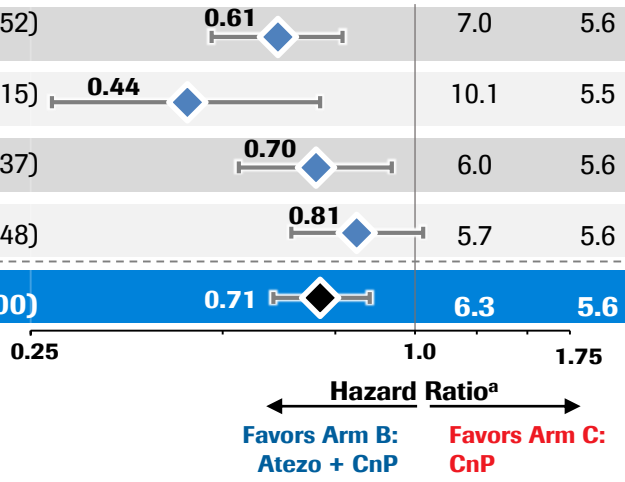
	Arm B	Arm C
Median PFS (95% CI), mo	6.3 (5.7, 7.1)	5.6 (5.5, 5.7)

HR[a], 0.71
(95% CI: 0.60, 0.85)
p<0.0001

Minimum follow-up: 9.8 mo; median follow-up: 17.1 mo

INV-assessed PFS in PD-L1 subgroups

Subgroup	n (%)	Median PFS, mo Arm B	Median PFS, mo Arm C
PD-L1 Positive (TC1/2/3 or IC1/2/3)	351 (52)	7.0	5.6
PD-L1 High (TC3 or IC3)	101 (15)	10.1	5.5
PD-L1 Low (TC1/2 or IC1/2)	250 (37)	6.0	5.6
PD-L1 Negative (TC0 and IC0)	331 (48)	5.7	5.6
ITT Population	**683 (100)**	**6.3**	**5.6**

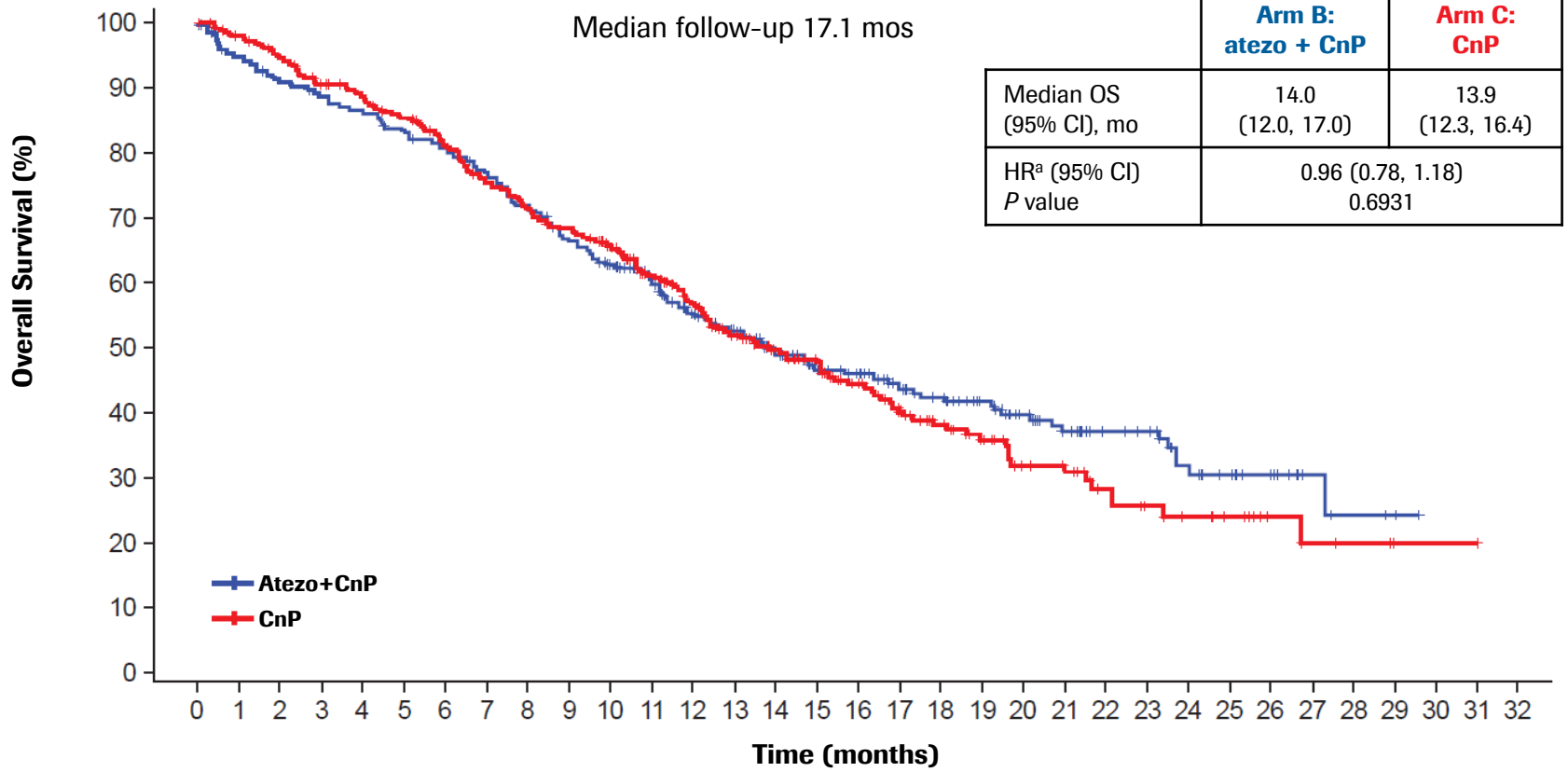


PFS benefit with Tecentriq + CnP (Arm B) vs CnP (Arm C) observed across all PD-L1–expressing subgroups, enriched with higher PD-L1 expression

Data cutoff: January 22, 2018,

[a] Unstratified HR; unstratified HRs for all PD-L1 subgroups. INV=investigator; CnP = carboplatin + nab-paclitaxel

IMpower131: First interim OS in ITT (Arm B vs Arm C)



	Arm B: atezo + CnP	Arm C: CnP
Median OS (95% CI), mo	14.0 (12.0, 17.0)	13.9 (12.3, 16.4)
HR[a] (95% CI) *P* value	0.96 (0.78, 1.18) 0.6931	

Next interim OS analysis anticipated in H2 2018

Data cutoff: January 22, 2018

[a] Unstratified HR, CNP = carboplatin + nab-paclitaxel

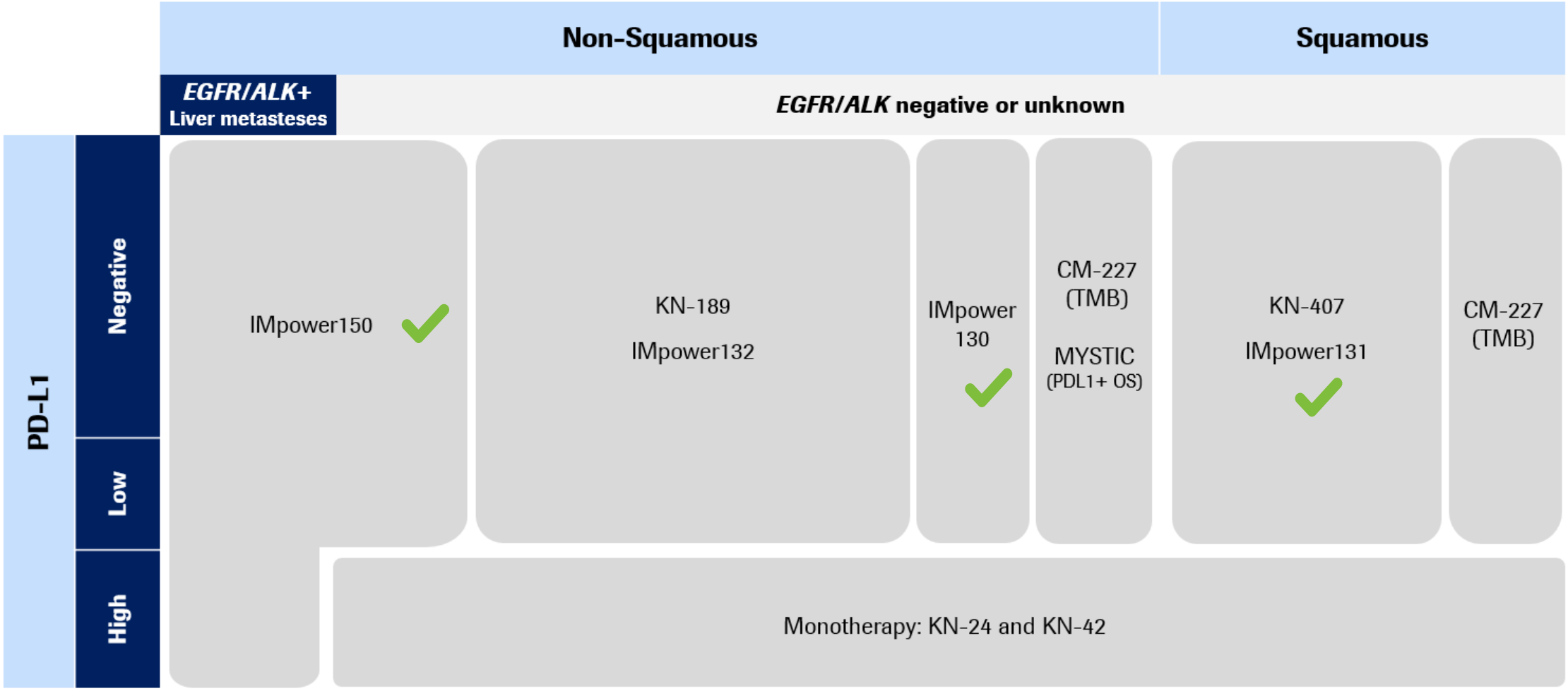
IMpower131 summary

- Study met co-primary endpoint of investigator-assessed PFS in Arm B vs Arm C in the ITT population
- PFS benefit with Tecentriq + CnP (Arm B) vs CnP (Arm C) was observed across all PD-L1–expressing subgroups, and was enriched in subgroups with higher PD-L1 expression
- Tecentriq + CnP median PFS in-line with other CIT + chemo combinations
- ORR numerically improved with enrichment by PD-L1 status
- OS benefit not significant at this time, with high cross-over to subsequent immunotherapy observed (42%). OS continues to be followed, with the next interim OS analysis anticipated later in 2018
- Tecentriq plus carboplatin and nab-paclitaxel has a manageable safety profile consistent with known safety risks of the individual therapies; no new safety signals were identified

CnP = carboplatin + nab-paclitaxel

Evolving landscape in 1L NSCLC

Treatment driven by histology and actionable mutations

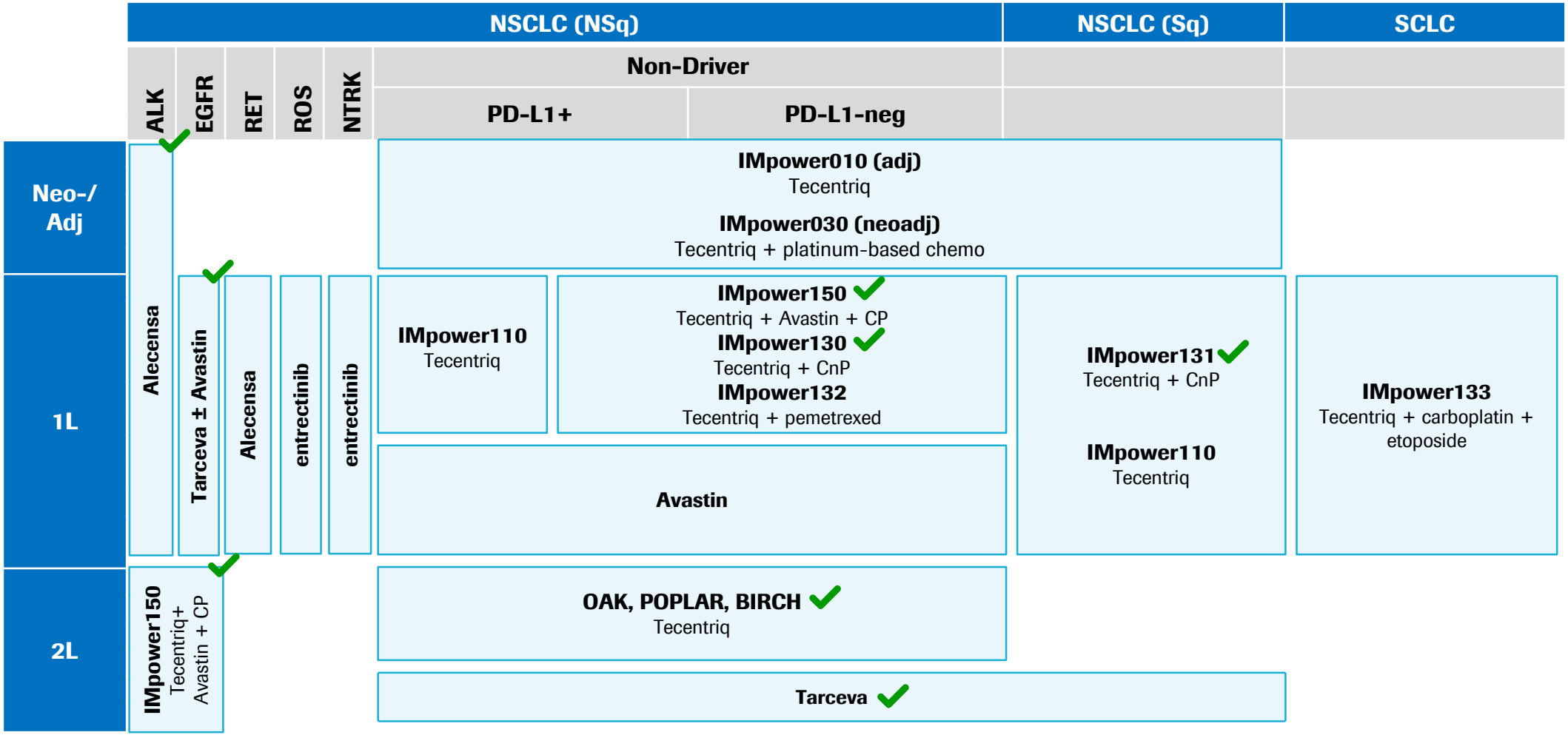


Illustrative

✔ = Positive Roche data

Broad portfolio in NSCLC today and looking ahead

Ability to cover all key segments



IMpower150: Tecentriq + chemo ± Avastin in 1L non-sq NSCLC

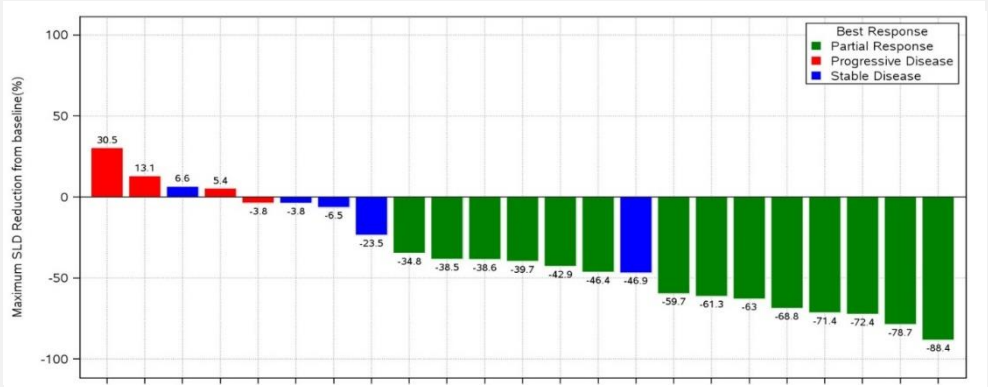
IMpower131: Tecentriq + chemo in 1L sq NSCLC

GO30140: Tecentriq + Avastin in 1L HCC

Tecentriq + Avastin in 1L hepatocellular carcinoma

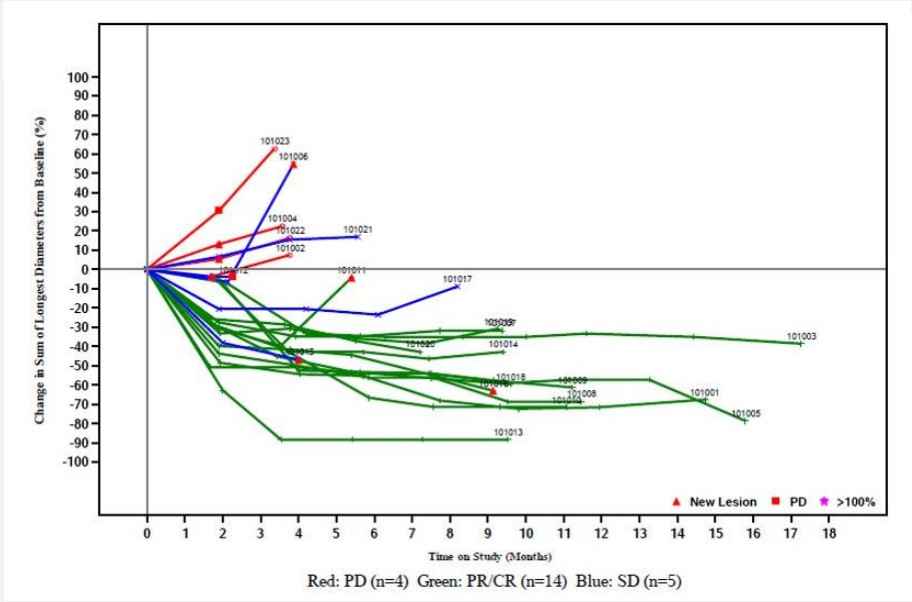
Encouraging phase 1 data, phase 3 study ongoing

Confirmed RECIST v1.1 responses* to Tecentriq + Avastin



	PFS rate %	OS rate %
6-month	65%	86%
12-month	60%	68%
mFU (range), months	10.3 (3.5-17.3)	

Tumor burden over time and response duration



- The combination of Tecentriq and Avastin shows promising early efficacy in patients with advanced HCC
- Confirmed ORR by RECIST v1.1 of 61% by INV; 10/14 responses are ongoing >6 months with 3 responses ongoing >12 months
- Median OS, PFS, and DOR have not yet been reached
- Combination of Tecentriq and Avastin was safe and well tolerated, no new safety signals
- Phase 3 (IMbrave150) of Tecentriq+Avastin vs. sorafenib ongoing

*minimum follow-up 16 weeks, median follow-up 10.3 months, evaluable patients (n=23)

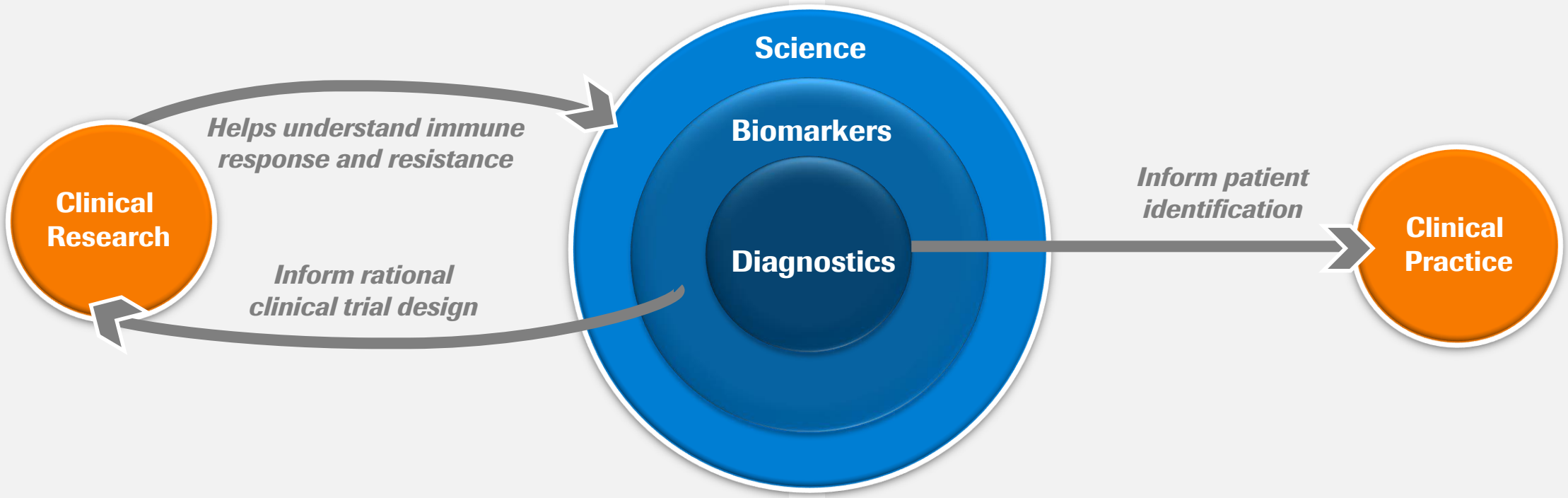
Biomarkers in the era of cancer immunotherapy

Priti S. Hegde, Ph.D.
Director, Oncology Biomarker Development

Scientific inquiry to identify increasingly effective & meaningful biomarkers that are predictive of patient response

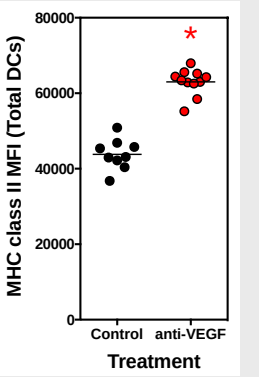
Incorporate science and biomarker findings into studies to develop best CIT regimen for each patient

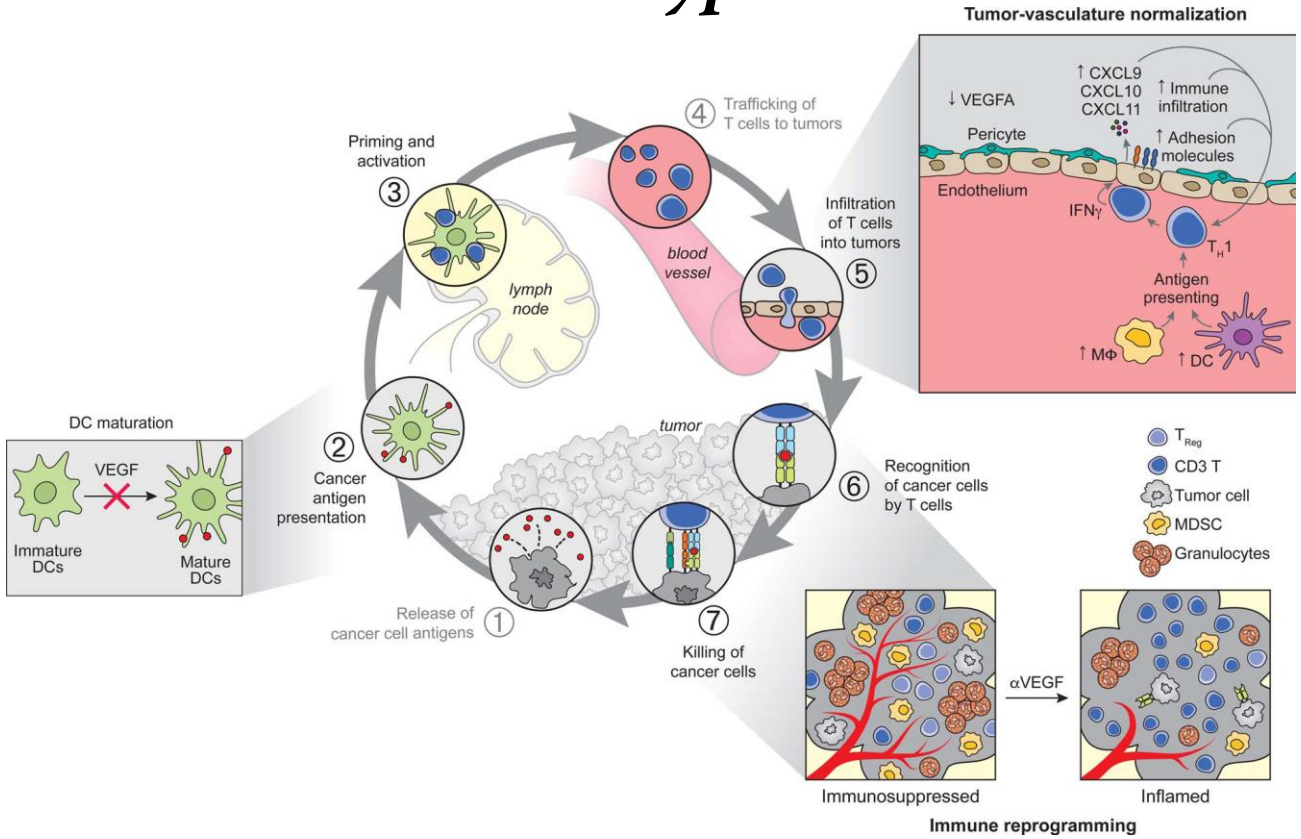
Develop and commercialize diagnostic tests to identify patients for best therapy

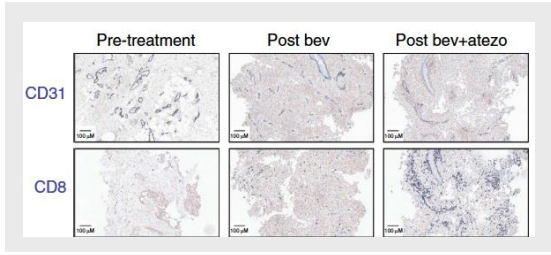


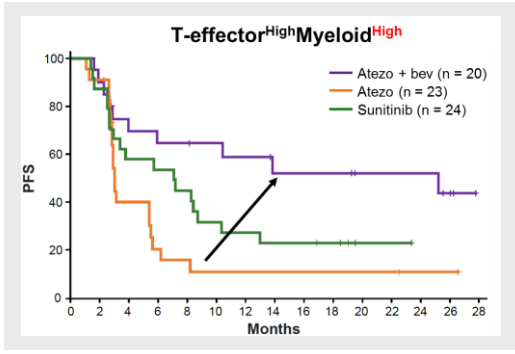
Scientific understanding to identify combinations

Establishing treatment options tailored to the specific immune biology associated with a tumor type









Understanding the immune modulatory properties of aVEGF has guided the regimens for IMpower150, IMmotion151 and IMbrave150

Hegde PS et al., Sem. Canc. Biol 2018; Chen and Mellman, Immunity, 2013; McDermott et al., Nat Med (accepted) 2018; Wallin J et al., Nat Comm 2016

Dx leadership in an increasingly fragmented treatment landscape

Moving from AC trials to disease-specific Dx subsets

PD-L1 IHC	• In the front-line setting, PD-L1 performs well in enriching for patients with PFS benefit (50-55% of the patient population)
T_{eff} gene signature	• T_{eff} gene signature is equivalent to PD-L1 IHC
TMB	• Response rate and duration of response to CPI correlate with TMB levels across different tumor types • TMB identifies a distinct patient population not currently captured by PD-L1 IHC
NGS testing	• NGS testing for rare biomarkers and as a standard test across tumor types

AC=all comers; Dx=diagnostic; TMB=tumor mutational burden; IHC=immunohistochemistry; NGS=next generation sequencing; CPI=checkpoint inhibitor

PD-L1 IHC assays are clinically equivalent

IMpower150 demonstrates high concordance between SP142 and SP263

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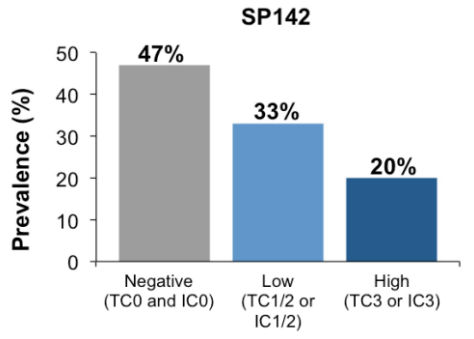
Science

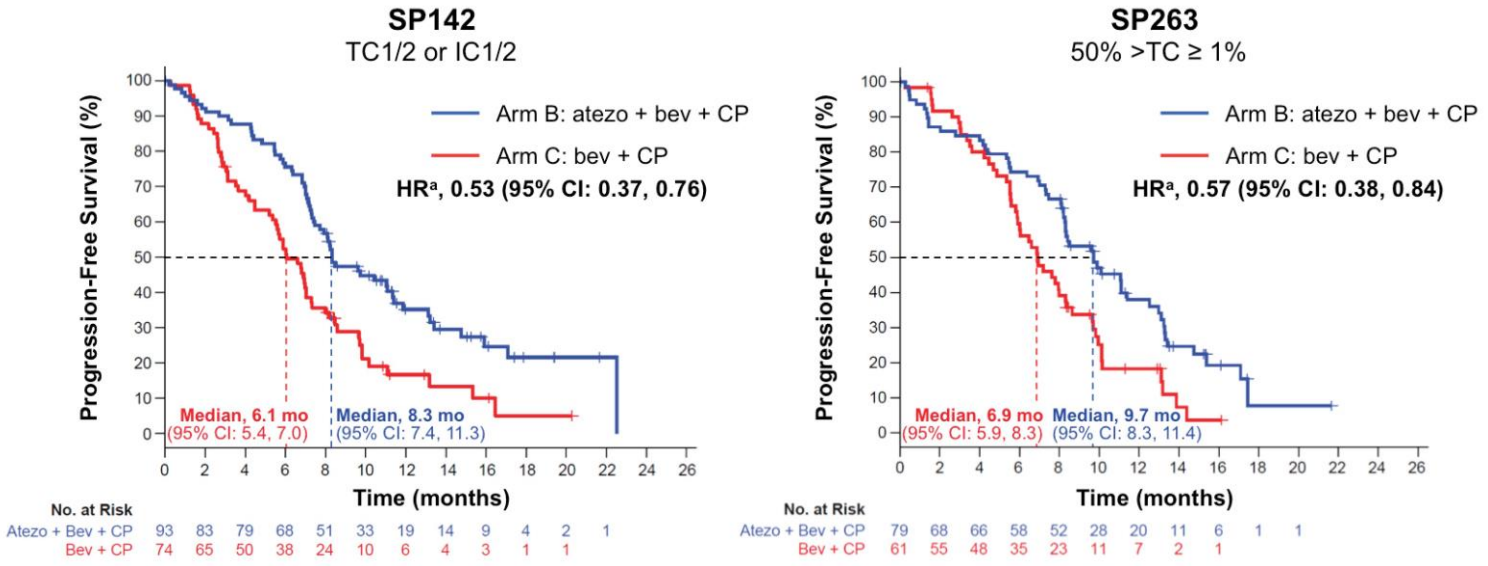
Biomarkers

Diagnostics

PD-L1 IHC prevalence[b]



Similar PFS HRs across PD-L1 subgroups



PFS Analysis in BEP of Arms B and C in ITT-WT (n=503)

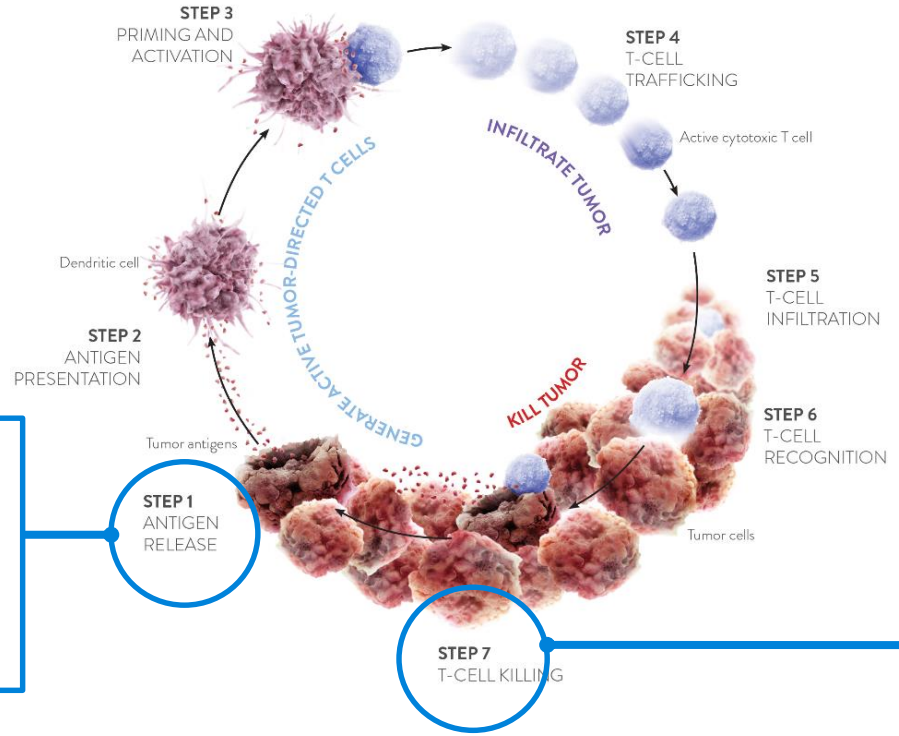
Kowanetz M et al., AACR 2018

[a]Unstratified HR. [b]Prevalence analysis of Arms B and C in the BEP (evaluable for SP263), n=503. TC3 or IC3=PD-L1+ ≥50% of TC or ≥10% of IC; TC1/2 or IC1/2=PD-L1+ <50% and ≥1% of TC or <10% and ≥1% of IC; TC0 and IC0=PD-L1+ <1% of TC and IC. Data cutoff: September 15, 2017

BEP=biomarker evaluable population; IC=tumor-infiltrating immune cells; TC=tumor cells; bev=bevacizumab; CP=carboplatin+paclitaxel

Complex biology behind efficacy of immune checkpoint inhibitors

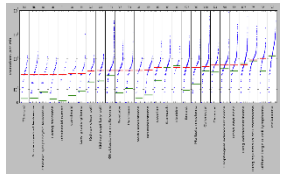
Capturing factors in addition to PD-L1 expression



Biomarker 1

Tumor mutational burden

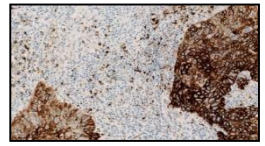
MSI, TMB



Biomarker 2

PD-L1 expression

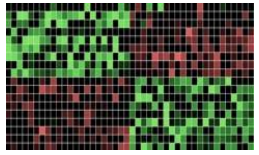
IHC



Tumor gene expression

IFNγ signature

NGS

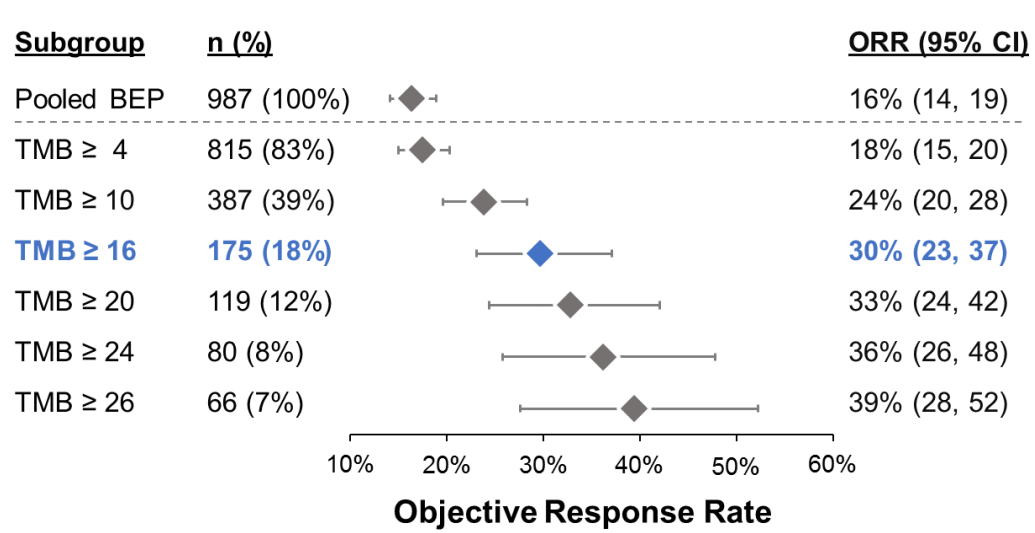


Robust biomarker research might allow to personalize cancer immunotherapy for patients in the future

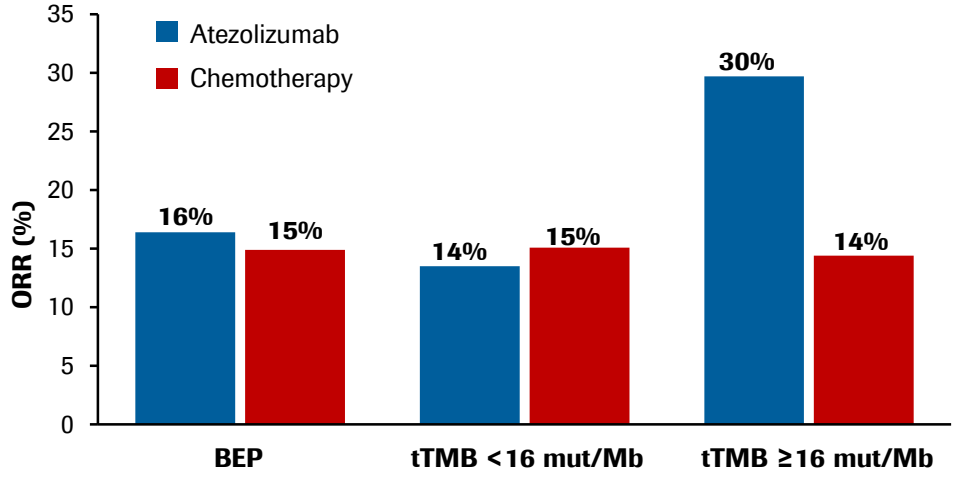
Hegde PS et al., Sem. Canc. Biol 2018; Chen and Mellman, Immunity, 2013; McDermott et al., Nat Med (accepted) 2018; Wallin J et al., Nat Comm 2016
TMB=tumor mutational burden; MSI=microsatellite instability; IHC=immunohistochemistry; NGS=next generation sequencing

High tissue-based TMB (tTMB) is associated with enriched ORR and DOR across tumor types and lines of therapy

ORR by tTMB cut-offs[a]



ORR and DOR in tTMB* ≥16 vs <16 subgroups



	BEP		tTMB <16 mut/Mb		tTMB ≥16 mut/Mb	
Median DOR (95% CI), mo	16.6 (13.8, 23.1)	6.2 (5.5, 6.7)	13.8 (12.5, 17.4)	6.2 (5.6, 6.9)	29.0 (18.6, NR)	6.2 (4.6, 8.3)

Legrand FA et al., ASCO 2018
Oral presentation on Tuesday, Jun 5th

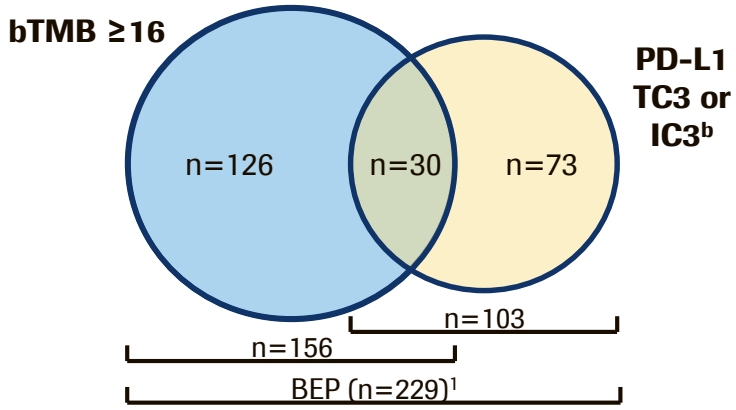
Results are encouraging in the understanding of the mechanisms underlying responses to cancer immunotherapy

Legrand FA et al., ASCO 2018
[a]TMB cutoffs shown are measured in mut/Mb (date of analysis: November 1, 2017); *Balar AV et al., Lancet. 2017 Jan 7;389(10064):67-76. tTMB was evaluated by the FoundationOne (F1) assay across 7 Tecentriq monotherapy studies: NSCLC n=342 (FIR, BIRCH, POPLAR, OAK), metastatic urothelial carcinoma (mUC) n=400 (IMvigor210, 211), and other advanced solid tumors n=245 (PCD4989g). ORR=objective response rate; DOR=duration of response; tTMB=tissue-based tumor mutational burden; BEP=biomarker evaluable population; NR=not reached

Blood-based TMB (bTMB): A non-invasive biomarker

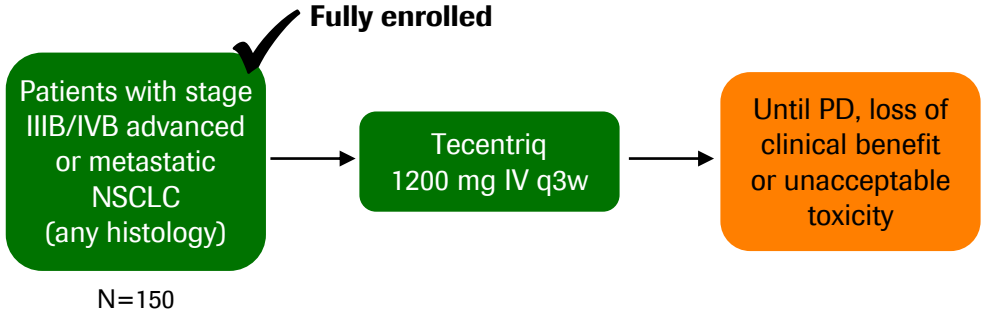
~30% of patients with NSCLC have inadequate tumor tissue for molecular testing

OAK Ph3: bTMB ≥16 predicts PFS benefit[a]



	PFS HR (95% CI)	OS HR (95% CI)
bTMB ≥16	0.64 (0.46, 0.91)	0.64 (0.44, 0.93)
TC3 or IC3	0.62 (0.41, 0.93)	0.44 (0.27, 0.71)
bTMB ≥16 and TC3 or IC3	0.38 (0.17, 0.85)	0.23 (0.09, 0.58)

B-F1RST Ph2: Prospective evaluation of bTMB



Interim Analysis: Prespecified at 6 mo after 50% of patients have been enrolled
Primary analysis: ORR and PFS (co-primary endpoints), expected later in 2018

bTMB identified patients who derived greater PFS benefit from Tecentriq as compared to the all-comer population in the two original NSCLC studies (POPLAR and OAK)

[1]Rittmeyer A et al., Lancet, 2017; [2]Gandara DR et al., ESMO 2017; [a]The bTMB assay uses hybridization-capture methodology and targets 1.1 Mb of genomic coding sequence (bTMB score of 16 ≈ 14 mutations/Mb). [b]PD-L1 expression on ≥50% of tumor cells or ≥10% of immune cells
bTMB=blood-based tumor mutational burden; CPI=checkpoint inhibitor; BEP=biomarker evaluable population; IC=tumor-infiltrating immune cells; TC=tumor cells; ORR=objective response rate

B-F1RST: bTMB enriches for PFS benefit of Tecentriq in 1L NSCLC

A potentially clinically relevant biomarker to inform treatment strategies

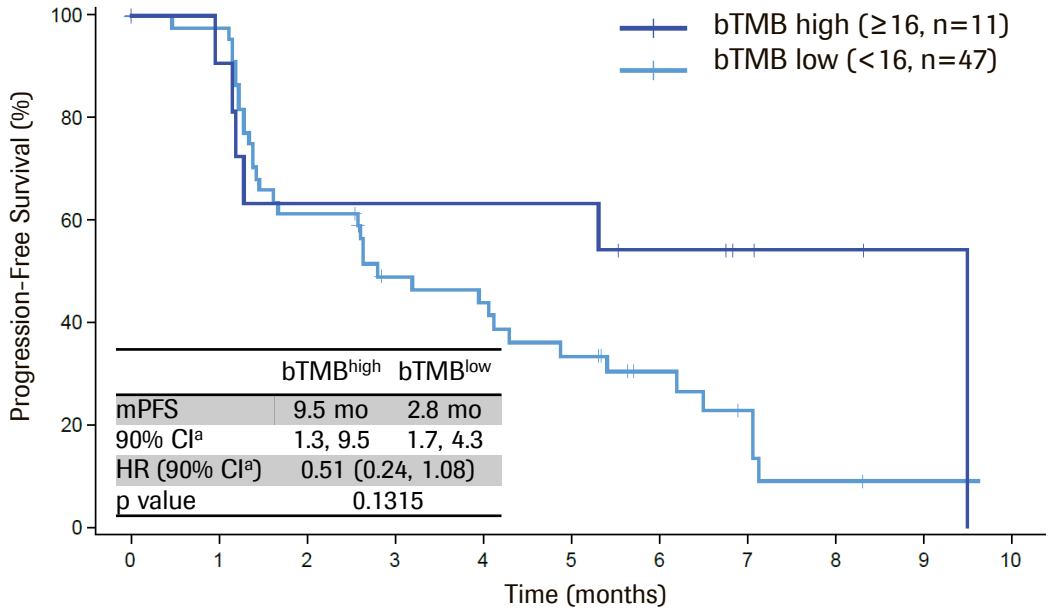
Roche

Science

Biomarkers

Diagnostics

Tecentriq PFS by bTMB subgroups



ORR[b] in bTMB ≥16 vs <16 subgroups

RECIST v1.1	IAP (n = 78)	BEP (n = 58)	bTMB low (n = 47)	bTMB high (n = 11)
ORR	15.4%	12.1%	6.4%	36.4%
PR	15.4%	12.1%	6.4%	36.4%
SD	33.3%	34.5%	36.2%	27.3%
PD	37.2%	37.9%	38.3%	36.4%

Minimum follow-up: 6 months

Velcheti V et al., ASCO 2018
Oral presentation on Tuesday, Jun 5th

Interim analysis results support the bTMB selection of patients in the ongoing, label-enabling Ph3 BFAST study

Velcheti V et al., ASCO 2018; Data cutoff: December 7, 2017.

[a]Per protocol, efficacy differences between bTMB high vs low subgroups are tested at a significance level of 0.1, and 90% CIs are provided. [b]Unconfirmed ORR (2 patients had only 1 scan prior to clinical cut-off). bTMB high, ≥16; bTMB low, <16. BEP comprised patients with a baseline evaluable blood sample with adequate tumor content (i.e. maximum somatic allele frequency [MSAF] ≥1%) to test on the FMI bTMB assay. IAP=interim analysis population; BEP=biomarker-evaluable population; bTMB=blood-based TMB; ORR=objective response rate; PR=partial response; SD=stable disease; PD=progressive disease

Dx leadership in an increasingly fragmented treatment landscape

Moving from AC trials to disease-specific Dx subsets

PD-L1 IHC	• Increasing PFS benefit associated with higher PD-L1 expression (IMmotion151) • Increasing OS benefit associated with higher PD-L1 expression (OAK, IMpower150) • SP142 and 22c3/SP263 are interchangeable (OAK, IMpower150)
T_{eff} gene signature	• Gene signatures are seen as the future to enable multiplex testing algorithms for patients • T_{eff} gene signature is equivalent to PD-L1 IHC
TMB	• tTMB: Pan tumor development for Tecentriq monotherapy (MYPATH, MX39795) • bTMB: Non-invasive biomarker for Tecentriq in 1L NSCLC (B-F1RST, B-FAST)
NGS testing	• Support NTRK pan-tumor, ROS1 in NSCLC, PI3K, PTEN alterations in breast cancer

AC=all comers; Dx=diagnostic; TMB=tumor mutational burden; IHC=immunohistochemistry; NGS=next generation sequencing

Highlights late stage portfolio outside cancer immunotherapy

Sandra Horning, M.D.
Executive VP
Chief Medical Officer and Head Global Product Development

ASCO Highlights

Hematology

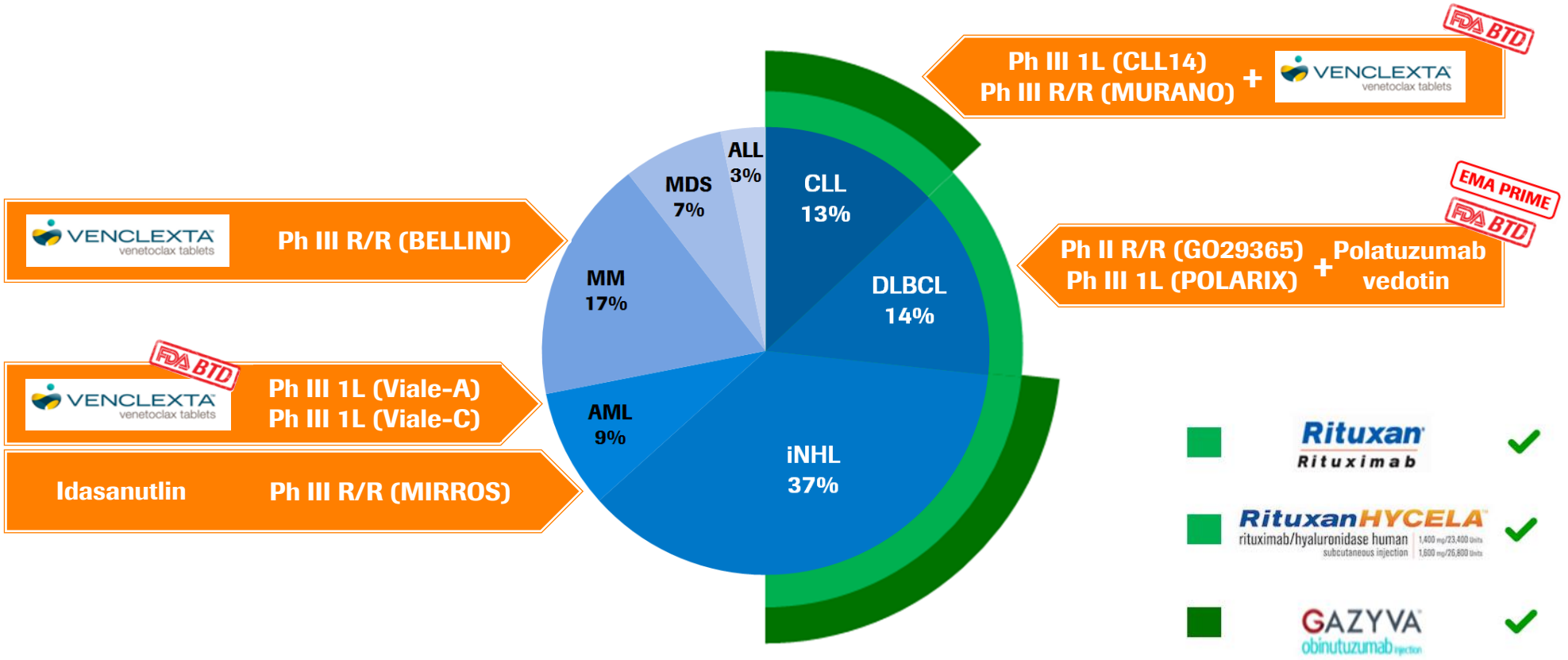
Breast

Lung

Late stage hematology

Improving standard of care and extending into new indications

Incidence rates (330,000 pts[1])

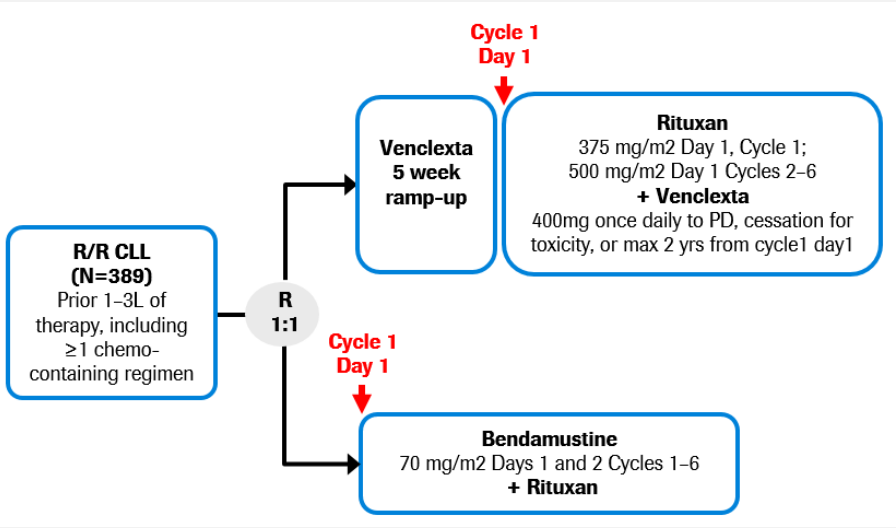


[1] Datamonitor; incidence rates includes the 7 major markets (US, Japan, France, Germany, Italy, Spain, UK); CLL=chronic lymphoid leukemia; DLBCL (aNHL)=diffuse large B-cell lymphoma; iNHL=indolent non-hodgkin`s lymphoma; AML=acute myeloid leukemia; MM=multiple myeloma; MDS=myelodysplastic syndrome; ALL=acute lymphoblastic leukemia; Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Polatuzumab vedotin in collaboration with Seattle Genetics

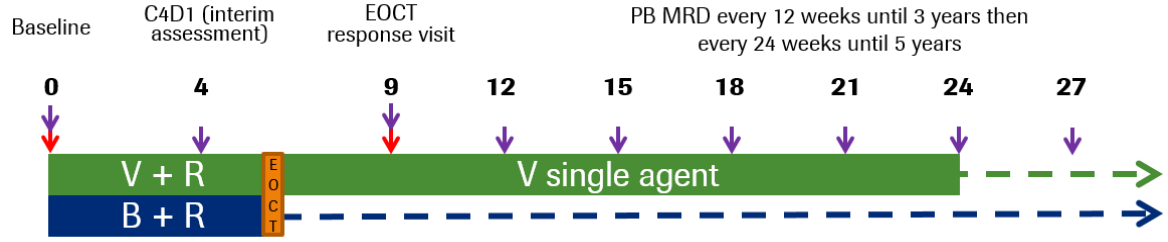
Venclexta + Rituxan in R/R CLL

MURANO results define new standard of care

Trial design



MRD assessment (2 EP)



- MRD negativity (MRD–) defined as <1 CLL cell per 10 000 leukocytes (10^{-4})
- Sample collection times for PB (↓) and BM (↓) identical in both arms
- MRD was centrally assessed by ASO-PCR and/or 8-color flow cytometry
- MRD status was reported: MRD+ if either ASO-PCR or flow-cytometry positive

Phase III results (MURANO) presented at ASH:

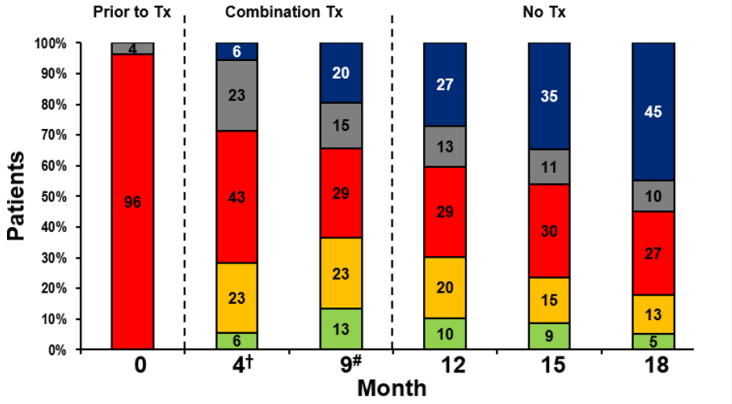
- Primary PFS endpoint met (HR of 0.17) with benefit across all sub-groups, including high-risk patients
- OS HR of 0.48 with a descriptive p-value of 0.0186; Landmark 2Y OS at 91.9% for V+R vs 86.6% for B+R

Seymour et al., *NEJM* (2018); Hillmen P. *et al*., ASCO 2018; Seymour J. *et al*., ASH 2017; MRD=minimal residual disease; EP=end point; PB=peripheral blood; BM=bone marrow; ASO-PCR=allele-specific PCR; EOCT=end of combination treatment; PFS=progression free survival; HR=hazard ratio; OS=overall survival; V=Venclexta in collaboration with AbbVie; R=Rituxan; B=bendamustine

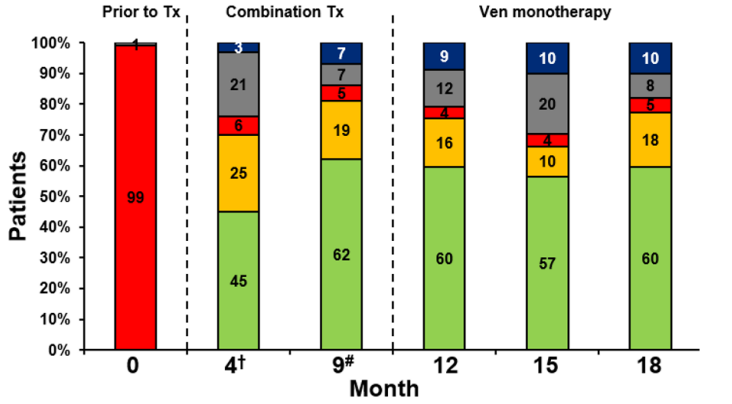
Venclexta + Rituxan in R/R CLL

PB MRD negativity maintained over time regardless of risk features

Bendamustine + Rituxan



Venclexta + Rituxan



MRD status: Negative: $<10^{-4}$ Intermediate-positive: 10^{-4} to $<10^{-2}$ High-positive: $\geq 10^{-2}$ Missing PD/death/withdrew

	V+R	B+R
ITT population	62	13
	p<0.0001**	
Del(17p) and/or TP53 mut		
Yes	57	5
No	66	20
IGVH		
Unmutated	61	15
Mutated	64	16

Phase III update (MURANO):

- PB MRD negativity kinetics for V+R are durable reflecting deep responses and correlate well with clinical outcome
- High PB MRD negativity for V+R achieved regardless of risk features (del17p, TP53mut, IGVH) contrary to B+R
- MURANO data filed in the US and EU; PDUFA date set for June 28
- Ph III (CLL14) results for Gazyva + Venclexta in 1L CLL expected in early 2019

Hillmen P. *et al*., ASCO 2018; PB MRD=peripheral blood minimal residual disease; PB MRD assessed by ASO-PCR and/or 8-color flow cytometry; PB MRD status was reported as follows: MRD+ if either ASO-PCR or flow-cytometry positive or if missing data or assay failure; V=Venclexta in collaboration with AbbVie; R=Rituxan; B=bendamustine

Venclexta + azacitidine/decitabine in 1L AML for older patients

Deep and durable responses regardless of risk status and age

Cohort	N	ORR N (%)	CR/CRi N (%)	uMRD after CR/CRi n/N (%)	Median (months)	
					mDOR of CR/CRi	mOS
All patients	**145**	**99 (68)**	**97 (67)**	**27/97 (29)**	**11.3 (8.9, NR)**	**17.5 (12.3, NR)**
V+aza/dec 400mg	**60**	**44 (73)**	**44 (73)**	**17/44 (39)**	**12.5 (7.8, NR)**	**NR (11.0, NR)**
V+azacitidine	29	22 (76)	22 (76)	10/22 (45)	NR (5.6, NR)	
V+decitabine	31	22 (71)	22 (71)	7/22 (32)	12.5 (5.1, NR)	
V+aza/dec 800mg	**74**	**50 (68)**	**48 (65)**	**10/48 (21)**	**11.0 (6.5,12.9)**	**17.5 (10.3,NR)**
V+azacitidine	37	22 (59)	21 (57)	7/21 (33)	11.7 (4.6, 12.9)	
V+decitabine	37	28 (76)	27 (73)	3/27 (11)	9.2 (5.9, NR)	
Historical azacitidine	**215**		**60 (28)**		**10.4**	**10.4**
Historical decitabine	**242**		**63 (26)**		**NR**	**7.7**

Phase Ib update (NCT02203773):

- Strong responses across risk subgroups and age >75 years compare favorably to historic results
- mOS not reached for the 400mg dose comparing favorably to historic results of 10.4m for aza and of 7.7m for dec
- 400mg V+aza/dec dose established due to best benefit-risk profile; Ph III (Viale-A) of V+aza in 1L AML on-going
- Accelerated filing of Ph Ib data expected by mid 2018

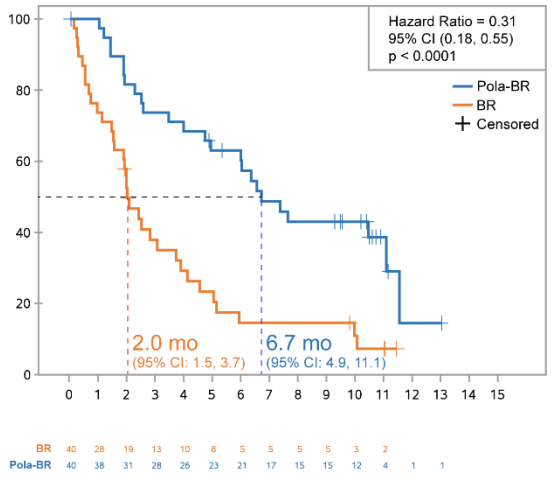
DiNardo C. D. *et al.*, ASCO 2018; Kantarjian J Clin Onc 2012; Dombret Blood 2015; aza=azacitidine; dec=decitabine; ORR=overall response rate; CR=complete remission; CRi=complete remission with incomplete marrow recovery; uMRD=undetectable minimal residual disease (less than 10^{-3} % leukemic cells as detected by multicolor flow cytometry in bone marrow aspirates at any measurement after achieving CR/CRi); mDOR=median duration of response; mOS=median overall survival; NR=not reached; V=Venclexta (in collaboration with AbbVie)

Polatuzumab vedotin + BR in R/R DLBCL

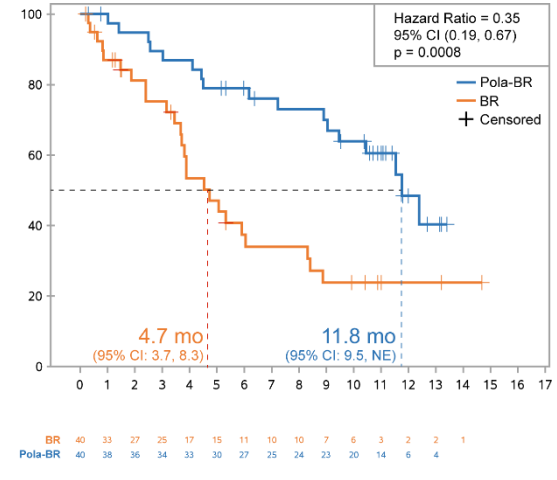
PFS/OS benefit regardless of prior treatment and disease status

	Pola + BR (N=40)	BR (N=40)
PET-CR at EOT (%)	40	15
mPFS (months)	**6.7 (4.9, 11.1)**	**2.0 (1.5, 3.7)**
HR (95% CI)	**0.31 (0.18, 0.55); p<0.0001**	
2 L	11.1 (10.4,NE)	3.7 (1.5, 5.1)
3 L+	6.0 (4.0, 7.6)	2.0 (1.5, 2.8)
Relapsed	11.1 (10.4, NE)	5.1 (2.5, 10.0)
Refractory	6.0 (3.5, 7.4)	1.9 (1.1, 2.8)
mOS (months)	**11.8 (9.5, NE)**	**4.7 (3.7, 8.3)**
HR (95% CI)	**0.35 (0.19, 0.67); p=0.0008**	
2 L	NR (10.5, NE)	5.9 (3.9, 8.4)
3 L+	11.5 (8.9, NE)	3.8 (3.2, 8.9)
Relapsed	NR (6.0, NE)	NR (NE, NE)
Refractory	11.5 (7.2, 12.4)	3.8 (3.2, 5.3)

Progression Free Survival



Overall Survival



Phase II update (GO29365):

- CR, PFS, OS were positive with a PFS HR of 0.31 (p<0.0001) and an OS HR of 0.35 (p=0.0008)
- OR, CR, PFS and OS were positive regardless of prior line of therapy (2L/3L+) or disease status (relapsed/refractory)
- Polatuzumab vedotin can be safely administered in combination with BR
- Accelerated filing of Ph II data expected in H2 2018

Sehn L. H. *et al*., ASCO 2018; PET-CR=positron emmission tomography complete responses; EOT=end of treatment; mPFS=median progression free survival; mOS=median overall survival; HR=hazard ratio; OR=overall reponse; CR=complete response; Pola=polatuzumab vedotin (in collaboration with Seattle Genetics); BR=bendamustine + Rituxan

ASCO Highlights

Hematology

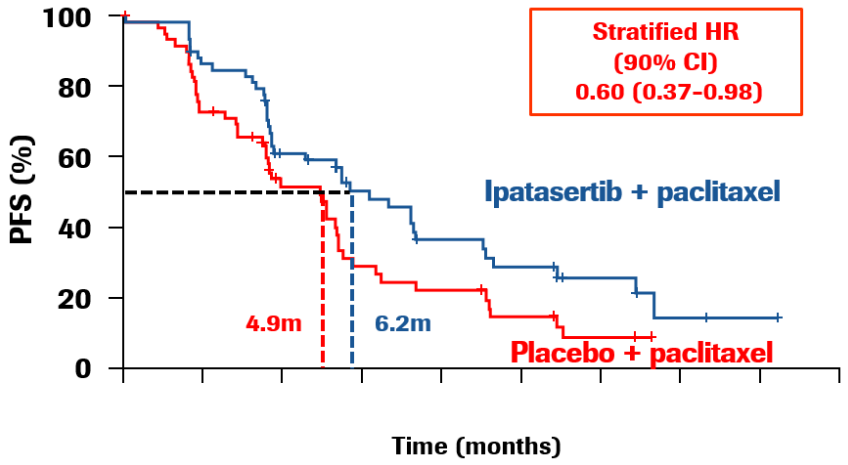
Breast

Lung

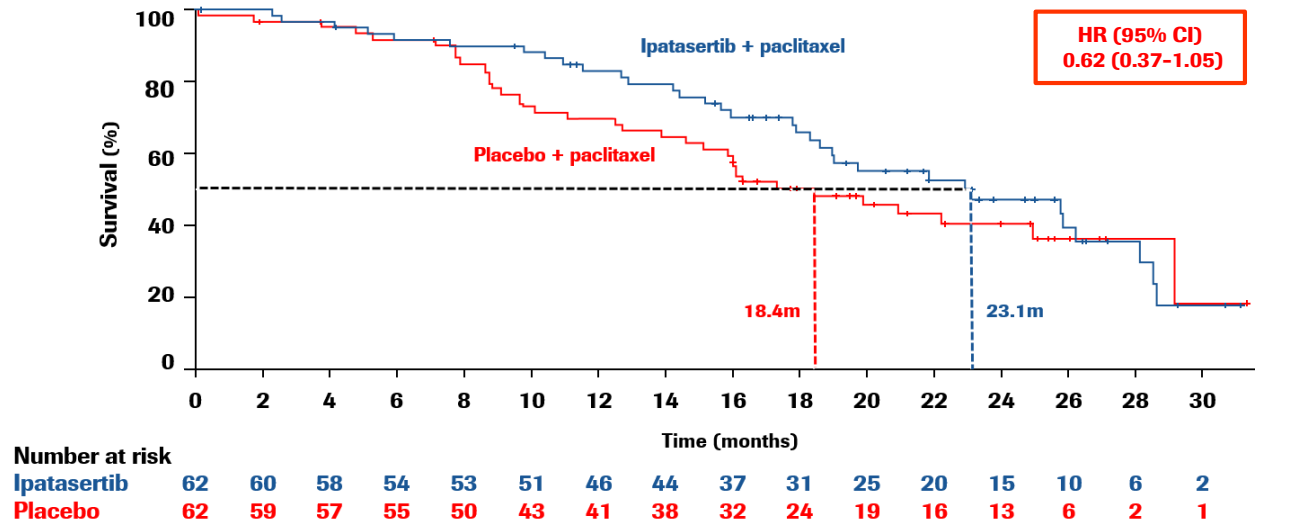
Ipatasertib + paclitaxel in 1L advanced TNBC

PFS benefit and OS update

PFS (ITT)



OS (ITT)



Ph II update (LOTUS):

- PFS HR in all comers was 0.6 vs 0.44 for patients with PIK3CA/AKT1/PTEN-altered tumors as determined by FMI`s FoundationOne NGS assay
- Trend towards improved OS with a stratified OS HR in all comers of 0.62; Final OS results expected in 2019
- IPATunity130 (NCT03337724), a randomized phase III trial, is evaluating ipatasertib + paclitaxel as 1L treatment for PIK3CA/AKT1/PTEN-altered advanced TNBC (cohort 1) and in HR+/HER2- mBC (cohort 2)

Dent R. *et al*., ASCO 2018; PFS=progression free survival; OS=overall survival; ITT=intent to treat; HR=hazard ratio; FMI=Foundation Medicine; NGS=next generation sequencing; HR=hormone receptor; mBC=metastatic breast cancer

ASCO Highlights

Hematology

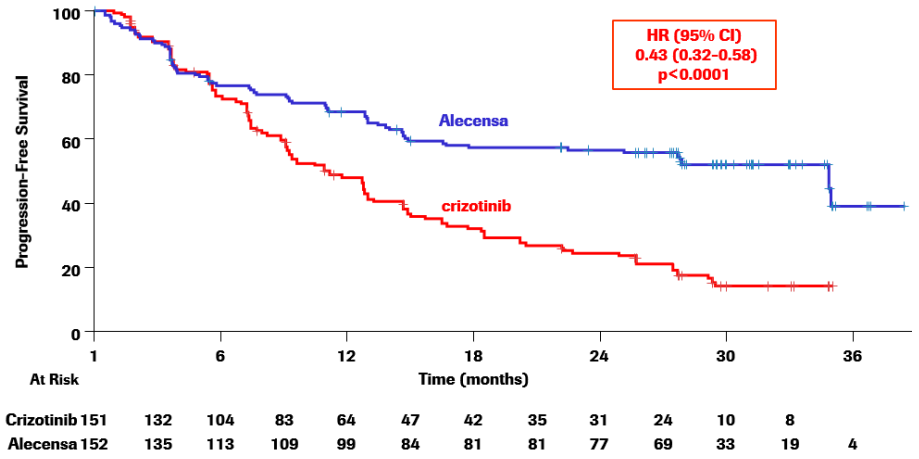
Breast

Lung

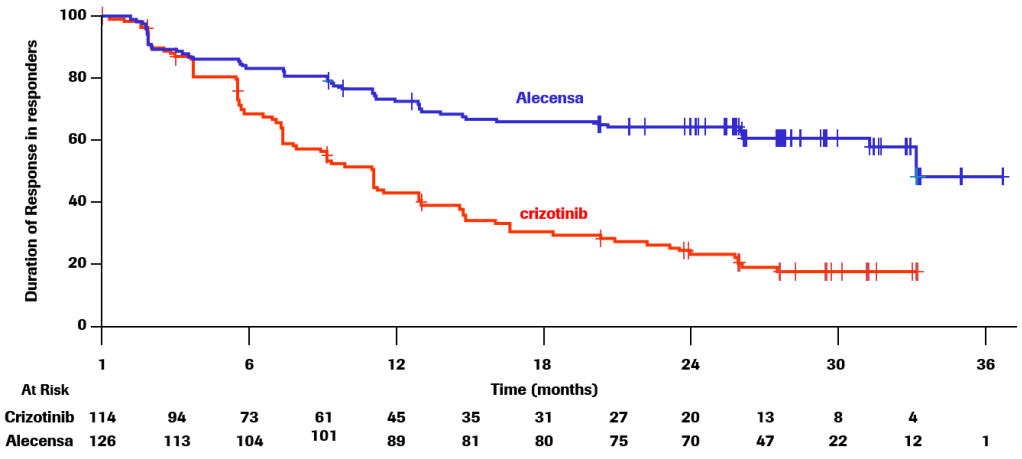
Alecensa in 1L ALK+ NSCLC

Alecensa currently more than triples PFS and DOR vs crizotinib

PFS* (ITT)



DOR* (responders)



Ph III update (ALEX):

- Median PFS for Alecensa was 34.8m vs 10.9m for crizotinib with a stratified HR 0.43 and in patients with baseline CNS metastases median PFS was 27.7m vs 7.4m (HR 0.35). Median DOR for Alecensa was 33.1m vs 11.1m for crizotinib. OS data are still immature.
- Alecensa established as standard of care in 1L ALK+ NSCLC due to significantly improved efficacy and better safety
- Alecensa`s efficacy likely reflects more potent inhibition (also in the CNS), as well as suppression of common on-target resistance mechanisms

Camidge D. R. *et al,* ASCO 2018; *Investigator assessment; PFS=progression free survival; ITT=intent to treat; DOR=duration of response; HR=hazard ratio; CNS=central nervous system; ORR=overall response rate; Alecensa (alectinib) in collaboration with Chugai

Phase III oncology pipeline keeps expanding

31 trials and unique combinations across multiple diseases

Lung: NSCLC, SCLC, ALK+NSCLC

1L non-sq	Tecentriq+carbo/pac+/-Avastin	**IMpower150**	✓
1L non-sq	Tecentriq+carbo+nab-pac	**IMpower130**	✓
1L sq	Tecentriq+carbo+pac/nab-pac	**IMpower131**	✓
1L non-sq	Tecentriq+cis/carbo+pem	**IMpower132**	
1L Dx+	Tecentriq	**IMpower110**	
Adj	Tecentriq	**IMpower010**	
1L SCLC	Tecentriq+carbo+etoposide	**IMpower133**	

Melanoma

1L BRAFwt	Tecentriq+Cotellic	**IMspire170**
1L BRAFmut	Tecentriq+Cotellic+Zelboraf	**IMspire150 TRILOGY**

Renal

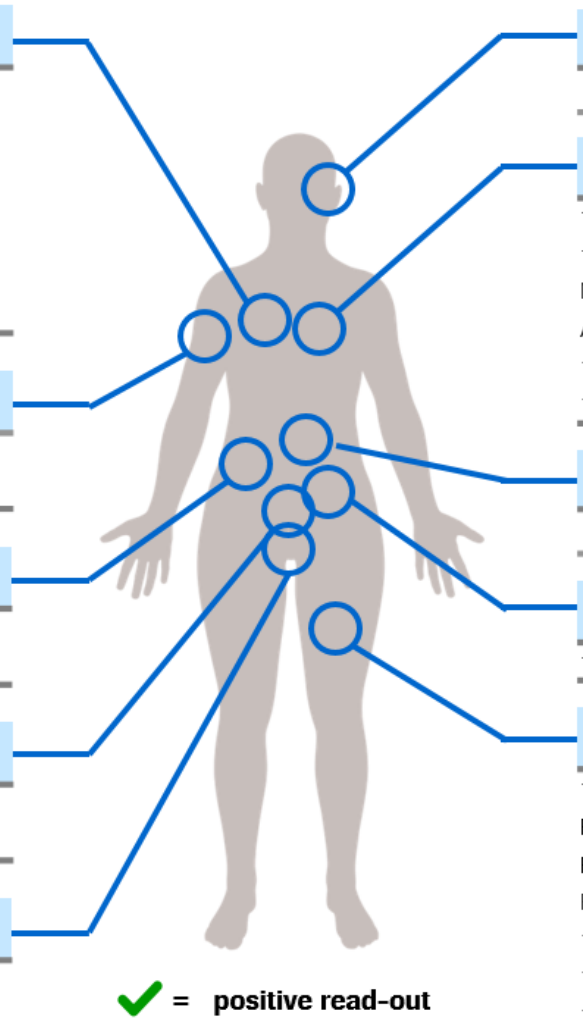
1L	Tecentriq+Avastin	**IMmotion151**	✓
Adj	Tecentriq	**IMmotion010**	

Bladder

1L	Tecentriq+/-gem/plat	**IMvigor130**
Adj MIBC	Tecentriq	**IMvigor010**

Prostate

1L CRPC	ipatasertib+abiraterone	**IPATential150**
2/3L CRPC	Tecentriq+enzalutamide	**IMbassador250**



✓ = **positive read-out**

Head and neck

Adj SCCHN	Tecentriq+/-chemo	**IMvoke010**

Breast: TNBC; HER2+; ER+/HER2-

1L TNBC	Tecentriq+nab-pac	**IMpassion130**
1L TNBC	Tecentriq+pac	**IMpassion131**
Neoadj TNBC	Tecentriq+nab-pac	**IMpassion031**
Adj TNBC	Tecentriq+paclitaxel	**IMpassion030**
1L Dx+ TNBC	ipatasertib+paclitaxel	**IPATunity130 C1**
1L Dx+ HR+ mBC	ipatasertib+paclitaxel	**IPATunity130 C2**

Hepatocellular carcinoma

1L	Tecentriq+Avastin	**IMbrave150**

Ovarian

1L	Avastin/carbo/pac+/-Tecentriq	**IMaGYN050**

Hematology: CLL, MM, AML, DLBCL

1L CLL	Venclexta*+Gazyva	**CLL14**	
R/R CLL	Venclexta*+Rituxan	**MURANO**	✓
R/R MM	Venclexta*+bortezomib/dexa	**BELLINI**	
R/R AML	idasanutlin+cytarabine	**MIRROS**	
1L AML	Venclexta*+azacitidine	**Viale-A**	
1L AML	Venclexta*+LDAC	**Viale-C**	
1L DLBCL	polatuzumab vedotin+Rituxan-CHP	**POLARIX**	

* Venclexta in collaboration with AbbVie; Gazyva in collaboration with Biogen; Polatuzumab vedotin in collaboration with Seattle Genetics

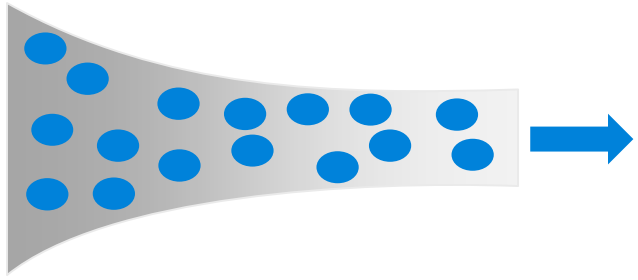
Oncology Strategy Update (Digital Health and PHC)

Daniel O'Day
CEO Roche Pharmaceuticals

Our innovation strategy remains unchanged

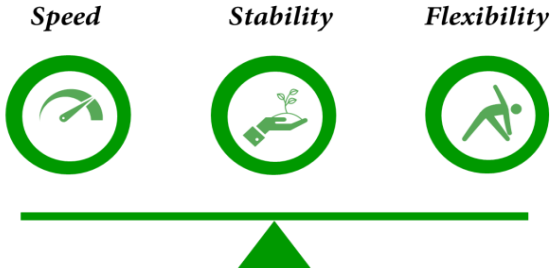
Accelerating data & advanced analytics efforts as central pillar of our strategy

Pipeline & commercial delivery



World-leading data & advanced analytics

Organisational transformation



Diverse, multidisciplinary talent base to drive innovation & execution

Rejuvenating the portfolio

Through continuously improving standard of care

Replace existing businesses

MabThera	Gazyva, Venclexta, polatuzumab vedotin, Sub Cut
Herceptin	Perjeta, Kadcyla, Sub Cut
Avastin	Tecentriq, entrectinib
Lucentis	VA2, port delivery
Tamiflu	baloxavir (Cap Endo)

Entering new franchises

MS:
Ocrevus

Hemophilia:
Hemlibra

CNS:
SMA, Autism, Huntington's

ASCO / WFH 2018 highlights

Hemlibra:	HAVEN 3 / 4 with superior profile
Tecentriq:	IMpower150: OS benefit IMpower 130: OS benefit IMpower 131: PFS benefit +Avastin in HCC: Meaningful responses
Venclexta:	MURANO in R/R CLL: New SoC showing high and durable MRD negativity 1L AML (1b): Deep & durable responses
Polatuzumab:	R/R DLBCL: Strong efficacy confirmed
Ipatasertib:	LOTUS (Ph II) in TNBC: PFS benefit
Alecensa:	ALEX 1L ALK+: >34 months PFS benefit

VA2=anti-VEGF/anti-angiopoietin-2 bispecific antibody; MS=multiple sclerosis; SMA=spinal muscular atrophy; HCC=hepatocellular carcinoma; R/R CLL=relapsed/refractory (R/R) chronic lymphocytic leukemia; AML=acute lymphocytic leukemia; DLBCL=diffuse large B-cell lymphoma; TNBC=triple negative breast cancer; ALK=anaplastic lymphoma kinase

Driving personalized healthcare forward

Personalize treatment through understanding of a patient's tumor

	Blockbuster medicines	Targeted therapies	Personalized treatments
			
Target population	Large: unspecified	Medium: sub-group	Small: individual patient
Diagnostics	No specific biomarkers	Single disease marker	Comprehensive NGS & response monitoring
Treatment	One medicine fits all	Targeted agents	Personalized combos of targeted & CIT agents

Increasing need for advanced data analytics capabilities

NGS=Next generation sequencing; CIT=Cancer Immunotherapy

Data insights leveraged along the value chain

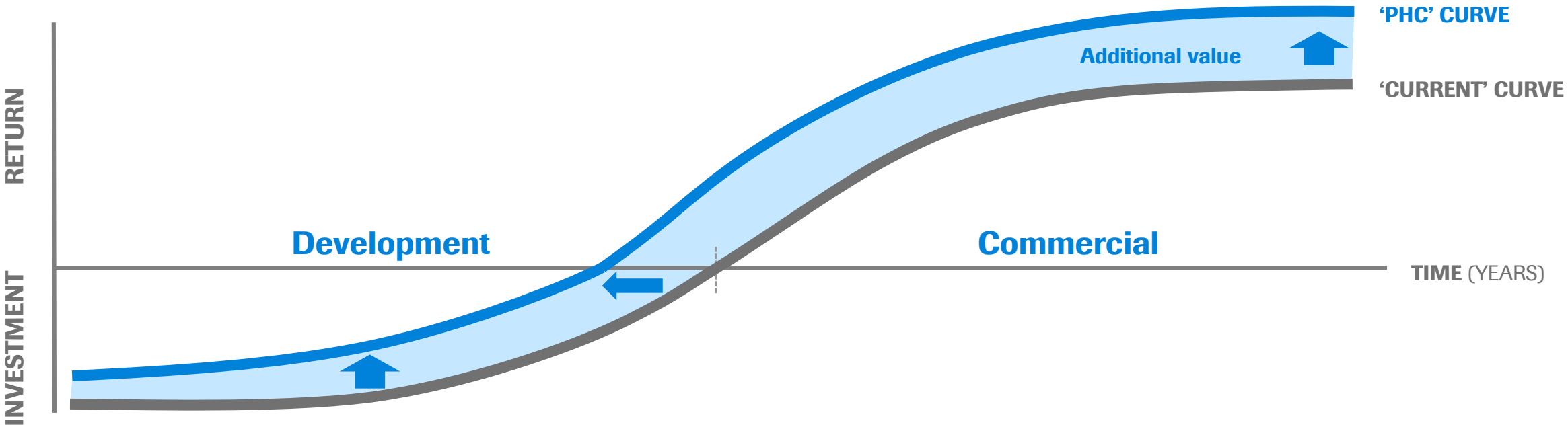
Foundation of future competitive differentiation

Smarter, more efficient R&D	Biological insights & target identification	Efficient trial design & recruitment	Improved regulatory & safety processes
Improved access & personalized patient care	Comprehensive Dx & personalized treatment options	Clinical decision support	Value proof and reimbursement

Dx=Diagnostics

… creating direct & indirect value to our business

More effective R&D and more differentiated products



Lower costs

Faster speed to market

Higher return

PHC=Personalized Healthcare

Acquisition of Flatiron

Leading player driving personalized patient care in oncology

Strong network in Oncology

- Leading EMR system and analytics solutions used by ~15% of US oncologists and covering ~15% of active patients

Leading real world data base

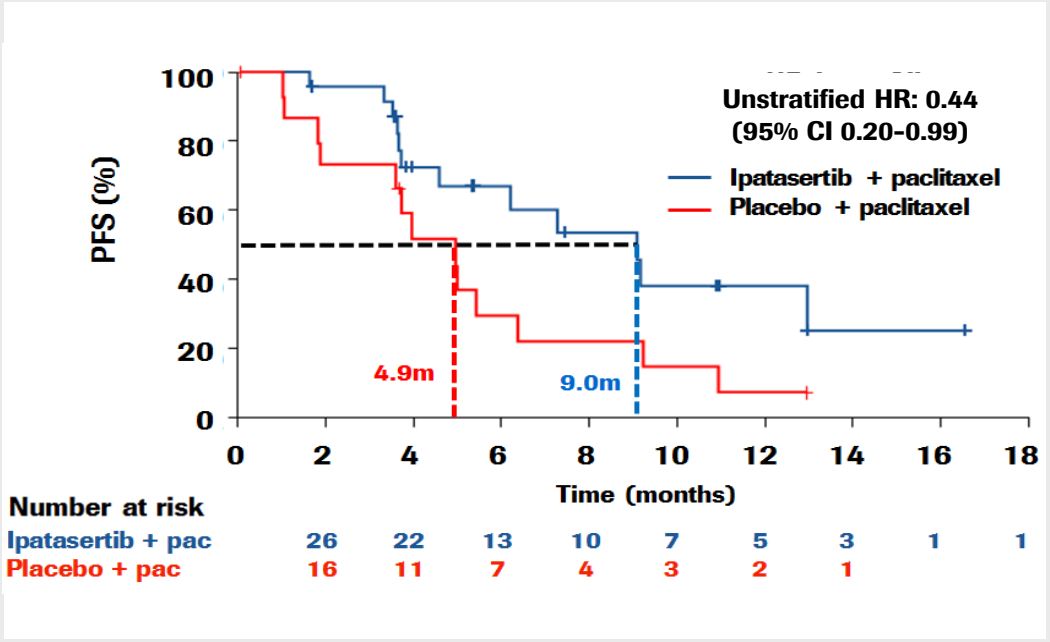
- Research-quality EMR data base covers 10m patients, over 2m of them active
- 90% of large Pharma companies are working with Flatiron data

While Flatiron will remain independent, acquisition will help to expand our existing partnership and provide required resources to accelerate key strategic projects in the field of personalized healthcare

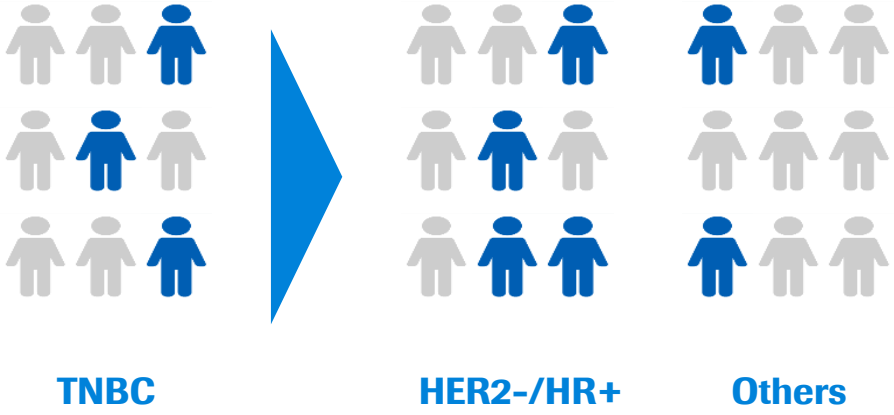
EMR=Electronic Medical Records

Generating new biologic insights and pan-tumor strategies
PIK3CA/AKT1/PTEN-altered tumors in the LOTUS trial

Retrospectively identified PIK3CA/AKT1/PTEN-altered sub-population with increased benefit



Utilizing FMI database to expand ipatasertib clinical trial program across different tumors



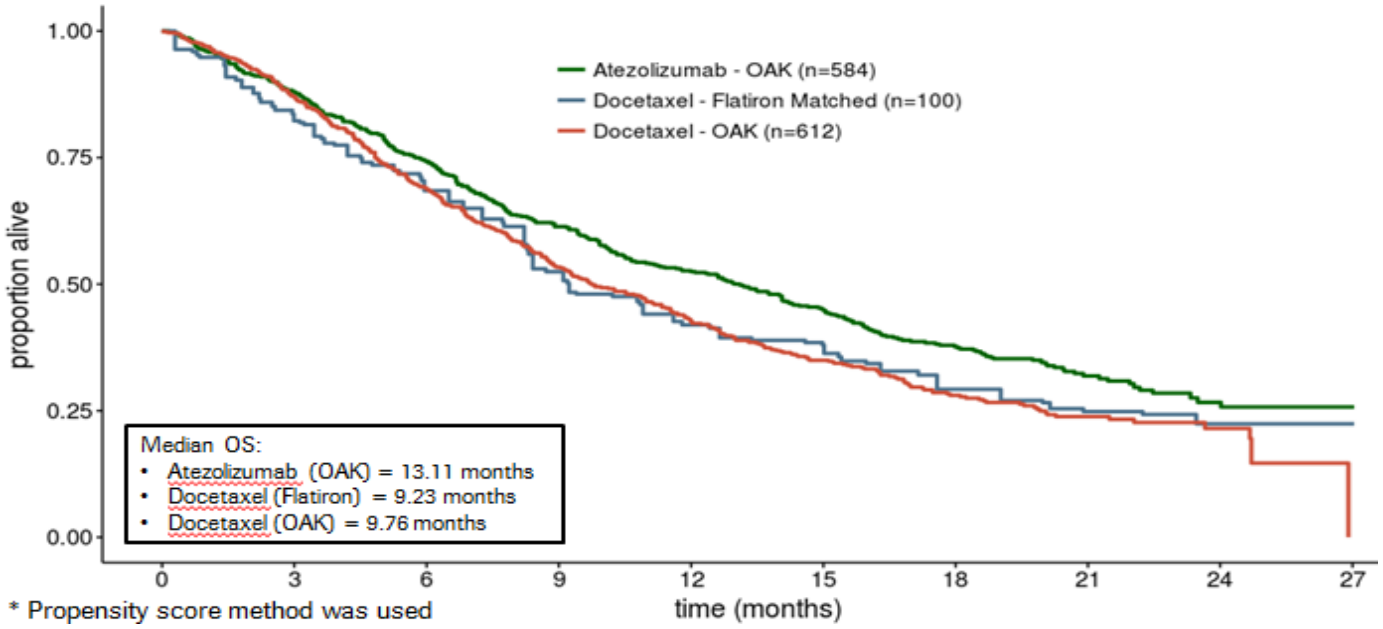
FMI key in identifying relevant patient sub-populations

FMI=Foundation Medicine; TNBC=Triple Negative Breast Cancer

Creating external control arm with RWD

Virtual control arm for Tecentriq in 2L NSCLC (OAK)

Retrospectively replicating docetaxel control arm in the Tecentriq OAK trial



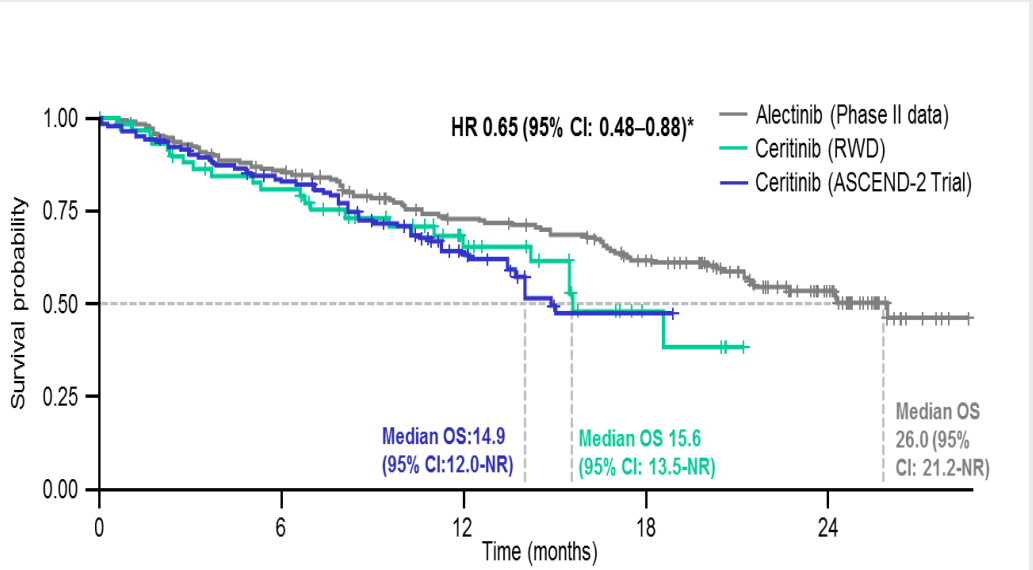
Leveraging FH EMR data comprehensiveness & quality for more effective clinical development

RWD=Real World Data; NSCLC=Non Small Cell Lung Cancer; FH=Flatiron Healthcare; EMR=Electronic Medical Records

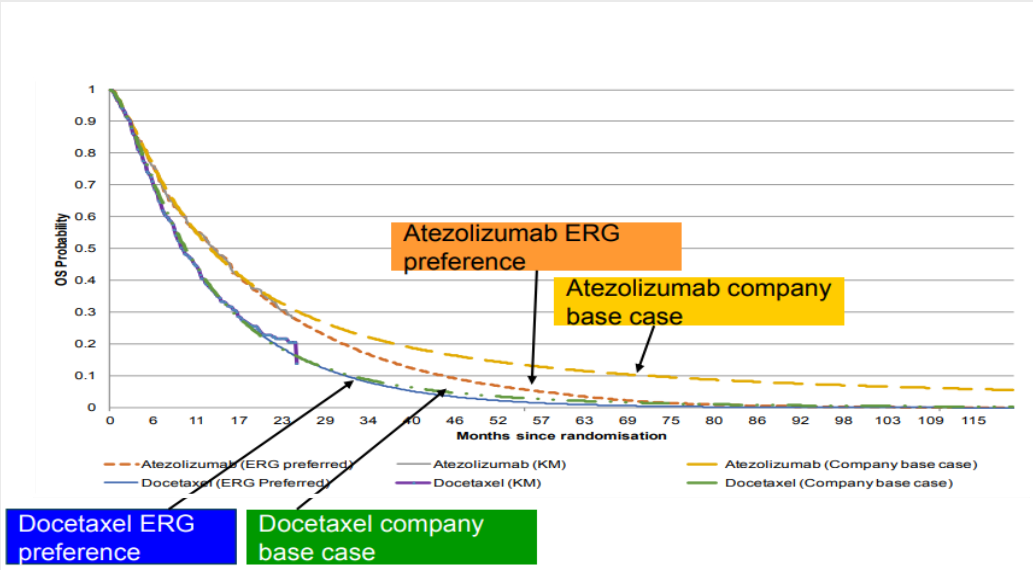
Leveraging RWD for regulatory approvals & HTA negotiations

Accelerating access and providing proof of value

Virtual control arm to supplement Alecensa in 2L ALK+ lung single-arm trials



NICE appraisal for Tecentriq in 2L NSCLC (OAK)



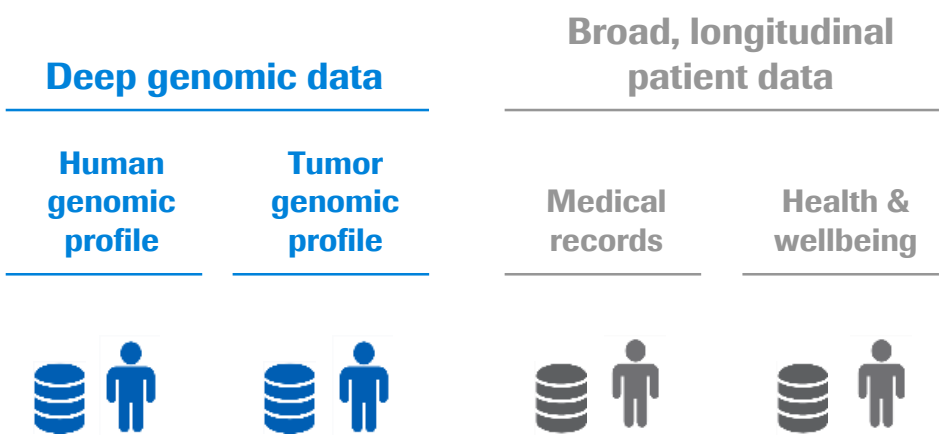
Leveraging FH EMR data in regulatory submissions and reimbursement discussions

RWD=Real World Data; HTA=Health Technology Assessment; NICE=National Institute for Health and Care Excellence; NSCLC=Non Small Cell Lung Cancer; FH=Flatiron Healthcare; ERG=Evidence Review Group; EMR=Electronic Medical Records

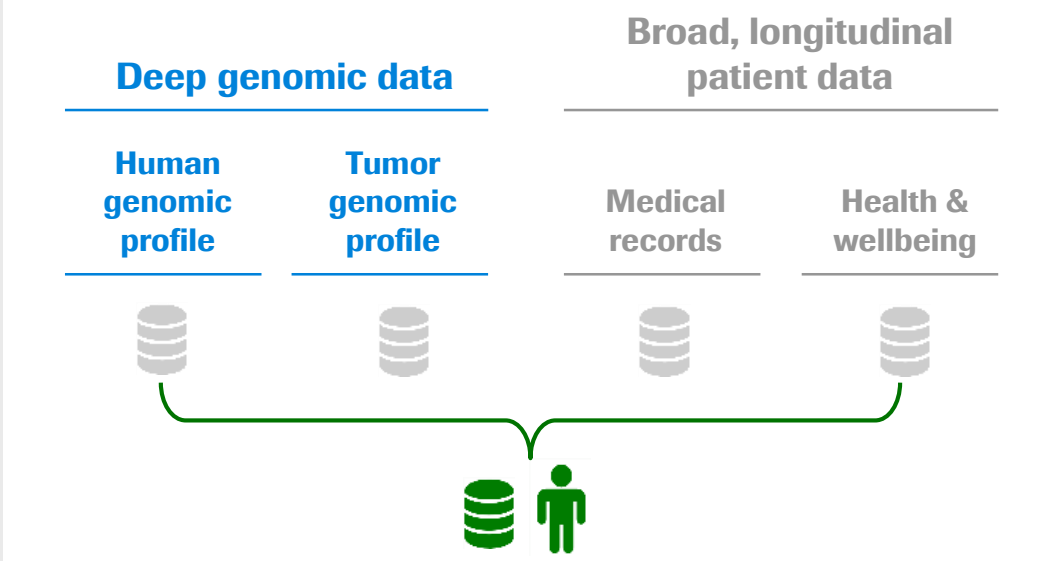
How to build true Meaningful Data at Scale?

Integrating complementary patient data will drive competitive advantage

From a world with specific, disconnected databases…



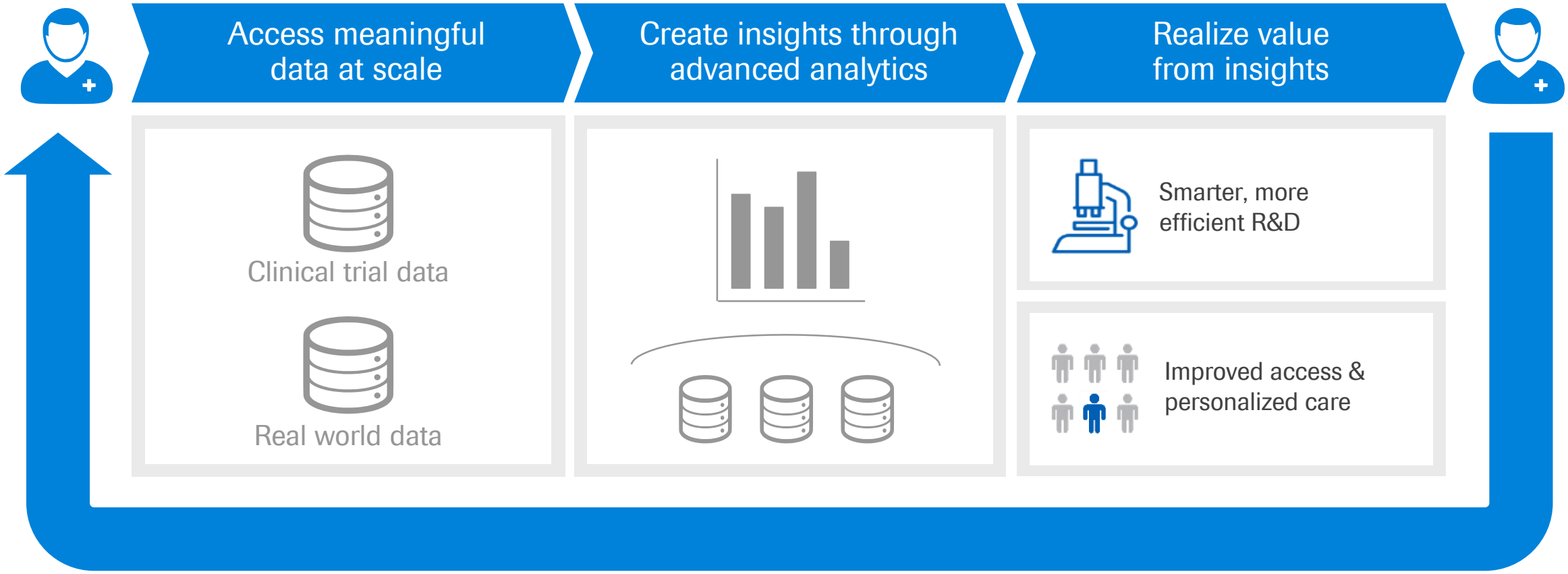
…to a world with truly integrated and meaningful data on each patient



Integrating deep and broad patient data has significant value potential to Roche and stakeholders

Our vision of personalized healthcare

Leveraging large data and advanced analytics



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FOUNDATION MEDICINE

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Doing now what patients need next