Roche Analyst Event

Tuesday, 08 June 2021

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2 legislative and regulatory developments and economic conditions;
3 delay or inability in obtaining regulatory approvals or bringing products to market;
4 fluctuations in currency exchange rates and general financial market conditions;
5 uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6 increased government pricing pressures;
7 interruptions in production;
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Welcome

Karl Mahler, Head of Investor Relations and Group Business Planning

Early pipeline programs in focus

William Pao, M.D., Ph.D., Head of Roche Pharma Research and Early Development

Ira Mellman, Ph.D., Vice President, Cancer Immunology, Genentech Research & Early Development

Late-stage pipeline programs in focus

Levi Garraway, M.D., Ph.D., Chief Medical Officer and Head of Global Product Development

ASCO 2021 Highlight

Tecentriq in adjuvant NSCLC: Phase 3 IMpower010 primary results

Heather Wakelee, M.D., Prof. of Medicine, Stanford Univ Medical Center / Deputy Director Stanford Cancer Institute

Q&A

Karl Mahler | Head of Investor Relations and Group Business Planning

Reflecting the quality of research and development at Roche

37 *Breakthrough Therapy Designations (BTD) since 2013*

Year	Molecule	Indication
2020	tiragolumab +Tcq	1L PD-L1+ NSCLC
	mosunetuzumab	3L+ FL
	Tecentriq	unresectable or metastatic ASPS
	Esbriet	uILD
2019	Gavreto	RET fusion-positive NSCLC
	Gavreto	RET mutation-positive MTC
	Cotellic	Histiocytic neoplasms
	Gazyva	Lupus nephritis
	rhPentraxin-2	IPF
	Venclexta + Gazyva	1L unfit CLL
	Kadcyla	Adjuvant HER2+ BC
2018	SPK-8011	Hemophilia A
	Enspryng	NMOSD
	Xolair	Food allergies
	Tecentriq + Avastin	1L HCC
	Hemlibra	Hemophilia A non-inhibitors
	Rozlytrek	NTRK+ solid tumors
2017	Polivy + BR	R/R DLBCL
	Venclexta + LDAC	1L unfit AML
	Zelboraf	BRAF-mutated ECD
	Rituxan	Pemphigus vulgaris

4 *Approvals under Real-Time Oncology review (RTOR) since start of the first pilot program in 2018*

Year	Molecule	Indication
2020	Gavreto	RET fusion-positive NSCLC
	Tecentriq + Avastin	1L HCC
2019	Venclexta + Gazyva	1L unfit CLL
	Kadcyla	Adjuvant HER2+ BC

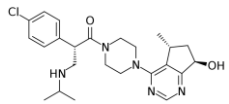
1 *NEW application under RTOR*

Tecentriq in adjuvant NSCLC Phase 3 IMpower010 interim analysis data

Our technology platforms in oncology

Roche pipeline includes differentiated therapeutic platforms

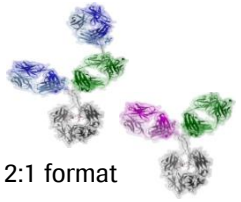
Small molecules



- **giredestrant**
- **belvarafenib**
- **SHP2i**
- **KRAS G12C**

Target oncogenes, induce apoptosis, supress tumor growth

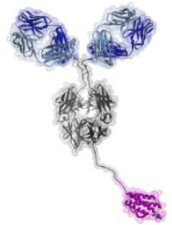
Bi-specific mAb



- **mosunetuzumab**
- **glofitamab**
- **cevostamab**
- **PD1xTIM3**
- **PD1xLAG3**
- **HLA-A2 WT1xCD3**

Engage and activate T cells to kill tumour cells

Fusion protein



- **PD1-IL2v**
- **CD19-4-1BBL**
- **FAP-4-1BBL**

Amplify immune response

mAb

- **tiragolumab**
- **CD25 mAb**

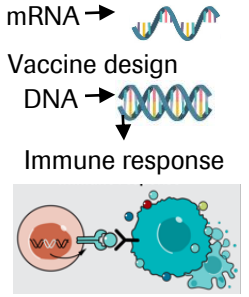
Amplify immune response

Antibody drug conjugate

- **Polivy**

Targeted toxic payload

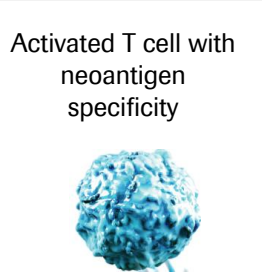
Personalized neoantigen vaccine



- **Autogene cevumeran[2]**
- **VB10.NEO[3]**

Patient's neo-antigens for anti-tumour immune response

Personalized T-cells



- **programmed T-cells[4]**

Patient's neo-antigens for anti-tumour immune response

Examples listed are highlighted during today's presentation

In collaboration with [1]Hanmi [2]Biontech; [3]Vaccibody; [4]Adaptive, [5]SQZ Biotechnology

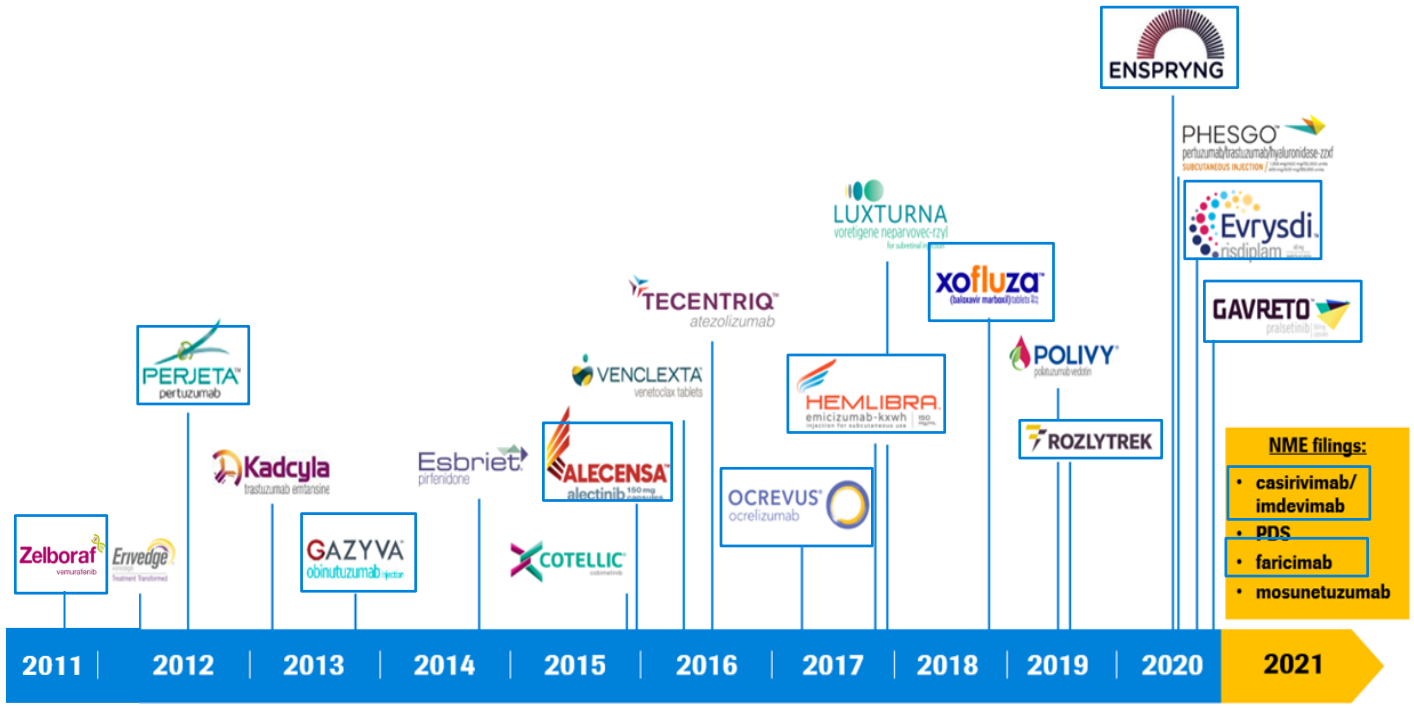
Early pipeline programs in focus

William Pao, M.D., Ph.D. | Head Roche Pharma Research & Early Development (pRED)

Roche pRED's contributions to launching new medicines

Science and innovation have been keys to success

Newly launched Roche medicines since 2011



Roche pRED supported development; *in collaboration with Chugai

Molecules under full development

- **glofitamab** - NHL
- **cibisatamab** – MSS CRC
- **gantenerumab** – AD
- **tominersen** - HD
- **crovalimab*** – PNH
- **SRP9001 –** DMD
- **AT-527** – COVID-19

NHL - Non-Hodgkin Lymphoma; MSS CRC - microsatellite stable colorectal cancer; AD - Alzheimer's Disease; HD - Huntington's Disease; PNH - paroxysmal nocturnal hemoglobinuria; DMD - Duchenne's Muscular Dystrophy

pRED oncology focus areas

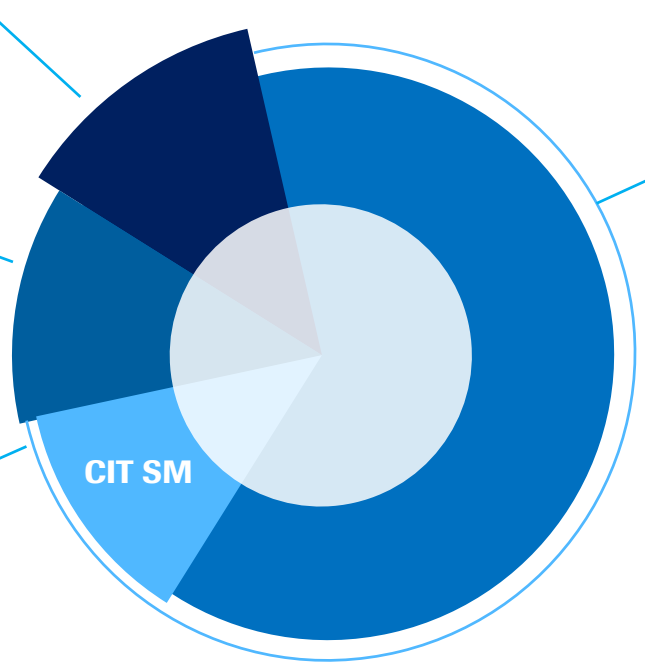
Covering a range of modalities in line with state of the art cancer biology

‘Game Changing’ Innovation

- New targets, technologies, collaborations and partnerships

Molecular Targeted Therapy (MTT) – small molecules

- Cancer signaling
- Targeted protein degradation



Cancer Immunotherapy large molecules

- Direct T-cell engagers
- Generators of tumor selective immune cells
- Modulators of T-cell activity & innate immunity

Cancer immunotherapy small molecules

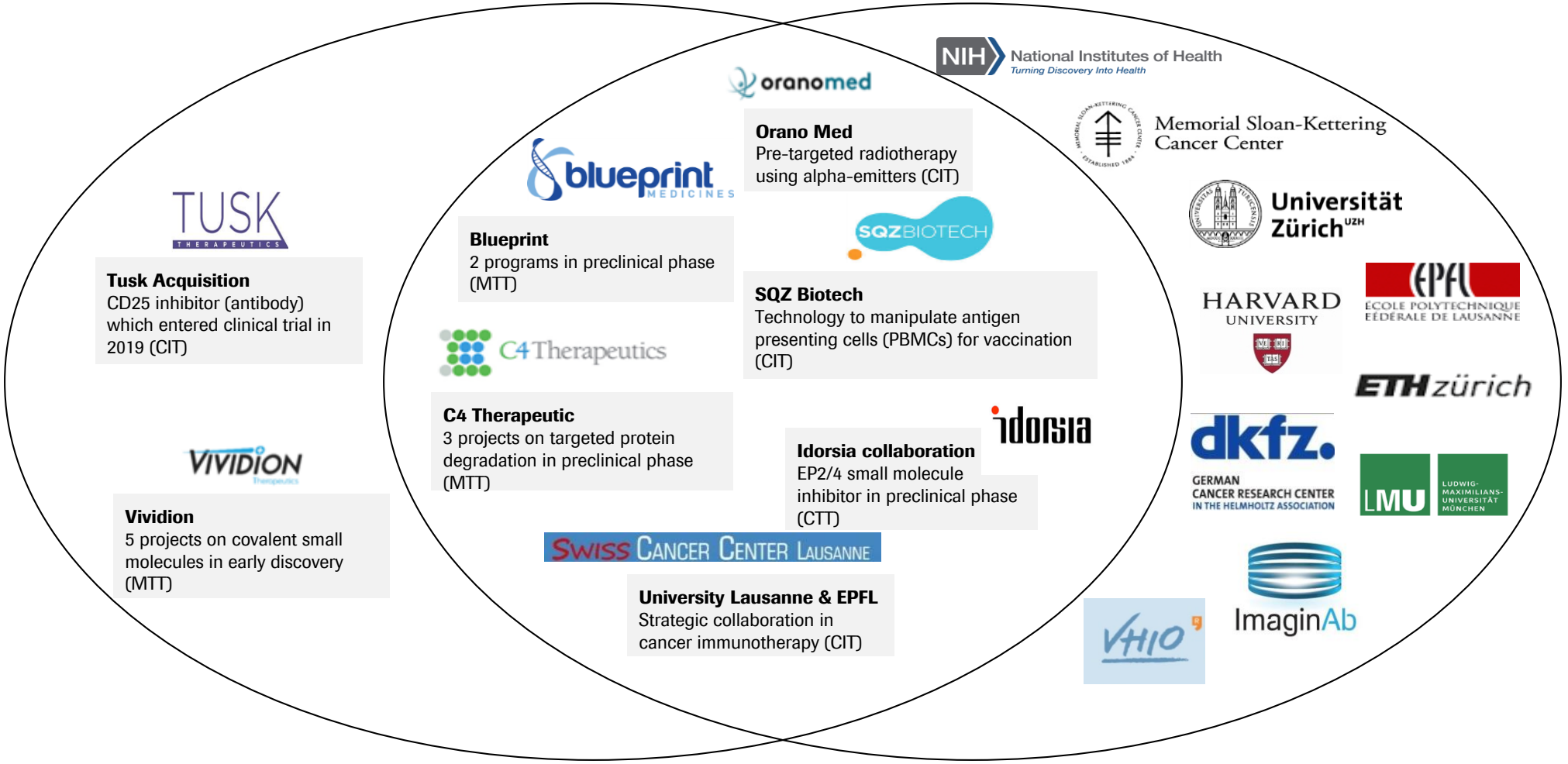
- Modulators of T-cell activity & innate immunity

Segment sizes are representative

Harnessing external innovation: 2018–2021

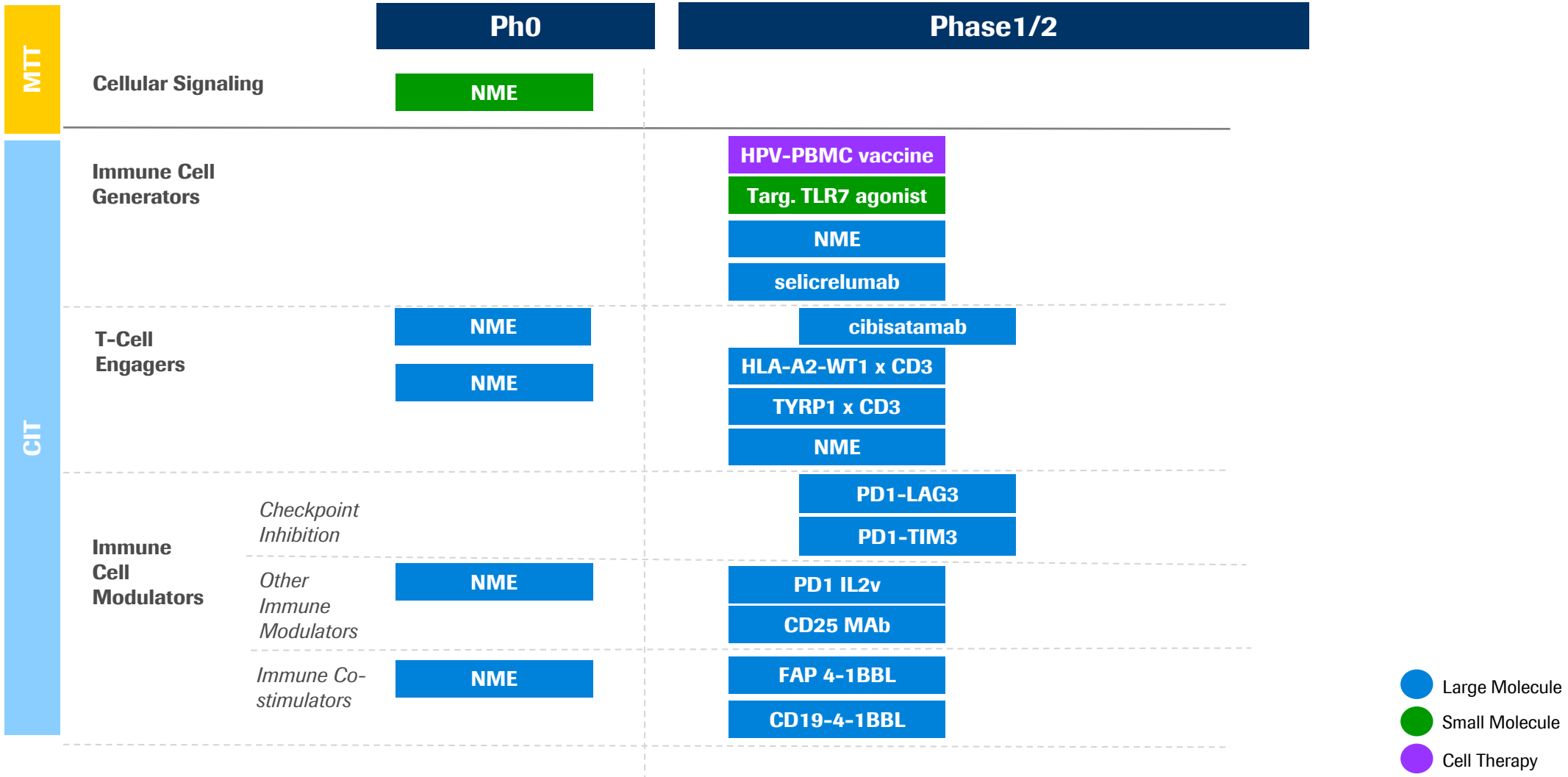
In-licensing projects of high scientific quality and strategic fit

Multiple strategic partnerships with biotech and academia



MTT - Molecular Targeted Therapy; CIT - Cancer Immunotherapy

pRED Oncology development pipeline

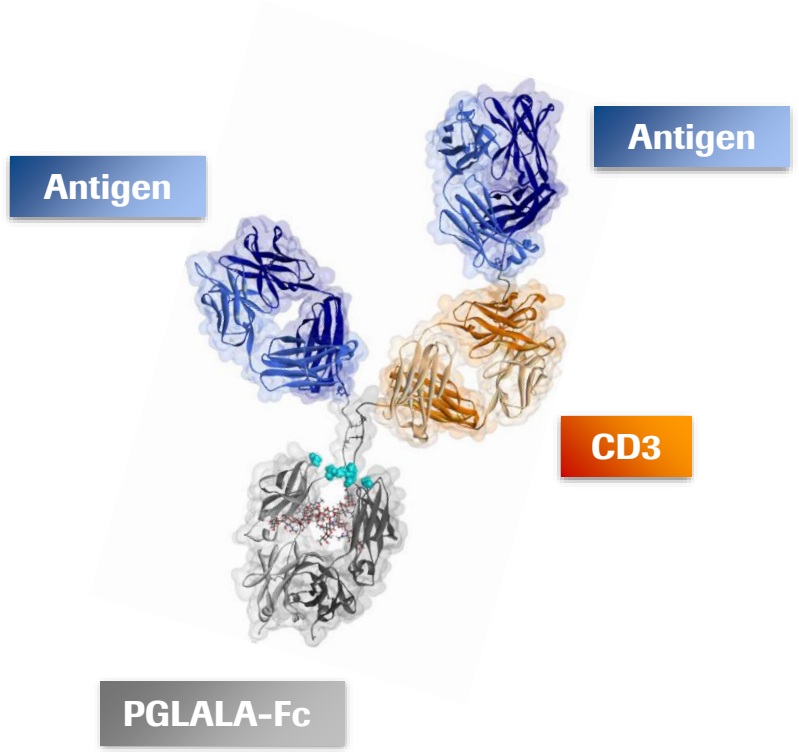


MTT - Molecular Targeted Therapy; CIT - Cancer Immunotherapy; NME – new molecular entity

T-cell Bispecifics in early clinical development: Redirect T-cell attack

Utilizing novel 2:1 format for maximal efficacy

2:1 format TCB, targeting tumor antigen and CD3[1]



Late clinical development

- Cibisatamab – carcinoembryonic antigen; colorectal cancer
- Glofitamab – CD20; Non-Hodgkin lymphoma

Early clinical development

- NME 1 – malignant hematology
- NME 2 – solid tumors
- TYRP1 x CD3 (RG6234) – melanoma

Early clinical development – TCR-like

- HLA-A2 WT1 (RMF peptide) – AML/ALL and solid tumors
- NME 3 – solid tumors

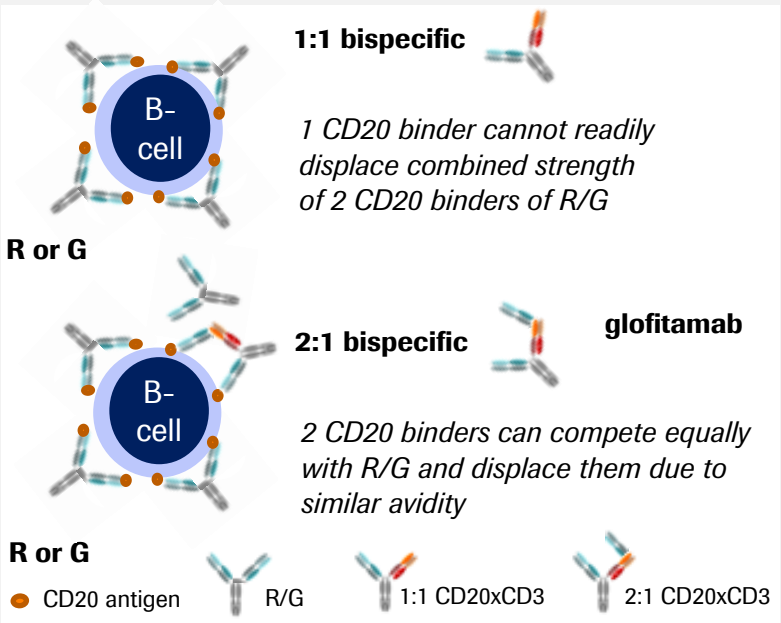
Preclinical development

- Enhance specificity and safety of TCBs by masking the anti-CD3 Fab fragment[2]

1. Bacac et al., *Oncoimmunology*. 2016; Jun 24;5(8); NME – new molecular entity; AML/ALL – acute myelogenous leukemia/acute lymphoblastic leukemia; 2. Geiger et al., *Nat Commun*. 2020; 11: 3196

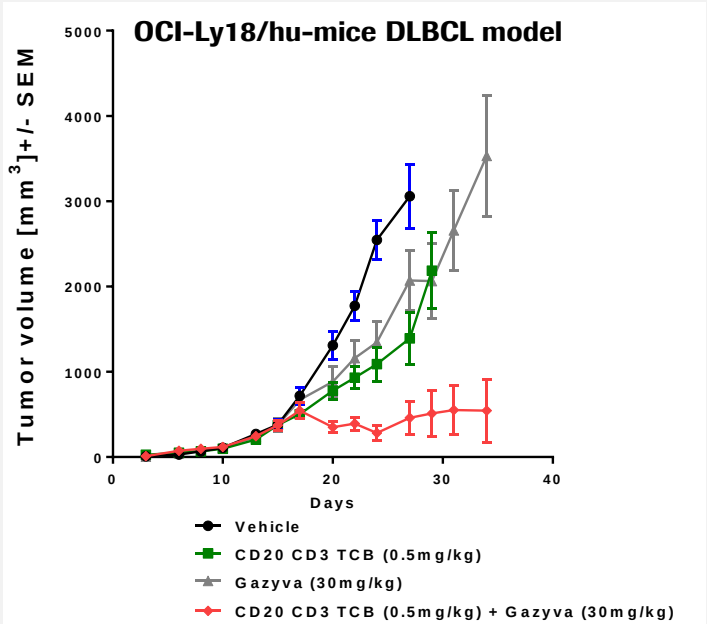
Glofitamab: Flexibility to combine with anti-CD20 mAbs

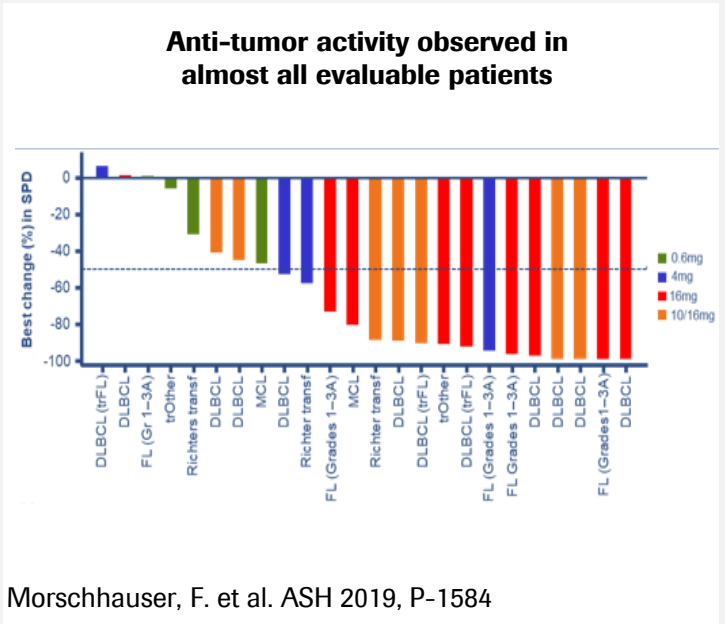
Glofitamab 2:1 format: Option to combine with Rituxan (R) and Gazyva (G)



- Bivalent binding of glofitamab on B-cell allows equal competition with bivalent aCD20s due to similar functional affinity for CD20
- CD20 B-cell occupancy by CD20 x CD3 only 2% for maximum efficacy

Glofitamab + Gazyva: strong efficacy demonstrated in preclinical and clinical studies



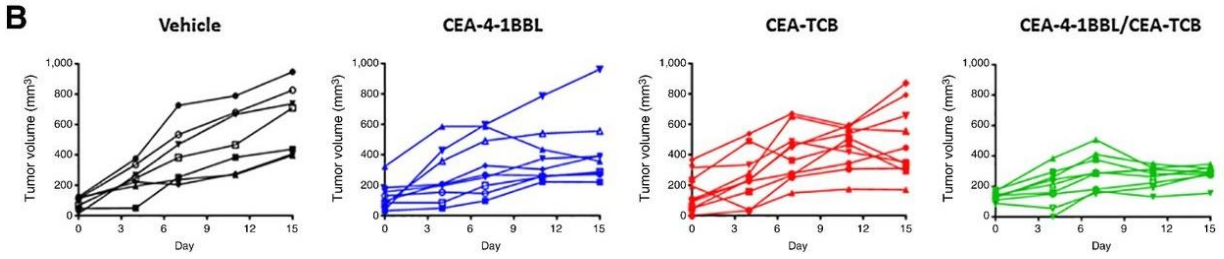


Morschhauser, F. et al. ASH 2019, P-1584

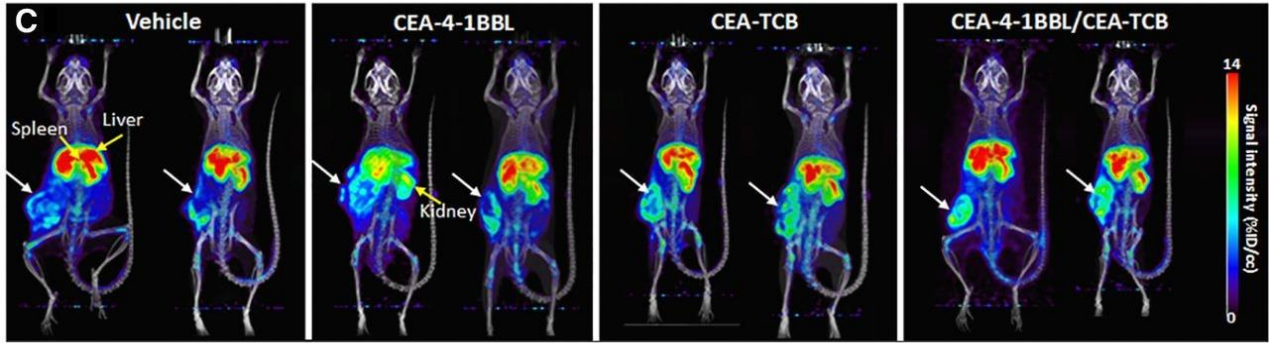
- Dual CD20-targeted therapy with concurrent glofitamab and Gazyva shows promising clinical activity and manageable safety in relapsed or refractory B-cell NHL in Ph Ib
- Comprehensive clinical development program in NHL as single-agent and in combinations

Assessing the potential of rapid non-invasive whole-body monitoring of patients with r/r NHL treated with glofitamab*

Preclinical studies with novel CD8 T-cell PET tracer using CEA TCB as proof of concept



PET/CT imaging of CD8 T-cell infiltration in humanized mice with CEA+ tumors



Griessinger et al., *Cancer Res* 2020;80:2903–13

- CEA-4-1BBL/CEA-TCB combination induced the strongest tumor regression
- PET distribution images 40 h post-injection showed homogenous signals throughout tumor borders and tumor center in CEA-TCB-treated and CEA-4-1BBL/CEA-TCB combo groups, respectively

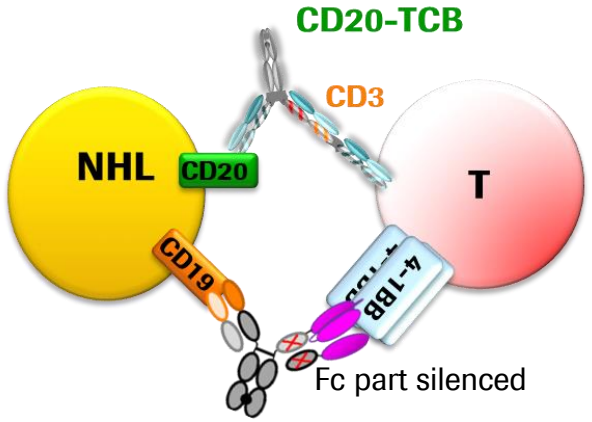
- High sensitivity of 89Zr-Df-IAB22M2C tracer for the detection of intra-tumoral CD8+ T-cell infiltrates as promising monitoring tool for patients' early response to cancer immunotherapy
- *FPI in sub-study of ongoing PhIb to assess potential of rapid non-invasive whole-body monitoring of patients with r/r NHL treated with glofitamab May 2021

*Glofitamab + ^{89}Zr-Df-IAB22M2C PET-Tracer combination, PhIb in r/r NHL, NCT03533283; in collaboration with ImaginAb

Glofitamab in combination with CD19-4-1BBL (RG6076)

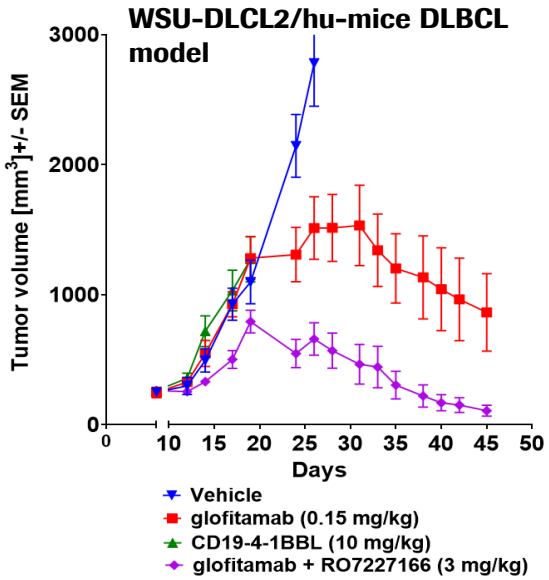
Potential for off-the-shelf alternative to 2nd generation CD19-CAR-T-cell

CD19-4-1BBL + CD20xCD3

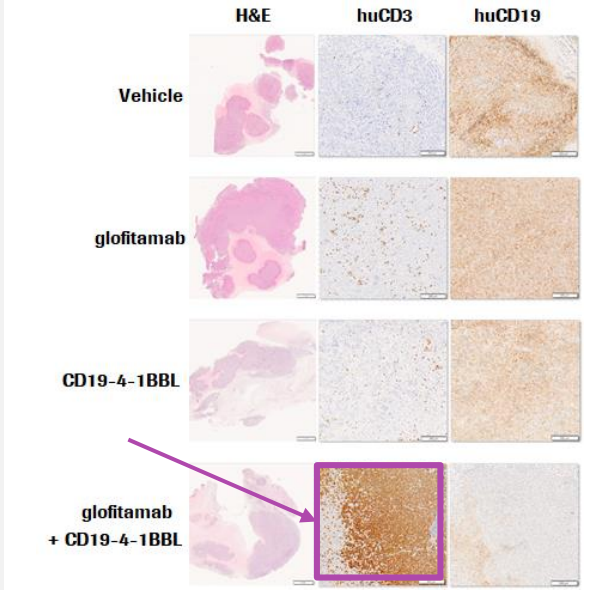


- Signal 1: NK or T-cell activation delivered by glofitamab
- Signal 2: CD19-4-1BBL leads to enhanced NK and T-cell activation and promotes a durable immune response

Improved tumor growth inhibition



Significantly enhanced T-cell infiltration



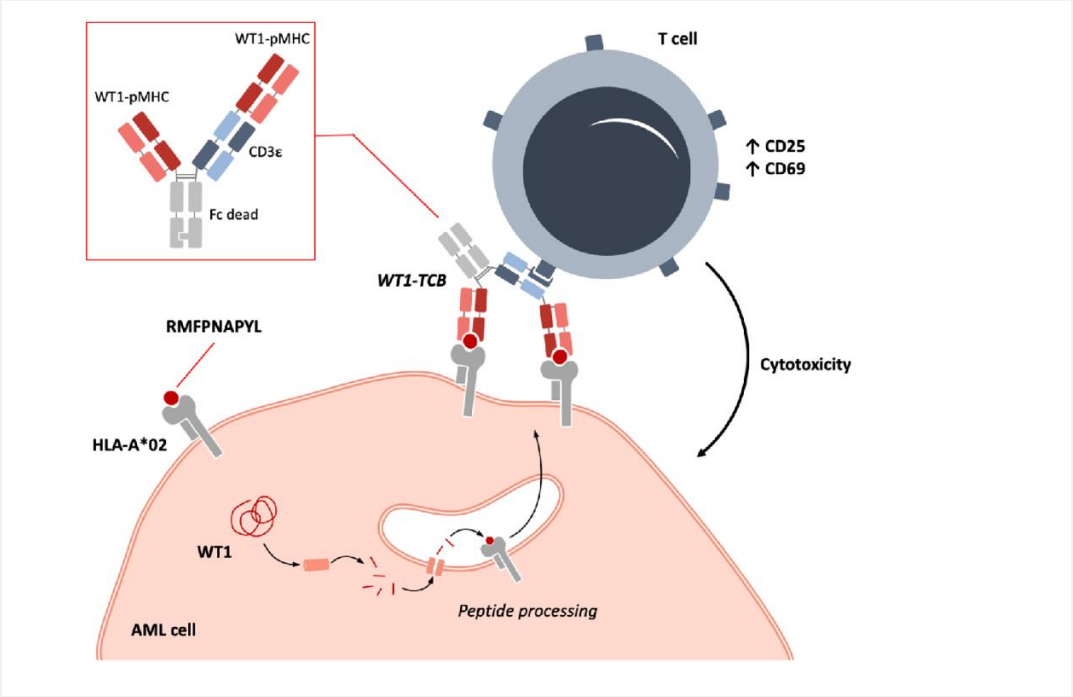
- CD19-4-1BBL enhances *in vivo* effector function of T or NK cells in the presence of CD19+ tumor targets in combination with glofitamab as well as obinutuzumab
- Ph I of CD19-4-1BBL in combination with glofitamab in r/r NHL ongoing

Umaña, P., AACR 2021

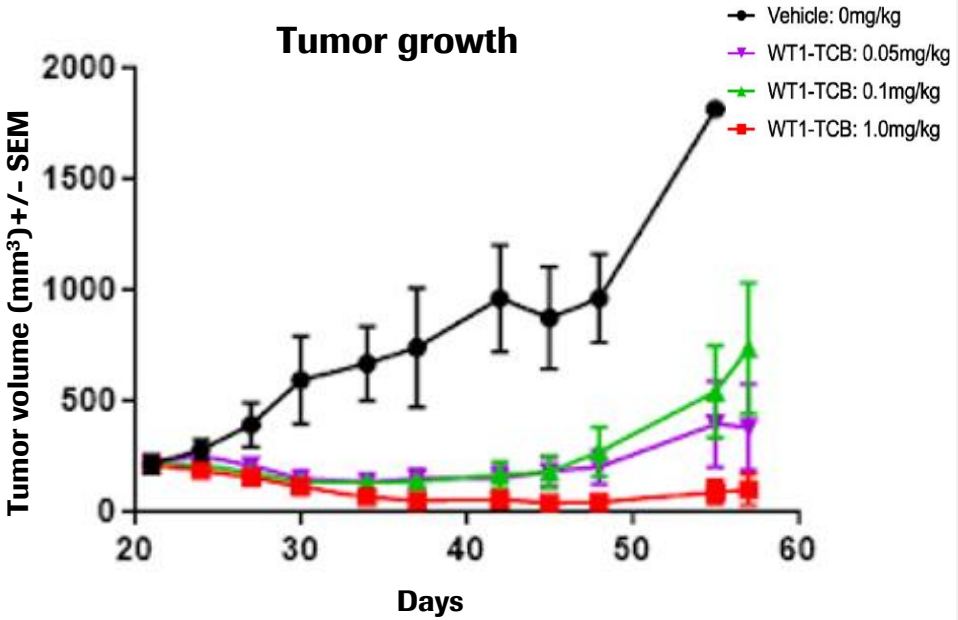
HLA-A2 WT1 x CD3 (RG6007) targeting intracellular oncoprotein WT1

TCR receptor-like T-cell bispecific for heme and solid tumors

Broadens potential tumor targets beyond cell surface proteins



RG6007 induced dose dependent reduction of tumor growth



SKM-1 Model in HSC-NSG Mice

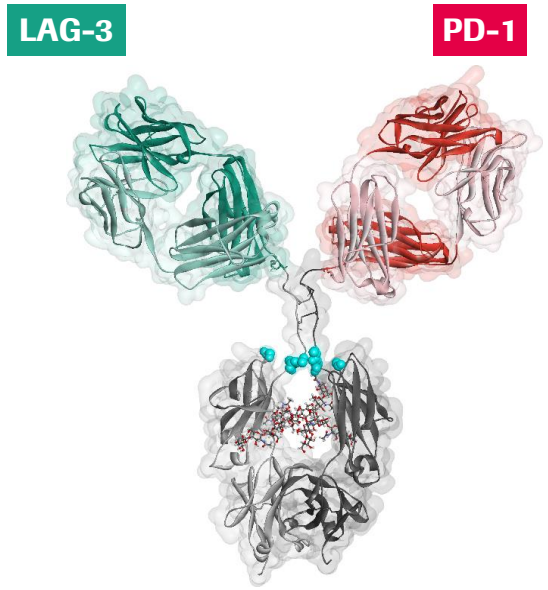
- Targets intracellular proteins via peptide MHC complexes (pMHC) and CD3 T-cells
- High specificity for tumor cells sparing healthy cells
- Potential for development in hematology and solid tumors, Ph I single agent dose escalation of RG6007 in AML ongoing

Haenel et al, 2021, submitted. Klein et al, ASH, 2019, collaboration with M. Subklewe, LMU Munich

PD1 mAbs in early clinical development

Enhancing activity of standard of care checkpoint inhibitors

PD1-LAG3/RG6139

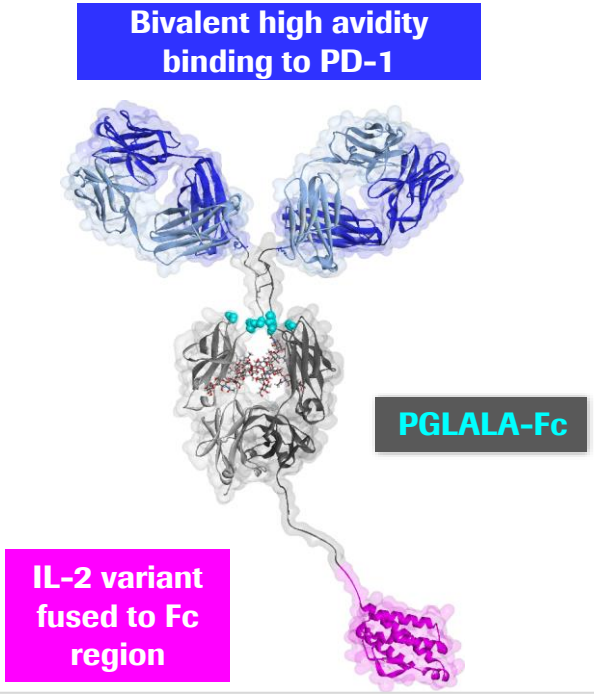


- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

PD1-TIM3/RG7769

- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

PD1-IL2v/RG6279

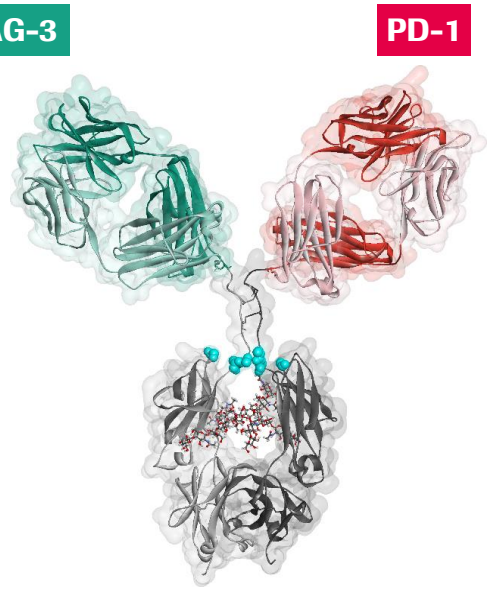


- Ph 1 dose escalation cohorts in solid tumors ongoing, data presented at AACR 2021

PD1 mAbs in early clinical development

Enhancing activity of standard of care checkpoint inhibitors

PD1-LAG3/RG6139

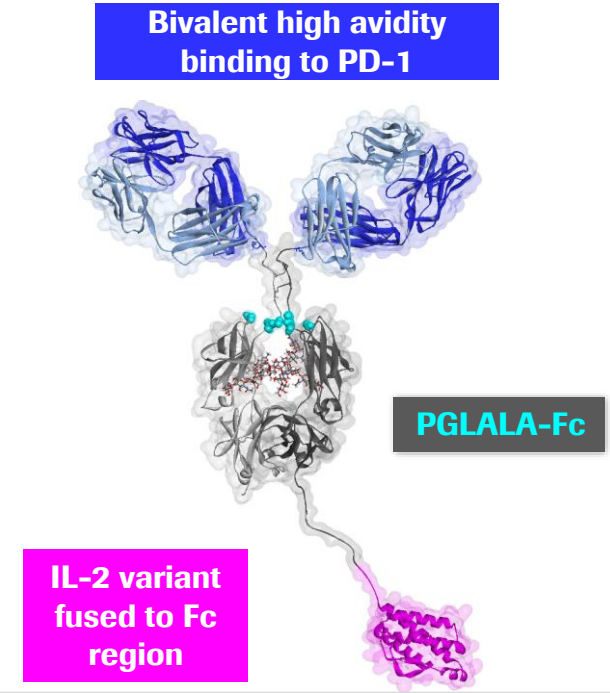


- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

PD1-TIM3/RG7769

- Ph 1 dose expansion cohorts in solid tumors ongoing
- Randomized Ph 2 start vs anti-PD1 exp. 2021

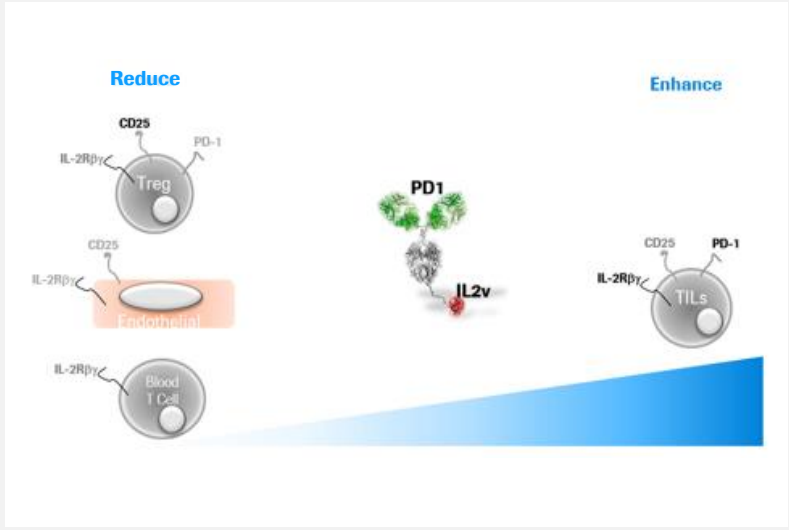
PD1-IL2v/RG6279



- Ph 1 dose escalation cohorts in solid tumors ongoing, **data presented at AACR 2021**

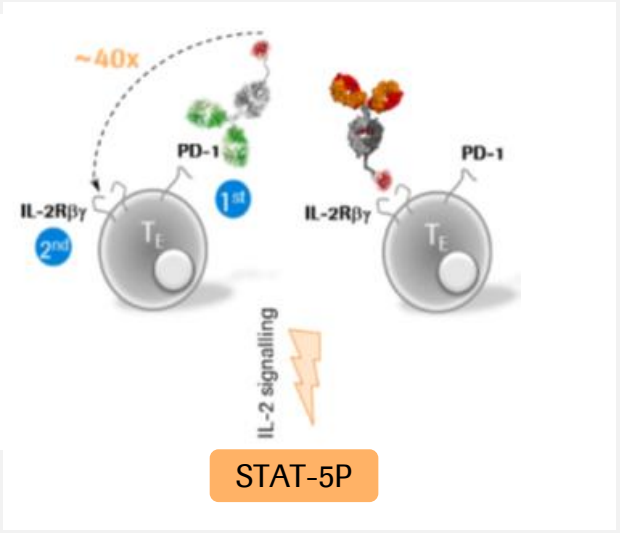
PD1-IL2v (RG6279): Delivering IL2 variant to PD-1+ T-cells

IL2v preferentially activates effector T cells



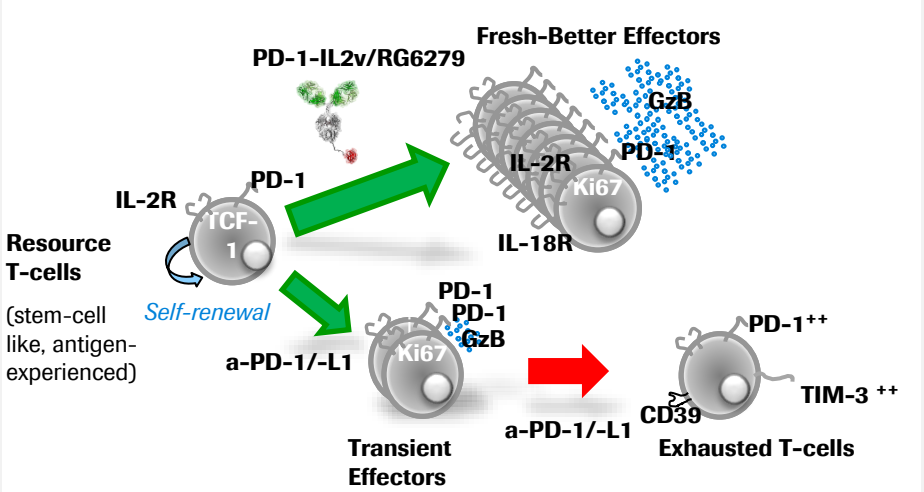
- IL2v engineered to eliminate binding to IL-2Rα (CD25), inducing only IL-2Rβγ agonism, thereby avoiding binding on endothelial cells and preferential expansion of Tregs

IL2v delivery to PD-1+ T cells



- PD1-targeting increases IL2v potency towards PD-1+ cells

Superior approach to exploit tumor-specific T-cells vs. CPI alone



Collaboration with R. Ahmed & M. Hashimoto, Emory University, Atlanta

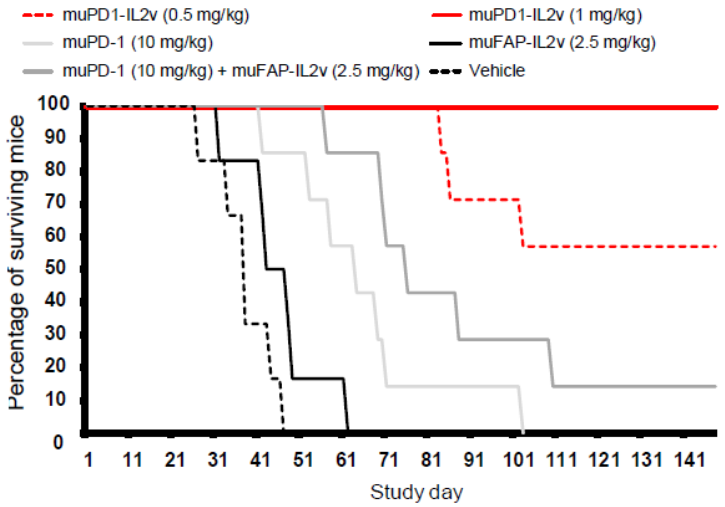
- PD1-IL2v treatment leads to greater expansion of proliferative and cytotoxic effector cells compared to non-PD-1-targeted IL2v and anti-PD-1

CPI - Check point inhibition

1. Umaña, P., AACR 2021; 2. Wullschleger, S., AACR 2021

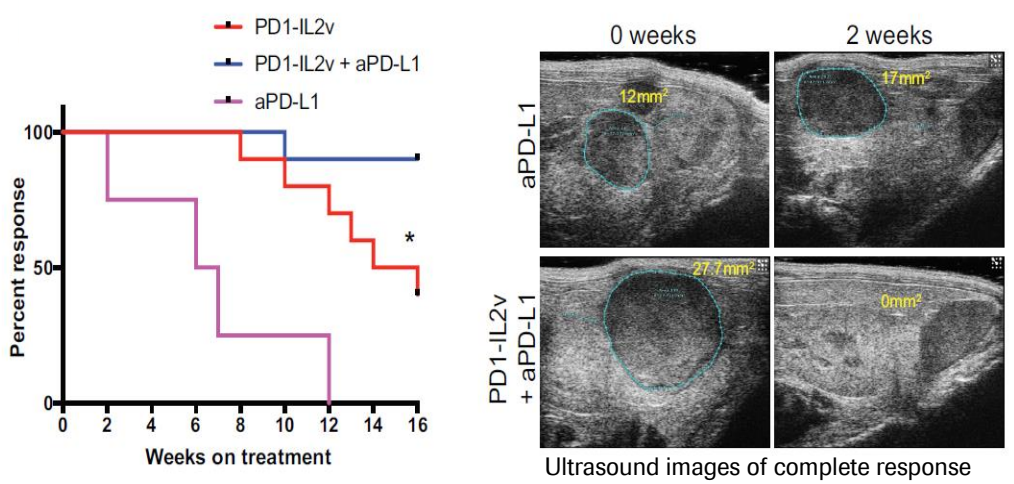
Encouraging preclinical activity of cis-targeted PD1-IL2v (RG6279)

PD1-IL2v: Superior efficacy vs. aPD-1 and aPD-1 + FAP-IL2v



Orthotopic PancO2-H7 model[1]

PD1-IL2v: Enhanced efficacy in combination with aPD-L1



Ultrasound images of complete response

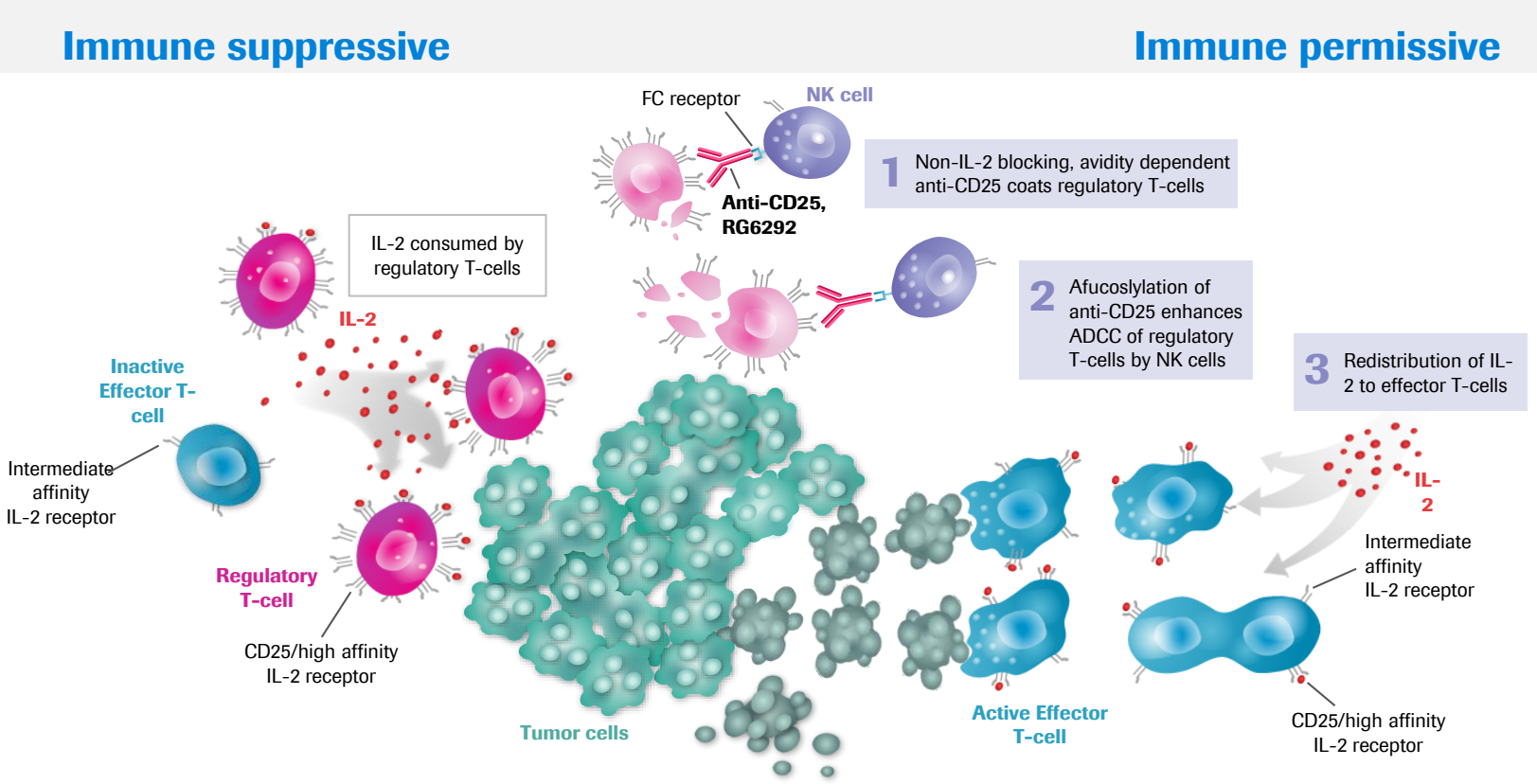
in RT5 model; collaboration with D. Hanahan, SLCC[2]

- Ph1 dose escalation with RG6279 in solid tumors ongoing (NCT04303858)

1. Umaña, P., AACR 2021; 2. Wullschleger, S., AACR 2021

Anti-CD25 (RG6292)

Selective regulatory T-cell depletion without affecting IL-2 signaling



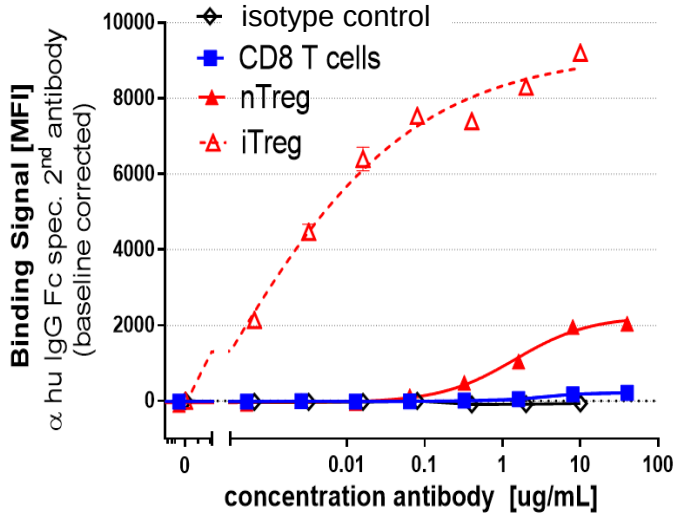
- RG6292-mediated Treg depletion leads to redistribution of IL-2 to effector T-cells

Solomon et al., Nature Cancer volume 1, 1153–1166 (2020), Amann AACR 2020

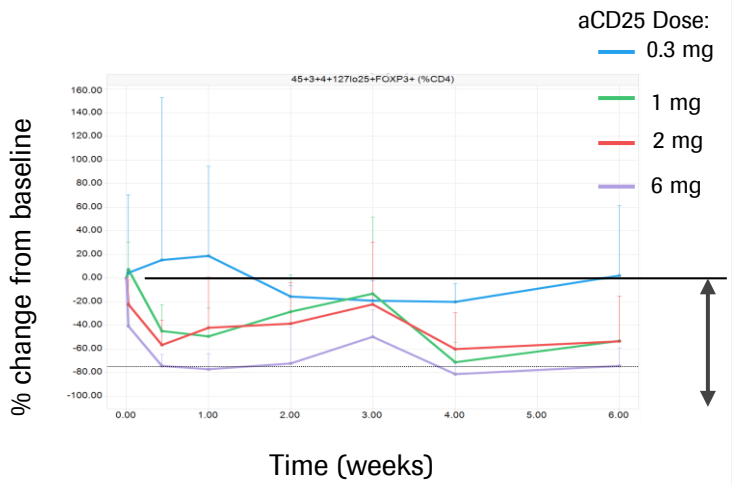
Anti-CD25 (RG6292)

Selective regulatory T-cell depletion without affecting IL-2 signaling

Preferential binding of RG6292 to iTregs *in vitro*

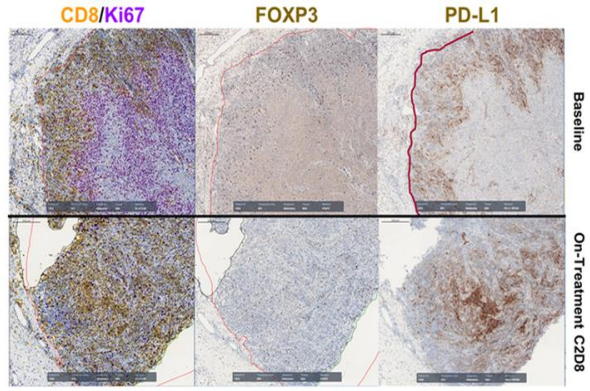


RG6292 induces dose dependent blood Treg depletion in patients



Consistent trend of Treg depletion observed from 2mg cohort onwards with > 75% Treg depletion from baseline

RG6292 induced an inflamed tumor type in patients



Melanoma, CPI experienced, dosed at 6mg

Immune cell relocation and conversion of tumors to a CD8 inflamed phenotype

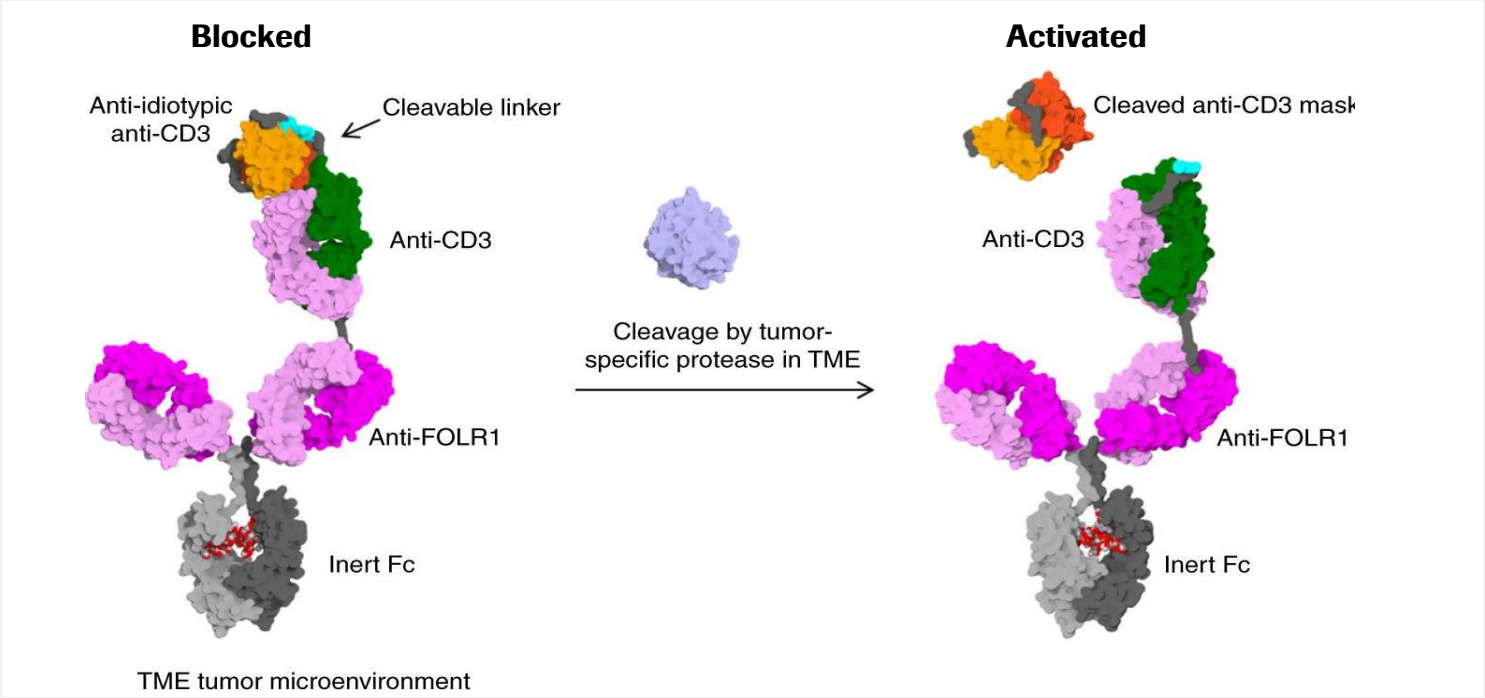
- Preliminary single agent dose escalation data indicate good tolerability with manageable skin toxicity being the most frequent AE
- PhI dose escalation as single agent (NCT04158583) and in combination with Tecentriq (NCT04642365) in solid tumors ongoing

Kolben, AACR 2021

nTreg: naive/resting Treg; iTreg: induced/activated Treg; AE: adverse event

Increasing the therapeutic index of T-cell Bispecifics via novel protein engineering

Enhancing specificity and safety of TCBs by masking the anti-CD3 Fab fragment



- Protease-activation using anti-idiotypic masks enables tumor specificity of a T-cell bispecific allowing for optimized on-target activity while minimizing off-tumor activity[1]

[1]Geiger et al., Nat Commun. 2020 Jun 24;11(1):3196

Early pipeline programs in focus

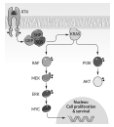
Ira Mellman, Ph.D. | Vice President, Cancer Immunology, Genentech Research & Early Development (gRED)

Robust gRED oncology portfolio

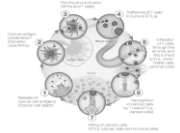
Genentech
A Member of the Roche Group

Oncology

Targeted Therapy



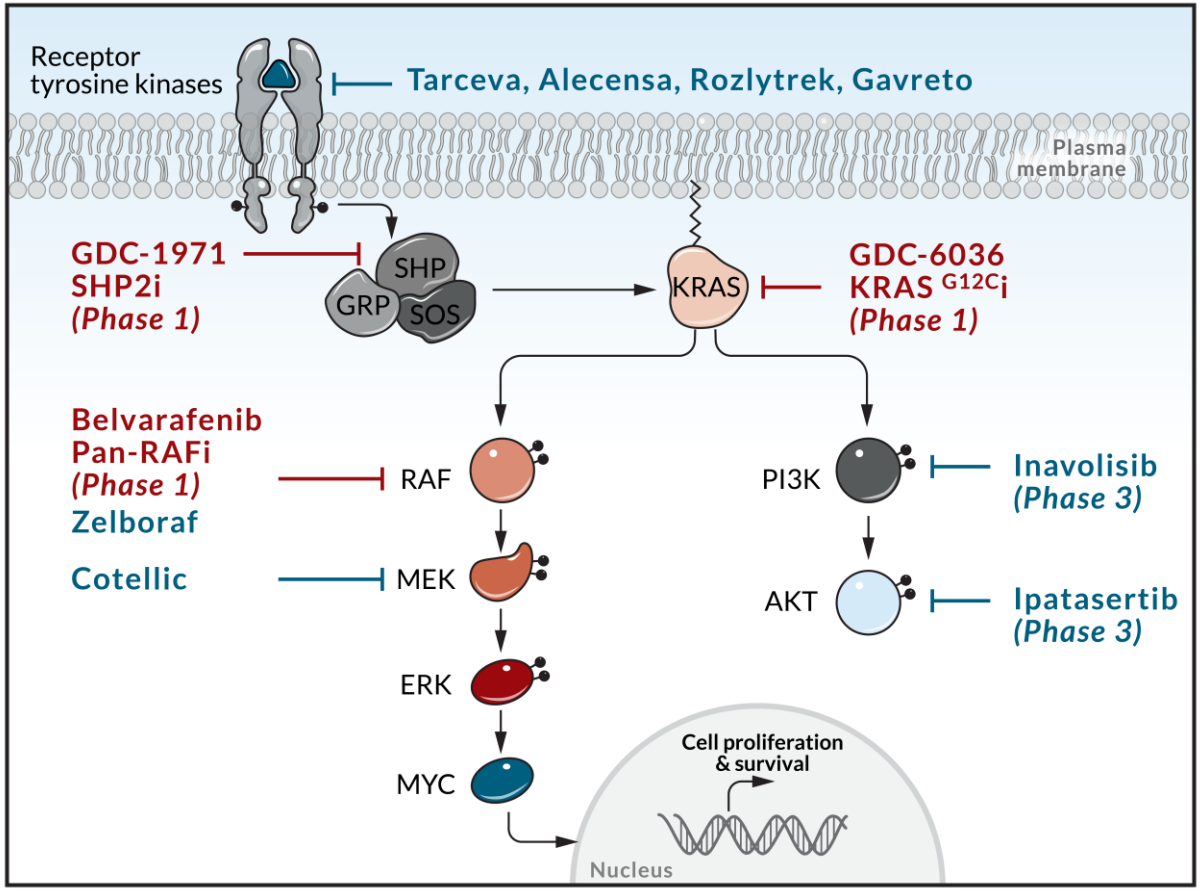
Cancer Immunotherapy



Phase 1	Phase 2	Phase 3
*Anti-BCMA/CD16a	*Autogene cevumeran	*ipatasertib
Anti-HER2/CD3 TDB		mosunetuzumab
*belvarafenib		inavolisib (mPI3Ka inh)
cevostamab (FcRH5xCD3)		giredestrant (SERD)
*IL15/IL15-Ra-Fc		tiragolumab
*DNA vaccine		
KRAS G12Ci		
*MAGE-A4 ImmTAC		
CIT-NME-1		
CIT-NME-2		
*SHP2i		

* partnered/acquired programs

Ras-MAPK pathway in cancer



Due to pathway cross-talk and feedback mechanisms, combination strategies are required for optimal clinical effectiveness and to tackle resistance

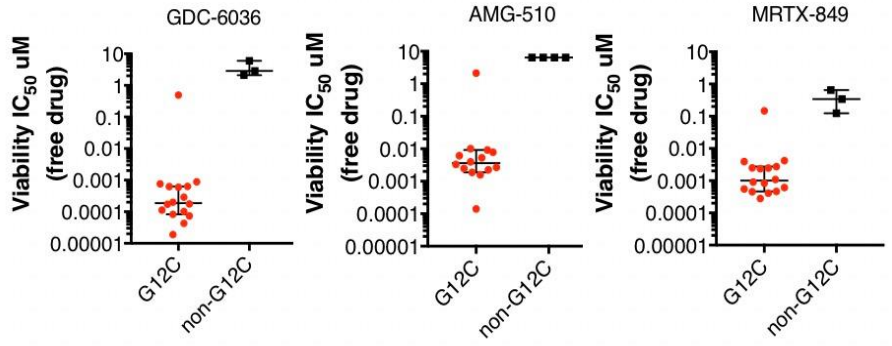
- *gRED portfolio*
- *Late stage portfolio / marketed*

GDC-6036 (KRAS G12C inhibitor) in solid tumors

G12C driver mutations found in 12% of all NSCLC patients

KRAS G12C inhibitor

***In vitro* cell line potency**

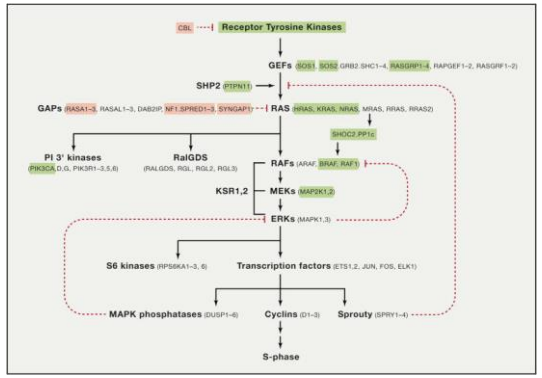


Genentech unpublished results

- Highly potent irreversible covalent inhibitor of the KRAS G12C mutant protein, which becomes locked in an inactive state
- Minimal safety findings leading to wide nonclinical safety margins
- Ph I dose escalation and expansion in KRAS G12C+ solid tumors started in Q2 2020

High unmet need remains in KRAS G12c mutant tumors

The RAS pathway



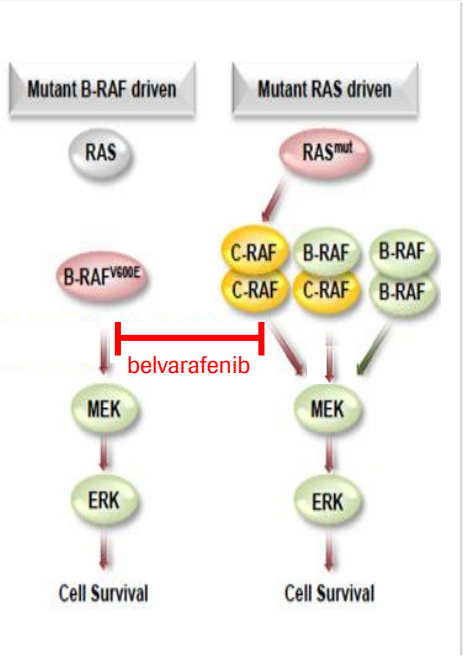
Simanshu, *Cell,* 2017

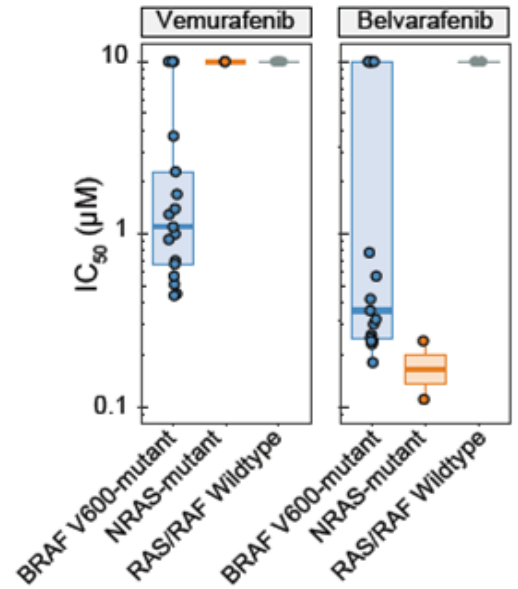
- GDC-6036 as a key combination partner for our portfolio, both targeted and immunotherapeutics
- RAS pathway activation can promote resistance to immunotherapy by reducing expression of MHC class I and tumor neoantigen presentation
- Cancer immunotherapy established as standard of care in 1L NSCLC, but inhibition of KRAS G12C is expected to deepen activity and extend durability

NSCLC = non small cell lung cancer

Belvarafenib is a potent and selective RAF dimer inhibitor

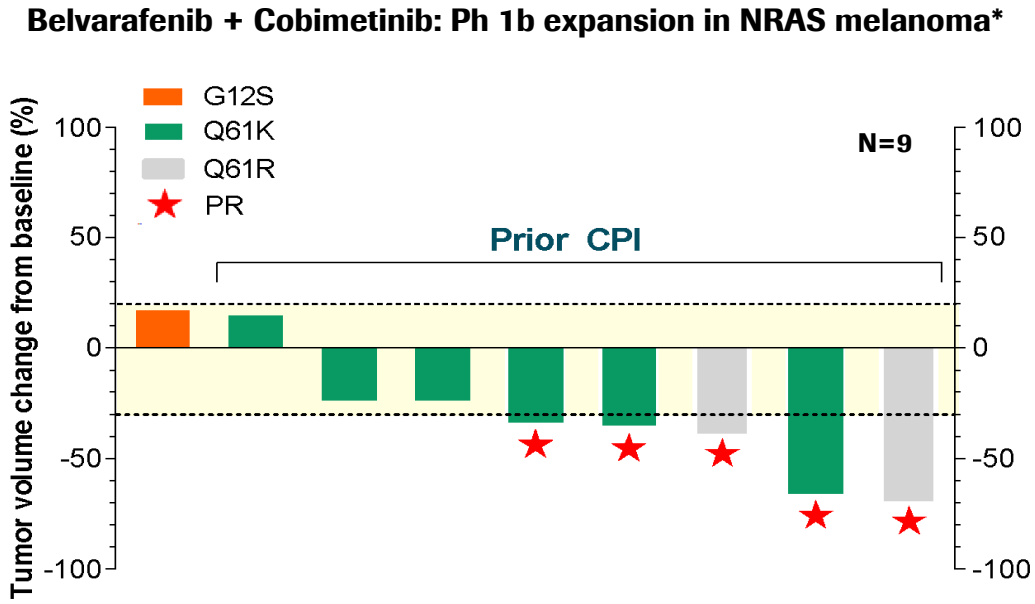
Selective inhibition of mutant RAF dimers





- Inhibition of RAF dimers, including downstream of RAS signaling (e.g. NRAS)
- Exceptional CNS penetration in preclinical studies

Promising efficacy in CPI-experienced NRAS melanoma



- Responses in 5/13 patients (38.5%) including in 5/11 patients with prior CPI (45.5%)*
- Belvarafenib + cobimetinib showed acceptable tolerability
- Further studies ongoing in NRAS melanoma (~25% of melanoma pts)

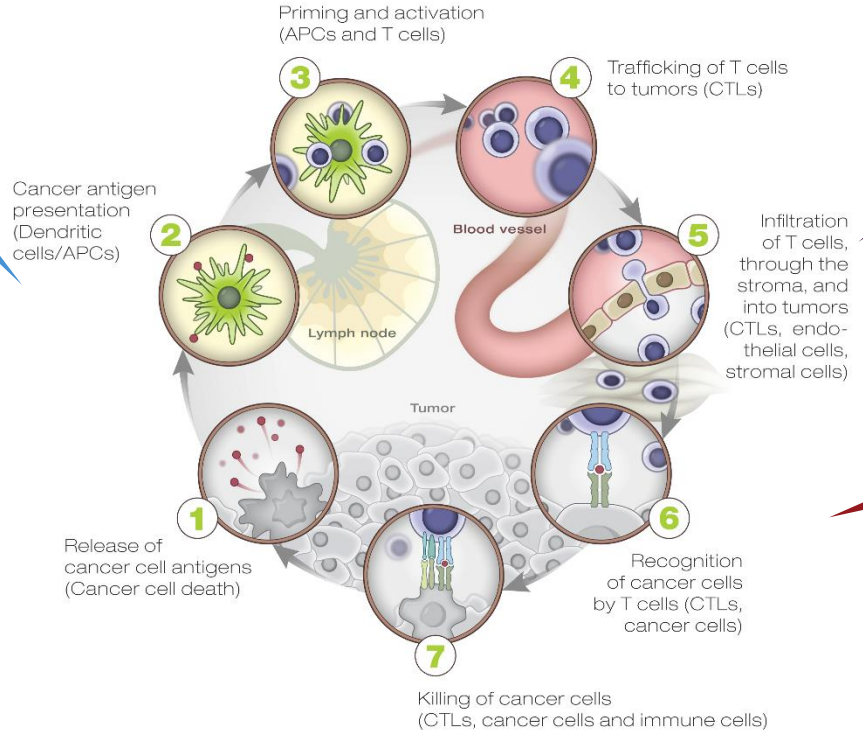
Belvarafenib in partnership with Hanmi, * 9 patients evaluable for response assessment; 4 non-evaluable patients at time of data cut; CPI=checkpoint inhibitor

Strategies to promote an antitumor immune response by phenotype

Target "rate limiting steps" associated with primary and secondary resistance

IMMUNE DESERT

- Generate/release/deliver antigens
- Enhance antigen presentation and T-cell priming
- Redirect and engage T cells



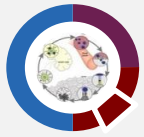
IMMUNE EXCLUDED

- Recruit T cells to tumour
- Address stromal barrier
- Redirect and engage T cells

INFLAMED

- Invigorate T cell response
- Redirect and engage T cells

Some patients may only require targeting of negative regulator (aPD-L1 monotherapy) to enable cancer immunity



Some patients will need two or more therapies to enable cancer immunity (e.g., to drive infiltration, boost MHC expression, etc)

Adapted from Chen and Mellman. Immunity 2013; Hegde, et al. Clin Cancer Res 2016; Kim and Chen. Ann Oncol 2016; Chen and Mellman. Nature 2017

Multiple modalities and approaches to leverage T cell immunotherapy

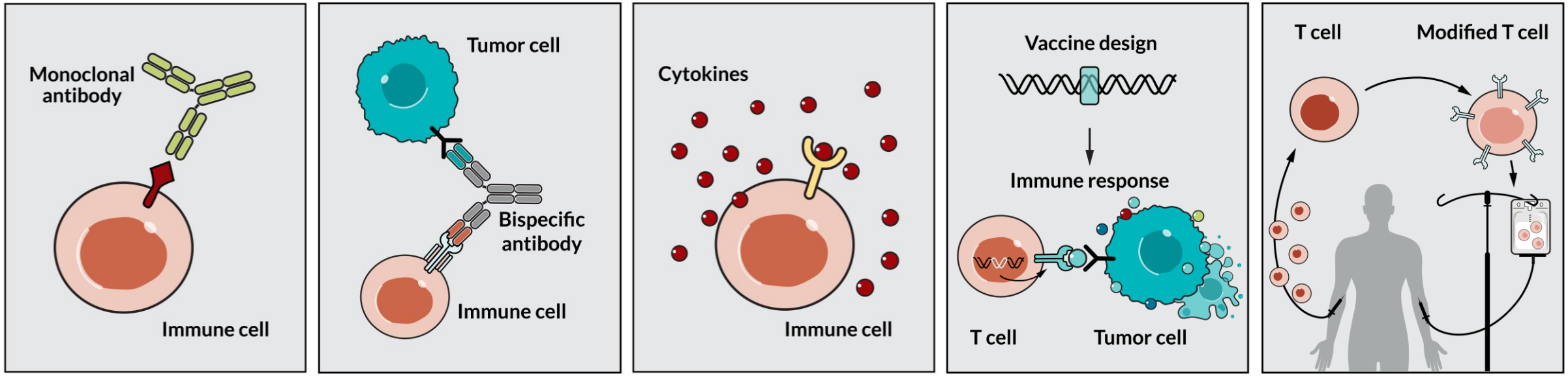
Monoclonal antibodies

Bispecific antibodies

Cytokines

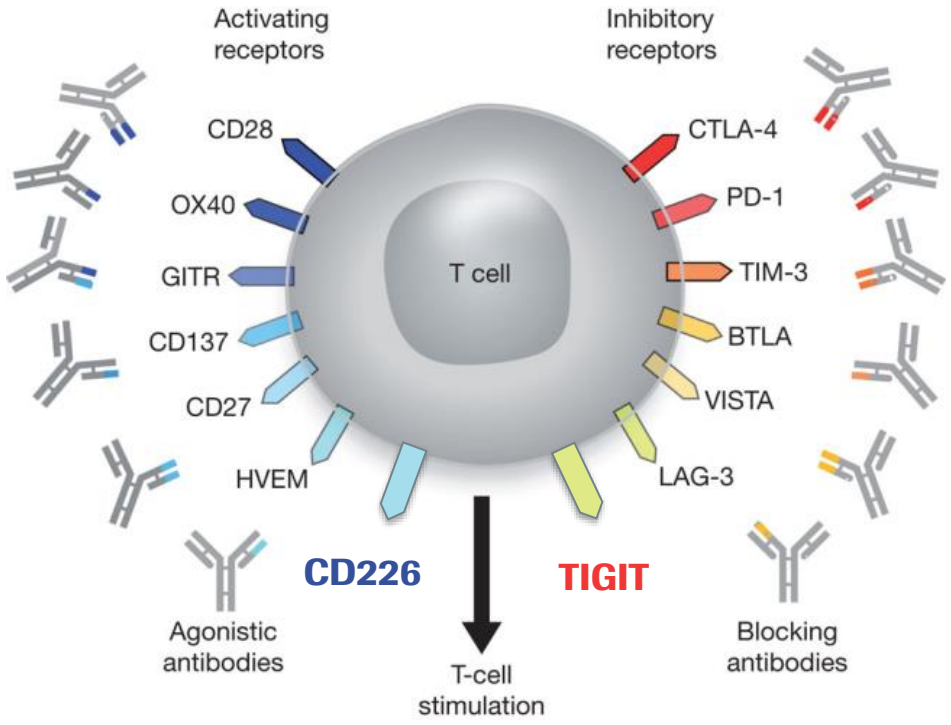
Neoantigen vaccines

NeoT cell therapy



There are many T cell checkpoints to combine with PD-1/L1 blockade, why choose TIGIT?

TIGIT is an inhibitory receptor discovered at Genentech

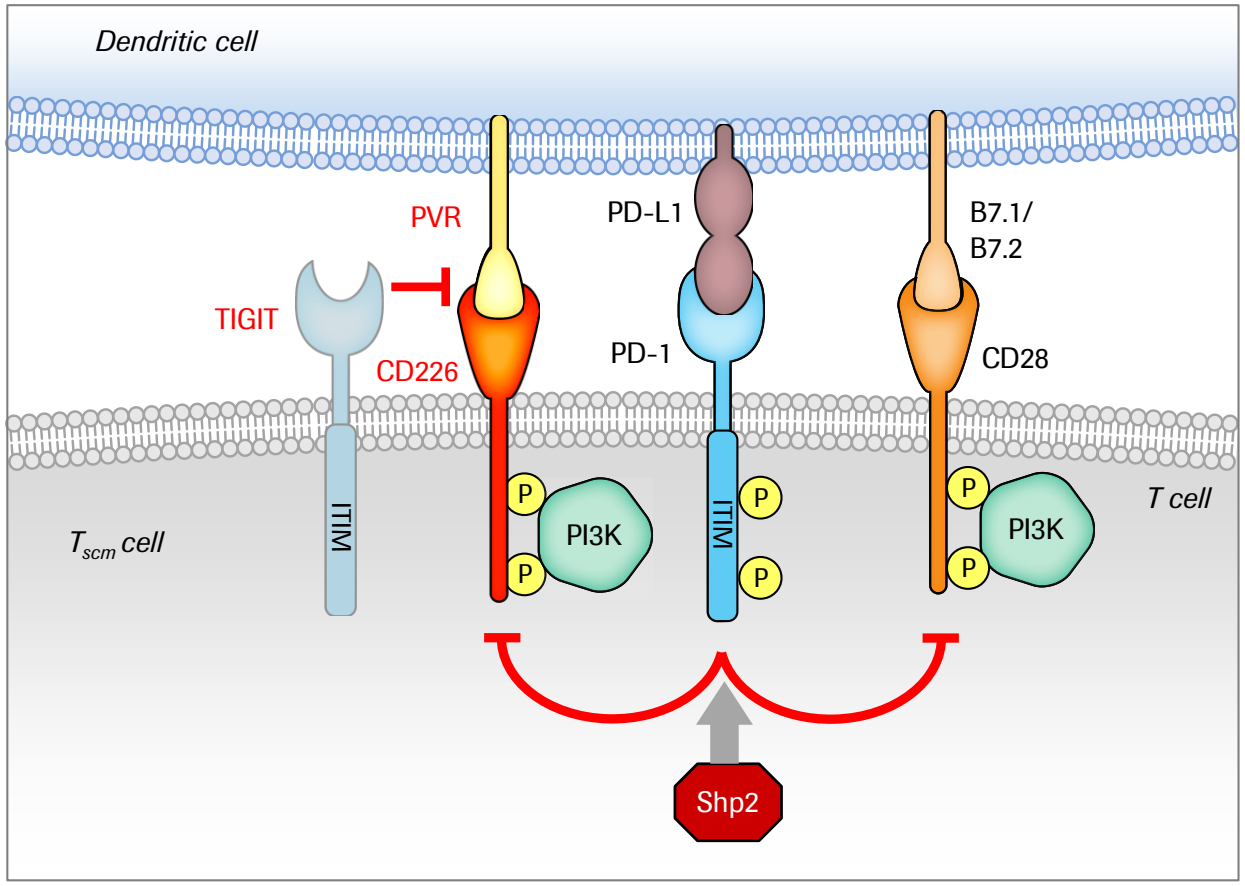


- First checkpoint inhibitor to yield positive randomized data in NSCLC in combination with PD-1/L1
- Only negative regulator besides PD-1 expressed by T_{scm} cells, a key target of aPD-1/L1
- Convergence with PD-1-mediated regulation of CD226 and CD28 costimulation
- Possible antibody-mediated modulation of dendritic cells, T_{regs}, & NK cells

NK, natural killer

1. Figure adapted from Mellman I et al. Nature 2011; 2. Manieri NA et al. Trends Immunol 2017; 3. Rotte A et al. Annals of Oncol 2018; 4. Yu X et al. Nature Immuno 2009

The convergence of the TIGIT and PD-1 pathways:
CD226 and CD28 are both "clients" of PD-1

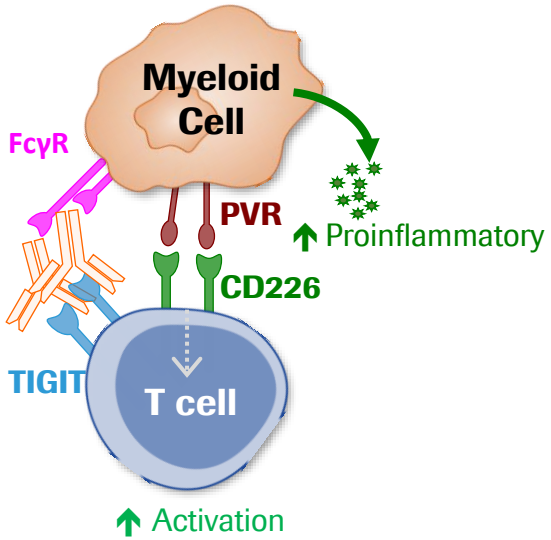


- TIGIT competes with CD226 for ligand binding
- PD-1 mediates dephosphorylation of both CD28 and CD226
- Optimal activation of costimulation requires coordinated inhibition of both TIGIT and PD-1
- TIGIT and PD-1 expressed on a likely target cell for PD-(L)1 therapy: T stem cell memory cells

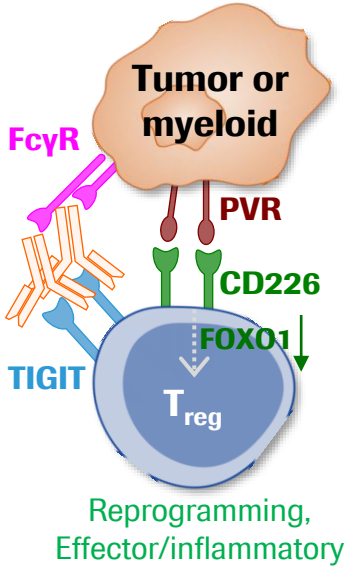
X. Xu, E. Hui, J. Hagar, K. Banta, E. Chiang, I. Mellman, et al., in preparation

TIGIT activity may also reflect modulation of myeloid cells, CD226 suppression of T_{regs}, NK cell activation

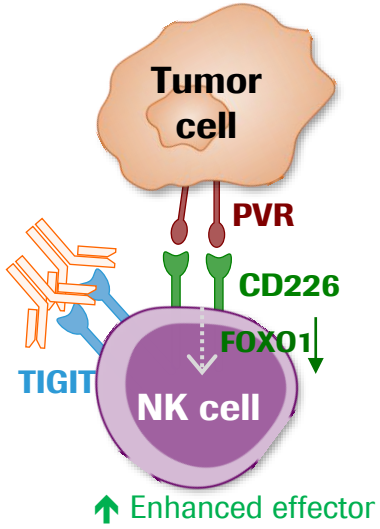
Modulation of myeloid (dendritic) cells creates proinflammatory tumor microenvironment[1]



CD226 signaling may dampen T_{reg} suppression, promote effector phenotype



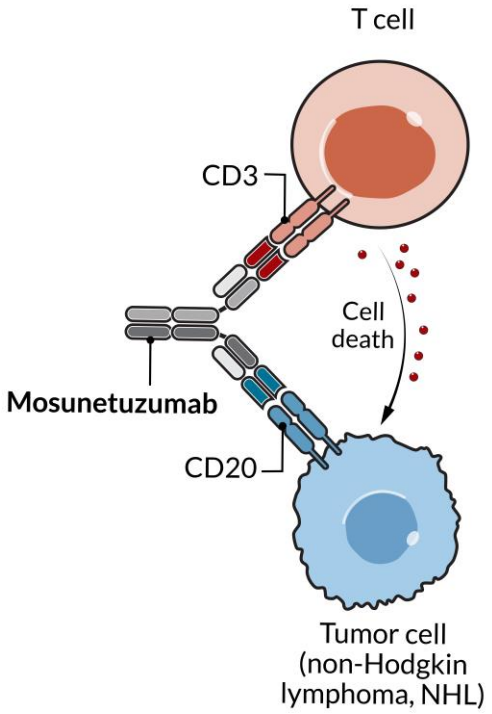
TIGIT is also expressed by NK cells, unlike PD-1



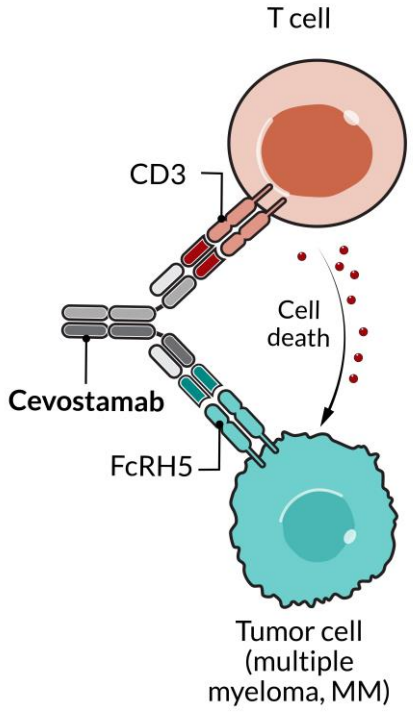
Anti-TIGIT Fc:FcγR interaction may sequester TIGIT away from the synapse, and play a role in reprogramming of myeloid cells

gRED bispecific antibody portfolio

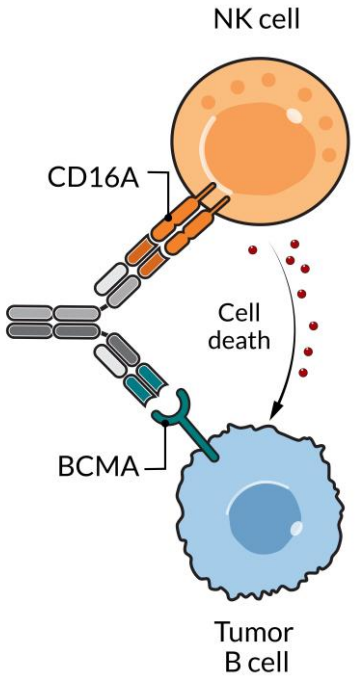
Mosunetuzumab
CD20 x CD3



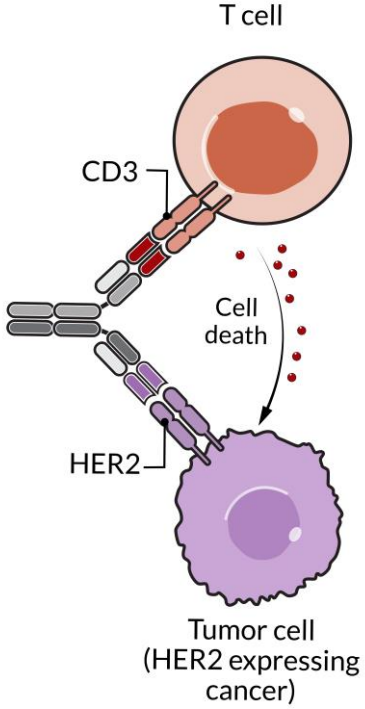
Cevostamab
FcRH5 x CD3



RG6296
BCMA x CD16A



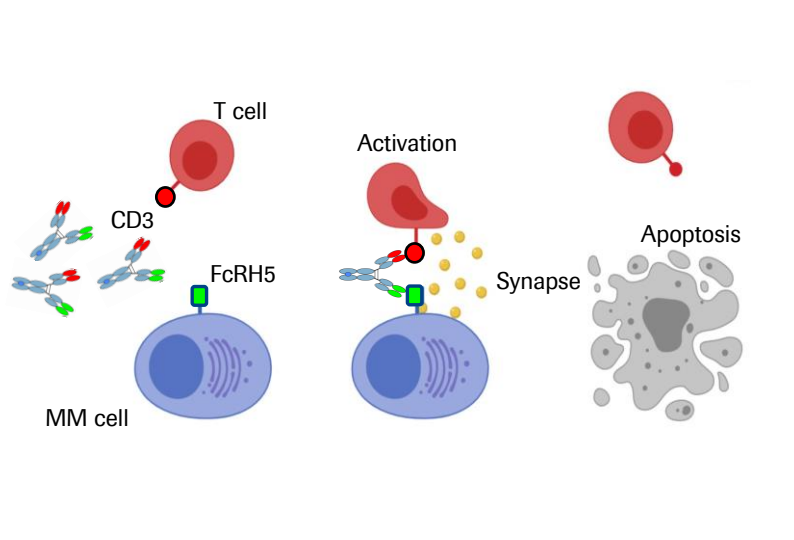
RG6194
HER2 x CD3



Cevostamab (FcRH5 x CD3)

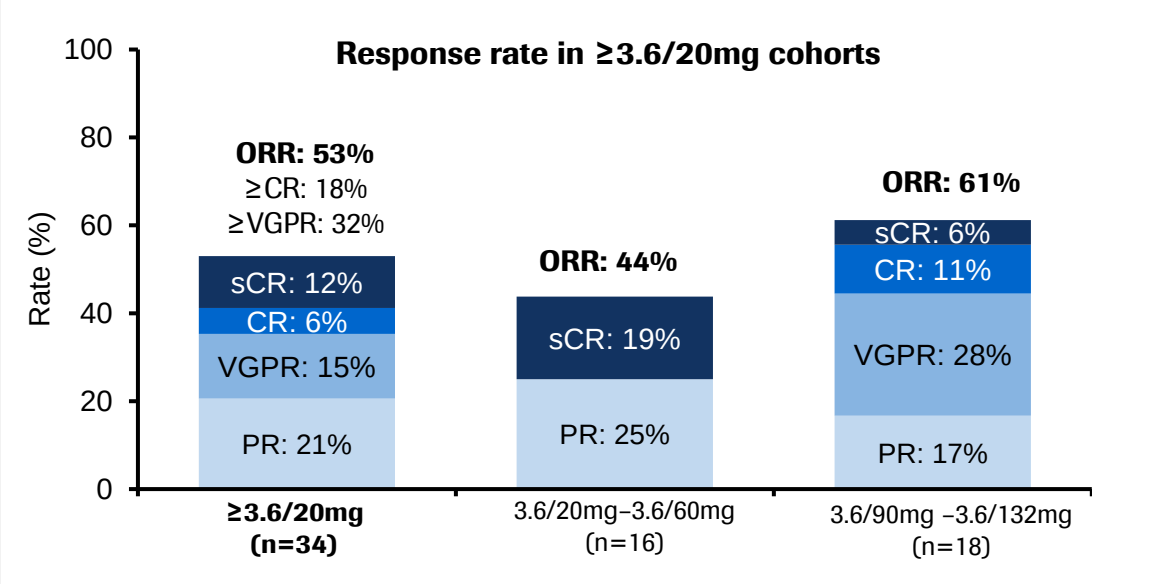
Promising activity in heavily pretreated R/R MM patients

FcRH5



- Humanized IgG-based T-cell-engaging bispecific ab
- FcRH5 expressed exclusively in the B-cell lineage and across all maturation stages (elevated in myeloma cells and normal plasma cells vs normal B cells[1])
- Expressed on myeloma cells with near 100% prevalence

Cevostamab Ph 1 dose escalation in R/R MM

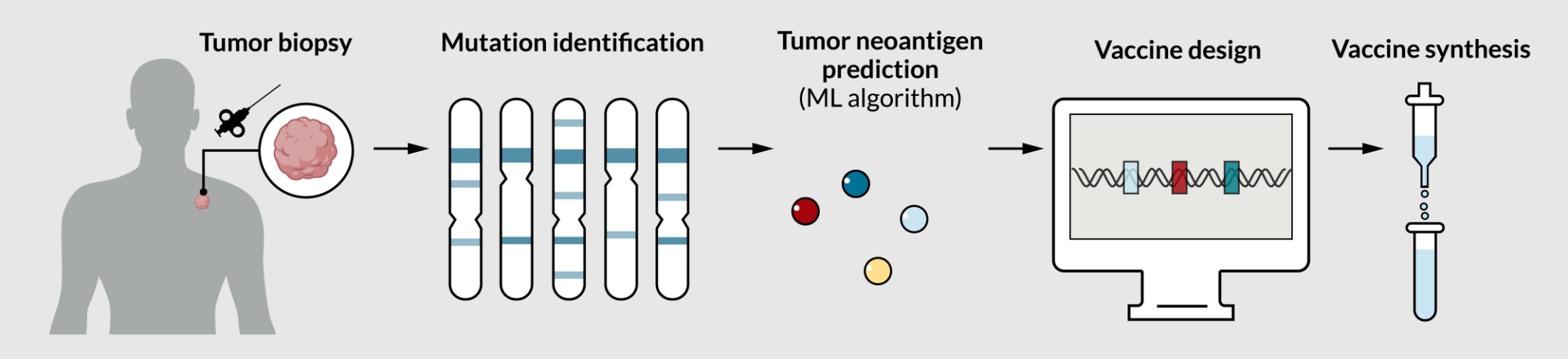


- Responses in penta-drug refractory pts (7/17, ORR:41%) and patients with prior BCMA (5/8, ORR:63%)
- Responses observed across all FcRH5 expression levels (FcRH5 expression on myeloma cells detected in all patients)
- Manageable toxicities with step-up dosing (CRS most common in C1; nearly all grade 1-2; one patient with grade 3 CRS)

1. Li et al. Cancer Cell 2017;31:383–95; Ig=immunoglobulin; MM=multiple myeloma; ab=antibody; CR = complete response; sCR=stringent CR; PR=partial response; VGPR=very good partial response; ORR=overall response rate

Autogene cevumeran, individualized neoantigen mRNA vaccine

Ph II studies underway in 1L melanoma



In collaboration with

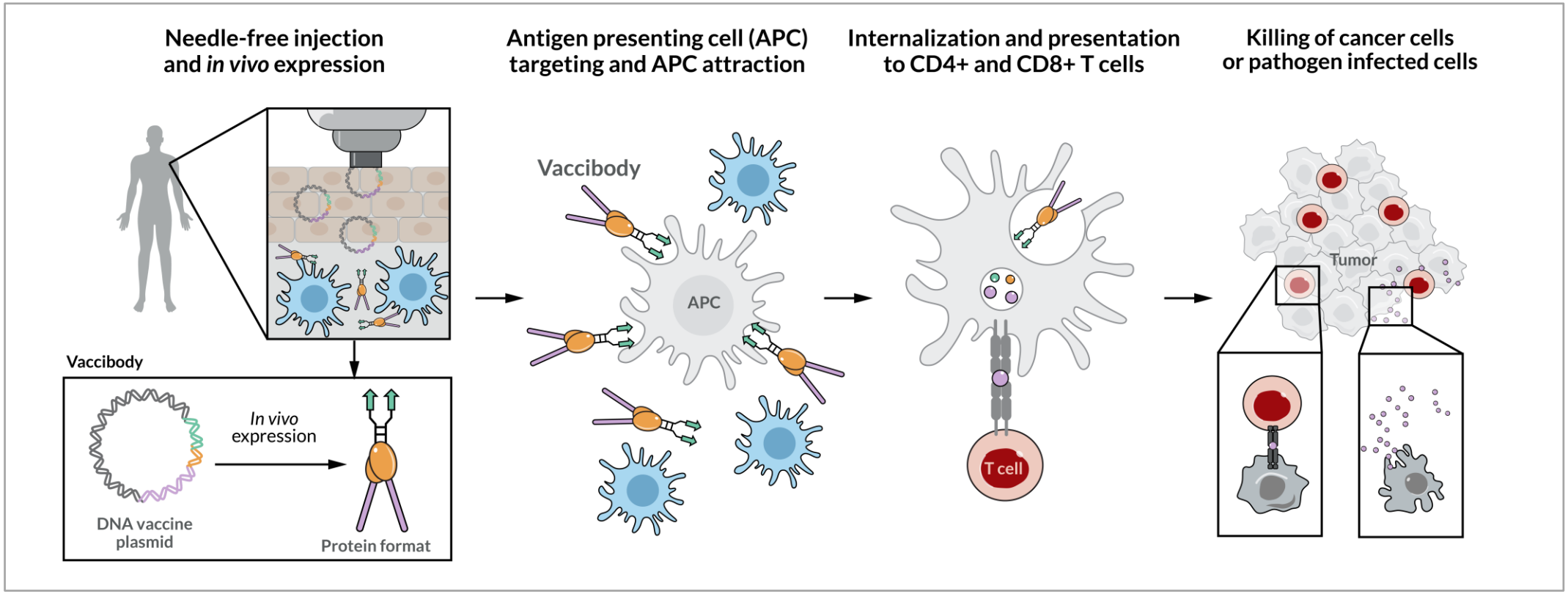
BIONTECH

- Fully individualized vaccine: mRNA vectors provide patient specific therapy
- Novel algorithms predict neoantigens recognized by T cells
- On demand-production (highly iterated and reproducible with low failure rate)
- Liposomal formulation for systemic delivery IV
- Ph1 showed neoantigen-specific T cell responses in the majority of patients (AACR 2020)

DNA vaccine with distinct mechanism to activate immune response

In collaboration with vaccibody

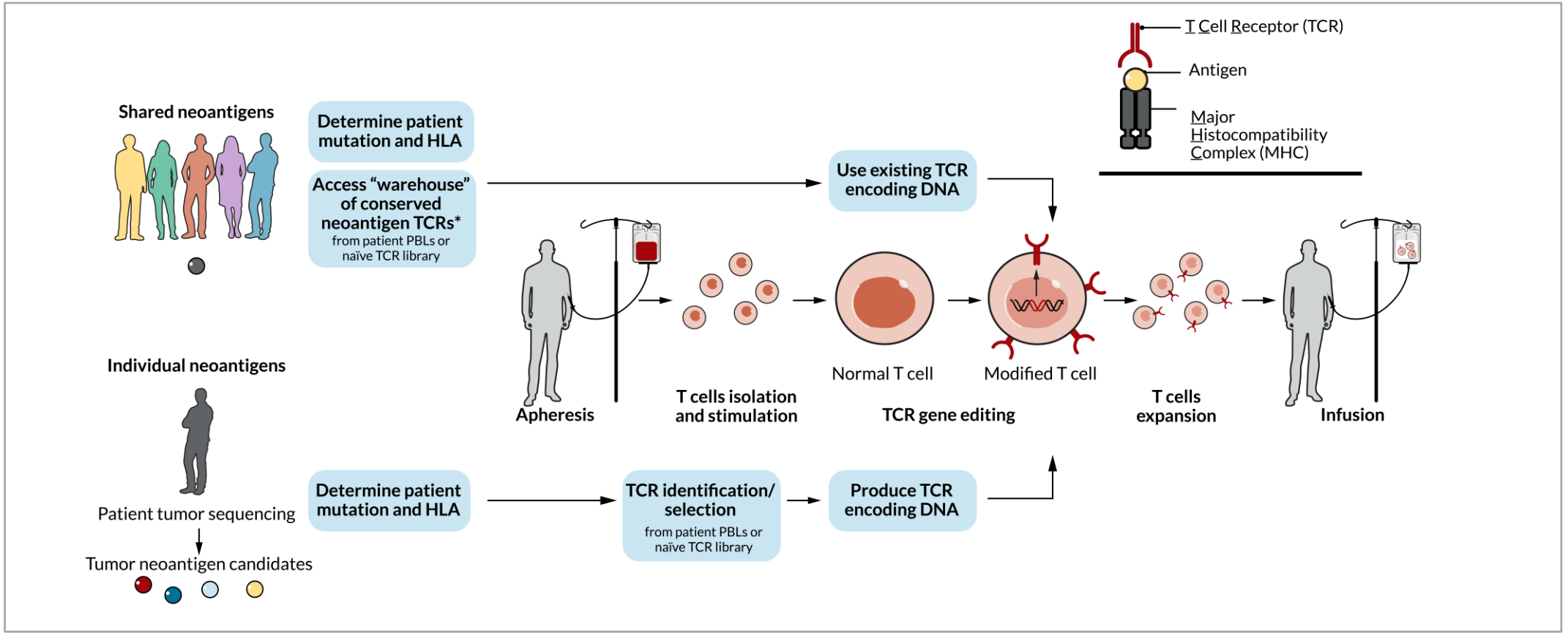
Ph1 showed neoantigen-specific T cell responses in patients (SITC 2019)



NeoT: Personalized T cell therapy directed at neoantigens

In collaboration with

Adaptive biotechnologies™



TCR: T cell receptor, HLA: human leukocyte antigen; PBL: peripheral blood leukocytes

Late-stage programs in focus

Levi Garraway, M.D., Ph.D | Chief Medical Officer and Head of Global Product Development

Significant near-term oncology news flow

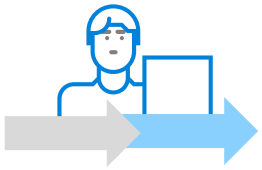
Key upcoming oncology news flow

New Molecular Entity (NME)
Additional Indication (AI)
Oncology / Hematology

Product	*Indication*	*Data/filing*
Tecentriq	NSCLC adj	2021
	SCCHN adj	2022
	RCC adj	2022
	1L mUC	2022
	NSCLC neoadj	2022
	HCC adj	2022
Alecensa	ALK+ NSCLC adj	2022
Polivy	1L DLBCL	2021
Venclexta	r/r MM t(11:14)	2022
mosunetuzumab	3L+ FL	2021
glofitamab	3L+ DLBCL	2021
tiragolumab	1L SCLC	2022
giredestrant	2L/3L ER+/HER2- mBC	2022
ipatasertib	1L CRPC	2022
inavolisib	Pi3K 1L HR+ BC	2022/2023

6 potential oncology NMEs with near-term pivotal data

Innovation for patients across solid tumors and hematology



Moving earlier in disease

- Curative potential for the largest number of patients
- Increasing screening, early detection technologies

Exploring rational combinations, new indications

- Combinations: tiragolumab+Tecentriq, Polivy+mosun/glofit
- New indications: MM (cevostamab), HR+/HER2- BC (giredestrant, inavolisib)

PHC 2.0

- Innovative trial design: TAPISTRY (tumor agnostic), AlphaT (decentralized)
- Building leading insights business

PHC = personalized healthcare; MM=multiple myeloma; HR+ BC = hormone receptor positive breast cancer

Earlier disease presents the opportunity for a cure

Need for high efficacy treatments that are well tolerated

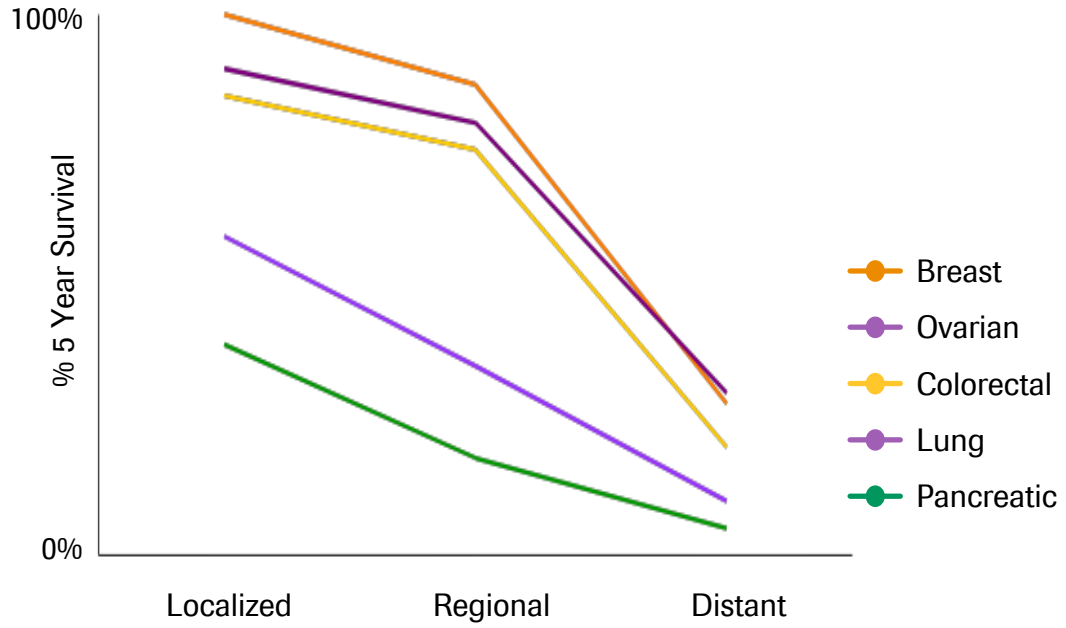
Chance for a cure: development earlier in the course of disease is critically important to improving the cure rate

Cost to society: treatment initiated in earlier stages of cancer reduces cost vs. treatment initiated later

Unmet need: large population with continued unmet needs including opportunity to improve long-term OS

Growing population: early disease population is expected to grow with the rise of early detection technologies, increasing screening

Outcomes by cancer type and stage at diagnosis[1]



1. National Cancer Institute, SEER database, literature review; OS= overall survival

Investing earlier in disease

Lung / Rare

Molecule	Indication	Ph 1	Ph 2	Ph 3
Tecentriq	Adjuvant NSCLC			*IMpower010* ✓
	Neoadjuvant NSCLC			*IMpower030*
	Adjuvant SCCHN			*IMvoke010*
tiragolumab[1]	Stage III unres. NSCLC			*SKYSCRAPER-03*
	Neoadj/Adj NSCLC			*SKYSCRAPER-05*
Alecensa	Adjuvant ALK+ NSCLC			*ALINA*

Breast / Gyn

Molecule	Indication	Ph 1	Ph 2	Ph 3
Tecentriq	Neoadj. TNBC [2]			*IMpassion031* ✓
	Adj TNBC			*IMpassion030*
giredestrant	Neoadj. HR+ BC			*coopERA*
	Adjuvant HR+ BC[4]			*lidERA*

✓ = met primary endpoint

GI / GU

Molecule	Indication	Ph 1	Ph 2	Ph 3
Tecentriq	Adjuvant RCC			*IMmotion010*
	Adjuvant HCC			*IMbrave050*
	HR NMIBC			*ALBAN*
	ctDNA+ HR MIBC			*IMvigor011*
	MSI-H CRC			*ATOMIC*
	BCG unresp. NMIBC			*SWOG S1605*
tiragolumab[1]	Locally adv. ESCC			*SKYSCRAPER-07*

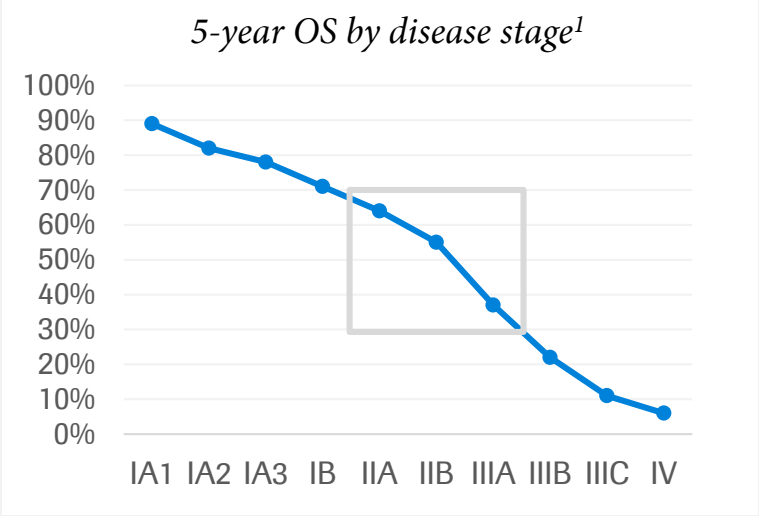
Heme

Molecule	Indication	Ph 1	Ph 2	Ph 3
Polivy	1L DLBCL			*POLARIX*
Venclexta	1L fit AML			*VIALE-M*
Glofit/Mosun[3]	1L DLBCL			*Ph 1b*

1. In combination with Tecentriq; 2. Positive for PCR, 3, +/- Polivy 4. Planned trial; NSCLC= non-small cell lung cancer; ESCC=esophageal squamous cell carcinoma; HCC=hepatocellular carcinoma; TNBC = triple negative breast cancer; RCC = renal cell carcinoma; NMIBC = non-muscle invasive bladder cancer; DLBCL = diffuse large b-cell lymphoma; AML = acute myeloid leukemia; CRC=colorectal carcinoma; ctDNA = circulating tumor DNA

High unmet need in adjuvant NSCLC
Tecentriq filed with FDA under RTOR

High unmet need in early NSCLC



- Many patients with Stage I-III NSCLC continue to have disease recurrence/progression post-surgery

TECENTRIQ® atezolizumab

Adjuvant NSCLC treatment is still evolving

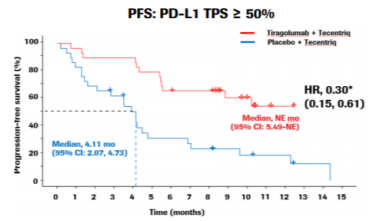
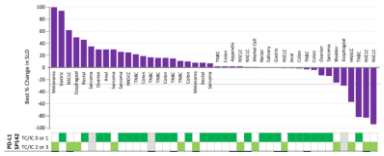
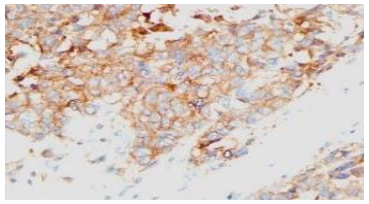
Screening: Early detection technologies expected to increase diagnosis at early stage

Testing: Increasing with adjuvant development for EGFR+, PD-L1+, ALK+ patients

Systemic therapy: Adjuvant treatment rates expected to increase with new therapeutic options

1. Chansky, et al Journal of Thoracic Oncology (2017); NSCLC = non-small cell lung cancer; RTOR = real time oncology review

Tiragolumab (anti-TIGIT) development program: scientific and clinical rationale

	Scientific / clinical evidence		*Example: Ph 3 investment*
	**CITYSCAPE Ph 2 trial** PFS benefit observed on top of Tecentriq in randomized trial	→	**SKYSCRAPER-01 (PD-L1+ NSCLC)** • Confirm CITYSCAPE results
	**Ph 1b expansion cohorts** Signal seeking across tumor types, with and without chemotherapy	→	**SKYSCRAPER-08 (ESCC)** • Early clinical data from Ph1b suggests Tecentriq+tira drives responses in ESCC
	**Biomarker data** Building scientific rationale, defining inclusion criteria	→	**SKYSCRAPER-02 (SCLC)** • High expression of TIGIT ligand PVR in SCLC[1]

1. Yu, et al, Journal of Thoracic Oncology (2018); ESCC = Esophageal squamous cell carcinoma; SCLC = Small-cell lung cancer

Tiragolumab development program

First Ph 3 data reading out in 2022: SKYSCRAPER-02 (SCLC)

Nine Ph II/III trials of tiragolumab + Tecentriq initiated

Lung Cancer

Indication	Ph 1	Ph 2	Ph 3
1L NSCLC: PD-L1 high			*SKYSCRAPER-01*
1L ES-SCLC			*SKYSCRAPER-02*
Stage III unres. NSCLC			*SKYSCRAPER-03*
Neoadj / Adj NSCLC			*SKYSCRAPER-05*
1L NSq NSCLC			*SKYSCRAPER-06*

Additional solid tumors

Indication	Ph 1	Ph 2	Ph 3
Locally advanced ESCC			*SKYSCRAPER-07*
1L ESCC			*SKYSCRAPER-08*
PD-L1+ Cervical Cancer			*SKYSCRAPER-04*
1L SCCHN			*SKYSCRAPER-09*

Additional trials ongoing in HCC, mUC, PDAC, TNBC, and hematology (MM, NHL)

Development Strategy

- **Build on Tecentriq**
- **Expand into early disease**
- **Compete in new indications**

NSCLC=Non-Small Cell Lung Cancer; ES-SCLC=extensive stage small cell lung cancer; ESCC=esophageal squamous cell carcinoma; HCC=hepatocellular carcinoma; mUC=metastatic urothelial carcinoma; PDAC= Pancreatic ductal adenocarcinoma; MM=multiple myeloma; NHL=non-hodgkins lymphoma

Giredestrant (SERD)

High unmet need remains across HR+/HER2- eBC and mBC

ET is a mainstay of HR+ BC treatment

20–50%
of HR+ eBC patients stop treatment within 5-yrs due to safety/adherence issues[1]

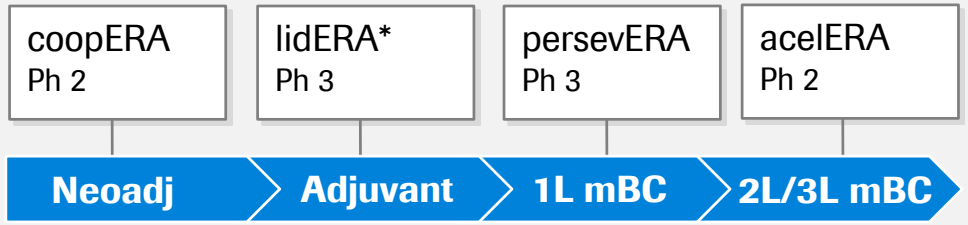
10–30%
of HR+ eBC patients become resistant to standard of care[2]

1. Bowels A, et al *J Oncol Pract* 2012
2. Ruhstaller, T. *J Clin Oncol* 2018

Potential for best-in-class profile in HR+ BC

- **Novel MOA**: immobilizes ER in the nucleus prior to degradation
- **High potency**: 7-15x more potent than other SERDs in development
- **Well tolerated** alone and in combination with CDK4/6i
- **Standardized dose**, 30mg once-daily selected for monotherapy/combo

Ongoing / planned trials:



* Planned trial; ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer; SERD = selective estrogen receptor degraer; ER = estrogen receptor

Giredestrant (SERD)

Promising activity across HR+/HER2- mBC and eBC

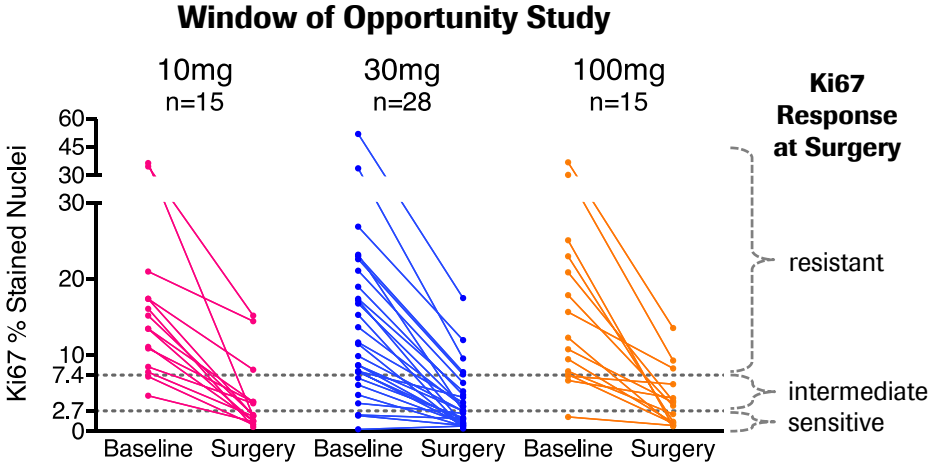
HR+/HER2- mBC

Ph 1b: giredestrant monotherapy

Clinical activity	30mg (n=41)
ORR*	20%
CBR	55%
Prior fulvestrant	3/8 (38%)
Prior CDK4/6i	11/26 (42%)
ESR1 mut	13/17 (76%)

- Promising clinical activity in all patient subgroups including patients with ESR1 mutations
- Well tolerated at all doses, with no DLTs
  - No clinically relevant bradycardia or ocular toxicity
  - Low treatment discontinuation
- Pivotal Ph 2 trial in 2L/3L HR+/HER2- BC reading out in 2022

Stage I-III neoadjuvant treatment



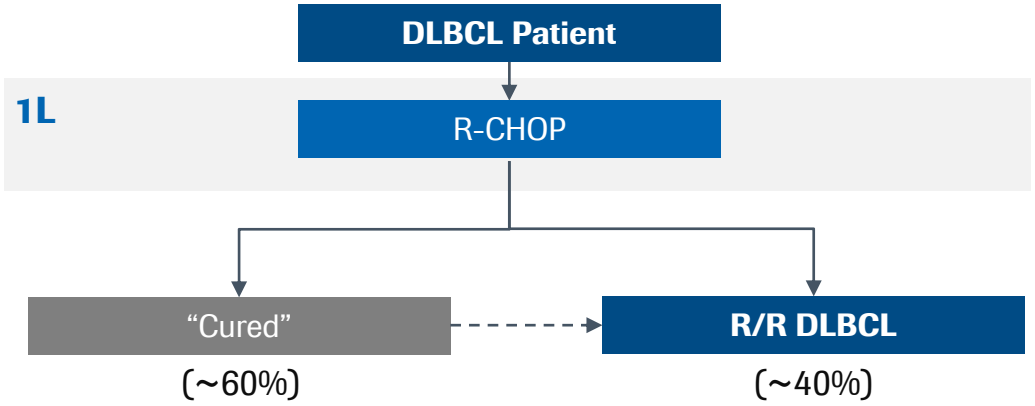
- Compelling pharmacodynamic effects observed in all dose cohorts (supportive of 30mg dose)
- Encouraging impact on proliferation (78% geomean reduction in Ki67); 55% of tumors exhibited complete cell cycle arrest (CCCA) at 2 weeks
- Ph 2 trial in neoadj HR+/HER2- BC reading out in 2021

*ORR in patients with baseline measurable disease; ET=endocrine therapy; HR+ BC=hormone receptor positive breast cancer; TNBC=triple negative breast cancer; eBC=early breast cancer; mBC=metastatic breast cancer; CCCA = complete cell cycle arrest, Ki67 ≤2.7%

Polivy readout in 1L DLBCL expected in 2021

Opportunity to establish Polivy as standard of care in curative setting

1L DLBCL treatment can be curative…



POLIVY® polatuzumab vedotin

…however high unmet need in remains in 1L DLBCL

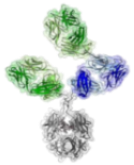
- ~40% of patients not cured with R-CHOP in 1L
- Patients with R/R DLBCL have poor prognosis: mOS <2yrs
- No new 1L therapies approved since R-CHOP
- 3x more drug treated patients in 1L than 2L DLBCL

Polivy in collaboration with Seattle Genetics; R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; R-CHOP=Rituxan + cyclophosphamide + hydroxydaunorubicin + vincristine+ prednisone; mOS=median overall survival

Roche CD20 x CD3 bispecific portfolio can be tailored to address diverse patient and customer needs

Mosunetuzumab

Attractive profile for the outpatient setting and across a broad range of indications and settings



Glofitamab

Potential to offer CAR-T like efficacy “off-the-shelf”, for patients with aggressive disease

Patients

- FL/DLBCL/other histologies
- 1L or R/R disease
- Patient characteristics, including risk/prognostic factors
- Single agent vs combination

Providers

- Academic centers vs. community
- SC or IV administration
- Off-the shelf administration

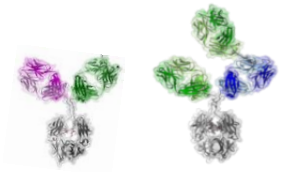
Payers

- Fixed duration vs. continuous

R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; SC=subcutaneous; IV=intravenous

Mosunetuzumab and glofitamab development plans

Moving into earlier lines of therapy in combination with SOC



Late line monotherapy

Pivotal cohorts reading out in 2021

- Mosun filing in 2021 in 3L+ FL
- Glofit filing in 2022 in 3L+ DLBCL

R/R NHL combinations

Randomized Ph 3 trials initiated

- Mosun + lenalidomide Ph 3 trial in R/R FL will begin enrolling soon
- Glofit + GemOx Ph 3 trial ongoing in 2L+ DLBCL

1L DLBCL

Developing in curative setting

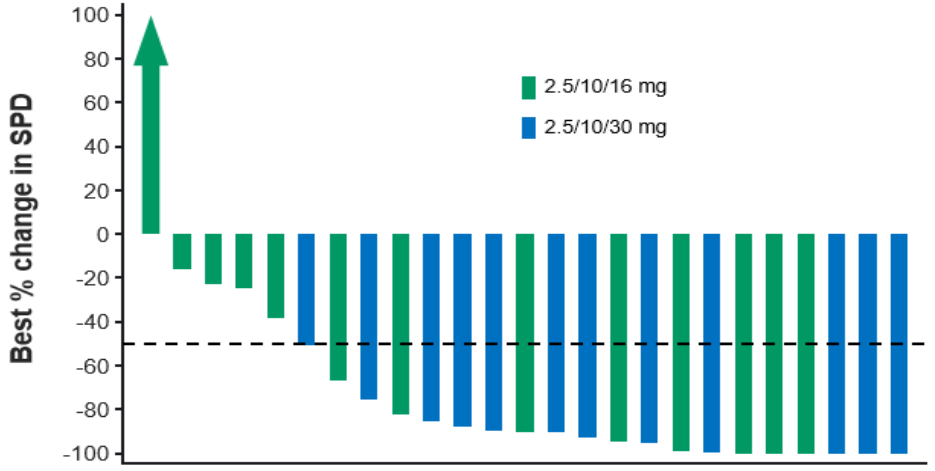
- Exploring combinations with and without Polivy
- Intriguing early data for mosun in 1L elderly / unfit patients

R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; NHL = non-Hodgkin Lymphoma; GemOx = gemcitabine + oxaliplatin; SOC = standard of care

Glofitamab

Potential for best-in-class efficacy with step-up dosing

Activity in R/R aNHL



Responses, n (%)	All aNHL pts (n=28)	aNHL 2.5/10/30mg cohort (n=14)
BOR	18 (64.3)	11 (78.6)
CR	16 (57.1)	10 (71.4)

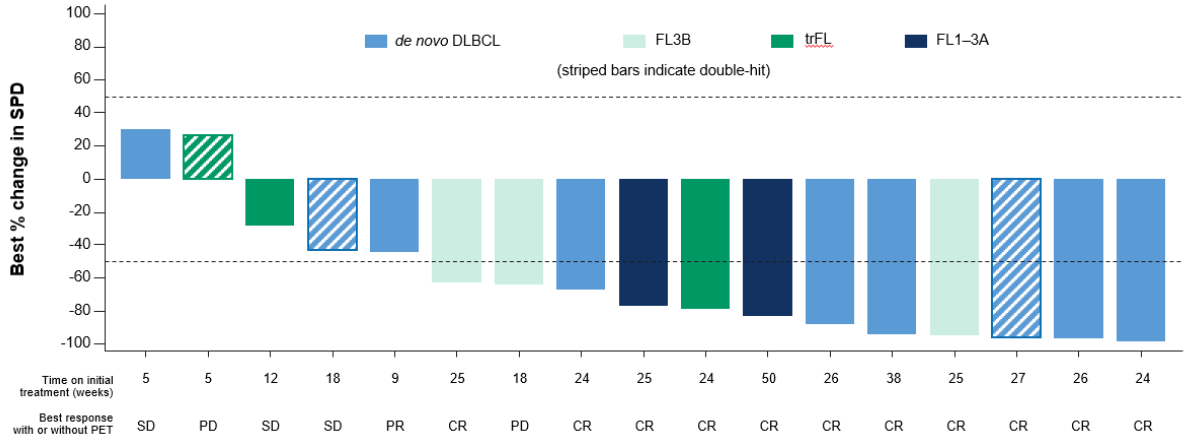
- High and durable response rates in R/R aggressive NHL patients who have failed multiple lines of therapy
  - CR rate of 71.4% at RP2D (2.5/10/30mg)
- CRS was mostly low grade, and confined to cycles 1-2

R/R = relapsed/refractory; aNHL = aggressive non-Hodgkin Lymphoma; CR = complete response; BOR = best overall response; CRS = cytokine release syndrome

Mosunetuzumab + Polivy

Novel combination with promising safety and efficacy

Phase Ib/II dose escalation



Responses, n (%)	All pts (N=22)	aNHL pts (n=19)	Post-CAR-T pts (n=7)	FL grade 1–3A pts (n=3)
BOR	15 (68.2)	12 (63.2)	4 (57.1)	3 (100)
CR	12 (54.5)	9 (47.4)	2 (28.6)	3 (100)

Median prior therapies: 3

- Promising efficacy in patients with R/R NHL, including in post-CAR-T patients
- M-Pola has an acceptable safety profile with low Gr 1 (2/22, 9%) and no Gr ≥2 CRS events observed
- Ph 2 expansion cohort in R/R DLBCL ongoing, with no mandatory hospitalization

R/R = relapsed/refractory; DLBCL=diffuse large B-cell lymphoma; FL=follicular lymphoma; aNHL = aggressive non-Hodgkin Lymphoma; CR = complete response; BOR = best overall response; CRS = cytokine release syndrome

ASCO 2021 Highlight

Tecentriq in adjuvant NSCLC: Phase 3 IMpower010 primary results

Heather Wakelee, M.D | Prof. of Medicine, Stanford University Medical Center / Deputy Director Stanford Cancer Institute

2021 ASCO ANNUAL MEETING

IMpower010: Primary Results of a Phase 3 Global Study of Atezolizumab vs Best Supportive Care After Adjuvant Chemotherapy in Resected Stage IB-IIIA Non-Small Cell Lung Cancer (NSCLC)

Heather A. Wakelee,[1] Nasser Altorki,[2] Caicun Zhou,[3] Tibor Csőszi,[4] Ihor O. Vynnychenko,[5] Oleksandr Goloborodko,[6] Alexander Luft,[7] Andrey Akopov,[8] Alex Martinez-Marti,[9] Hirotsugu Kenmotsu,[10] Yuh-Min Chen,[11] Antonio Chella,[12] Shunichi Sugawara,[13] Fan Wu,[14] Jing Yi,[15] Yu Deng,[15] Mark McCleland,[15] Elizabeth Bennett,[15] Barbara J. Gitlitz,[15] Enriqueta Felip[16]

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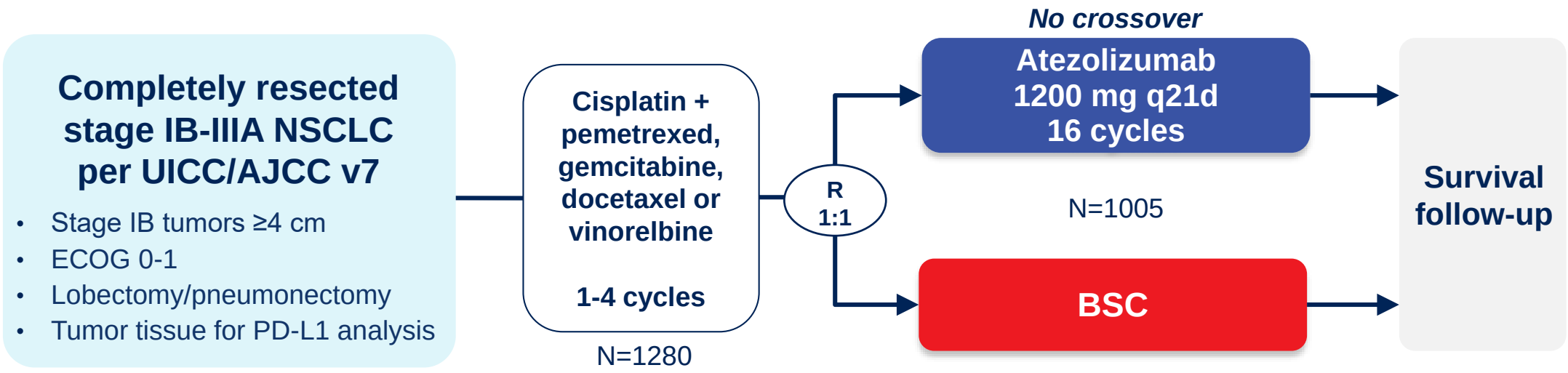
IMpower010: introduction

- Adjuvant platinum-based chemotherapy changed the standard of care for completely resected early-stage NSCLC (stage IB-IIIA) over 15 years ago[1-4]
  - DFS HR, 0.84 (95% CI: 0.78, 0.91)
  - OS HR, 0.89 (95% CI: 0.82, 0.96)
  - Leads to 4%-5% OS improvement at 5 years vs observation
- Osimertinib provides substantial DFS benefit in patients whose tumors harbor *EGFR* activating mutations,[5] but there remains a high unmet need for improved adjuvant treatment in other patients with NSCLC
- IMpower010 evaluated the efficacy and safety of adjuvant atezolizumab vs best supportive care (BSC) after adjuvant chemotherapy in patients with completely resected NSCLC

1. Pignon J-P, et al. J Clin Oncol 2008;26:3552-9; 2. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V8.2020; 3. Postmus PE, et al. Ann Oncol 2017;28(suppl 4):iv1-21.
4. Vansteenkiste J, et al. Ann Oncol 2019;30(8):1244-53; 5. Wu Y-L, et al. N Engl J Med 2020;383:1711-23.

IMpower010: study design



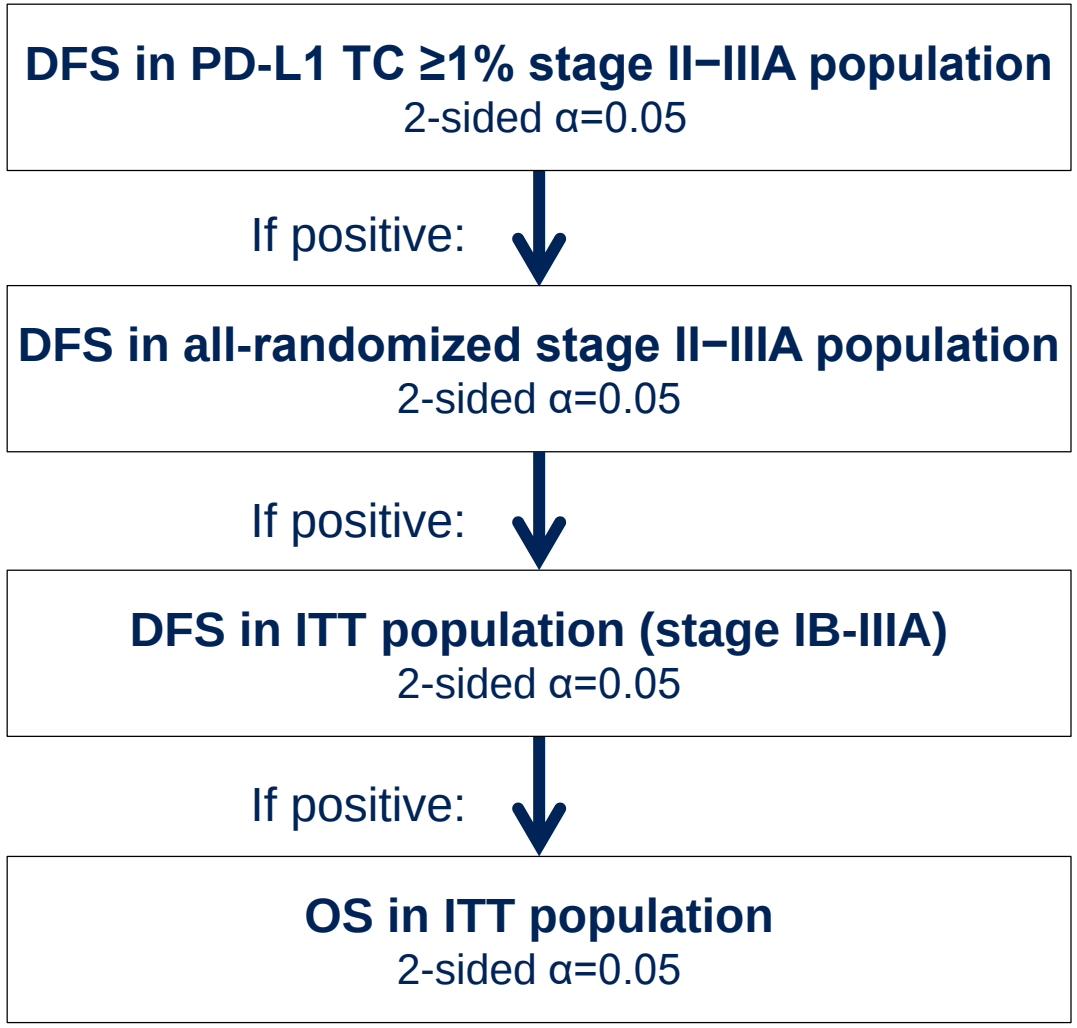
Stratification factors
- Male/female
- Stage (IB vs II vs IIIA)
- Histology
- PD-L1 tumor expression status[a]: TC2/3 and any IC vs TC0/1 and IC2/3 vs TC0/1 and IC0/1

Primary endpoints
- Investigator-assessed DFS tested hierarchically:
  - PD-L1 TC ≥1% (per SP263) stage II-IIIA population
  - All-randomized stage II-IIIA population
  - ITT population (stage IB-IIIA)

Key secondary endpoints
- OS in ITT population
- DFS in PD-L1 TC ≥50% (per SP263) stage II-IIIA population
- 3-y and 5-y DFS in all 3 populations

Both arms included observation and regular scans for disease recurrence on the same schedule.
ECOG, Eastern Cooperative Oncology Group; IC, tumor-infiltrating immune cells; ITT, intent to treat; TC, tumor cells. [a] Per SP142 assay.

IMpower010: statistical analysis plan



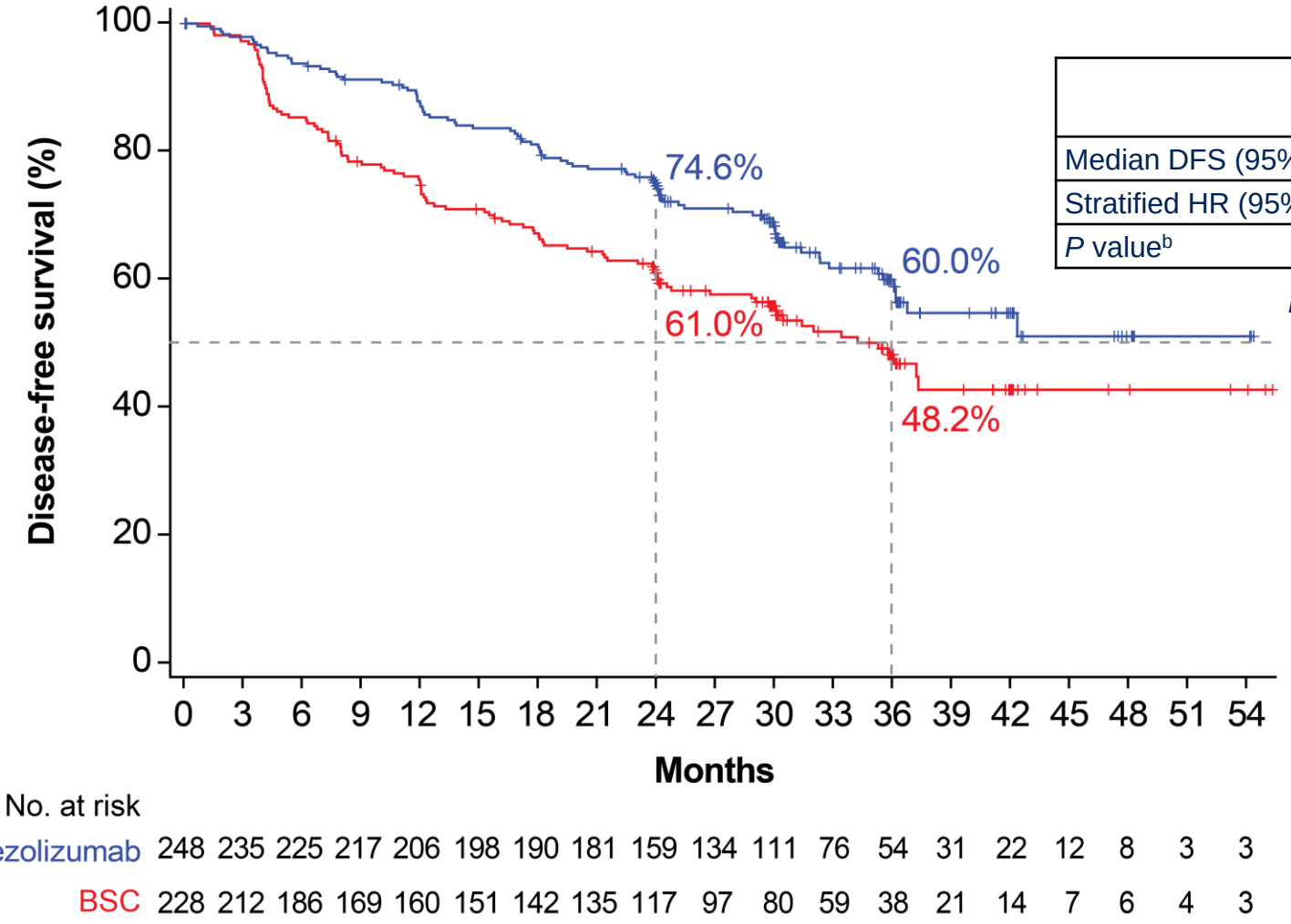
- The primary DFS endpoint was tested hierarchically in 3 primary analysis populations

IMpower010: baseline characteristics

Characteristic	All patients (N=1005)	PD-L1 TC ≥1% (SP263) (stage II-IIIA)		All randomized (stage II-IIIA)		ITT (stage IB-IIIA)	
		Atezolizumab (n=248)	BSC (n=228)	Atezolizumab (n=442)	BSC (n=440)	Atezolizumab (n=507)	BSC (n=498)
Median (range) age, y	**62 (26-84)**	61 (34–82)	62 (26–84)	62 (33–82)	62 (26–84)	62 (33–83)	62 (26–84)
Age ≥65 y, n (%)	**382 (38.0)**	92 (37.1)	97 (42.5)	161 (36.4)	177 (40.2)	184 (36.3)	198 (39.8)
Sex, male, n (%)	**672 (66.9)**	171 (69.0)	147 (64.5)	295 (66.7)	294 (66.8)	337 (66.5)	335 (67.3)
Race, n (%)							
White	**738 (73.4)**	162 (65.3)	166 (72.8)	307 (69.5)	324 (73.6)	362 (71.4)	376 (75.5)
Asian	**242 (24.1)**	78 (31.5)	56 (24.6)	121 (27.4)	106 (24.1)	130 (25.6)	112 (22.5)
Other	**25 (2.5)**	8 (3.2)	6 (2.6)	14 (3.2)	10 (2.3)	15 (3.0)	10 (2.0)
ECOG PS, n (%)							
0	**556 (55.3)**	140 (56.5)	125 (54.8)	239 (54.1)	252 (57.3)	273 (53.8)	283 (56.8)
1	**446 (44.4)**	107 (43.1)	102 (44.7)	201 (45.5)	187 (42.5)	232 (45.8)	214 (43.0)
Histology, non-squamous, n (%)	**659 (65.6)**	152 (61.3)	143 (62.7)	292 (66.1)	296 (67.3)	328 (64.7)	331 (66.5)
Stage, n (%)							
IB	**123 (12.2)**	–	–	–	–	65 (12.8)	58 (11.6)
IIA	**295 (29.4)**	85 (34.3)	76 (33.3)	147 (33.3)	148 (33.6)	147 (29.0)	148 (29.7)
IIB	**174 (17.3)**	46 (18.5)	37 (16.2)	90 (20.4)	84 (19.1)	90 (17.8)	84 (16.9)
IIIA	**413 (41.1)**	117 (47.2)	115 (50.4)	205 (46.4)	208 (47.3)	205 (40.4)	208 (41.8)
Tobacco use history, n (%)							
Never	**222 (22.1)**	51 (20.6)	41 (18.0)	100 (22.6)	96 (21.8)	114 (22.5)	108 (21.7)
Current/previous	**783 (77.9)**	197 (79.4)	187 (82.0)	342 (77.4)	344 (78.2)	393 (77.5)	390 (78.3)
PD-L1 by SP263, TC≥1%, n (%)[a]	**535 (54.6)**	248 (100)	228 (100)	248 (57.8)	228 (53.0)	283 (57.4)	252 (51.9)
EGFR mutation status, n (%)[b]							
Positive	**117 (11.6)**	23 (9.3)	20 (8.8)	49 (11.1)	60 (13.6)	53 (10.5)	64 (12.9)
Negative	**527 (52.4)**	123 (49.6)	125 (54.8)	229 (51.8)	234 (53.2)	261 (51.5)	266 (53.4)
Unknown[c]	**361 (35.9)**	102 (41.1)	83 (36.4)	164 (37.1)	146 (33.2)	193 (38.1)	168 (33.7)
ALK rearrangement status, n (%)[b]							
Positive	**33 (3.3)**	12 (4.8)	11 (4.8)	14 (3.2)	17 (3.9)	15 (3.0)	18 (3.6)
Negative	**574 (57.1)**	133 (53.6)	121 (53.1)	251 (56.8)	256 (58.2)	280 (55.2)	294 (59.0)
Unknown[c]	**398 (39.6)**	103 (41.5)	96 (42.1)	177 (40.0)	167 (38.0)	212 (41.8)	186 (37.3)

Clinical cutoff: January 21, 2021. [a] 26 patients in the ITT population had unknown PD-L1 status as assessed by SP263. [b] For patients with non-squamous NSCLC, *EGFR/ALK* status was assessed locally or centrally. [c] 89.2% of patients with unknown *EGFR* status and 80.7% of patients with unknown *ALK* status had squamous NSCLC and were not required to undergo local or central testing.

IMpower010: DFS in the PD-L1 TC ≥1%[a] stage II-IIIA population (primary endpoint)



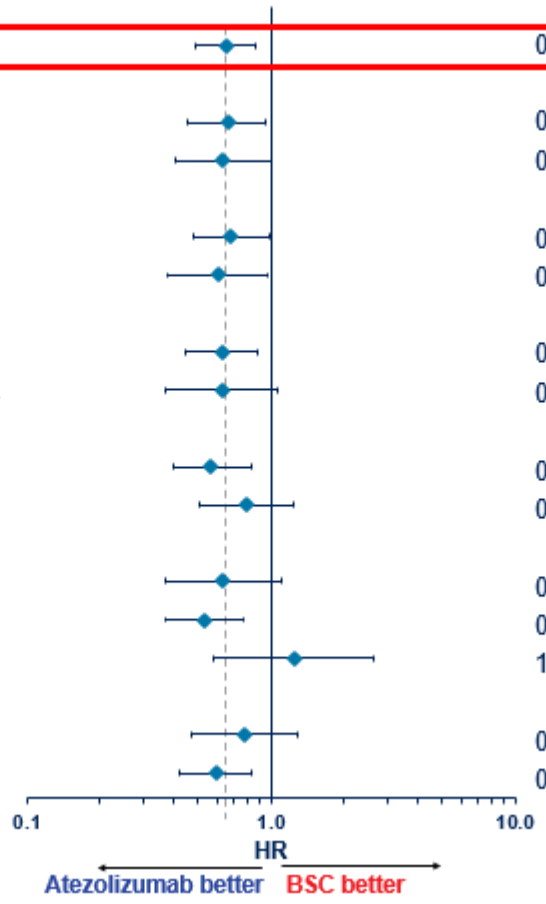
	Atezolizumab (n=248)	BSC (n=228)
Median DFS (95% CI), mo	NE (36.1, NE)	35.3 (29.0, NE)
Stratified HR (95% CI)	0.66 (0.50, 0.88)	
P value[b]	0.004[c]	

Median follow-up: 32.8 mo (range, 0.1-57.5)

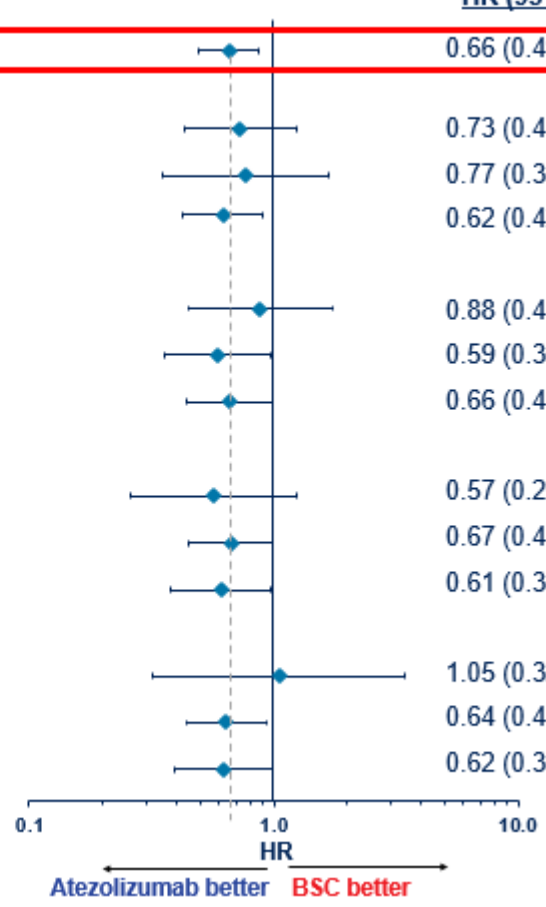
Clinical cutoff: January 21, 2021. CI, confidence interval; HR, hazard ratio; NE, not evaluable. [a] Per SP263 assay. [b] Stratified log-rank. [c] Crossed the significance boundary for DFS.

IMpower010: DFS in key subgroups of the PD-L1 TC ≥1%[a] stage II-IIIA population

Subgroup	N	HR (95% CI)[b]
All patients	476	0.66 (0.49, 0.87)
Age		
<65 y	287	0.67 (0.46, 0.96)
≥65 y	189	0.64 (0.41, 1.01)
Sex		
Male	318	0.69 (0.48, 0.99)
Female	158	0.61 (0.38, 0.97)
Race		
White	328	0.63 (0.45, 0.89)
Asian	134	0.63 (0.37, 1.06)
ECOG PS		
0	265	0.57 (0.40, 0.83)
1	209	0.79 (0.51, 1.23)
Tobacco use history		
Never	92	0.63 (0.37, 1.10)
Previous	309	0.54 (0.37, 0.78)
Current	75	1.24 (0.58, 2.64)
Histology		
Squamous	181	0.78 (0.47, 1.29)
Non-squamous	295	0.60 (0.42, 0.84)

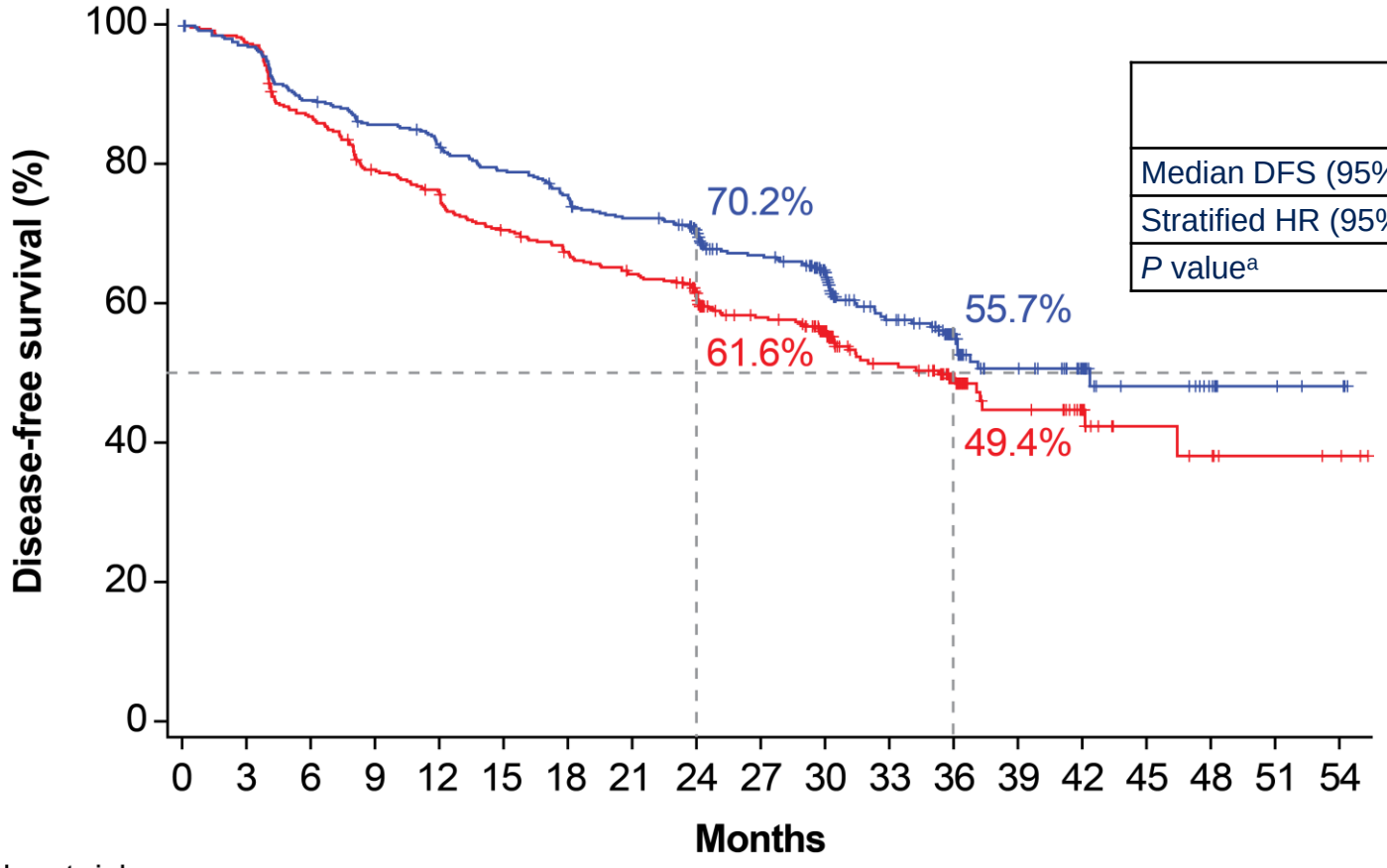


Subgroup	N	HR (95% CI)[b]
All patients	476	0.66 (0.49, 0.87)
Stage		
IIA	161	0.73 (0.43, 1.24)
IIB	83	0.77 (0.35, 1.69)
IIIA	232	0.62 (0.42, 0.90)
Regional lymph node stage (pN)		
N0	106	0.88 (0.45, 1.74)
N1	194	0.59 (0.36, 0.97)
N2	176	0.66 (0.44, 0.99)
***EGFR* mutation status**		
Yes	43	0.57 (0.26, 1.24)
No	248	0.67 (0.45, 1.00)
Unknown[c]	185	0.61 (0.38, 0.98)
***ALK* rearrangement status**		
Yes	23	1.05 (0.32, 3.45)
No	254	0.64 (0.44, 0.93)
Unknown[c]	199	0.62 (0.39, 1.00)



Clinical cutoff: January 21, 2021. [a] Per SP263 assay. [b] Stratified for all patients; unstratified for all other subgroups.
[c] 89.2% and 80.7% of patients with unknown *EGFR* or *ALK* status, respectively, had squamous NSCLC and were not required to undergo local or central testing.

IMpower010: DFS in the all-randomized stage II-IIIA population (primary endpoint)



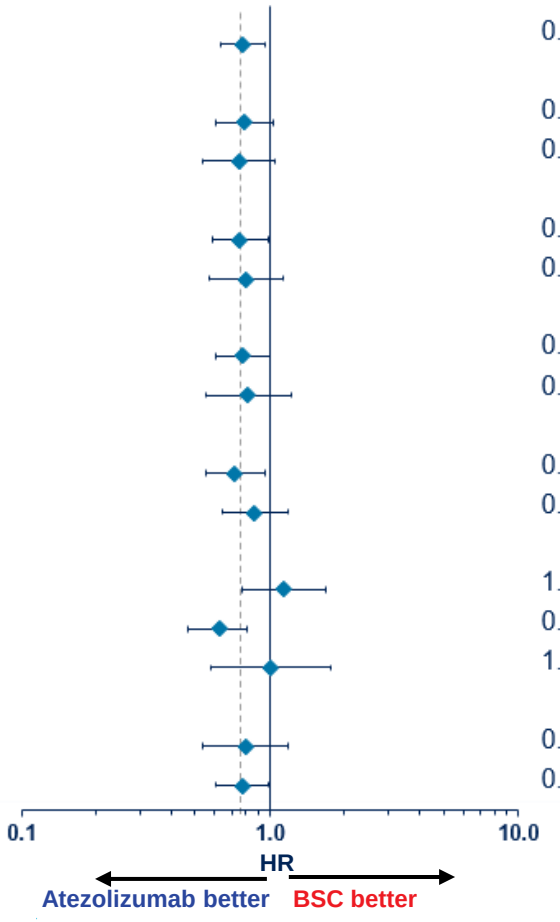
	Atezolizumab (n=442)	BSC (n=440)
Median DFS (95% CI), mo	42.3 (36.0, NE)	35.3 (30.4, 46.4)
Stratified HR (95% CI)	0.79 (0.64, 0.96)	
P value[a]	0.02[b]	

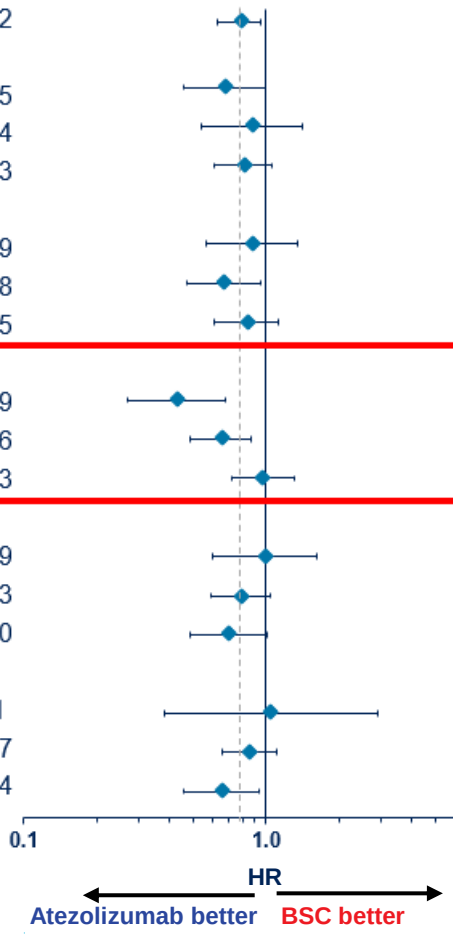
Median follow-up: 32.2 mo (range, 0-57.5)

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] Crossed the significance boundary for DFS.

IMpower010: DFS in key subgroups of the all-randomized stage II-IIIA population

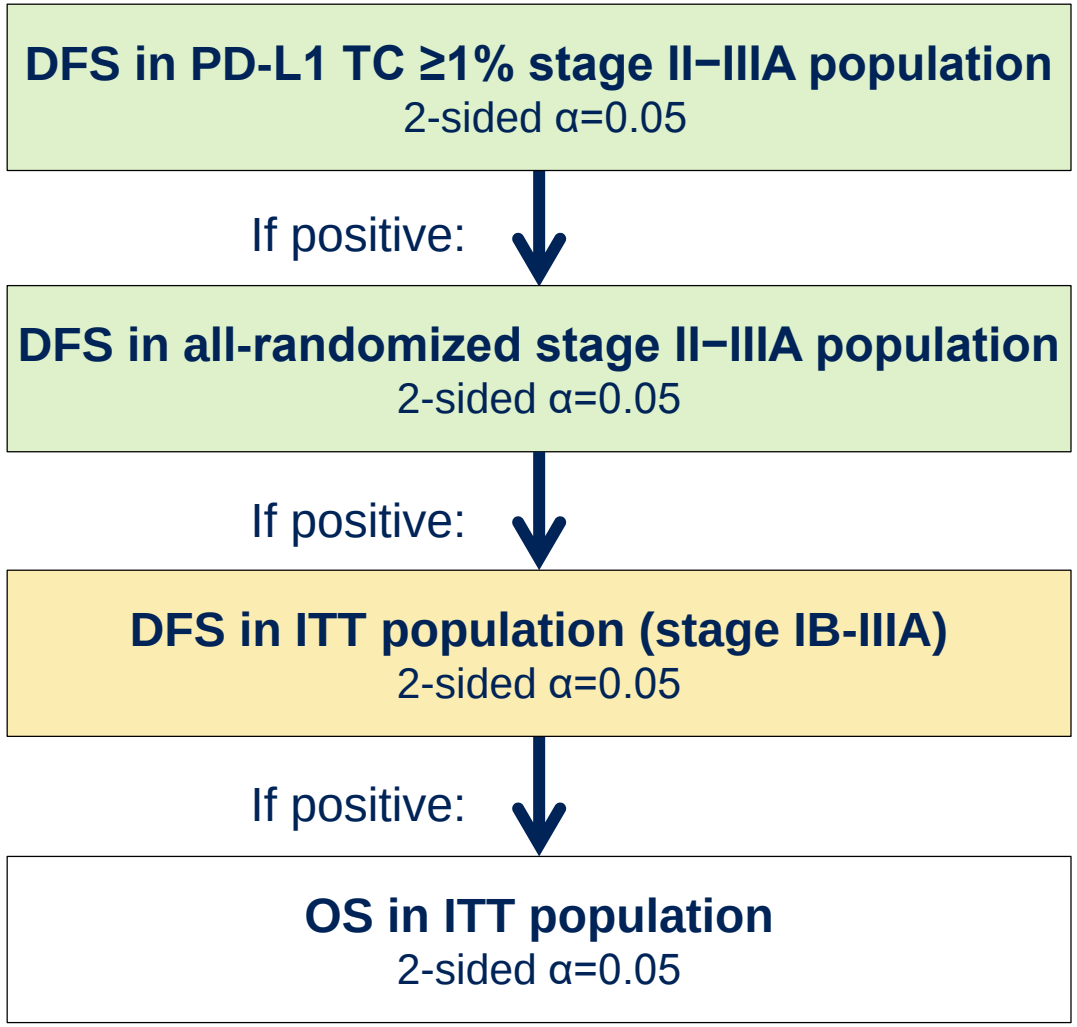
Subgroup	N	HR (95% CI)[a]
All patients	882	0.79 (0.64, 0.96)
Age		
<65 y	544	0.79 (0.61, 1.03)
≥65 y	338	0.76 (0.54, 1.05)
Sex		
Male	589	0.76 (0.59, 0.99)
Female	293	0.80 (0.57, 1.13)
Race		
White	631	0.78 (0.61, 1.00)
Asian	227	0.82 (0.55, 1.22)
ECOG PS		
0	491	0.72 (0.55, 0.95)
1	388	0.87 (0.64, 1.18)
Tobacco use history		
Never	196	1.13 (0.77, 1.67)
Previous	547	0.62 (0.47, 0.81)
Current	139	1.01 (0.58, 1.75)
Histology		
Squamous	294	0.80 (0.54, 1.18)
Non-squamous	588	0.78 (0.61, 0.99)
All patients	882	0.79 (0.64, 0.96)
Stage		
IIA	295	0.68 (0.46, 1.00)
IIB	174	0.88 (0.54, 1.42)
IIIA	413	0.81 (0.61, 1.06)
Regional lymph node stage (pN)		
N0	229	0.88 (0.57, 1.35)
N1	348	0.67 (0.47, 0.95)
N2	305	0.83 (0.61, 1.13)
SP263 PD-L1 status		
TC≥50%	229	0.43 (0.27, 0.68)
TC≥1%	476	0.66 (0.49, 0.87)
TC<1%	383	0.97 (0.72, 1.31)
***EGFR* mutation status**		
Yes	109	0.99 (0.60, 1.62)
No	463	0.79 (0.59, 1.05)
Unknown	310	0.70 (0.49, 1.01)
***ALK* rearrangement status**		
Yes	31	1.04 (0.38, 2.90)
No	507	0.85 (0.66, 1.10)
Unknown	344	0.66 (0.46, 0.93)





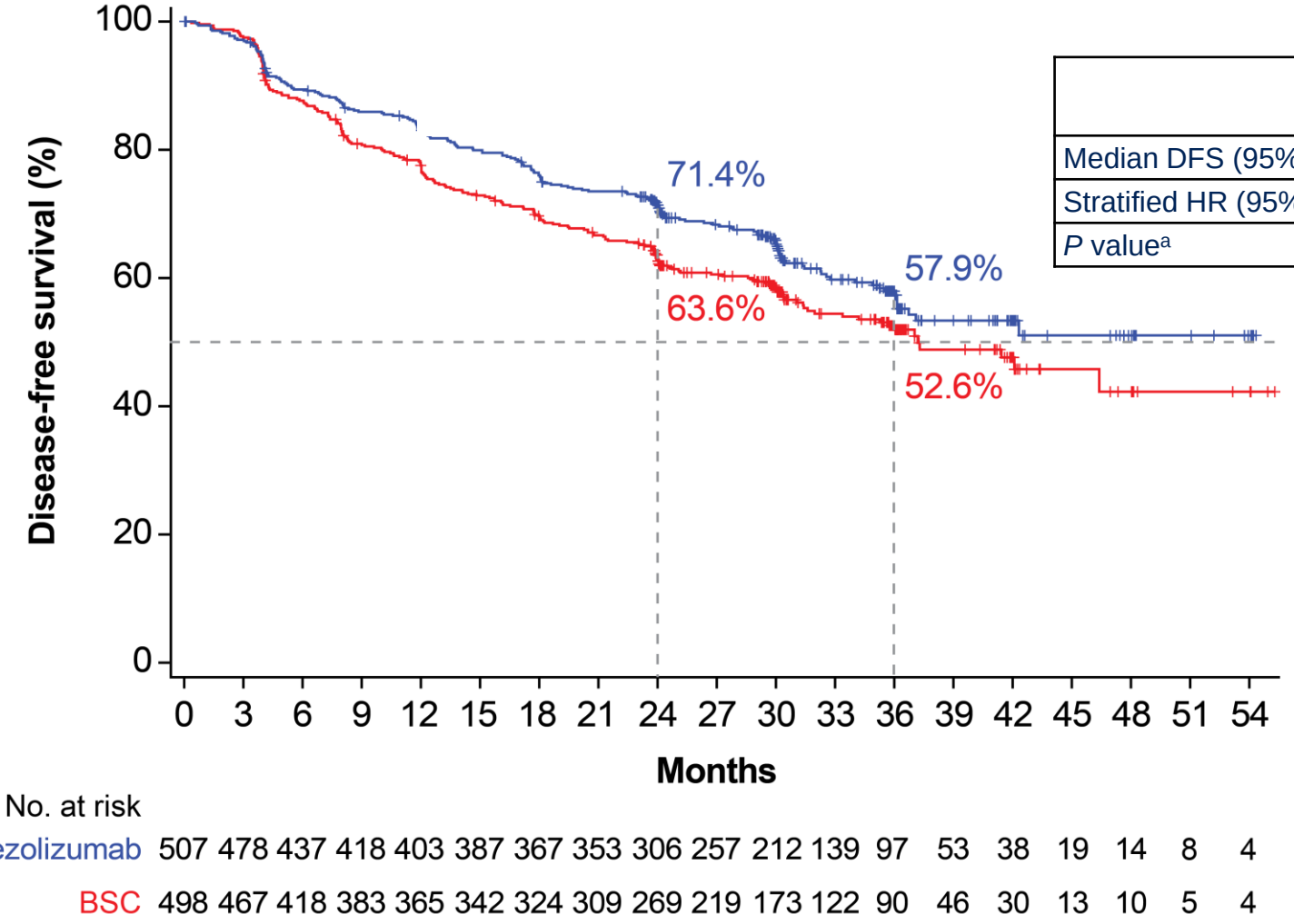
Clinical cutoff: January 21, 2021. [a] Stratified for all patients; unstratified for all other subgroups.

IMpower010: statistical analysis plan



- The significance boundary was not crossed at this DFS interim analysis in the ITT population (stage IB-IIIA) and testing will continue to the final DFS analysis in this population

IMpower010: DFS in the ITT population (stage IB-IIIA; primary endpoint)



	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[a]	0.04[b]	

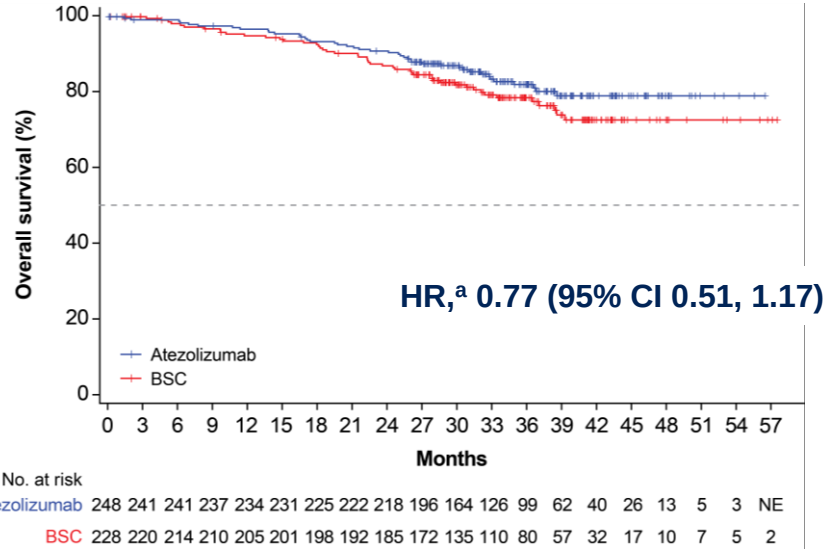
Median follow-up: 32.2 mo (range, 0-58.8)

- DFS in the ITT population did not cross the significance boundary at this interim DFS analysis

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] The statistical significance boundary for DFS was not crossed.

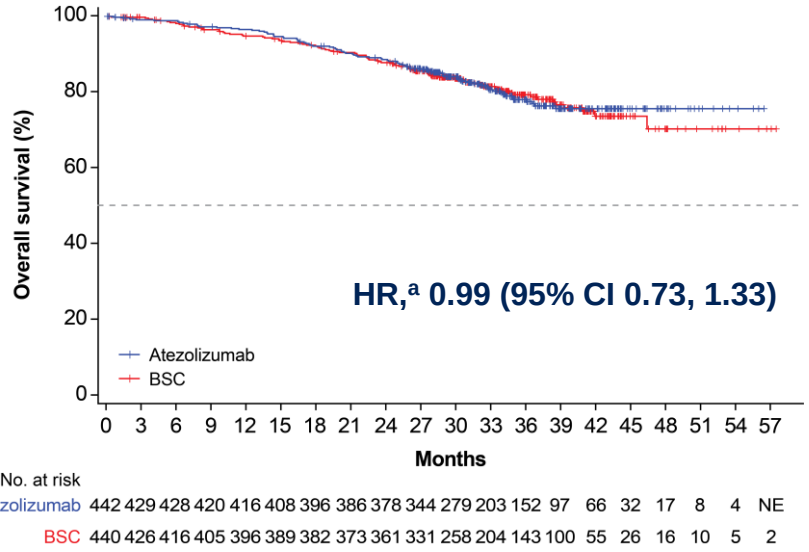
IMpower010: early OS data at interim DFS analysis

PD-L1 TC ≥ 1% stage II-IIIA



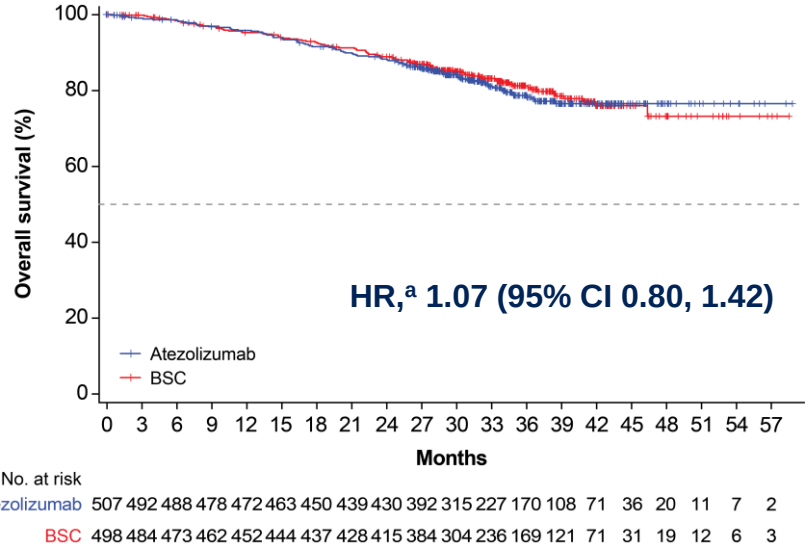
No. at risk																				
Atezolizumab	248	241	241	237	234	231	225	222	218	196	164	126	99	62	40	26	13	5	3	NE
BSC	228	220	214	210	205	201	198	192	185	172	135	110	80	57	32	17	10	7	5	2

All-randomized stage II-IIIA



No. at risk																				
Atezolizumab	442	429	428	420	416	408	396	386	378	344	279	203	152	97	66	32	17	8	4	NE
BSC	440	426	416	405	396	389	382	373	361	331	258	204	143	100	55	26	16	10	5	2

ITT



No. at risk																				
Atezolizumab	507	492	488	478	472	463	450	439	430	392	315	227	170	108	71	36	20	11	7	2
BSC	498	484	473	462	452	444	437	428	415	384	304	236	169	121	71	31	19	12	6	3

- OS data were immature at this pre-planned DFS interim analysis
  - OS in the ITT population was not formally tested
  - A trend toward OS improvement with atezolizumab was seen in the PD-L1 TC ≥1% stage II-IIIA population

Clinical cutoff: January 21, 2021. [a] Stratified.

IMpower010: safety summary[a]

n (%)	Atezolizumab (n=495)	BSC (n=495)
Any-cause AE	459 (92.7)	350 (70.7)
Treatment-related AE	335 (67.7)	–
Grade 3-4 AE	108 (21.8)	57 (11.5)
Treatment-related grade 3-4 AE	53 (10.7)	–
Serious AE	87 (17.6)	42 (8.5)
Treatment-related serious AE	37 (7.5)	–
Grade 5 AE	8 (1.6)[b]	3 (0.6)[c]
Treatment-related grade 5 AE	4 (0.8)	–
AE leading to dose interruption of atezolizumab	142 (28.7)	–
AE leading to atezolizumab discontinuation	90 (18.2)	–
Immune-mediated AEs	256 (51.7)	47 (9.5)
Grade 3-4 immune-mediated AEs	39 (7.9)	3 (0.6)
Immune-mediated AEs requiring the use of systemic corticosteroids	60 (12.1)	4 (0.8)

Clinical cutoff: January 21, 2021. AE, adverse event; [a] Data are from the safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). [b] Interstitial lung disease*; pneumothorax; multiple organ dysfunction syndrome*; cerebrovascular accident; arrhythmia; myocarditis*; acute myeloid leukemia*; acute cardiac failure. [c] Pneumonia; pulmonary embolism; cardiac tamponade and septic shock in the same patient. *, Treatment related per investigator.

IMpower010: immune-mediated AEs[a]

imAEs occuring in ≥1% of patients

	Atezolizumab (n=495)		BSC (n=495)	
n (%)	Any grade	Grade 3-4	Any grade	Grade 3-4
Any immune-mediated AEs	256 (51.7)[b]	39 (7.9%)	47 (9.5)	5 (0.6)
Rash	91 (18.4)	7 (1.4)	11 (2.2)	0
Hepatitis (diagnosis and laboratory abnormalities)	86 (17.4)	20 (4.0)	22 (4.4)	1 (0.2)
Hepatitis (laboratory abnormalities)	81 (16.4)	16 (3.2)	21 (4.2)	1 (0.2)
Hepatitis (diagnosis)	7 (1.4)	4 (0.8)	1 (0.2)	0
Hypothyroidism	86 (17.4)	0	3 (0.6)	0
Hyperthyroidism	32 (6.5)	2 (0.4)	4 (0.8)	0
Pneumonitis	19 (3.8)[c]	4 (0.8)	3 (0.6)	0
Infusion-related reaction	7 (1.4)	1 (0.2)	0	0
Adrenal insufficiency	6 (1.2)	2 (0.4)	0	0

imAEs occuring in <1% of patients

	Atezolizumab (n=495)		BSC (n=495)	
n (%)	Any Grade	Grade 3-4	Any grade	Grade 3-4
Meningoencephalitis	4 (0.8)	3 (0.6)	0	0
Colitis	4 (0.8)	2 (0.4)	1 (0.2)	0
Diabetes mellitus	4 (0.8)	0	1 (0.2)	0
Myositis (myositis and rhabdomyolysis)	4 (0.8)	0	1 (0.2)	0
Pancreatitis	2 (0.4)	1 (0.2)	1 (0.2)	1 (0.2)
Encephalitis	2 (0.4)	2 (0.4)	0	0
Severe cutaneous adverse reaction	2 (0.4)	0	0	0
Autoimmune hemolytic anemia	2 (0.4)	0	0	0
Myocarditis	2 (0.4)[c]	0	0	0
Meningitis	2 (0.4)	1 (0.2)	0	0
Guillain-Barre syndrome	1 (0.2)	1 (0.2)	0	0
Ocular inflammatory toxicity	1 (0.2)	0	1 (0.2)	1 (0.2)
Hypophysitis	1 (0.2)	0	0	0
Nephritis	1 (0.2)	0	0	0
Vasculitis	0	0	1 (0.2)	1 (0.2)

Clinical cutoff: January 21, 2021. [a] Data are from the safety population (all randomized patients who received ≥1 atezolizumab dose or for BSC, had ≥1 post-baseline assessment). [b] Includes 2 (0.4%) Grade 5 events. [c] Includes 1 (0.2%) Grade 5 event.

IMpower010: conclusions

- IMpower010 is the first Phase III study of cancer immunotherapy to demonstrate DFS improvement in the adjuvant NSCLC setting after platinum-based chemotherapy
  - Adjuvant atezolizumab following complete resection and adjuvant chemotherapy showed statistically significant DFS benefit in the PD-L1 TC ≥1% stage II-IIIA (HR, 0.66; 95% CI: 0.50, 0.88) and all-randomized stage II-IIIA (HR, 0.79; 95% CI: 0.64, 0.96) populations, with enriched clinical benefit in patients whose tumors express PD-L1
- IMpower010 will continue for DFS and OS analyses in the ITT population
  - DFS in the ITT population, including patients with stage IB disease, did not cross the significance boundary at this interim DFS analysis
  - At this pre-planned interim DFS analysis, OS data were immature and not formally tested
- The safety profile of atezolizumab was consistent with prior experience of atezolizumab monotherapy across indications and lines of therapy
- Atezolizumab may be considered a practice-changing adjuvant treatment option for patients with PD-L1 TC ≥1% stage II-IIIA NSCLC

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