
Roche

Combinations in Cancer Immunotherapy

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16 May 2017

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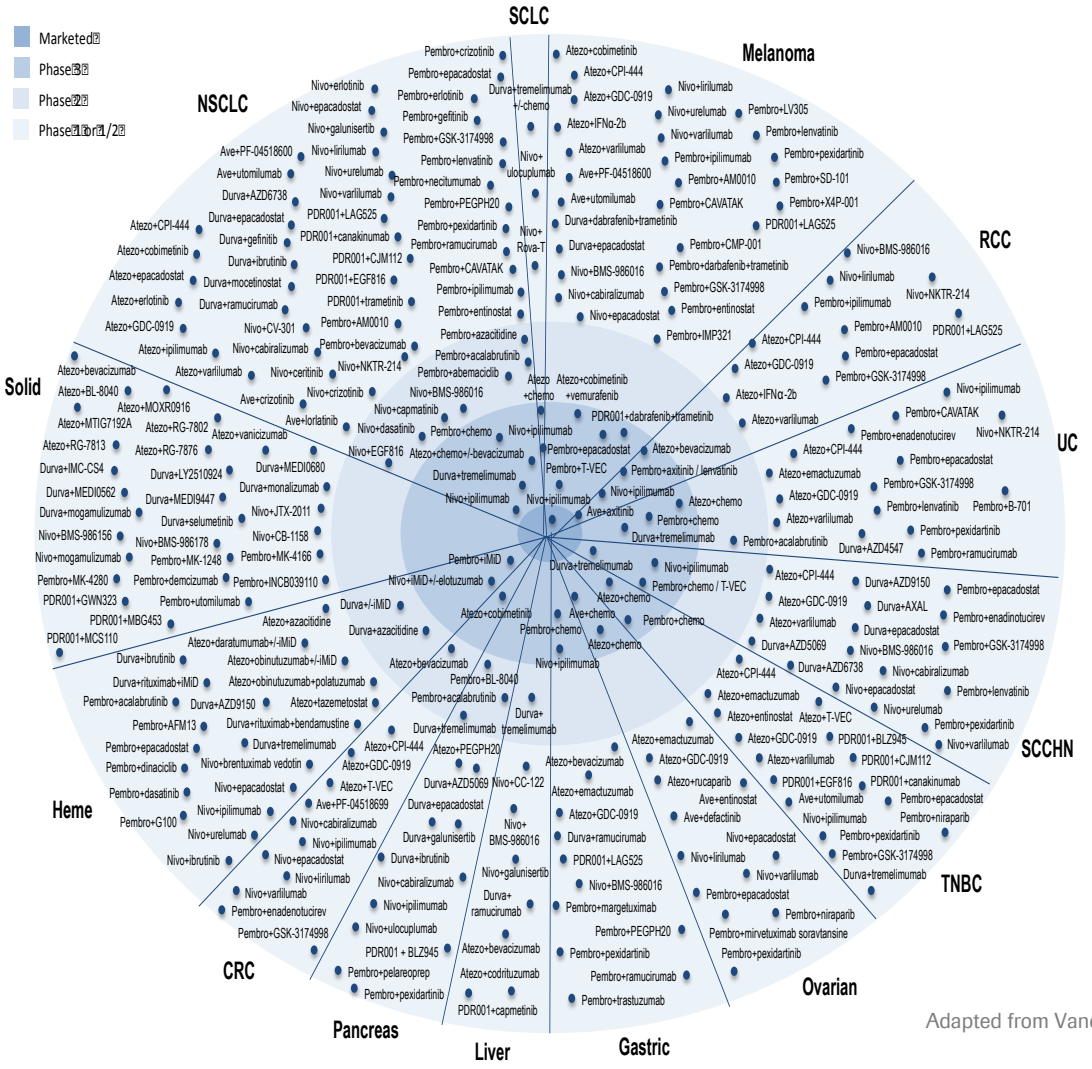
Intense CIT combination landscape evolving:

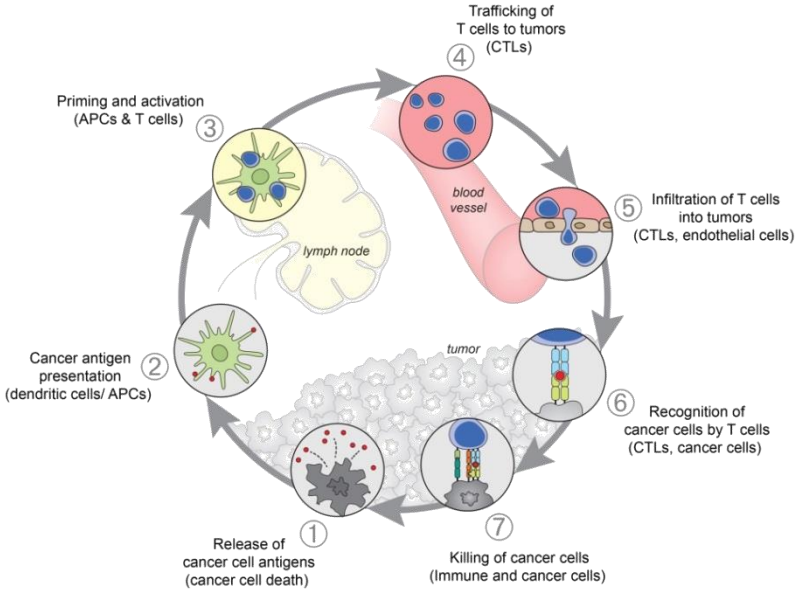
Over 800+ cancer immunotherapy combination studies already in the clinic



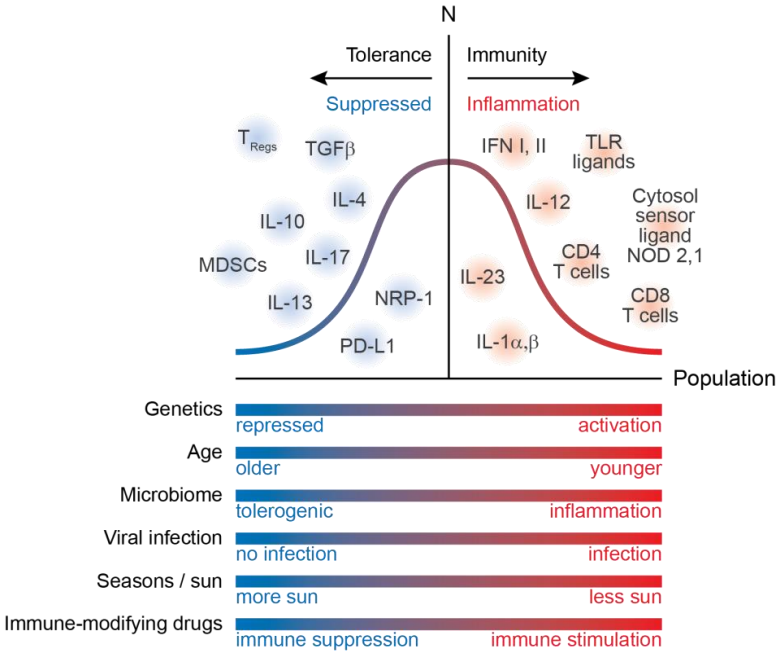
Adapted from Vanessa Lucey of CRI by Gergely Jarmy, Chen and Mellman, *Nature 2017*

Immune biology

A complex set of tumor, host and environmental factors govern strength, and timing of anti-cancer immune responses



Chen and Mellman. *Immunity* 2013

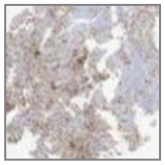


Chen and Mellman. *Nature 2017*

Human cancer *immunology*

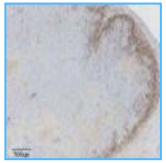
Inflamed — Non-inflamed

INFLAMED



CD8+ T cells infiltrated, but non-functional

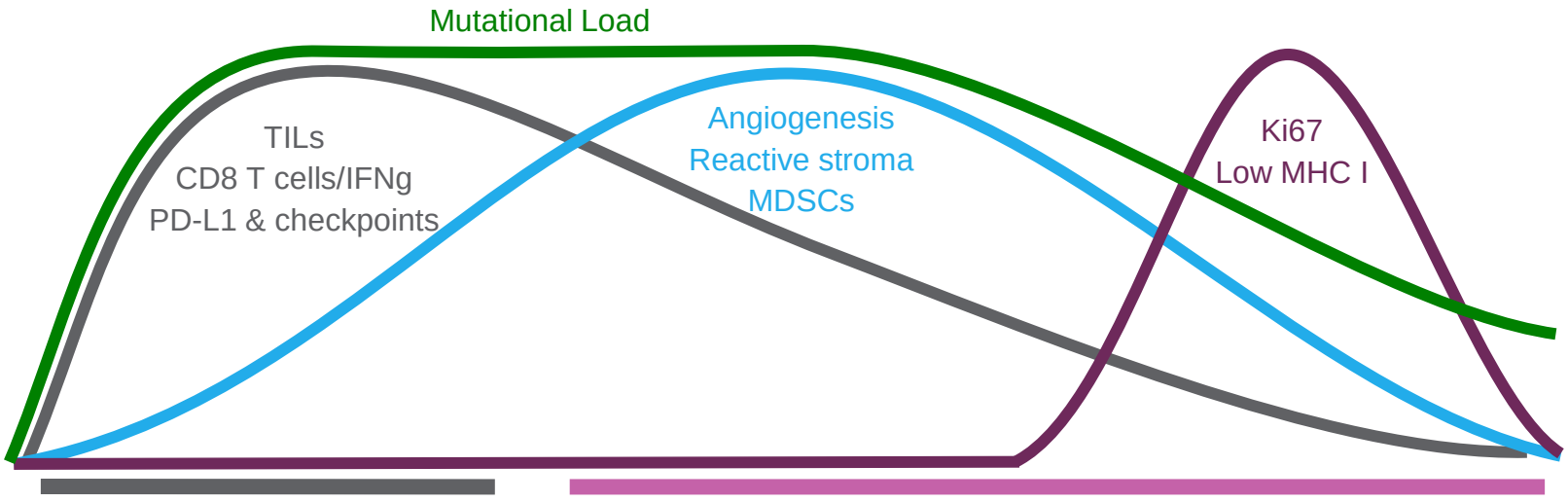
IMMUNE EXCLUDED



CD8+ T cells accumulated but have not efficiently infiltrated

IMMUNE DESERT

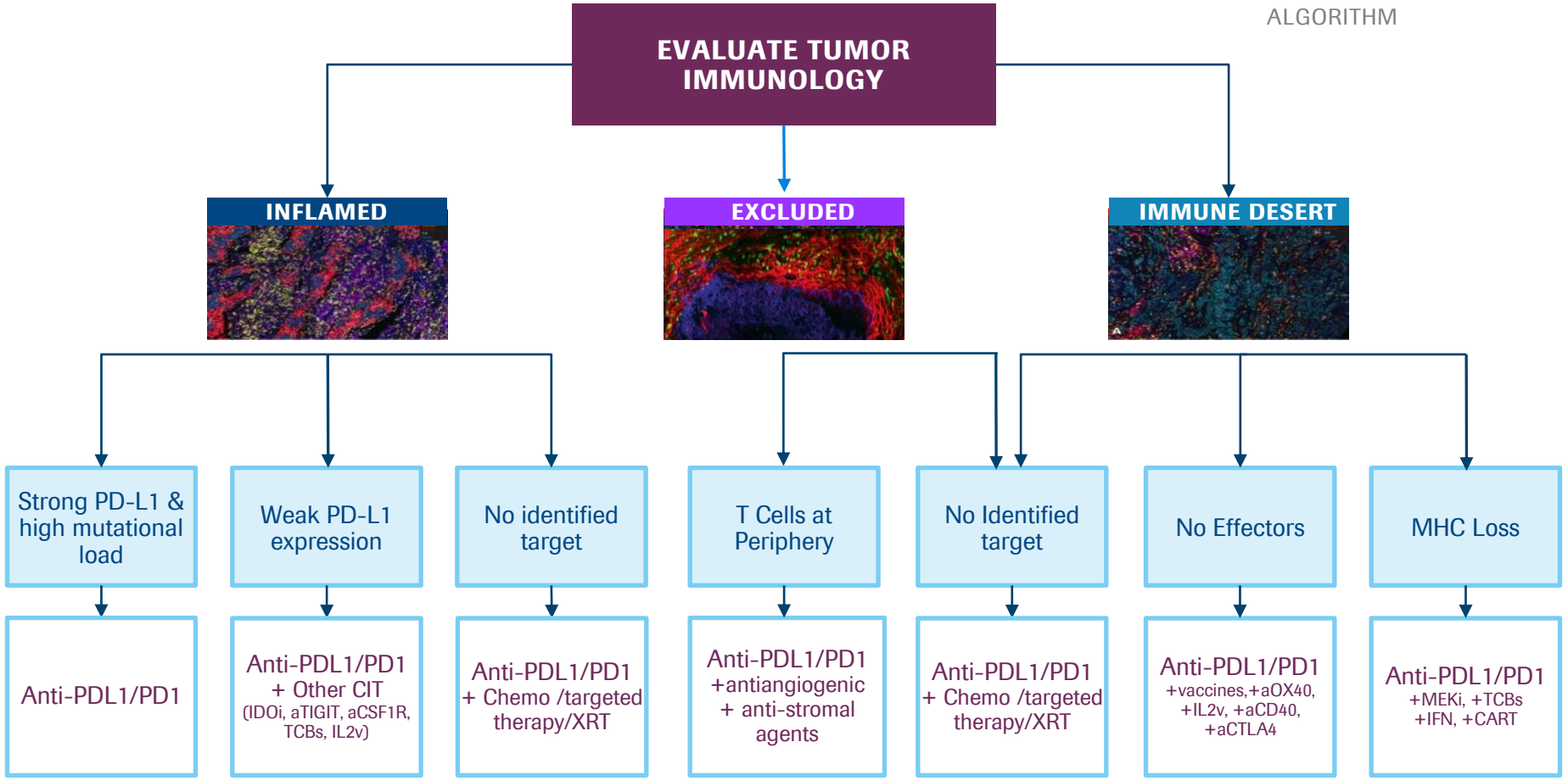
CD8+ T cells are absent from tumor and its periphery



Modified from Hegde PS et al., Clin Canc Res 2016

Towards a personalized cancer immunotherapy paradigm

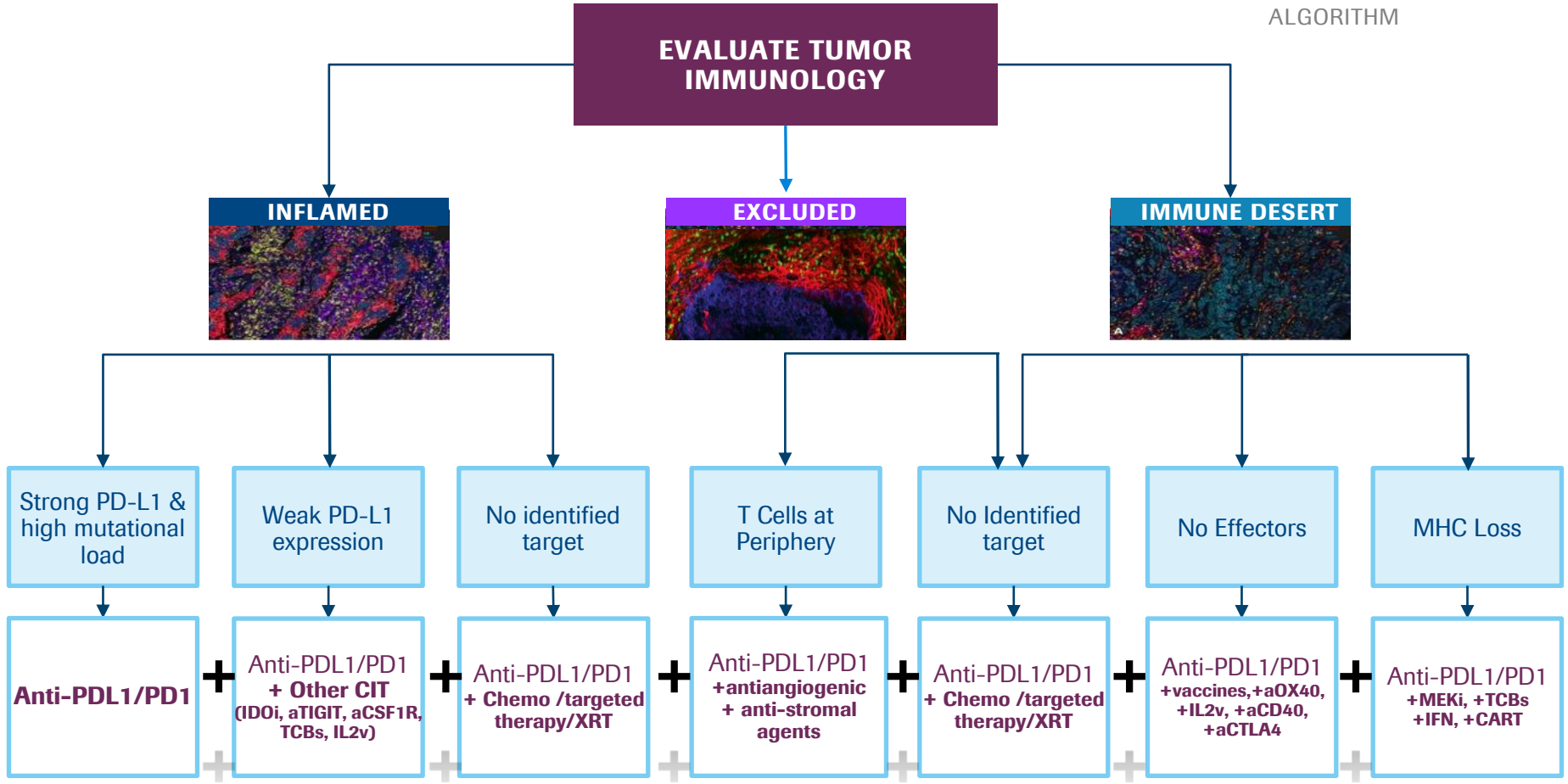
HYPOTHETICAL TREATMENT ALGORITHM



Modified from Kim and Chen, Annals of Oncology 2016

Or *maybe* we can put them all together?

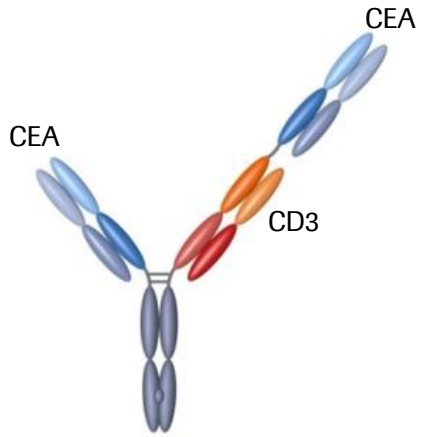
HYPOTHETICAL TREATMENT ALGORITHM



Modified from Kim and Chen, Annals of Oncology 2016

CEA CD3 T-cell bispecific (TCB) for solid tumors

Ph Ib data to be presented at ASCO 2017

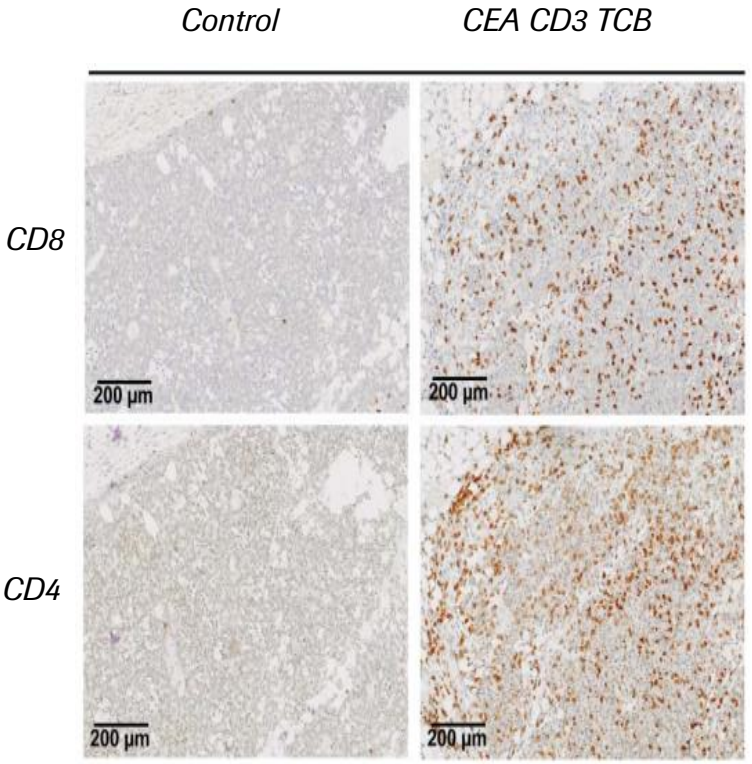


Simultaneous binding to tumor and T cells results in:

- T cell engagement, activation and killing of tumor cells by delivery of cytotoxic granules
- T-cell engagement independent of specificity and activation status

CEA CD3 TCB generates synthetic immunity in preclinical models

Intra-tumor T cell staining



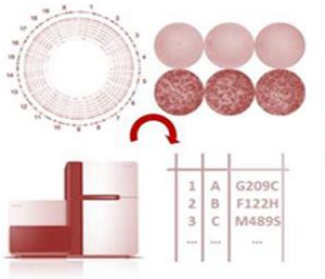
Bacac, Klein, and Umana. *OncoImmunology 2016*

Personalized Cancer Vaccines (PCV)

Enhanced antigen recognition may benefit all immunological phenotypes

Tumor Biopsy

Mutation Identification



Vaccine Design

Vaccine Synthesis

mRNA backbone | Neo-antigen 1 | Neo-antigen 2 | Neo-antigen 3 | Neo-antigen 4 | Neo-antigen 5 | mRNA backbone

Cancer immunotherapy pipeline overview

Phase I (11 NMEs + 28 AIs)

RG6026	CD20 CD3 TCB	hematopoietic tumors
RG6058	TIGIT ± Tecentriq	solid tumors
RG6078	IDO inh	solid tumors
	IDO inh + Tecentriq	solid tumors
RG6180	personalized cancer vaccine	oncology
RG7155	emactuzumab + Tecentriq	solid tumors
	emactuzumab + CD40 iMAb	solid tumors
RG7421	Cotellic + Tecentriq + Avastin	2/3L CRC
RG7446	Tecentriq	solid tumors
	Tecentriq	NMIBC
	T + Zelboraf ± Cotellic	melanoma
	T ± Avastin ± chemo	HCC-GC-PaC
	T ± Avastin ± chemo	solid tumors
	T + Cotellic	solid tumors
	T + Ipi/IFN	solid tumors
	T + Tarceva/Alecensa	NSCLC
	T + anti-CD20 multiple combos	lymphoma
	T ± lenalidomide ± daratumumab	MM
	T + K/HP	HER2+ BC
	T + HMA	MDS
	T + radium 223	mCRPC
	T + guadecitabine	AML
RG7461	FAP IL2v FP + Tecentriq ± Avastin	RCC
RG7802	CEA CD3 TCB ± Tecentriq	solid tumors
RG7813	CEA* IL2v FP+Tecentriq	solid tumors
RG7828	CD20/CD3 TDB	heme tumors
RG7876	CD40 iMAb + Tecentriq	solid tumors
	CD40 iMAb + vanucizumab	solid tumors
RG7888	OX40 iMAb	solid tumors
	OX40 iMAb + Tecentriq	solid tumors
INCY**	Tecentriq + epacadostat	solid tumors
CLDX**	Tecentriq + varlilumab	solid tumors
CRVS**	Tecentriq + CPI-4444	solid tumors
KITE**	Tecentriq + KTE-C19	r/r DLBCL
AMGN**	Tecentriq + talimogene laherp	TNBC, CRC
JNJ**	Tecentriq ± daratumumab	solid tumors
CLVS**	Tecentriq + rucaparib	ovarian ca
EPZM**	Tecentriq + tazemetostat	r/r DLBCL
BLRX**	Tecentriq + BL-8040	AML, solid tumors

Phase II (4 AIs)

RG3502	Kadcyla + Tecentriq	HER2+ 2L mBC
RG7421	Cotellic + Tecentriq ± taxane	TNBC
IMDZ**	Tecentriq + NY-ESO-1	soft tissue sarcoma
SNDX**	Tecentriq + entinostat	TNBC

Phase III (15 AIs)

RG7421	Cotellic + Tecentriq	3 L CRC
	Cotellic + T + Zelboraf	BRAFm melanoma
RG7446	Tecentriq	NSCLC adj
	Tecentriq	MIBC adj
	T + Abraxane	1L non-sq NSCLC
	T + chemo+Avastin	1L ovarian cancer
	T + chemo + Avastin	1L non-sq NSCLC
	T + chemo + pemetrexed	1L non-sq NSCLC
	T + Abraxane	1L sq NSCLC
	T + Abraxane	TNBC
	T + Avastin	RCC
	T ± chemo	1L mUC
	T + chemo	1L extens. stage SCLC
	T + enzalutamide	CRPC
	Tecentriq Dx+	1L sq+non-sq SCLC
	Tecentriq	RCC adj

Registration (1 NMEs + 1 AIs)

RG7446	Tecentriq[1]	2L mUC
	Tecentriq[2]	2L+ NSCLC

1. Filing based on IMvigor210, accelerated approval in US for 1L & 2L; phase III in 2L ongoing
2. Approved in US

** External collaborations: INCY- Incyte IDO inh; CLDX – Celldex CD27 MAb; CRVS – Corvus ADORA2A antag; KITE – Kite KTE-C19; AMGN – Amgen oncolytic virus; JNJ – Janssen CD38 MAb; CLVS – Clovis PARP inh; EPZM – Epizyme EZH2 inh; BLRX - BioLine Rx CXCR4 antag; IMDZ – Immune Design CMB305; SNDX – Syndax HDAC inh

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

RG-No Roche/Genentech
*INN: cergutuzumab amunaleukin
T=Tecentriq

Status as of April 27, 2017

ASCO 2017: Major oral presentations

Roche Analyst Event

Monday, June 5

5:15pm CDT

Tumor type	Trials
Breast	• Herceptin + Perjeta: Ph III (APHINITY) in adjuvant HER2+ BC
Lung	• Alecensa: Ph III (ALEX) in 1L ALK+ NSCLC • Tecentriq: Ph III (OAK) in 2L NSCLC
Colorectal	• aCEA/CD3 TCB +/- Tecentriq: Ph I in 3L CRC
Solid tumors	• Tecentriq + IDOi: Ph I
Renal	• Tecentriq + Avastin: Update Ph II (IMmotion150) in 1L RCC

IDOi in collaboration with NewLink Genetics; Alecensa in collaboration with Chugai

Doing now what patients need next