Society for Immunotherapy of Cancer

Impact of the Tumor Microenvironment for CAR-T cell Therapy Efficacy

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Disclosures

Co-founder and chairman of the scientific advisory board:

- *HalioDx*

Collaborative Research Agreement (grants) :

- *Perkin-Elmer, IObiotech, MedImmune, Janssen, Imcheck Therapeutics*

Participation to Scientific Advisory Boards:

- *BMS, MedImmune, Astra Zeneca, Novartis, Definiens, Merck Serono, IObiotech, ImmunID, Nanostring, Illumina, Northwest Biotherapeutics, Actelion, Amgen, Merck MSD*

Consultant :

- *BMS, Roche, GSK, Compugen, Mologen, Gilead, Sanofi*

A Novel Paradigm for Cancer

Science
AAAS

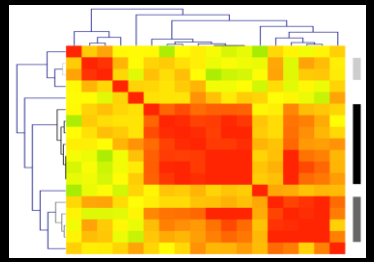
Type, Density, and Location of Immune Cells Within Human Colorectal Tumors Predict Clinical Outcome

Jérôme Galon,[1*†] Anne Costes,[1] Fatima Sanchez-Cabo,[2] Amos Kirilovsky,[1] Bernhard Mlecnik,[2] Christine Lagorce-Pagès,[3] Marie Tosolini,[1] Matthieu Camus,[1] Anne Berger,[4] Philippe Wind,[4] Franck Zinzindohoué,[5] Patrick Bruneval,[6] Paul-Henri Cugnenc,[5] Zlatko Trajanoski,[2] Wolf-Herman Fridman,[1,7] Franck Pagès[1,7†]

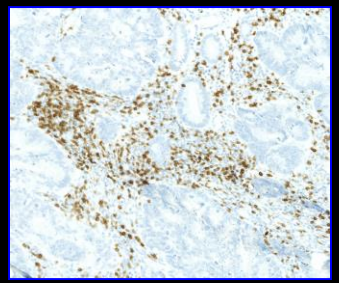
29 SEPTEMBER 2006 VOL 313 SCIENCE www.sciencemag.org

The foundation a new concept ↓

Immune contexture



Quality

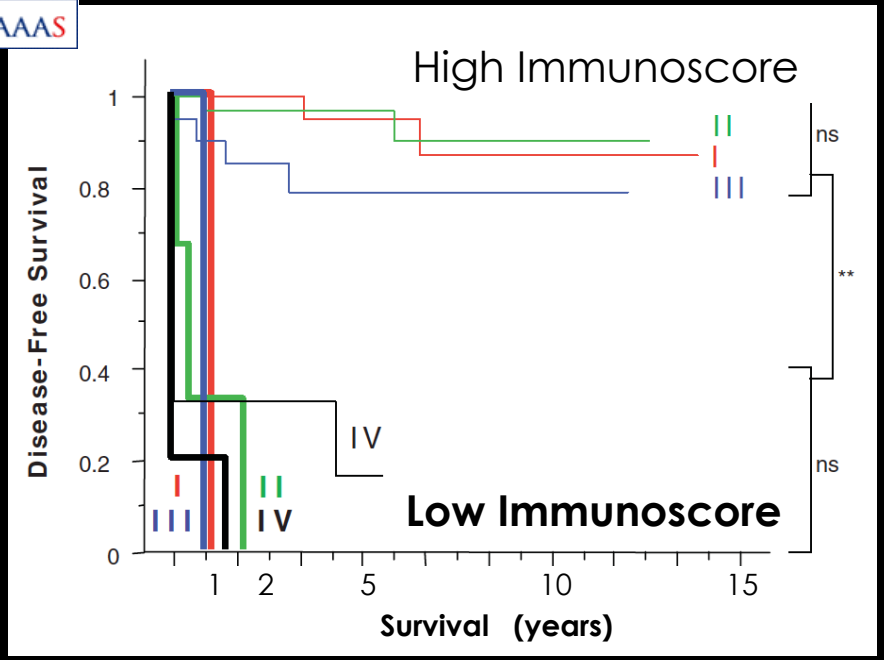


Type/Density/Location

Optimized Immunosign

Galon J et al. ***Science*** 2006

Immunoscore: a novel paradigm for cancer



- ✓ High Immunoscore
- ✓ Inflammed tumors
- ✓ Strong pre-existing adaptive immunity

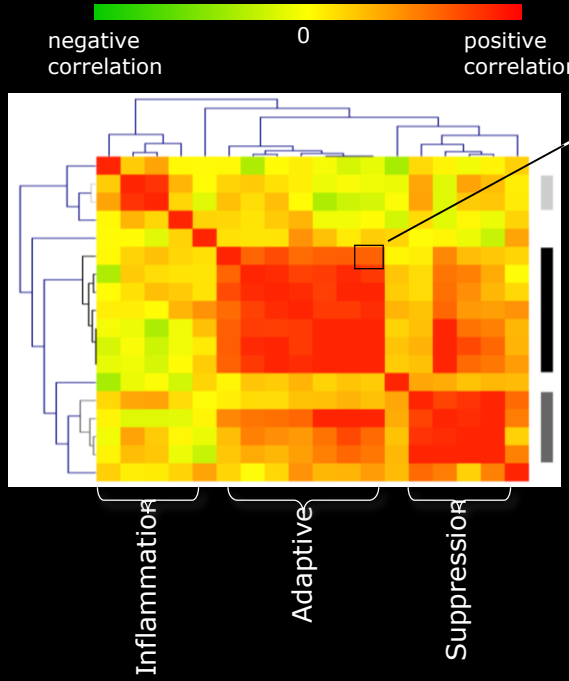
- ✓ Low Immunoscore
- ✓ Non-Inflammed tumors
- ✓ Weak/absent pre-existing adaptive immunity

Coordinated adaptive immune reaction (Immunoscore) more than tumor invasion predicts clinical outcome

Galon et al. ***Science*** 2006

Analysis of immune function

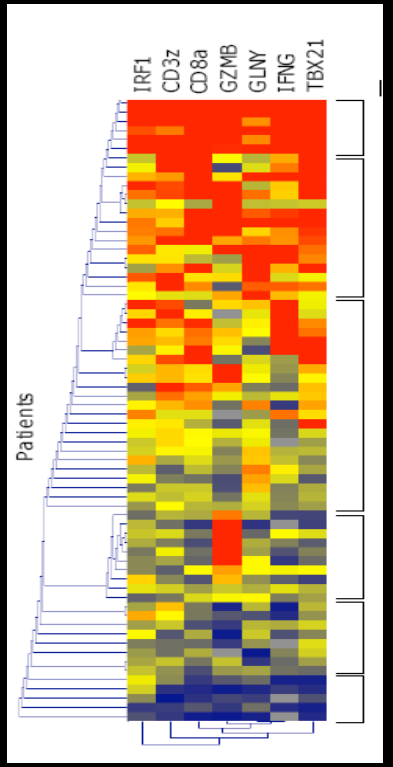
Real-time quantitative PCR
Correlation matrix - HCL clustering
n=75 patients



Inflammation

Adaptive immunity

Immune suppression



Relapse (%)
20
32
38
64
75
80

Coordinated adaptive immune response correlated with relapse

A Novel Paradigm for Cancer

Multivariate Cox Analysis

Parameters	*HR*	*P* value
• T-stage	1.2	0.25
• N-stage	1.4	0.15
• Differentiation	1.1	0.84
• **Immunoscore**	1.9	0.00001

"***Immune Contexture***" :

Cells -> ✓**Type**

Quantity -> ✓**Density**

Spatial -> ✓**Location**

-> Immunoscore

Quality -> ✓Immune **functional** orientation

-> Immunosign

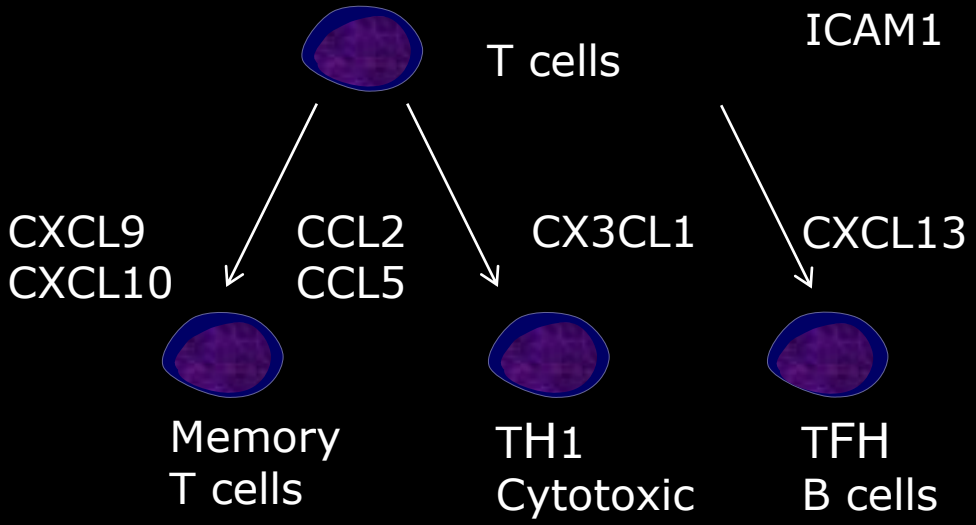
Galon J et al. ***Science*** 2006

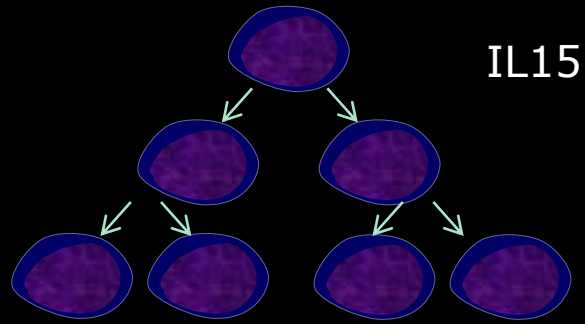
Mechanisms associated with T cells infiltration

Attraction

Adhesion
MADCAM1
VCAM1
ICAM1

Local lymphocyte proliferation



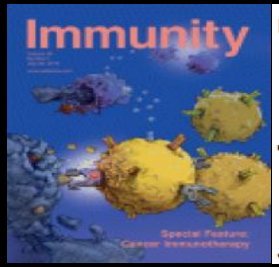


Mlecnik et al. ***Gastroenterology*** 2010

Mlecnik et al. ***Science Transl Med*** 2014

Bindea et al. ***Immunity*** 2013

The continuum of cancer immunosurveillance



Immunity
Review

Cell PRESS

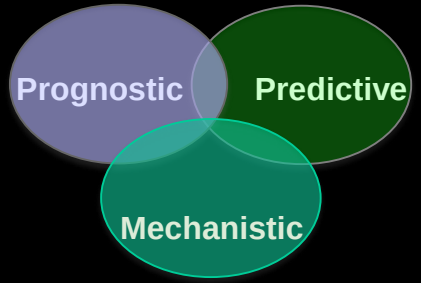
The Continuum of Cancer Immunosurveillance: Prognostic, Predictive, and Mechanistic Signatures

Jérôme Galon,[1,2,3,*] Helen K. Angell,[1,2,3] Davide Bedognetti,[4] and Francesco M. Marincola[4,5,*]

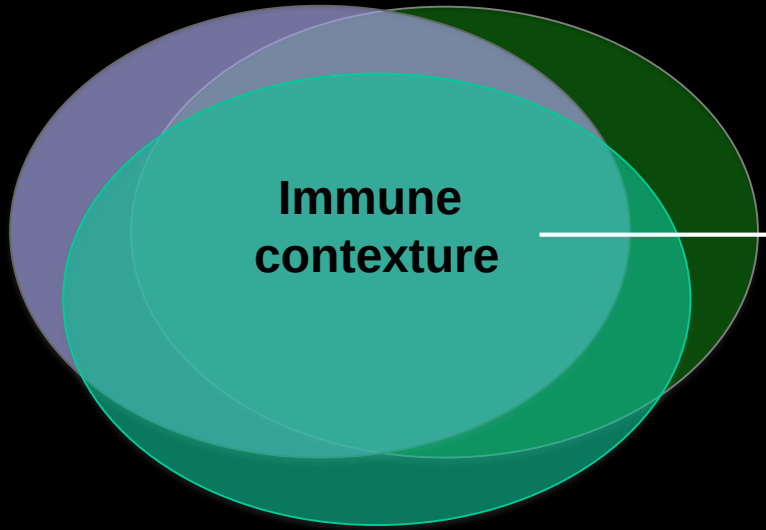
Galon J et al. ***Immunity*** 2013

The overlap between prognostic, predictive and mechanistic immune signatures

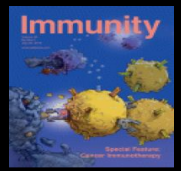
NON-Immune signatures



IMMUNE signatures



Immunoscore
Th1
Cytotoxicity
Chemokines
Cytokines
Adhesion



Galon J et al. ***Immunity*** 2013

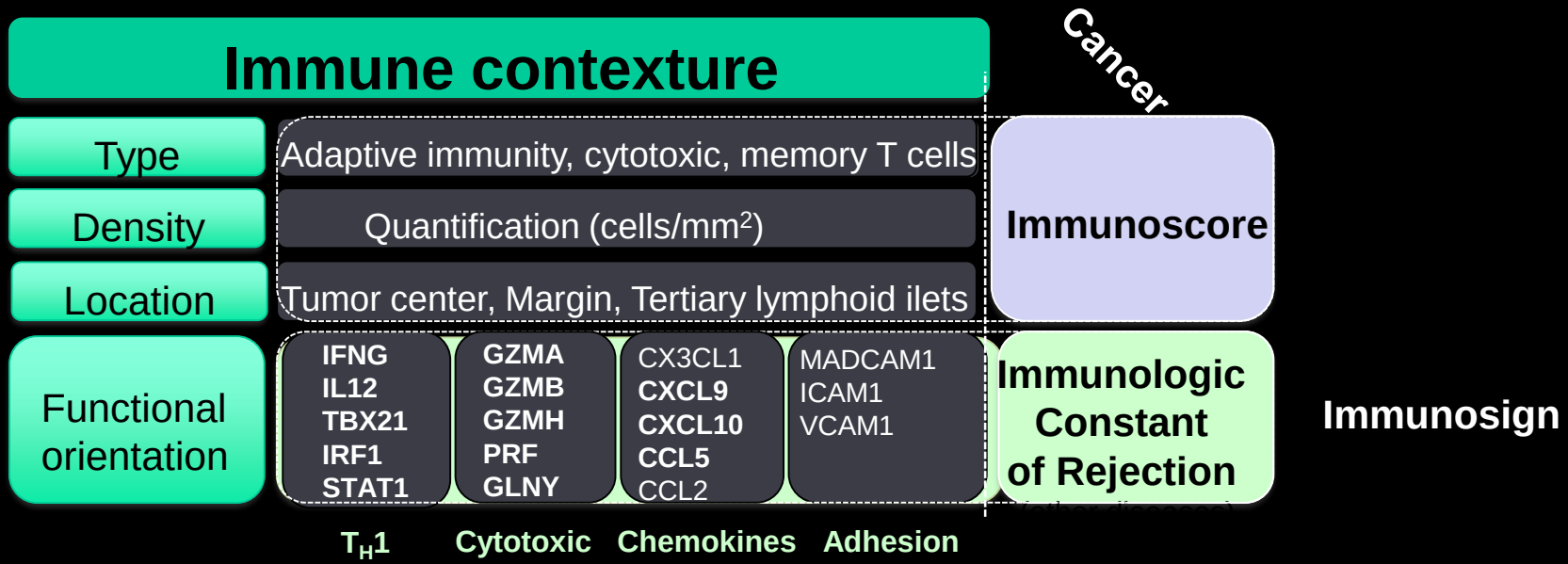
The overlap between prognostic, predictive and mechanistic immune signatures

IMMUNE signatures

Immune contexture

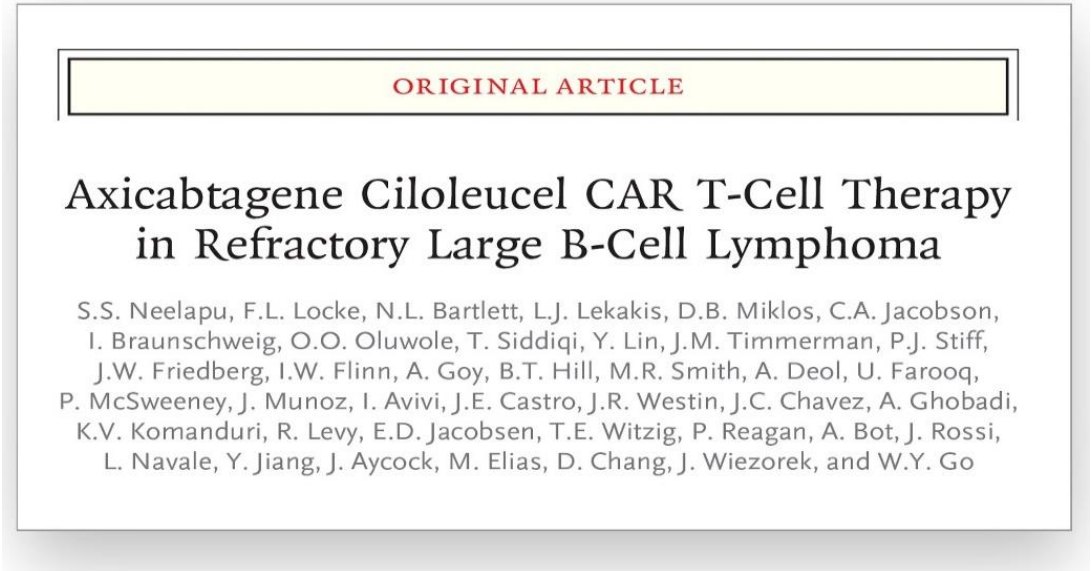
	STAT-1 IRF-1/IFN-γ-SG Pathway	CXCR3/ CXCL9-11 Pathway	CCR5/ CCL3-5 Pathway	Granzyme Perforin Granulisin/ TIA-1/CASPs Pathway	Adhesion Molecules	References
Prognostic						
Breast		+		+	+	Ascierto et al., 2012
	+	+	+			Curtis et al., 2012
Ovarian	+		+	+		Leffers et al., 2010
	+	+			+	Zhang et al., 2003
Melanoma	+	+	+			Messina et al., 2012
	+	+				Mann et al., 2013
Colorectal	+	+	+	+	+	Mlecnik et al., 2010
	+			+		Galon et al., 2006
	+			+		Pagès et al., 2005
	+		+	+		Tosolini et al., 2011
		+				Jiang et al., 2010
Lung			+			Moran et al., 2002
Hepatocellular	+	+	+		+	Chew et al., 2012
	+		+	+	+	Chew et al., 2010
Predictive						
Breast (Chemo)		+				Denkert et al., 2010
	+	+				Desmedt et al., 2008
	+	+				Teschendorff et al., 2007
	+	+				Ignatiadis et al., 2012
Melanoma (IL-2/ vaccine/ adoptive therapy/anti-CTLA-4)	+					Wang et al., 2002
	+		+		+	Weiss et al., 2011
	+	+				Gajewski et al., 2010
		+	+			Bedognetti et al., 2012
	+	+	+	+		Ji et al., 2012
	+	+	+	+		Ulloa-Montoya et al., 2013
Lung	+	+	+	+		Ulloa-Montoya et al., 2013
Mechanistic						
Melanoma (IL-2/ vaccine/anti-CTLA-4)		+	+	+	+	Panelli et al., 2002
	+					Wang et al., 2002
	+		+		+	Weiss et al., 2011
				+		Aarntzen et al., 2012
	+	+	+	+		Ji et al., 2012
Basal Cell (Imiquimod)	+	+	+			Panelli et al., 2007

Galon J et al.
Immunity 2013



Galon J et al. ***Immunity*** 2013

CD19-CAR-T immunotherapy: ZUMA-1 Trial



The NEW ENGLAND JOURNAL of MEDICINE

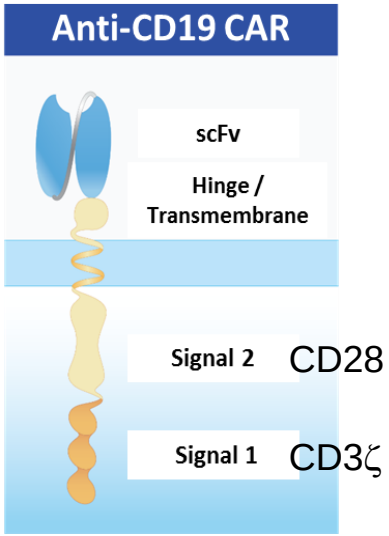
ORIGINAL ARTICLE

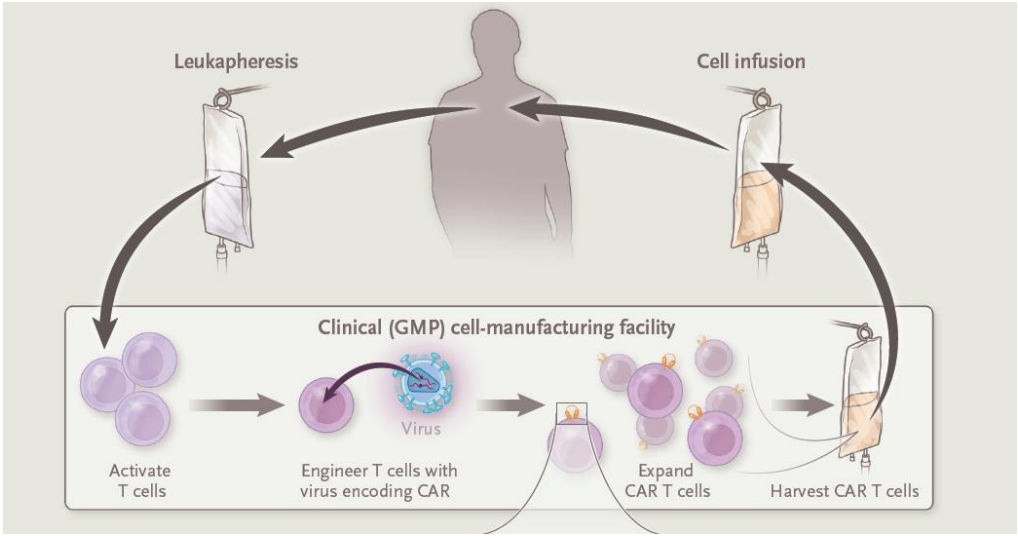
Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma

S.S. Neelapu, F.L. Locke, N.L. Bartlett, L.J. Lekakis, D.B. Miklos, C.A. Jacobson, I. Braunschweig, O.O. Oluwole, T. Siddiqi, Y. Lin, J.M. Timmerman, P.J. Stiff, J.W. Friedberg, I.W. Flinn, A. Goy, B.T. Hill, M.R. Smith, A. Deol, U. Farooq, P. McSweeney, J. Munoz, I. Avivi, J.E. Castro, J.R. Westin, J.C. Chavez, A. Ghobadi, K.V. Komanduri, R. Levy, E.D. Jacobsen, T.E. Witzig, P. Reagan, A. Bot, J. Rossi, L. Navale, Y. Jiang, J. Aycock, M. Elias, D. Chang, J. Wiezorek, and W.Y. Go

Neelapu et al. *NEJM* 2017

CAR-T Design and Product Manufacturing





Adapted from Tran et al, NEJM 2017

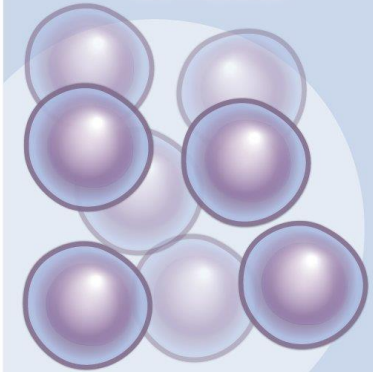
The CAR-T was approved by the US FDA and European Commission for the treatment of adult patients with relapsed/refractory large B cell lymphoma after ≥ 2 lines of systemic therapy

ZUMA-1 Trial: Clinical Outcomes

CAR T-Cell Therapy for Refractory Large B-Cell Lymphoma

MULTICENTER, PHASE 2 CLINICAL TRIAL

CAR T-cell Therapy
N=101



82% Objective response

54% Complete response

(20% Objective response in historical controls)

52% Overall survival at 18 months

96 Patients Had grade ≥3 adverse events:

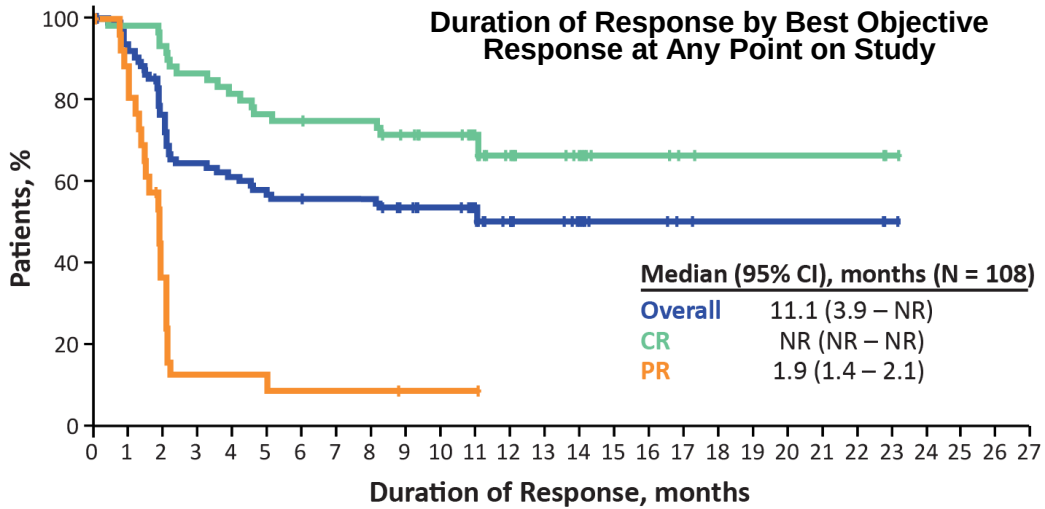
13 Patients Had cytokine release syndrome (including 2 deaths)

28 Patients Had neurologic events

The NEW ENGLAND JOURNAL of MEDICINE

Neelapu et al. 2017

ZUMA-1 Trial: Long-Term Follow Up



Patients at Risk

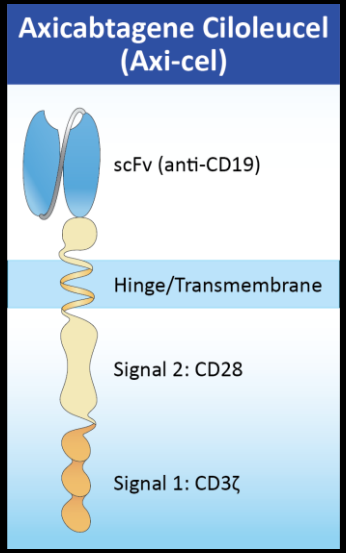
Overall	89	82	67	56	53	49	48	47	47	42	38	31	19	16	12	6	6	4	3	3	3	3	1	0
CR	63	61	58	53	50	47	46	45	45	41	37	30	19	16	12	6	6	4	3	3	3	3	1	0
PR	26	21	9	3	3	2	2	2	2	1	1	1	0											

CR, complete response; PR, partial response; NR, not reached; CI, confidence interval.

Locke et al, ASCO 2018

CAR-T cell therapy

CAR Design and Schematic Representation of ZUMA-1 Trial



Phase 1

Refractory DLBCL/PMBCL/TFL
(cohort of n = 7)

Phase 2

Cohort 1
Refractory DLBCL
(n = 77)

Cohort 2
Refractory PMBCL/TFL
(n = 24)

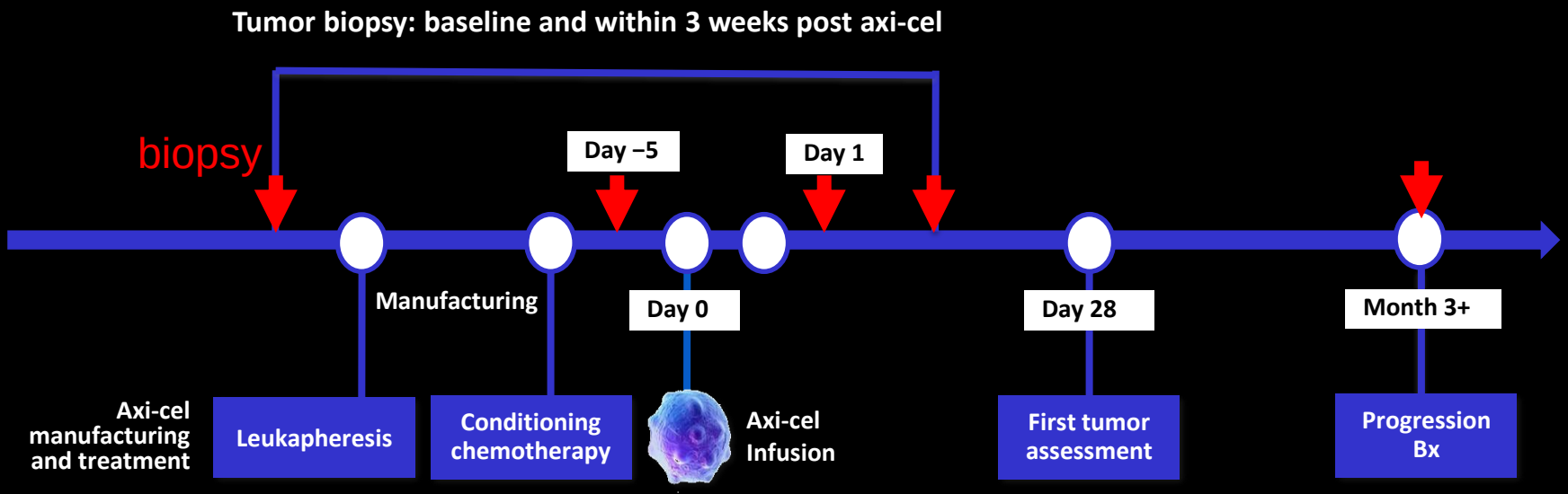
Of 101 patients in Phase 2 ZUMA-1 with refractory large B cell lymphoma treated with axi-cel :
ORR, 83%
CR, 58%
Ongoing responses: 39% including 37% CR

CRS and NE were mostly reversible (n = 108 from Phases 1 & 2):
Grade ≥ 3 CRS, 11%
Grade ≥ 3 NE, 32%
4 Grade 5 AEs (2 axi-cel related and 2 unrelated)

Axi-Cel Maintained Ongoing Responses at Median Follow-Up of 27.1 Months

AE, adverse event; axi-cel, axicabtagene ciloleucel; CR, complete response; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; DLBCL, diffuse large B cell lymphoma; NE, neurologic event; NHL, non-Hodgkin lymphoma; ORR, objective response rate; PMBCL, primary mediastinal B cell lymphoma; TFL, transformed follicular lymphoma.

Tumor microenvironment analysis: Zuma 1 - Protocol and Timing of Paired Biopsies



axi-cel, axicabtagene ciloleucel.

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- ***What are the changes in TME Post-CAR-T?***
- ***Which patients are responding to CAR-T?***
- ***What are the mechanisms of relapse?***
- ***Can we predict toxicities?***

TME: Tumor MicroEnvironment

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- ***TME Tx related signature***
- ***Predictive TME signature (baseline and early post Tx)***
- ***Biomarkers at relapse***
- ***Toxicity signature***

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- ***TME Tx related signature***
- ***Predictive TME signature (baseline and early post Tx)***
- ***Mechanisms of relapse***
- ***Toxicity signature***

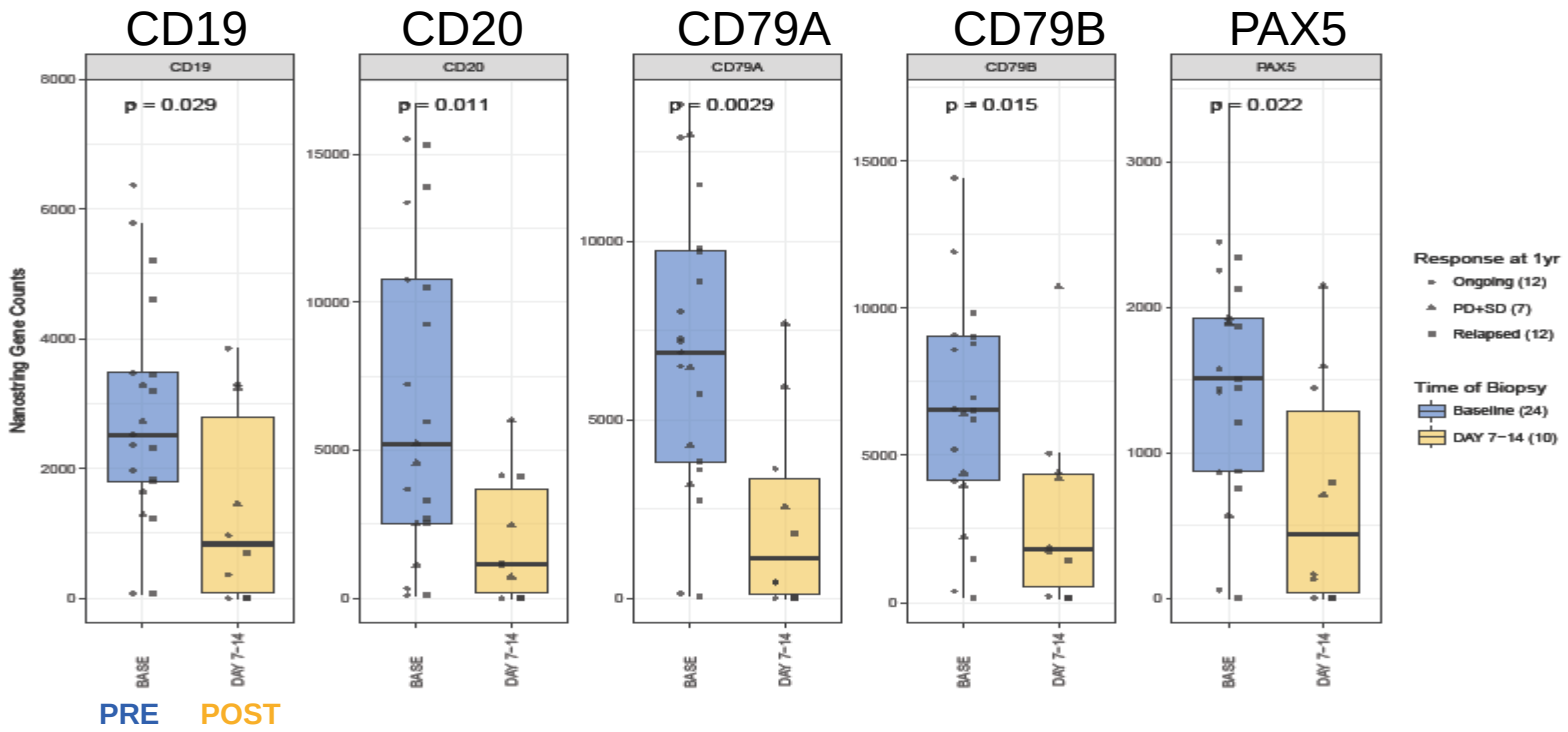
Prespecified Gene Sets Analyzed

Immunosign 21		Expanded 43 Immune Gene Panel				PanCancer Immune Profiling Panel (763 genes)	
CD3G	STAT4	CTLA4	GZMH	CD8A	PDCD1	**Adaptive immune response**	
CD3E	CD3D	CD3G	IRF1	CX3CL1	TNFRSF9	B cells	T cells
GZMK	GZMM	CD3E	GZMA	CXCL10	TSLP	eg, BLK, CD19, CR2, MS4A1, TNFRSF17	eg, CD2, CD2E, CD3G, CD6
PRF1	CD8A	REN	GZMB	TNFRSF18	CCL2		
ICOS	CXCL10	GZMK	CXCL11	CD69	CD247		
STAT1	IL15	CCL5	STAT4	CD274	GNLY		
CCR2	CCL2	ITGAE	LAG3	IL15	LTK	**Innate immune response**	
IRF1	TBX21	PRF1	CD3D	PF4	TBX21	Cytotoxic cells	Dendritic cells
GZMA	CXCR3	ICOS	CXCL9	IFNG	VEGFA	eg, CD8, BLC2	eg, CCL12, CCL17
GZMB	CD69	STAT1	GZMM	CXCL13	CXCR3	Macrophages	Granulocytes
CXCL11		CCR2	IL17A	PROM1		eg, APOE, CCL7	eg, CMA1, CSF3R

Changes in Tumor Micro-Environment (TME) immune genes after CAR-T (Yescarta)

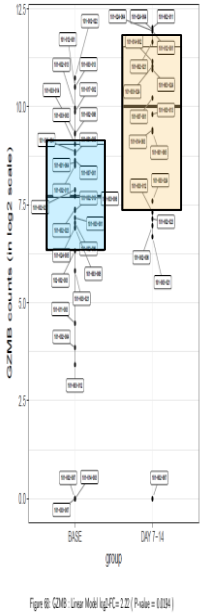
Changes in TME PRE and POST CAR-T

Changes in Gene Expression in TME Post Axi-Cel: Decreased B Cell Lineage Gene Expression Post Treatment

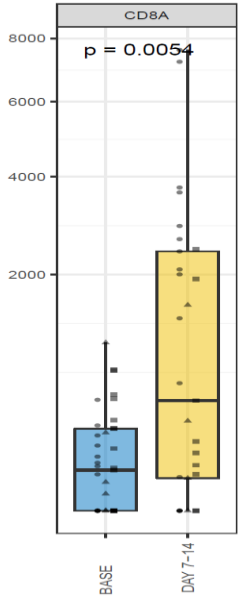


Changes in Gene Expression in TME Post Axi-Cel: Increase of Cytotoxic T Cells and Interferon-Program Related Genes (Immunosign) Post Treatment

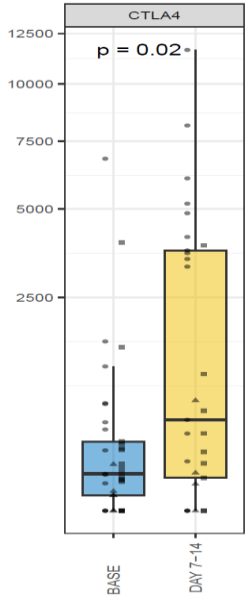
GZMB



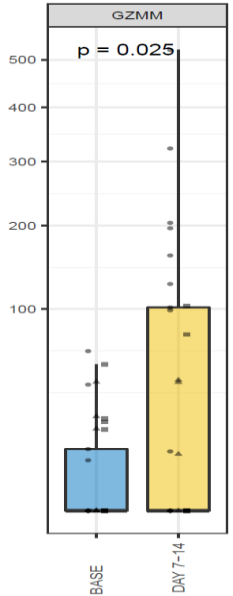
CD8A



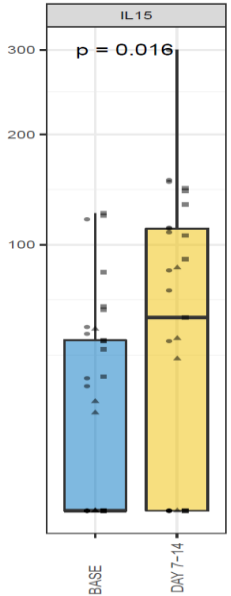
CTLA4



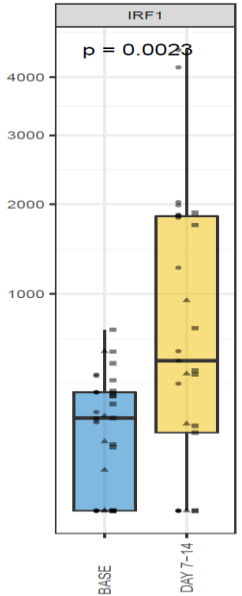
GZMM



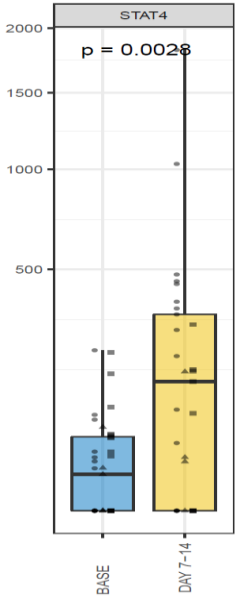
IL15



IRF1



STAT4



Nanostring Gene Counts

PRE POST

Time of Biopsy
Baseline (37)
DAY 7−14 (29)

Response at 1yr
Ongoing (30)
PD+SD (10)
Relapsed (26)

Changes in Gene Expression in TME Post Axi-Cel: Increase Post Treatment

Activating checkpoints

GITR

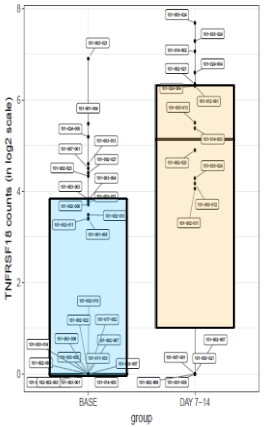


Figure 64: TNFRSF18 : Linear Model log2-FC= 2.12 (P-value = 0.00786)

ICOS

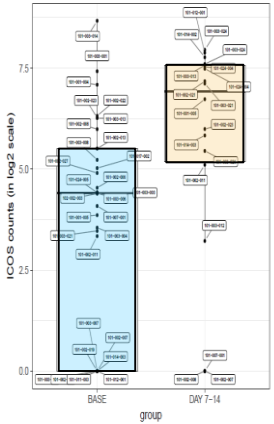


Figure 70: ICOS : Linear Model log2-FC= 1.81 (P-value = 0.0315)

PRE POST

Chemokines

CXCL9 (MIG)

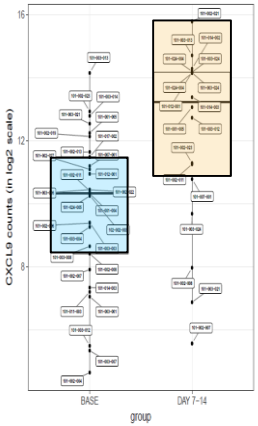


Figure 58: CXCL9 : Linear Model log2-FC= 2.28 (P-value = 0.00564)

CCL5 (RANTES)

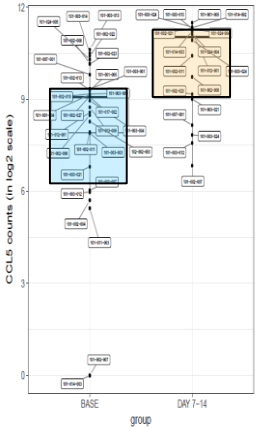


Figure 60: CCL5 : Linear Model log2-FC= 1.99 (P-value = 0.00624)

CCL2 (MCP-1)

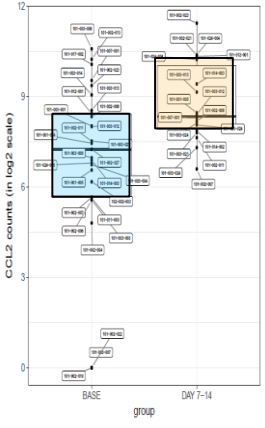
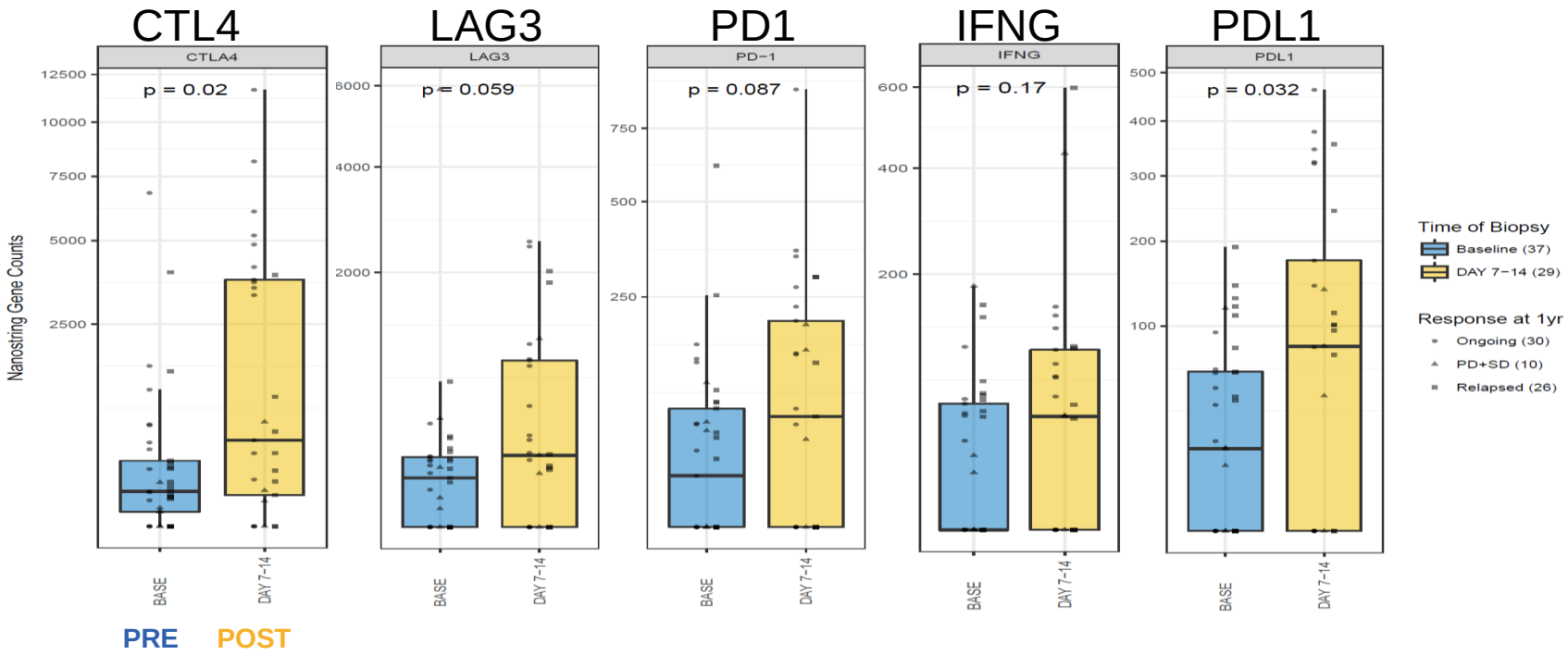


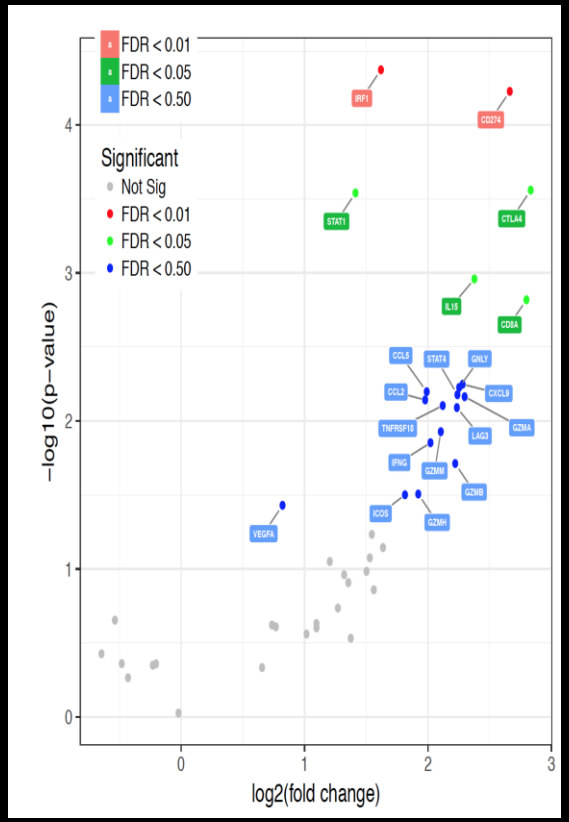
Figure 63: CCL2 : Linear Model log2-FC= 1.98 (P-value = 0.0072)

PRE POST

Changes in Gene Expression in TME Post Axi-Cel: IFNg-Program Related Checkpoints (Immunosign panel) Post Treatment



Treatment with Axi-Cel Results in Rapid and Dramatic Changes in the Tumor Immune Microenvironment



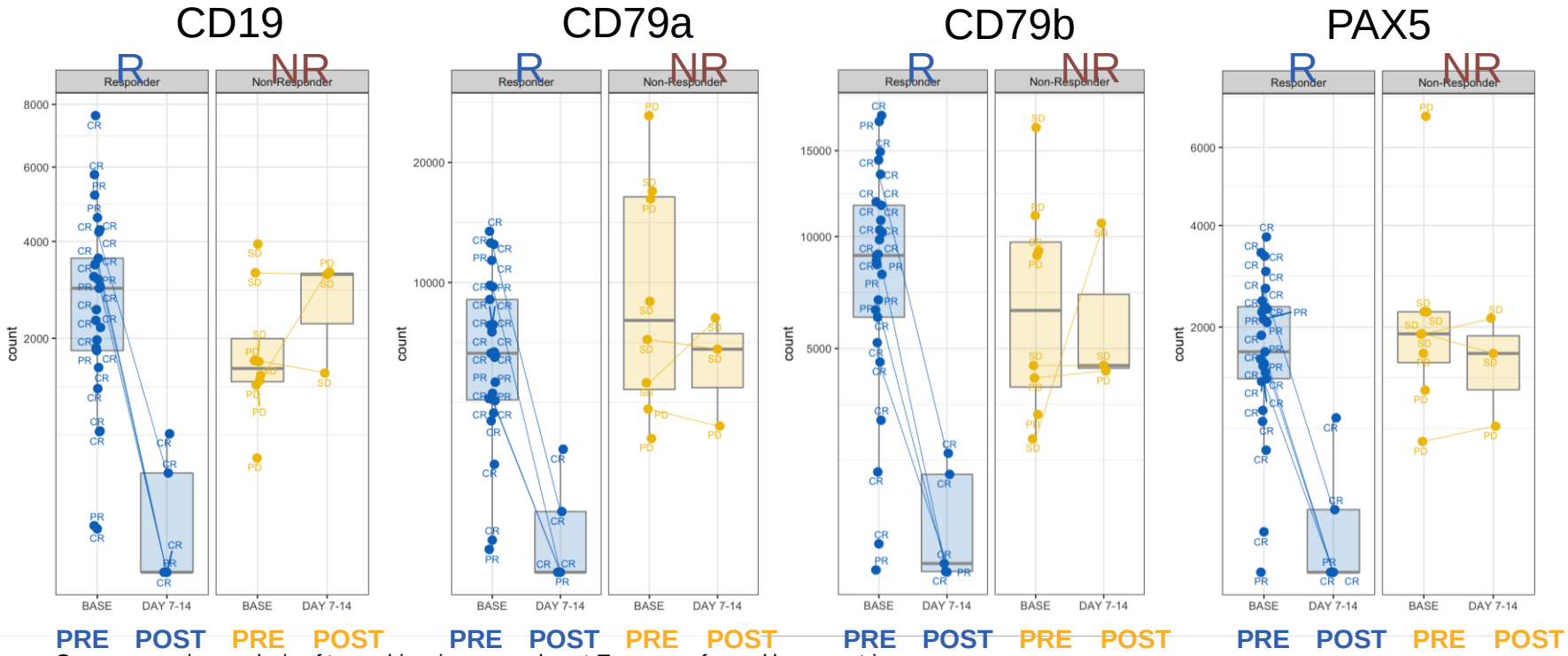
Top transcripts from a pre-specified 43 immune gene panel upregulated in tumor 7-21 days after treatment. IDO1 and other genes not in the 43 panel are pending.

Checkpoints	IFN related	Effectors	Proliferative	Chemokines
PD-L1	IRF1	CD8A	IL15	CXCL9
CTLA4	STAT1	GNLY		CCL2
	STAT4	GZMA		CCL5
LAG3		GZMM		
TNFRSF18	IFNγ	GZMB		
ICOS		GZMH		

Changes in Tumor Micro-Environment (TME) immune genes after CAR-T (Yescarta)

Changes in TME POST CAR-T in Responders (R) and Non-Responders (NR)

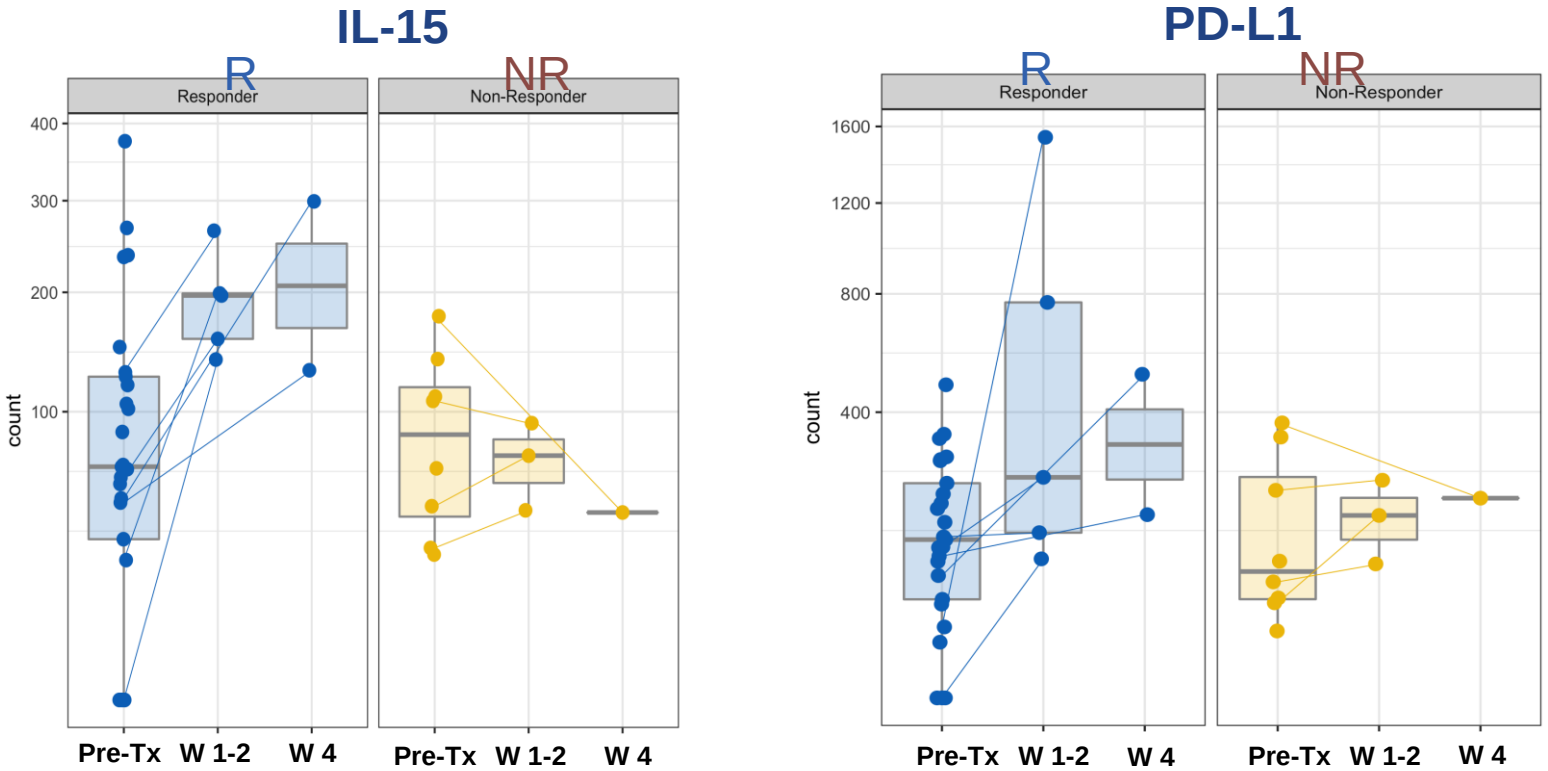
Rapid Decline in Expression Levels of B Cell-Related Genes Post Axi-Cel in Responding Patients



Gene expression analysis of tumor biopsies pre and post-Tx was performed by nanostring.
Zuma-1 trial, 1 year follow up

Bot et al, Cell Therapies and Bioengineering Conference, 2018

Changes in IL-15 and PD-L1 Gene Expression in the Tumor Microenvironment in Responding *vs* Non-Responding Patients



Gene expression analysis of tumor biopsies pre and post-Tx was performed by nanostring.

Responder: Best response was complete or partial response. Non-responder: best response was progression or stable disease.

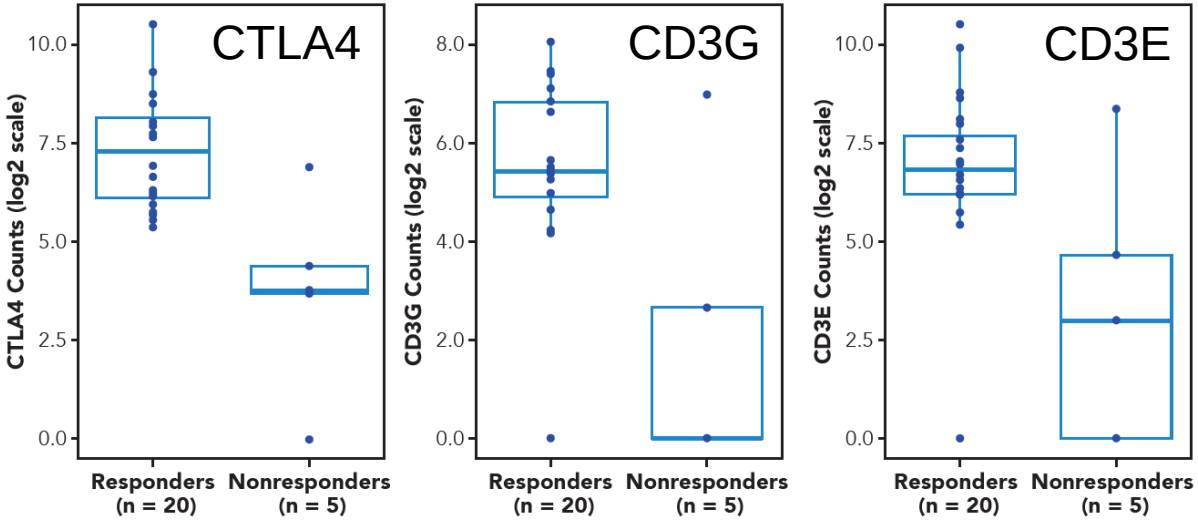
Zuma-1 trial, 1 year follow up

Bot et al, Annual CAR TCR Summit, 2018

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- *TME Tx related signature*
- ***Predictive TME signature (baseline and early post Tx)***
- *Mechanisms of relapse*
- *Toxicity signature*

Immune Genes Elevated in Tumor Biopsies Measured Before CAR T Cell Treatment From Responders From a Prespecified 43 Immune Gene Panel[a]



	CTLA4	CD3G	CD3E
Log2 fold change	3.56	3.4	3.27
***P* value**	< .001	.007	.023
False discovery rate	0.058	0.678	1
Gene set	Adaptive, B cell functions	Adaptive, Regulation, Immunosign 21	Adaptive, T cell functions, Immunosign 21

[a]This analysis was performed on samples from 25 patients treated with axi-cel with a minimum follow-up of 9 months. One patient subsequently converted from a “nonresponder” to a “responder” at 12-month follow-up.

Pre-specified Immunosign21 custom signature separates OR from non-OR

Hi

Immunosign21

Lo

Pre-specified cutoff
Hi/Lo: (25% percentile)

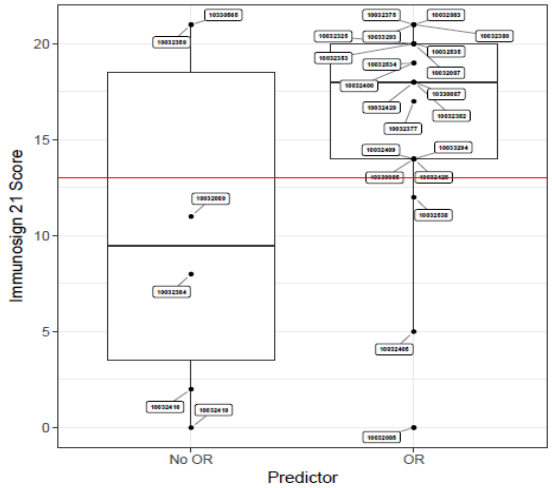


Figure 22: Immunosign 21 Scores. The red line is the low/high score cut-off

ImmunoSign 21	High	Low
Objective.Response		
No OR	2	4
OR	18	3

Table 15: Contingency table for ImmunoSign 21 Level and Objective.Response. Associated Fisher test p.value is: 0.024

N=27

-> Validation on N=51 samples

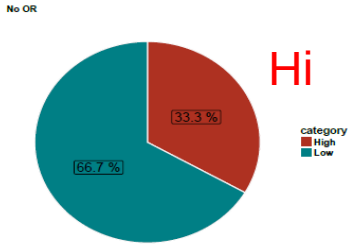


Figure 23: Immunosign 21 Scores. Repartition of scores for No OR samples

No OR
67% Lo

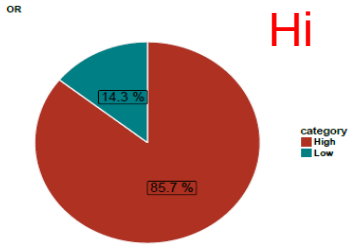


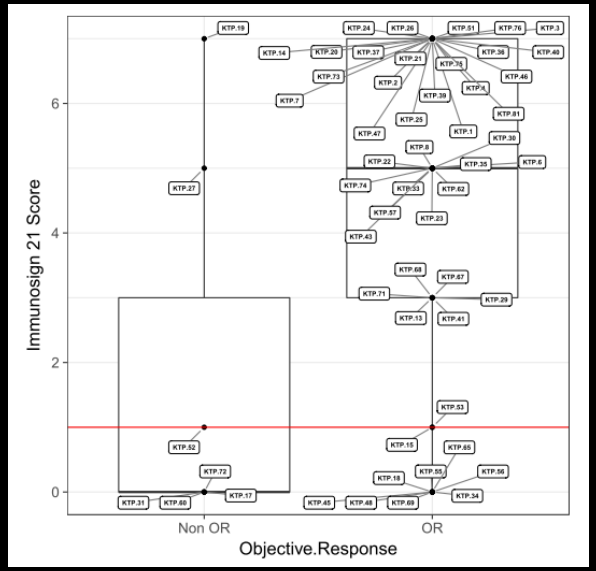
Figure 24: Immunosign 21 Scores. Repartition of scores for OR samples

OR
86% Hi

Chi2 Pvalue, P=0.023

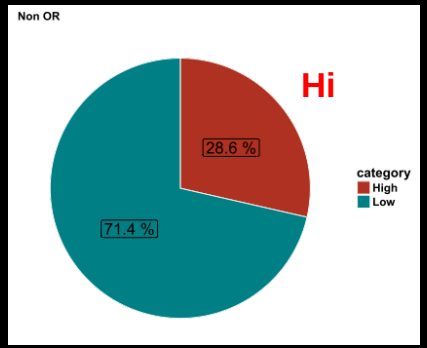
Pre-specified Immunosign® 21 separates OR from non-OR

OR vs No OR (Objective.Response) in pre-treatment Population

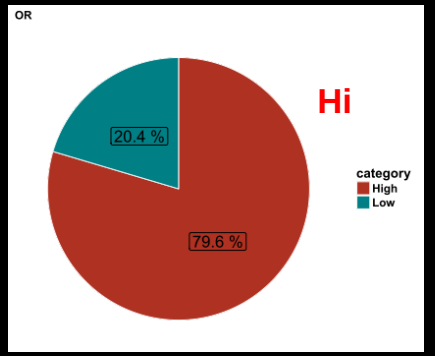


Fisher test P=0.012

non OR



OR

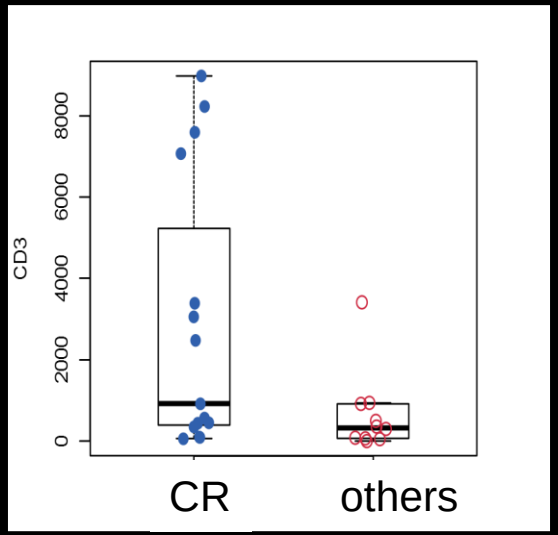


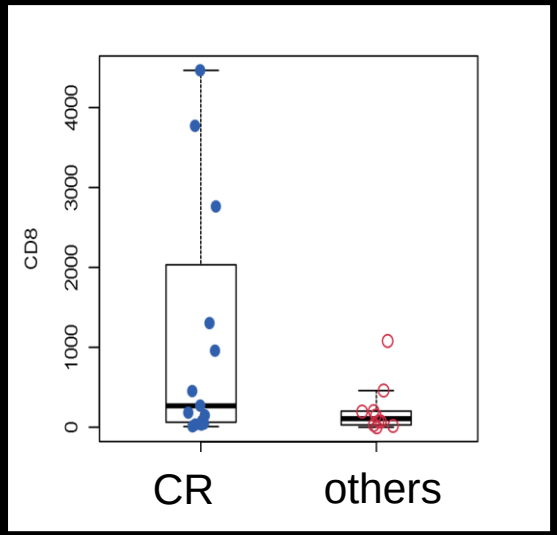
N=64

Immunosign® 21 pre-CAR-T infusion predicts Objective Response

Pre-treatment T-cell densities

Association Between Intratumoral Densities of CD3+ and CD8+ T Cells and Clinical Outcome



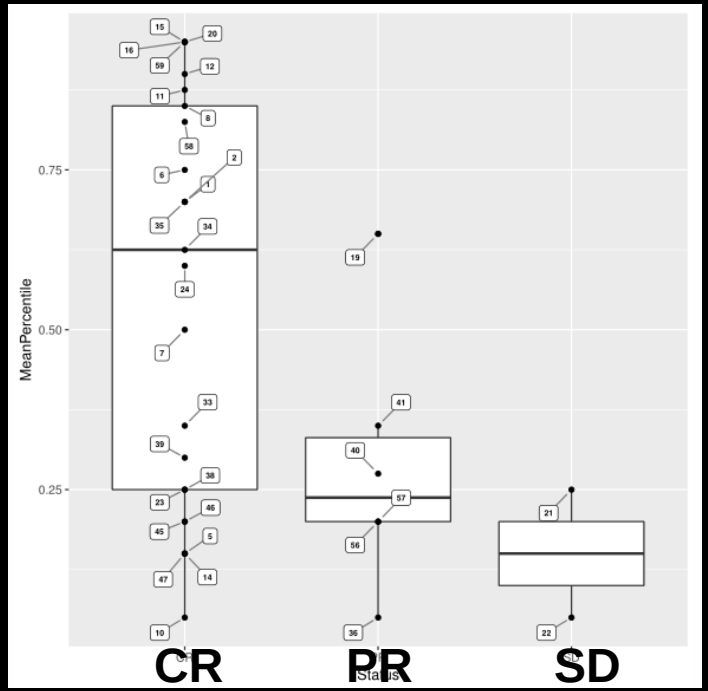


Pretreatment intratumoral densities of CD3+ and CD8+ T cells trends positively with achievement of CR (*P* = .025 and .049, respectively)

CR, complete response.

Immunoscore analysis

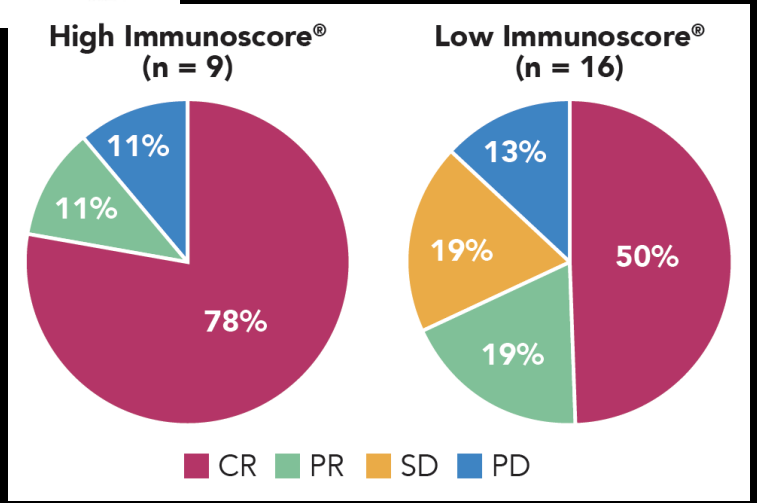
Mean Percentile Immunoscore®



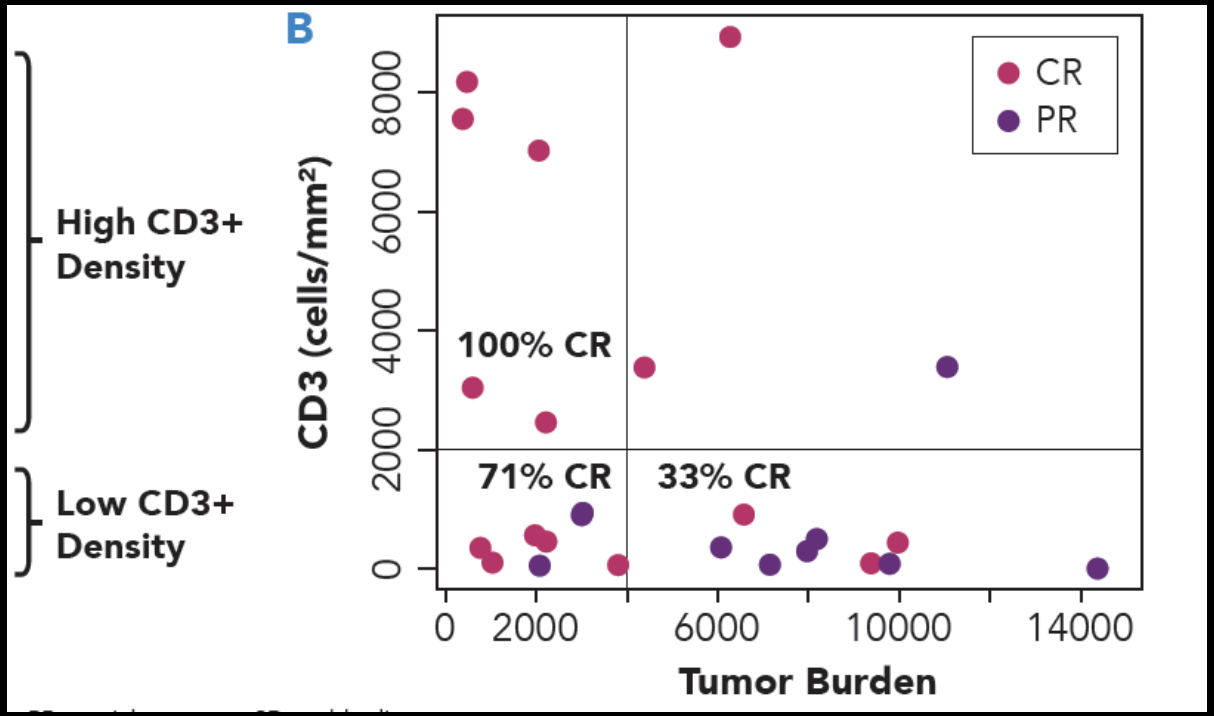
Significant Increase of Biopsy Immunoscore® on patient with CR

Immunoscore®	High	Low
CR	14	11
PR	1	5
SD	0	2

Exact fisher test
p-value: 0.028



T cell densities & Tumor burden analysis



CR after CAR-T treatment correlates with “Hot” TME pretreatment.
However, a subset of patients with “Cold” TME pretreatment and low intratumoral T cell density, achieved CR.
Data suggest that CAR T cells may overcome a detrimental TME defined by low density of intratumoral CD3+ T cells pretreatment

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- *TME Tx related signature*
- *Predictive TME signature (baseline and early post Tx)*
- ***Mechanisms of relapse***
- *Toxicity signature*

Change in TME upon progression: mechanisms of relapse

Enhancement of expression of select genes upon progression

PRAME

5.3.2.6 PRAME

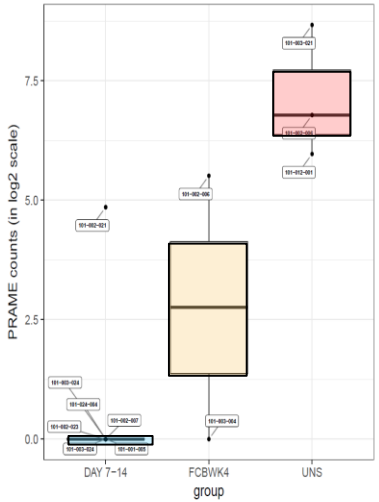


Figure 160: PRAME : Linear Model log2-FC= NA (Anova P-value = 0.00514) in post-treatment+OR (Treatment.Status.Objective.Response) population.

CCL22

5.3.2.14 CCL22

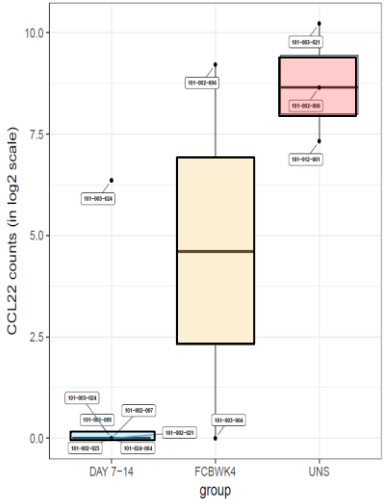


Figure 168: CCL22 : Linear Model log2-FC= NA (Anova P-value = 0.0131) in post-treatment+OR (Treatment.Status.Objective.Response) population.

AICDA

5.3.2.20 AICDA

(The protein is involved in somatic hypermutation, gene conversion, and class-switch recombination of immunoglobulin genes)

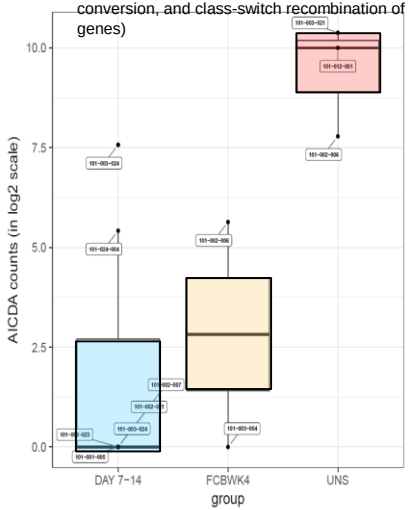


Figure 174: AICDA : Linear Model log2-FC= NA (Anova P-value = 0.0168) in post-treatment+OR (Treatment.Status.Objective.Response) population.

POST Biopsy Wk14 Biopsy After Relapse (Progressor)

POST Biopsy Wk14 Biopsy After Relapse (Progressor)

POST Biopsy Wk14 Biopsy After Relapse (Progressor)

Diminution of CAR and immune related genes upon progression

CAR-T

5.3.2.50 CD28_CD3z

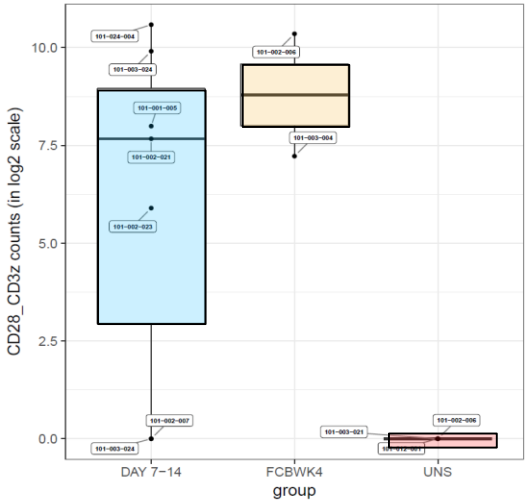
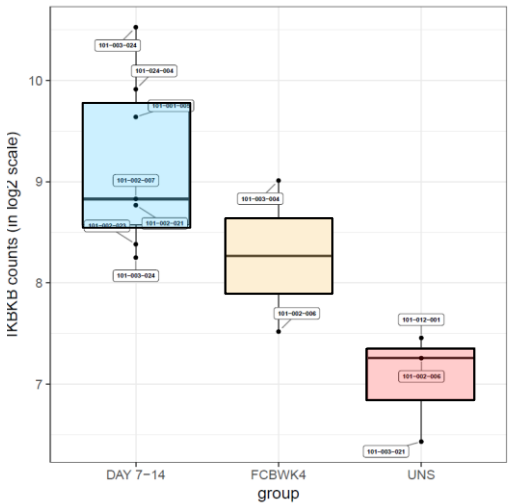


Figure 204: CD28_CD3z : Linear Model log2-FC= NA (Anova P-value = 0.0527) in post-treatment+OR (Treatment.Status.Objective.Response) population.

IKKb (Inh NFKb)

IKBKB



: IKBKB : Linear Model log2-FC= NA (Anova P-value = 0.0134) in post-treatment+OR (Tr
s.Objective.Response) population.

IFNL1, IL29 (binds IL28RA, IL10RB)

5.3.2.39 IFNL1

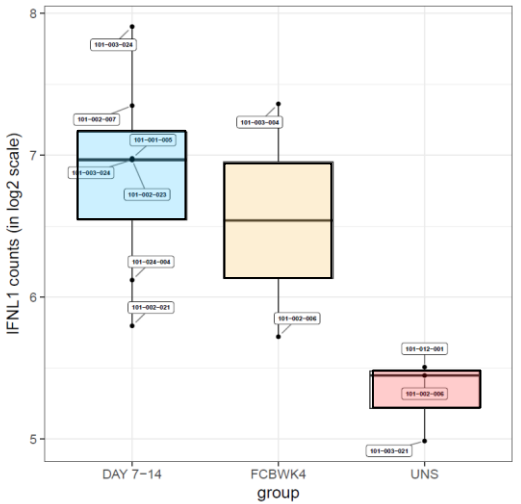


Figure 193: IFNL1 : Linear Model log2-FC= NA (Anova P-value = 0.0338) in post-treatment+OR (Treatment.Status.Objective.Response) population.

POST **Biopsy Wk14** **Biopsy After Relapse (Progressor)**

POST **Biopsy Wk14** **Biopsy After Relapse (Progressor)**

POST **Biopsy Wk14** **Biopsy After Relapse (Progressor)**

Diminution of CAR and immune related genes upon progression

SAA1

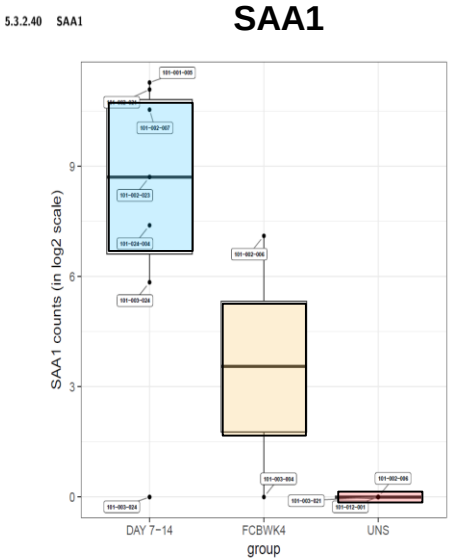


Figure 194: SAA1 : Linear Model log2-FC= NA (Anova P-value = 0.0344) in post-treatment+OR (Treatment.Status.Objective.Response) population.

IL15

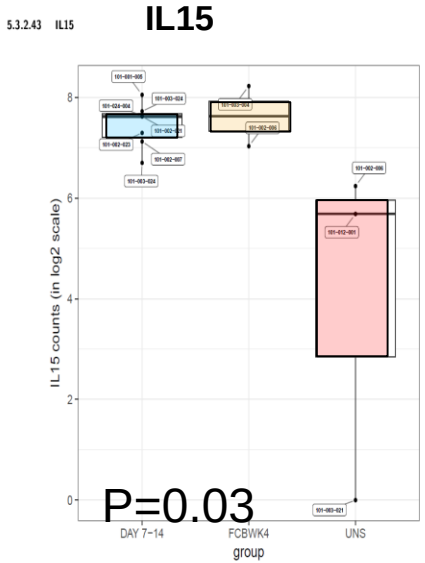


Figure 197: IL15 : Linear Model log2-FC= NA (Anova P-value = 0.0369) in post-treatment+OR (Treatment.Status.Objective.Response) population.

Immunosign 21

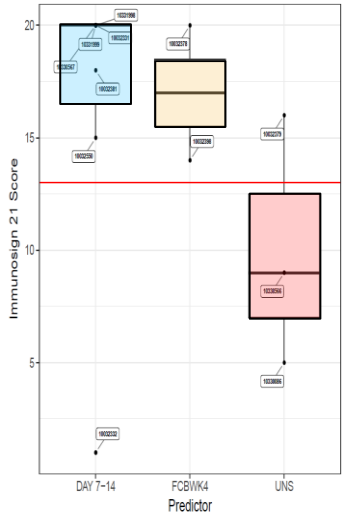


Figure 206: Immunosign 21 Scores. The red line is the low/high score cut-off

Hi

Lo

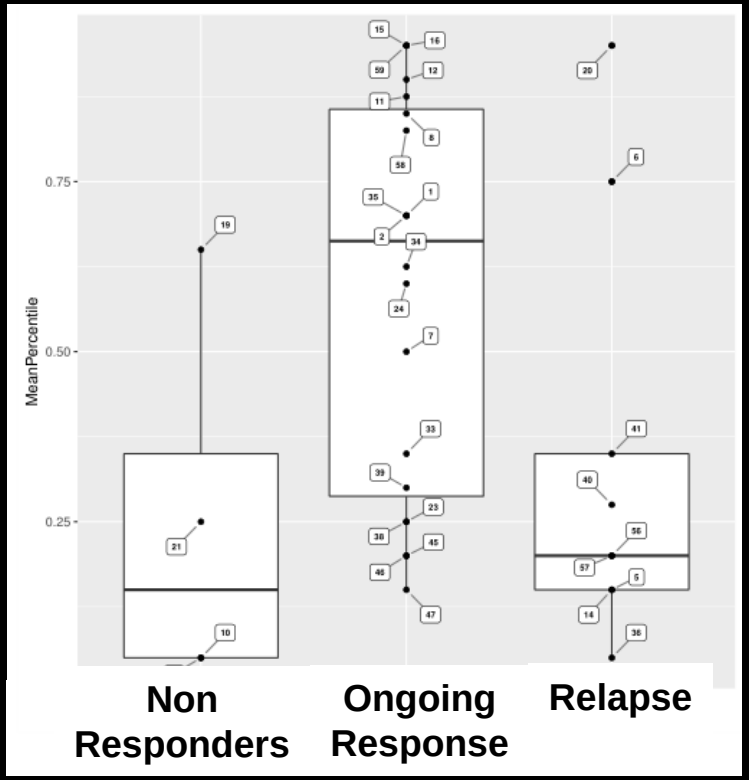
POST Biopsy Wk14 Biopsy After Relapse (Progressor)

POST Biopsy Wk14 Biopsy After Relapse (Progressor)

POST Biopsy Wk14 Biopsy After Relapse (Progressor)

Decrease of IL15 and of Immunosign21 upon progression (to be confirmed on larger dataset)

Immunoscore in Ongoing Response



Significant Increase of Biopsy Immunoscore® on Ongoing Response

Exact fisher test p-value: 0.030

Immunoscore®	High	Low
Non-responder	1	3
Ongoing	12	8
Relapsed	2	7

DO NOT POST

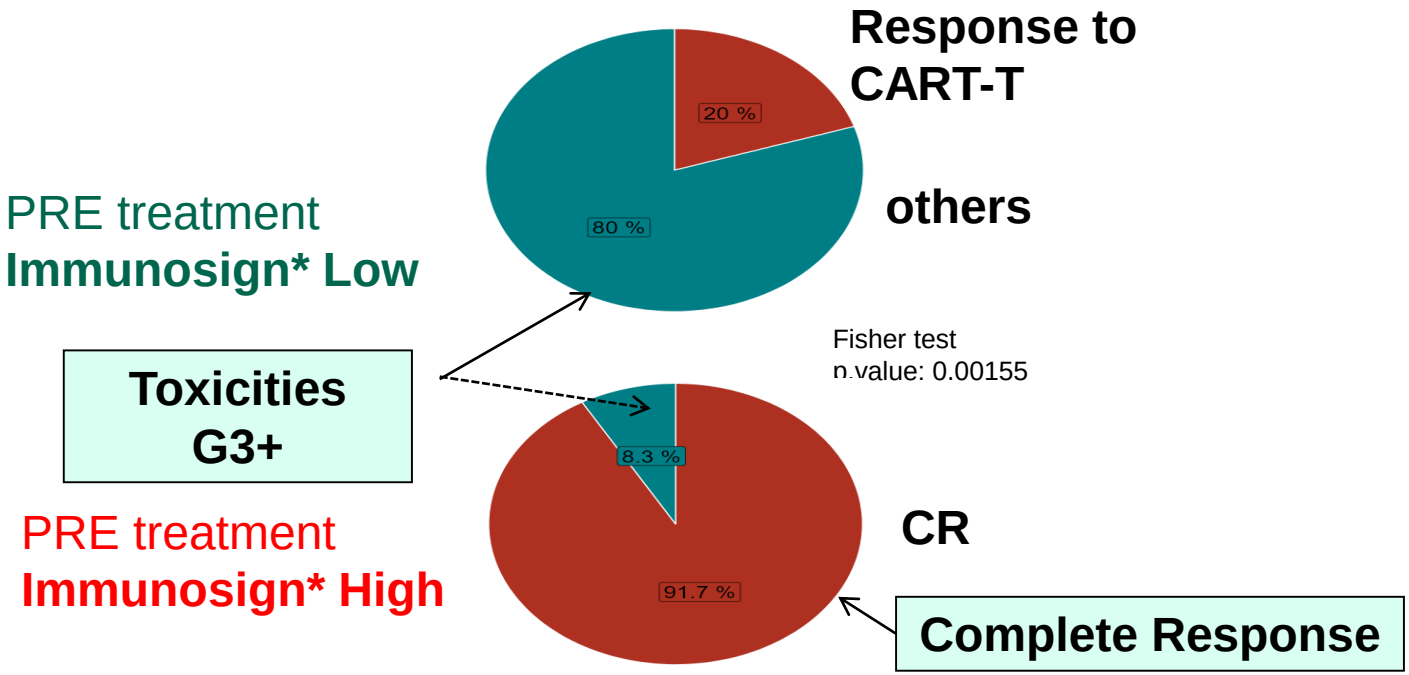
Immunoscore® may be decreased in relapse samples

KITE ZUMA-1 clinical trial Translational Biomarkers analysis

- *TME Tx related signature*
- *Predictive TME signature (baseline and early post Tx)*
- *Mechanisms of relapse*
- ***Toxicity signature***

Conclusion / Interpretation:

KITE ZUMA-1 clinical trial Translational Biomarkers

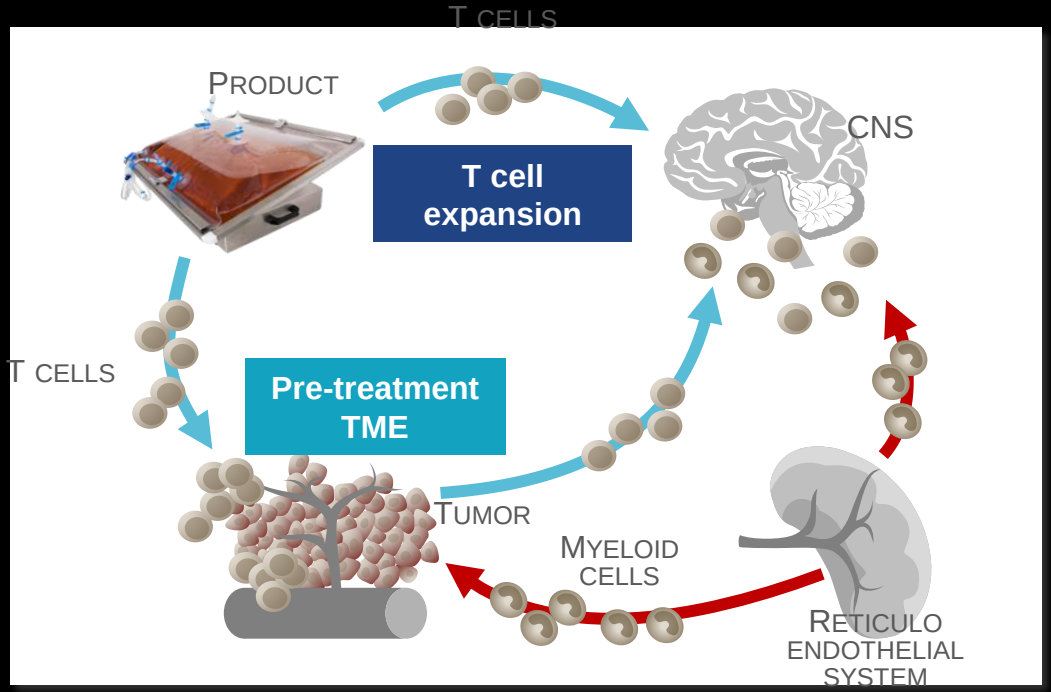


Conclusion / Interpretation:

KITE ZUMA-1 clinical trial Translational Biomarkers

CAR-T : A Mechanistic Model of Efficacy and Toxicities

- T cell "fitness" (juvenile, proliferative, polyfunctional)
- Dose of CD8 T cells
- Pre-treatment tumor burden
- Pre-treatment pre-existing immunity / tumor microenvironment
- Target antigen "loss"



- Efficacy
- Toxicities
- Both

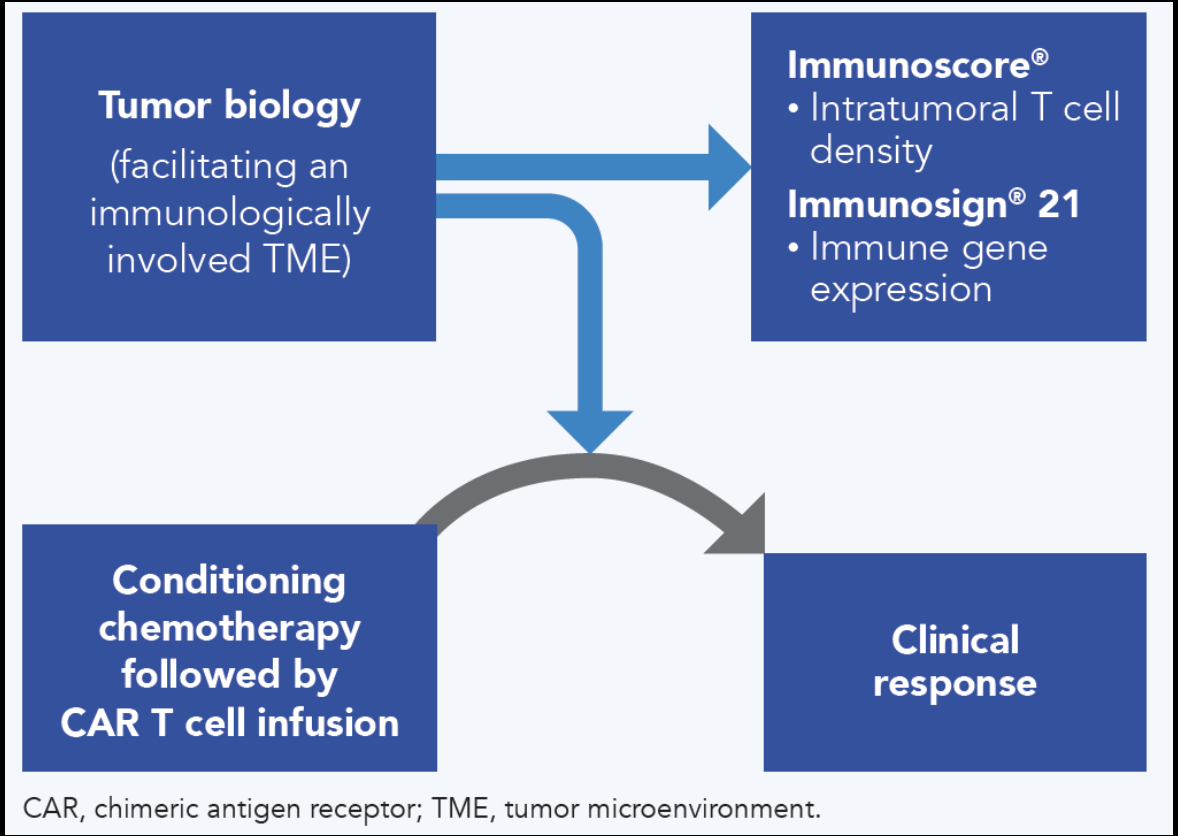
DO NOT POST

*Based on: Kochenderfer, JCO 2017; Neelapu, NEJM 2017; Locke, AACR 2017; Galon, ASCO 2017; Rossi, SITC 2017; Locke, ASH 2017; Rossi, Blood 201Z, ASH 2018, AACR2018, AACR 2019. TME – Tumor microenvironment .

CONCLUSIONS

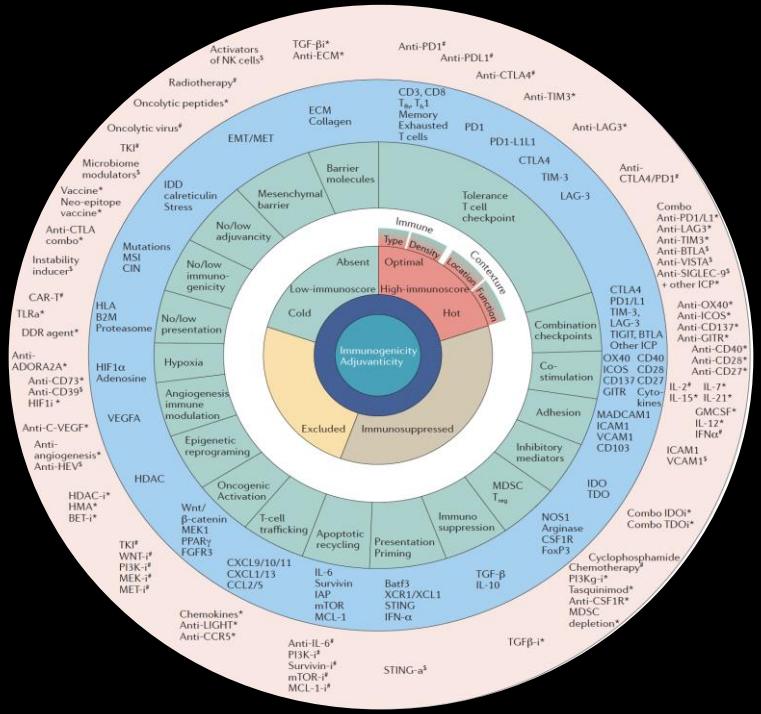
- ✓ Pre-existing T cell-involved features of the TME (High Immunoscore, High Immunosign) may be associated with a response to CAR-T
- ✓ Factors intrinsic to tumor biology may influence CAR T cell efficacy through the immune microenvironment (Pre-treatment TME enriched in T cell and innate immune-related genes)
- ✓ CAR-T could overcome an unfavorable TME (low Immunoscore) in a subset of patients
- ✓ CAR T cell treatment is associated with rapid and profound changes in the TME
  - Increase of immune checkpoints, IFN-related genes and chemokines
  - Elevation of IL-15 and PD-L1 gene expression in CR and PR
- ✓ These results support anti-CD19 CAR T cell treatment optimizations designed to overcome an immune-detrimental TME

Model Linking Tumor Biology Features With TME and Response to CAR T Cell Therapy



CAR, chimeric antigen receptor; TME, tumor microenvironment.

Treating hot, altered and cold immune tumors with immunotherapy



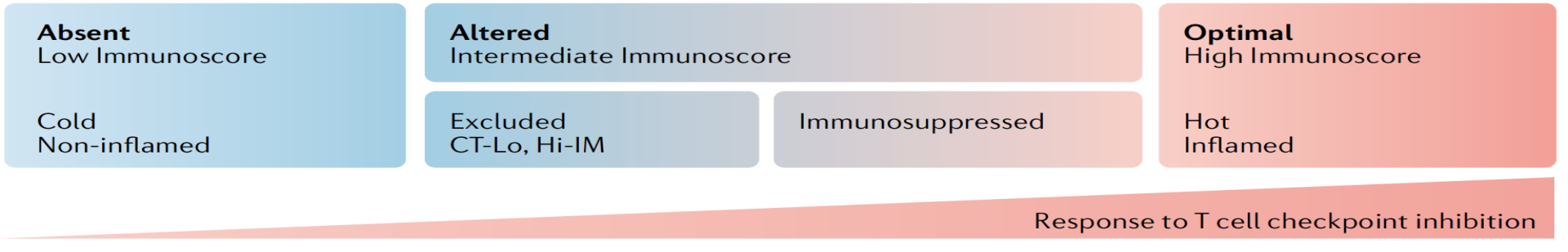
Galon J. & Bruni D.
Nature Reviews Drug Discovery 2019

NATURE REVIEWS | DRUG DISCOVERY

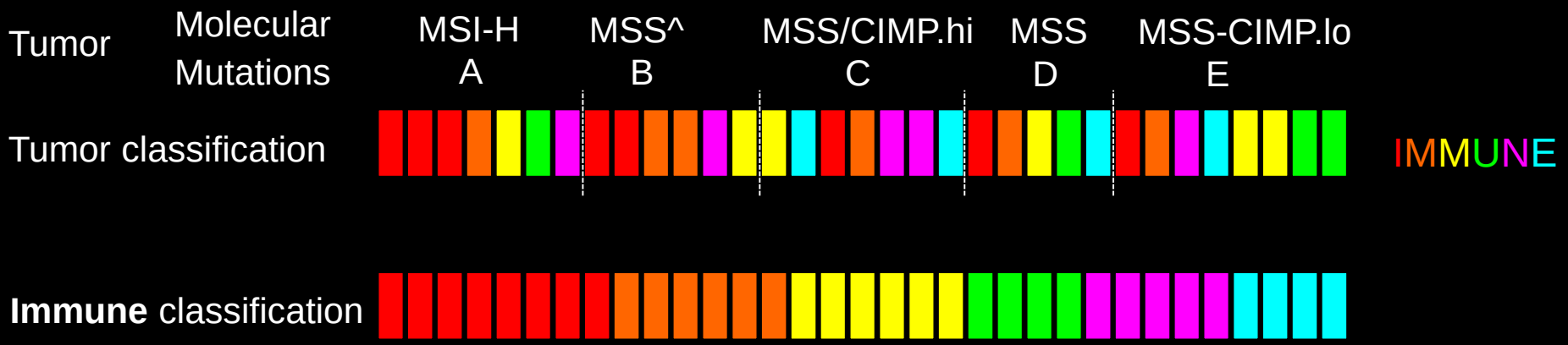
Approaches to treat immune hot, altered and cold tumours with combination immunotherapies

Jérôme Galon * *and Daniela Bruni*

2019



Stratification of cancer based on the immune status



-> Importance of having standardized immune Assays

Galon lab.

INSERM, CRC, Paris, France

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Tessa Fredriksen
Florence Marliot
Lucie Lafontaine
Stéphanie Mauger
Amélie Bilocq
Bénédicte Buttard
Amos Kirilovsky
Marie Tosolini
Maximilian Waldner
Sarah Church
Pauline Maby
Helen Angell
Mihaela Angelova
Angela Vasaturo
Bernhard Mlecnik
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Daniela Bruni
Anastasia Lanzi

HalioDx, France ; HalioDx Inc. USA

Corinne Danan
Sarah Turcan
Naouel Elasri
Regis Perbrost
Stephane Debono
Jacque Fieschi
Vincent Fert
Fabienne Hermitte

Kite Pharma, Gilead company, USA

Adrian Bot
John Rossi
Nathalie Scholler
Marika Sherman
Yueh Wei-Shen
Edmund Chang
Geoff Houghton
Sharon Mu
Allen Xue
Lianqing Zheng
Bin Hao
Lynn Navale
Joe Jiang
William Go
Jeff Aycock
Meg Elias
Jeff Wiezorek

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James Kochenderfer
Steven Rosenberg

MDACC, USA

Sattva Neelapu

Moffit CC, USA

Frederick Locke

Stanford, USA

David Miklos

Patients, families, investigators