LMU KLINIKUM
Gemeinsam. Fürsorglich. Wegweisend.

Gene Center Munich

Bispecifics in AML

Marion Subklewe, M.D.
Head of the Cellular Immunotherapy Program at the LMU – Munich

Subklewe Lab for Translational Cancer Immunology

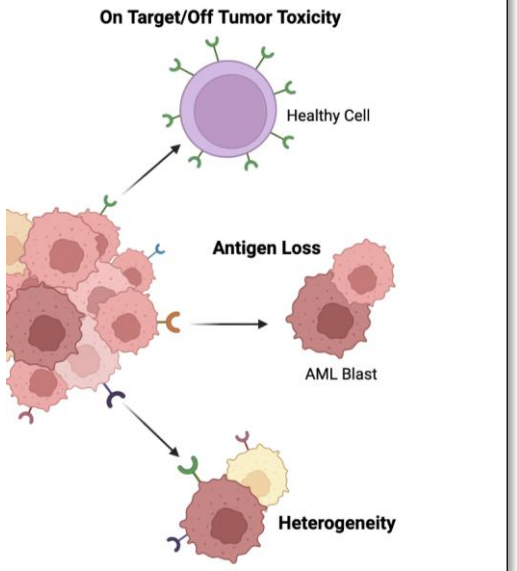
Early Clinical Trial Unit / ImmunoTaskForce

Disclosures

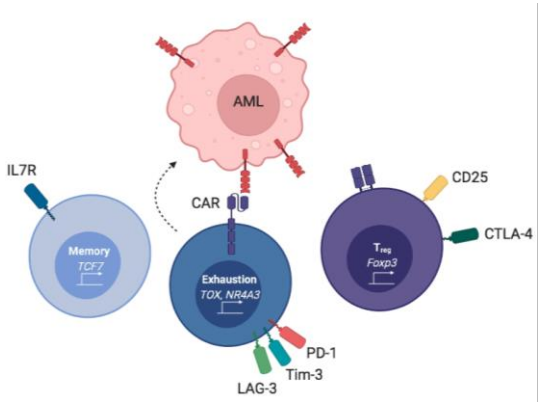
- Research Support: Amgen, BMS/Gilead, Miltenyi, Morphosys, Novartis, Roche, Seattle Genetics
- Advisory Board: Amgen, BMS/Celgene, Gilead, Janssen, Novartis, Pfizer, Seattle Genetics
- Speaker’s Bureau: Amgen, BMS/Celgene, Gilead, Novartis, Pfizer

Challenges of T cell-based Immunotherapy in AML

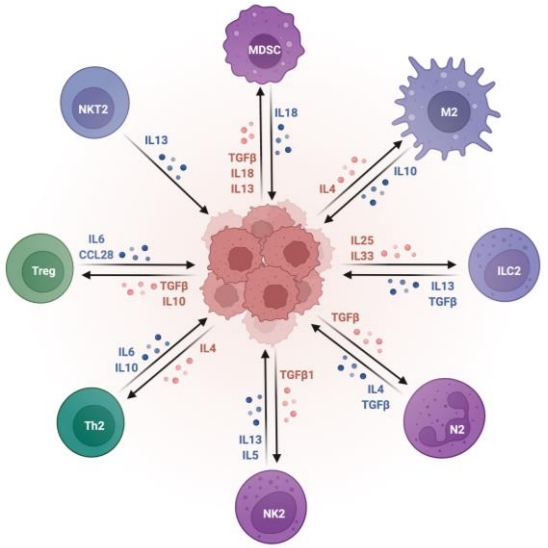
Target Antigen Heterogeneity / Specificity



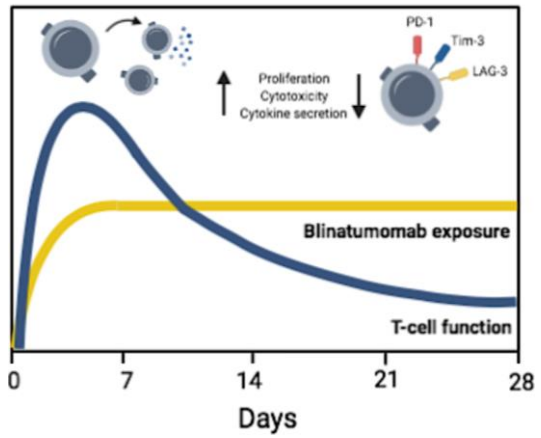
T-cell Subsets / T-cell Function



TME / BM Niche Inflammatory Signature



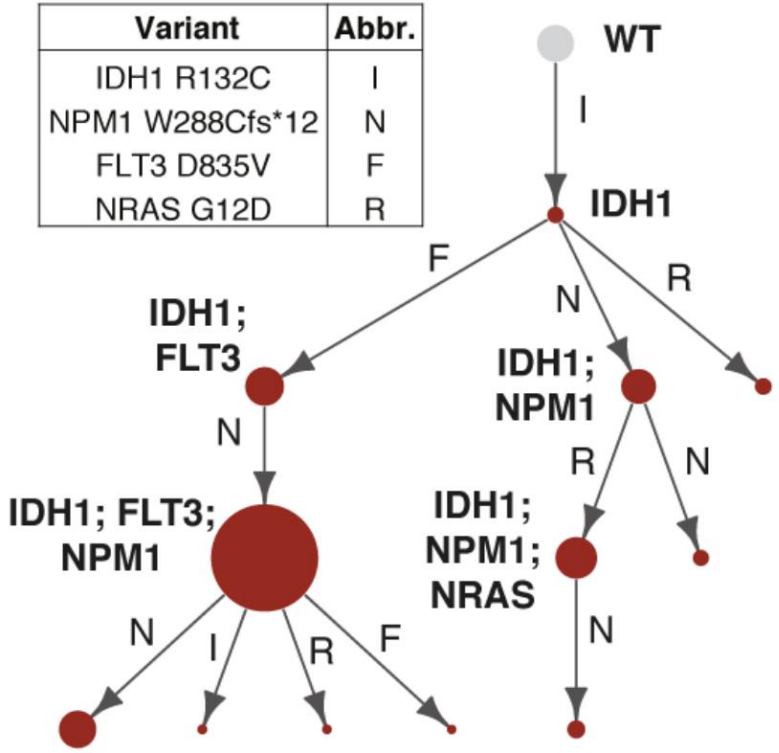
Schedule of Application / Trial Design



Target Antigens for Bispecifics in AML: Inter- & Intra Patient Heterogeneity

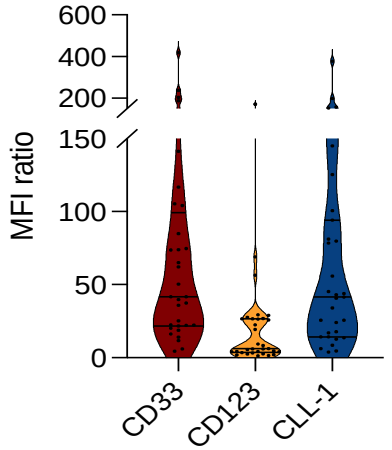
Clonal Complexity

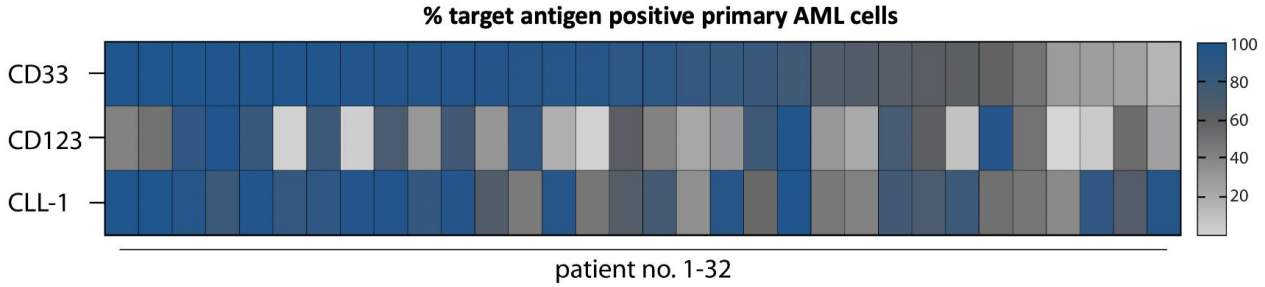
Variant	Abbr.
IDH1 R132C	I
NPM1 W288Cfs*12	N
FLT3 D835V	F
NRAS G12D	R



Miles et al, Nature 2020

Target Heterogeneity



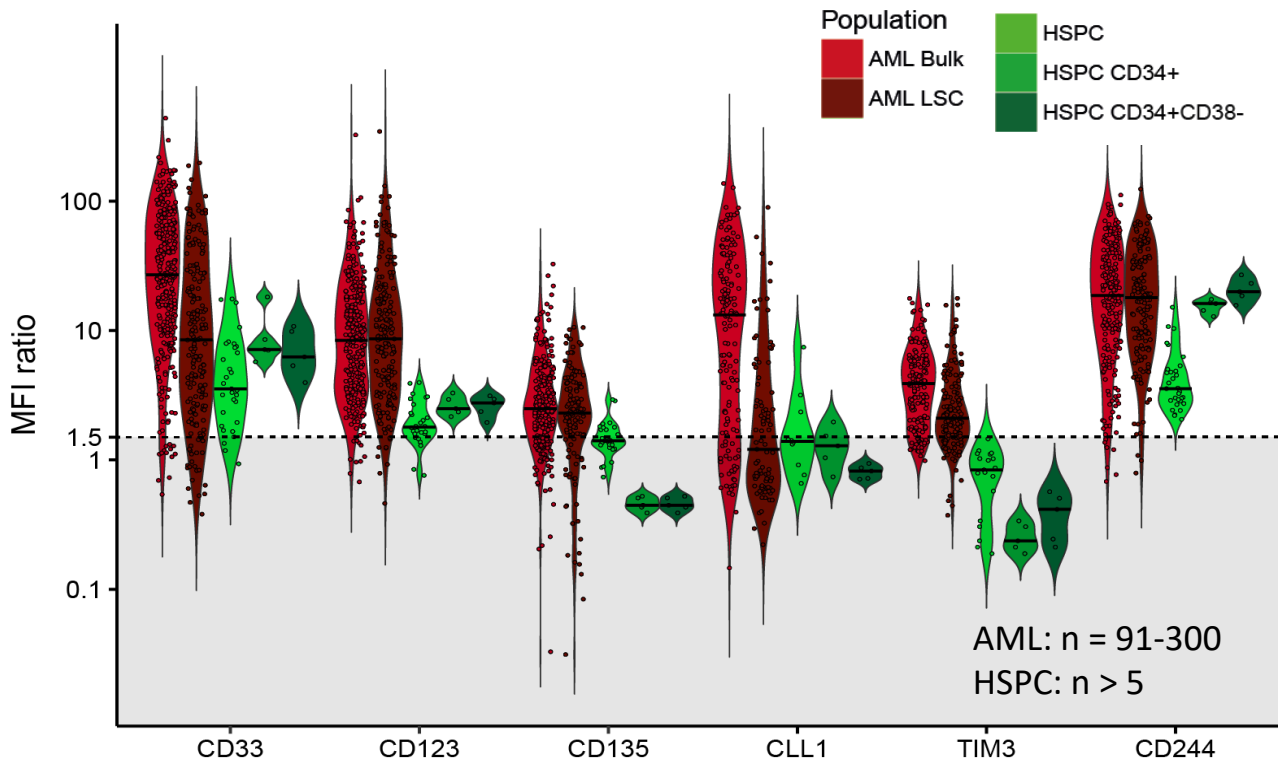


Nixdorf et al, EHA 2022

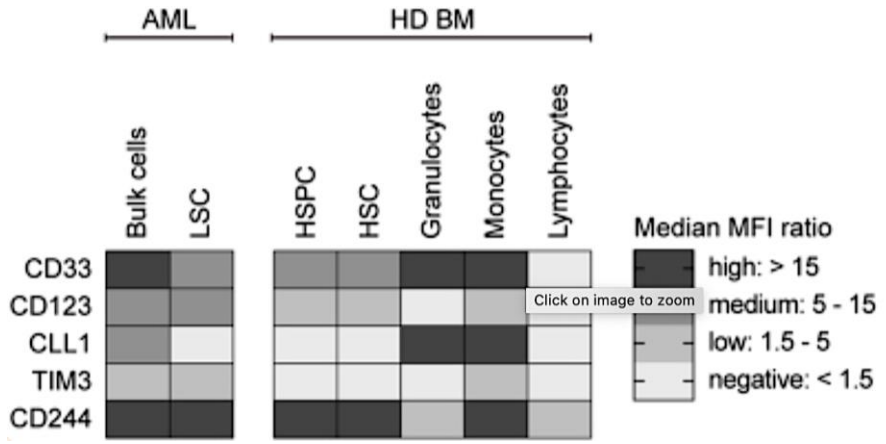
Target Antigens for Bispecifics in AML: On-Target-Off-Leukemia Toxicity

A small Therapeutic window

Antigen Expression in AML and Normal Hematopoiesis



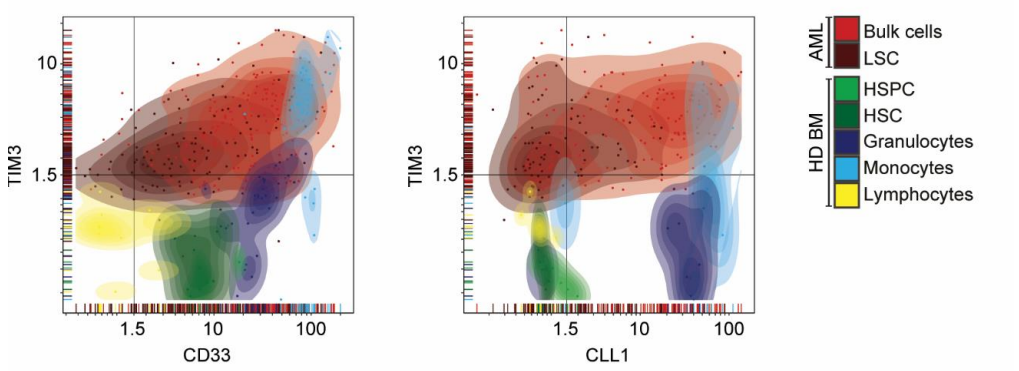
Common Target Antigens are Lineage Derived

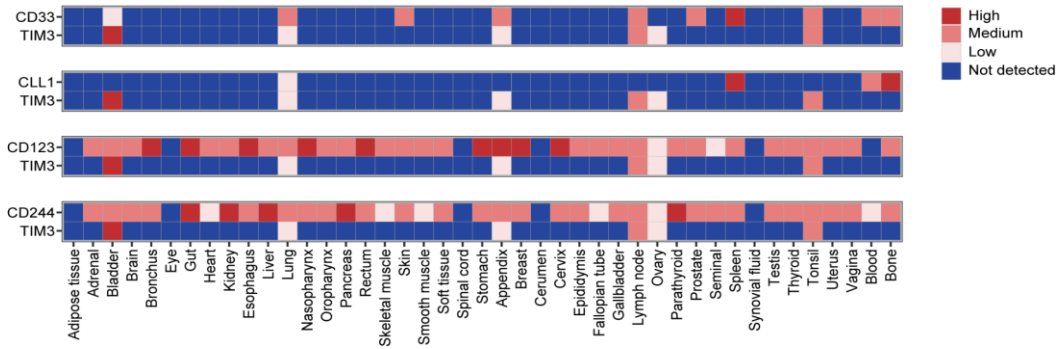


Haubner et al, Leukemia 2019

Dual Targeting Strategy in AML: Construct Design determines Specificity vs Escape

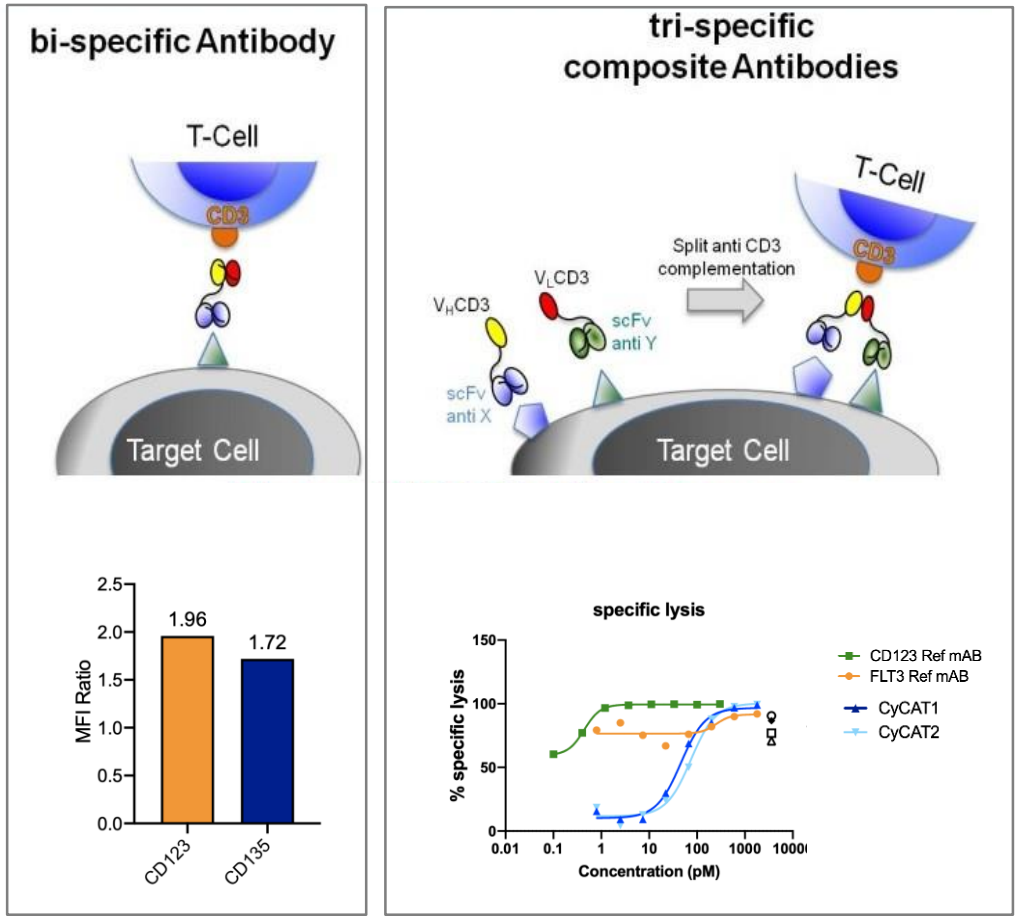
Identification of Suitable Target Antigen Combinations





Haubner et al, Leukemia 2019

Hemibodies to Eliminate dual Antigen positive cells while sparing single positive bystanders

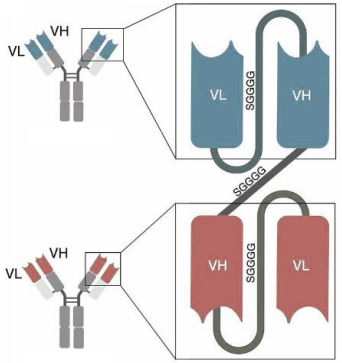


Work in progress

Bispecific Antibody Formats Targeting Surface & Intracellular Antigens

Anti-CD3

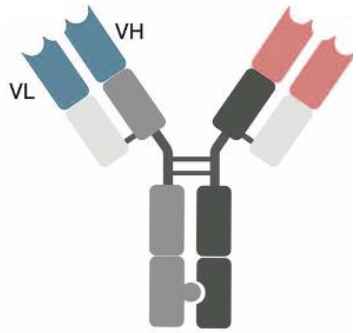
Bispecific T cell engager, BiTE



Anti-TAA,
e.g. anti-CD19

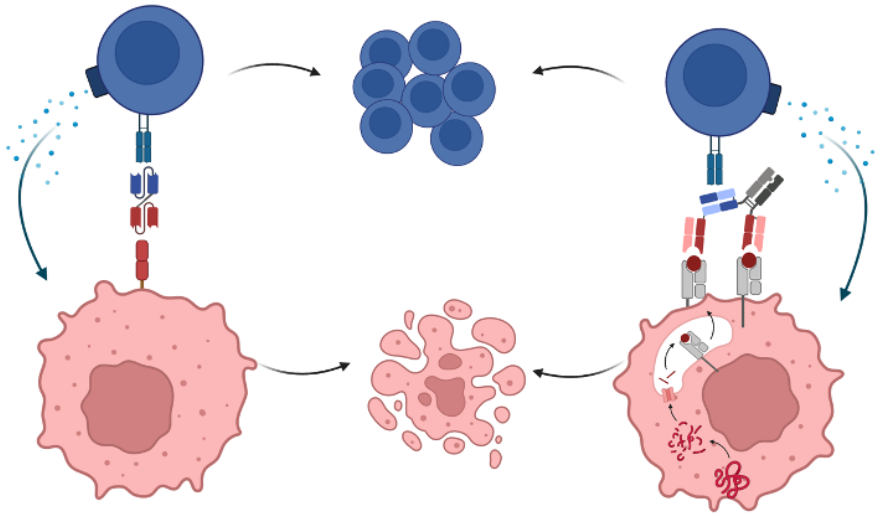
50 – 60 kDa

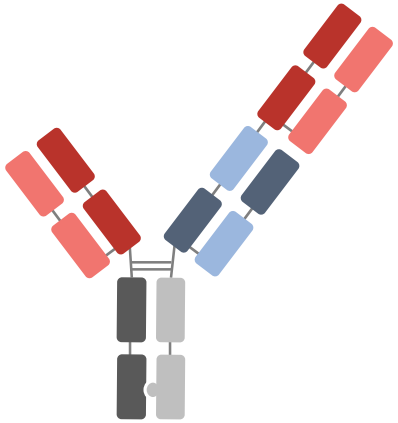
Extended Half-Life BiTEs



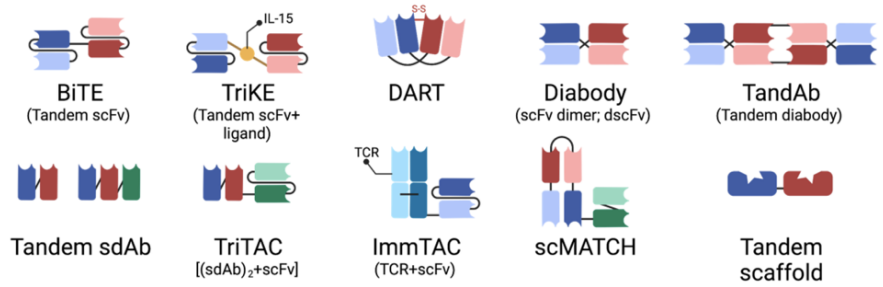
often non-functional
Fc domain; Extended half-life

ca. 150 kDa

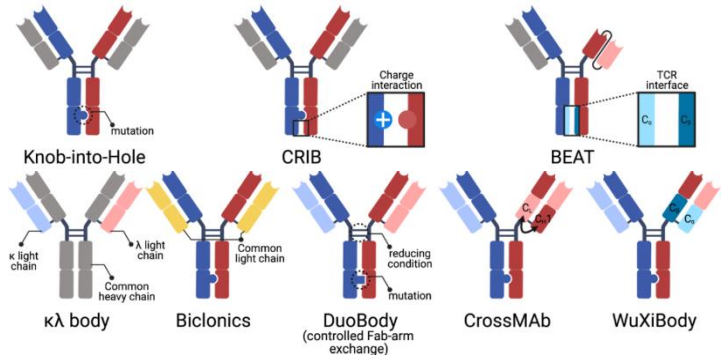




Fragment-based BsAbs; can be linked to Fc



Heterodimerization of heavy or light chains



Adpated from You et al, Vaccines 2021, Augsberger et al, Blood 2021

A New Universe of Targets: Bispecific „TCR Mimickry“ Molecules

Selected TCR and TCR-like bispecifics in development

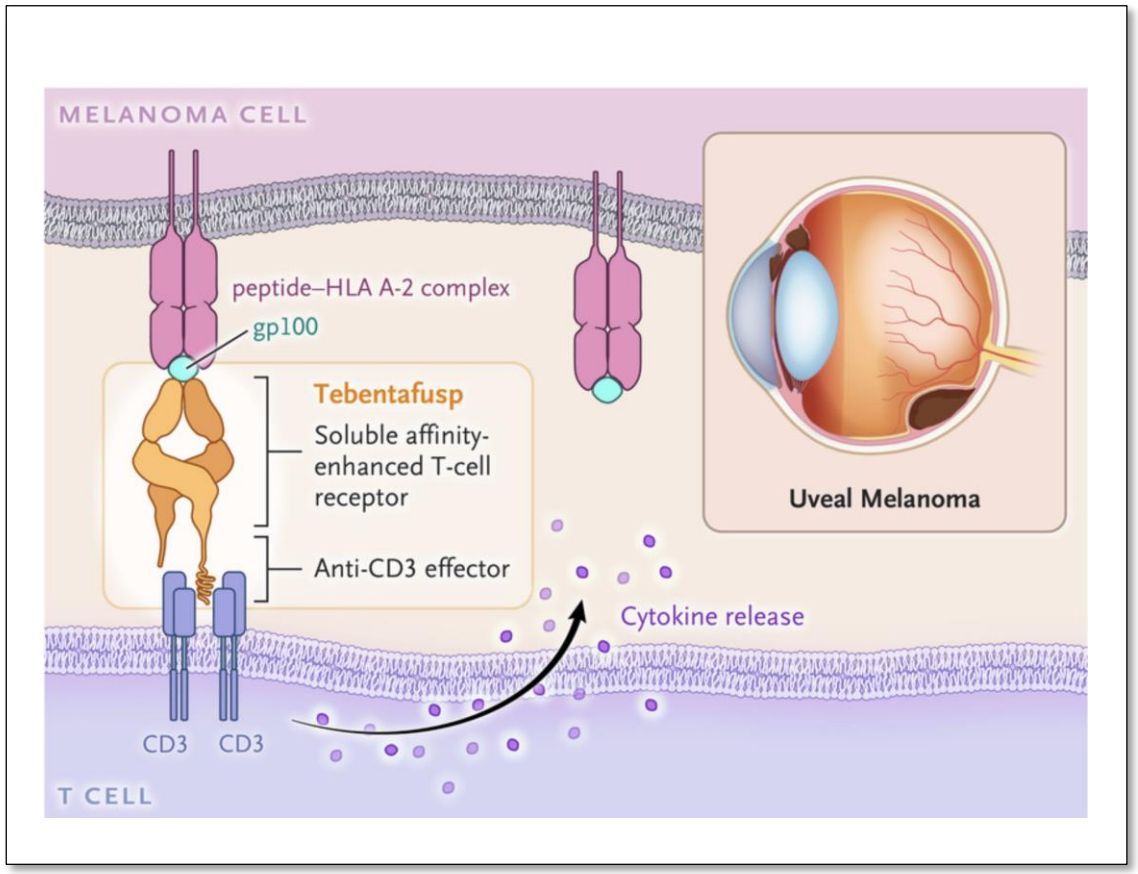
Drug	Sponsor	Target	Lead indication	Status
TCR-based target binder				
Tebentafusp	Immunocore	Gp100	Unresectable or metastatic uveal melanoma	Approved
IMC-F106C	Immunocore	PRAME	Various solid tumours	Phase I/II
IMC-C103C	Immunocore/Roche	MAGE-A4	Various solid tumours	Phase I/II
IMC-I109V	Immunocore	Env	Hepatitis B virus	Phase I
IMA401	Immatics/BMS	MAGE-A4/8	Various solid tumours	CTA filed"
IMA402	Immatics	PRAME	Various solid tumours	Preclinical
ABBV-189	AbbVie/Harpoon Therapeutics	Survivin	Cancer	Preclinical
Antibody-based target binder				
RG6007	Roche	WT1	Acute myeloid leukaemia	Phase I
RG6129	Roche	MAGE-A4	Various solid tumours	Phase I
Unnamed candidate	Gritstone	CT86	Various solid tumours	Preclinical

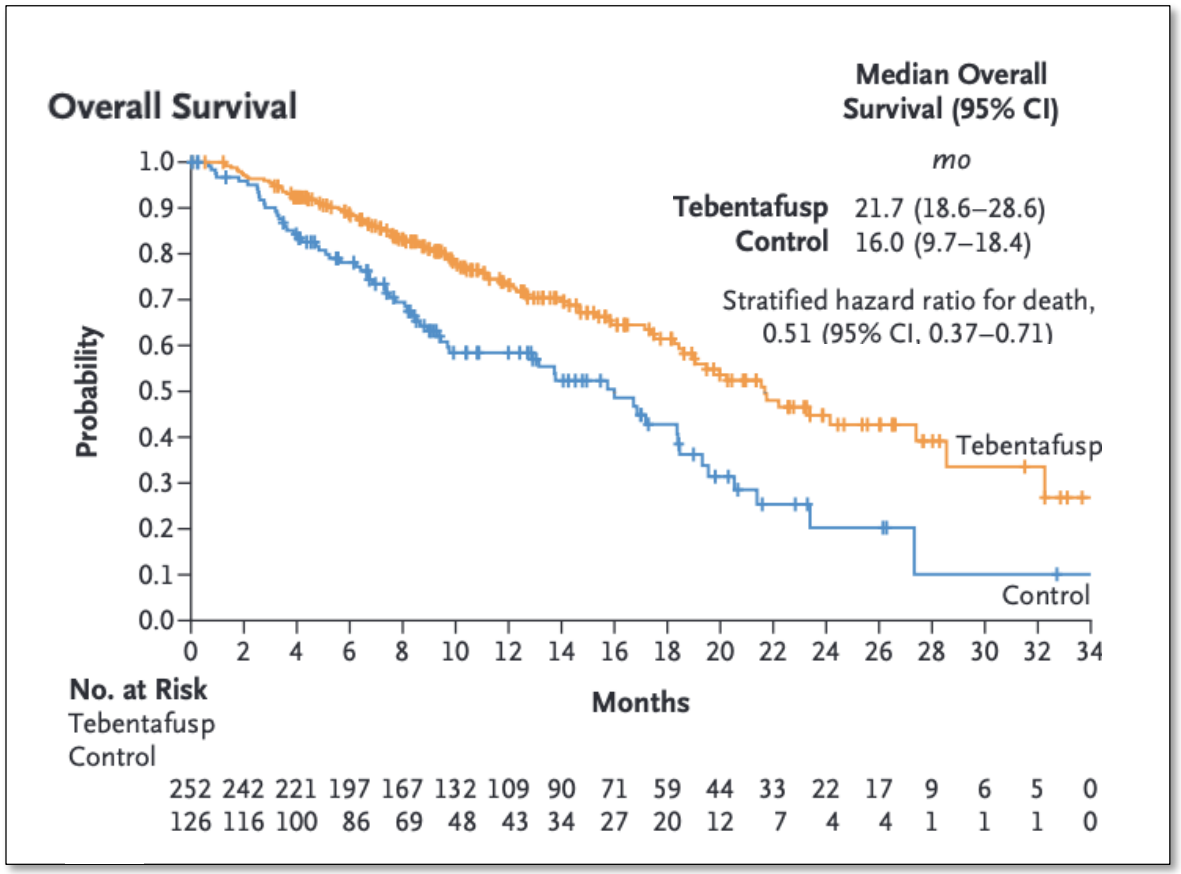
Katie Kingwell, Nature Drug Discovery 2022

First Approved T-Cell Recruiting Bispecific directed against an intracellular TAA

Tebentafusp (gp100-TCRxCD3)

- Indication: HLA-A*02:01-positive Adults with inoperable/metastatic uvea Melanoma





Nathan et al, N Engl J Med, 2021

A New Universe of Targets: Bispecific „TCR Mimickry“ Molecules

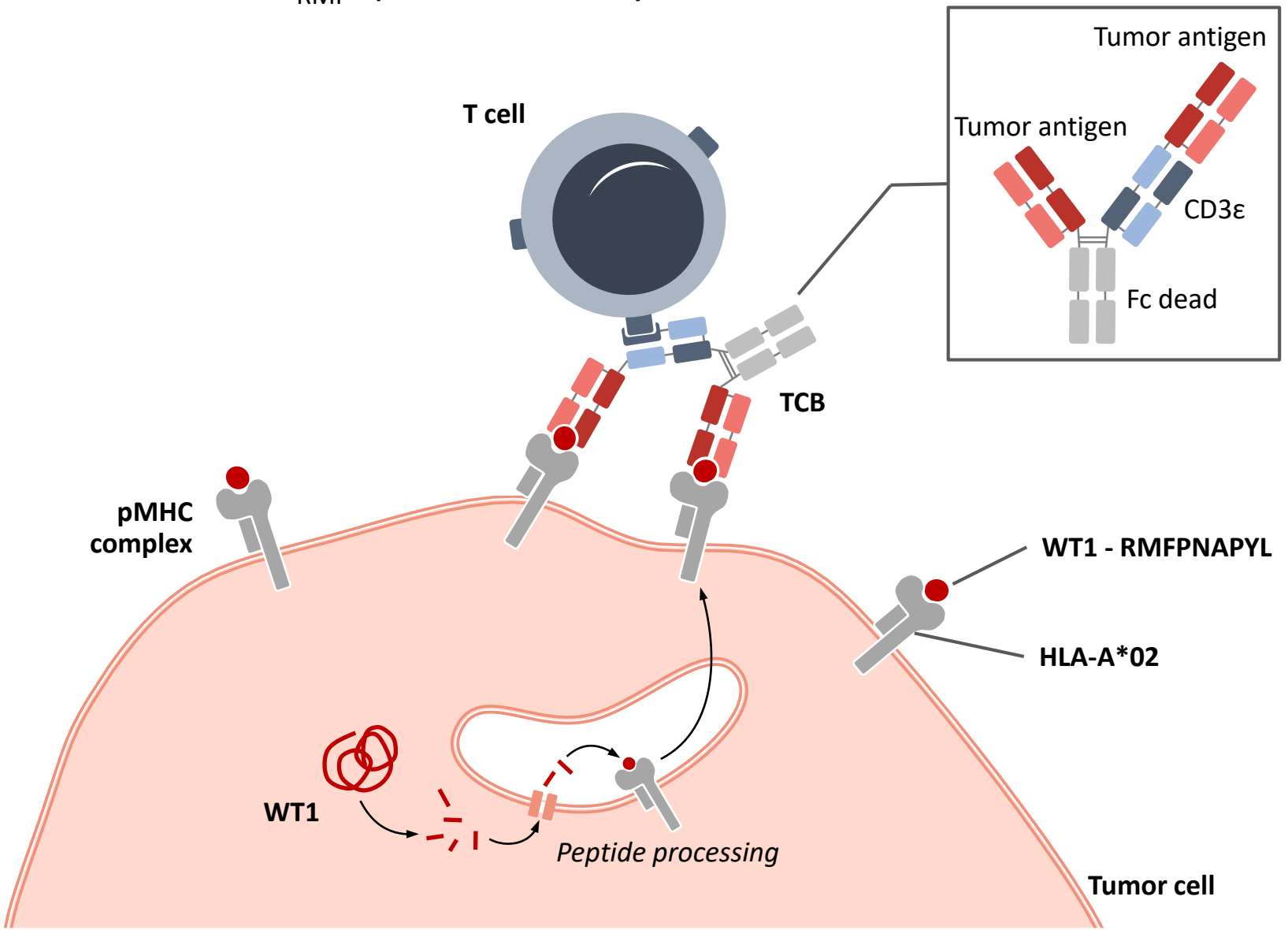
Selected TCR and TCR-like bispecifics in development

Drug	Sponsor	Target	Lead indication	Status
TCR-based target binder				
Tebentafusp	Immunocore	Gp100	Unresectable or metastatic uveal melanoma	Approved
IMC-F106C	Immunocore	PRAME	Various solid tumours	Phase I/II
IMC-C103C	Immunocore/Roche	MAGE-A4	Various solid tumours	Phase I/II
IMC-I109V	Immunocore	Env	Hepatitis B virus	Phase I
IMA401	Immatics/BMS	MAGE-A4/8	Various solid tumours	CTA filed"
IMA402	Immatics	PRAME	Various solid tumours	Preclinical
ABBV-189	AbbVie/Harpoon Therapeutics	Survivin	Cancer	Preclinical
Antibody-based target binder				
RG6007	Roche	WT1	Acute myeloid leukaemia	Phase I
RG6129	Roche	MAGE-A4	Various solid tumours	Phase I
Unnamed candidate	Gritstone	CT86	Various solid tumours	Preclinical

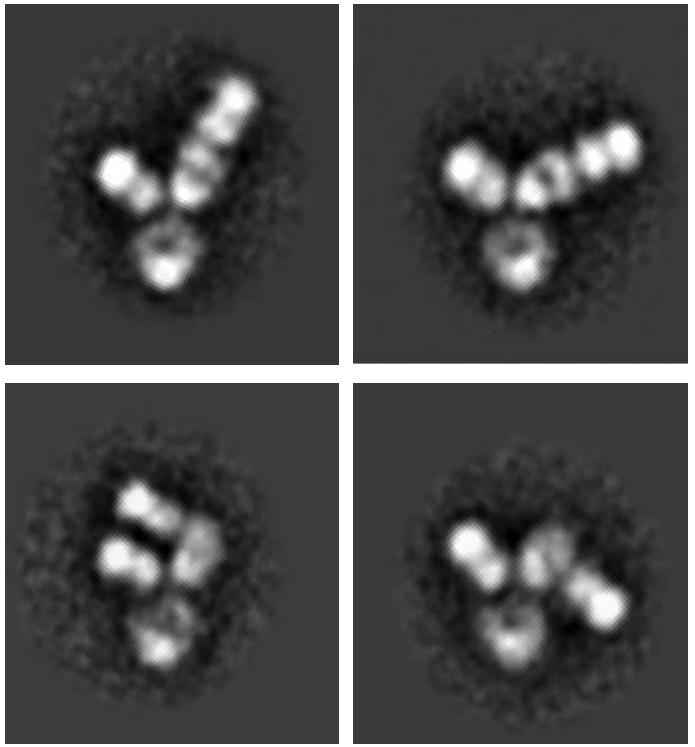
Katie Kingwell, Nature Drug Discovery 2022

Intracellular Antigens as Targets for Bispecific Antibodies „2+1“

HLA-A2^{+}-WT1$_{RMF}$ specific Antibody

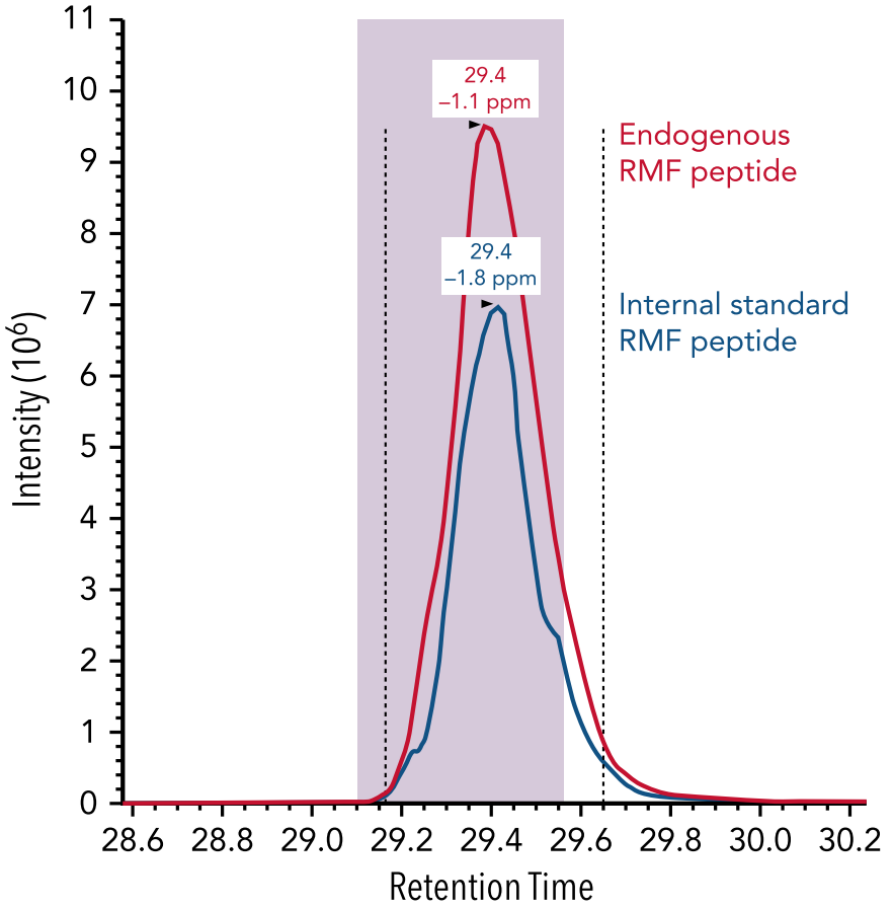


Fc dead domain:
extended half-life/
IgG-like PK properties



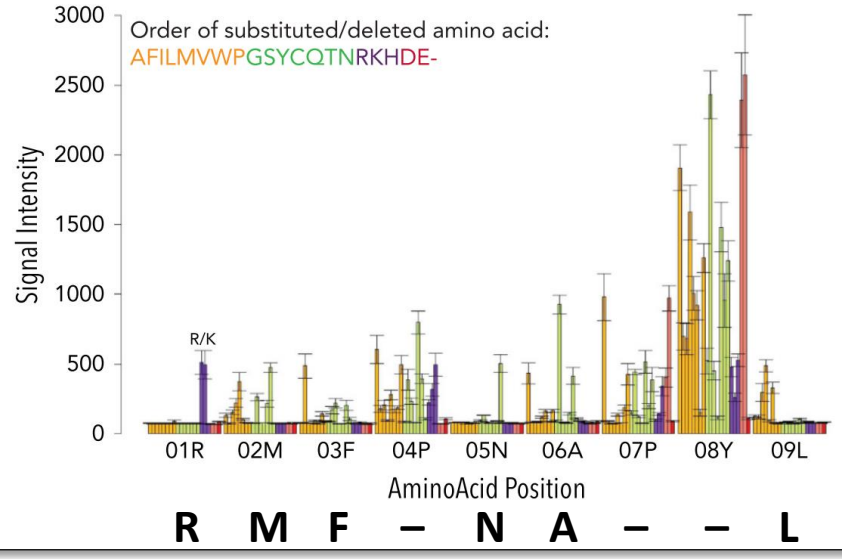
$WT1_{RMF}$ is Presented on HLA-A*02^{+} AML Cells and is Specifically Recognized by WT1-TCB

Peptide presentation by AML cells



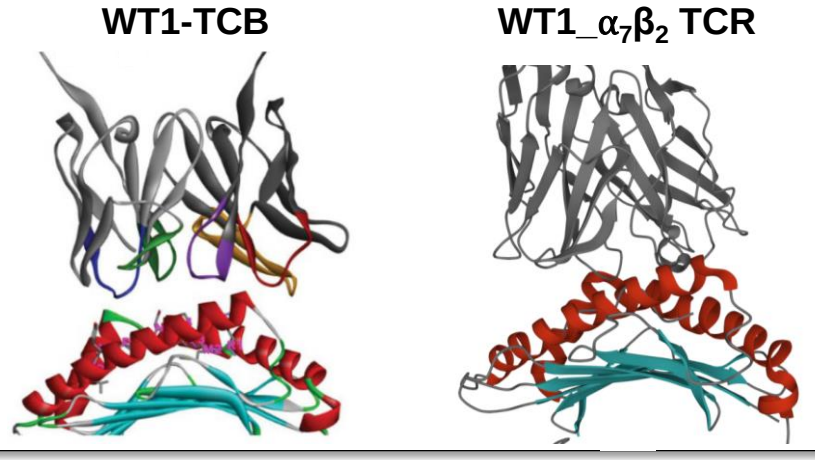
→ 154 copies/cell

Peptide specificity screening



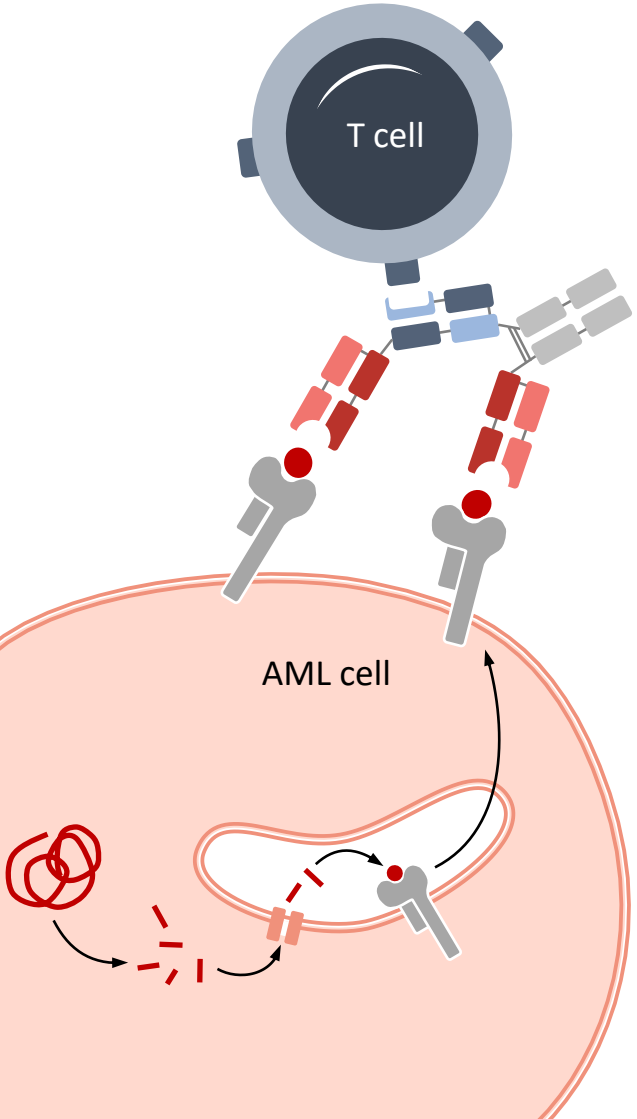
R M F – N A – – L

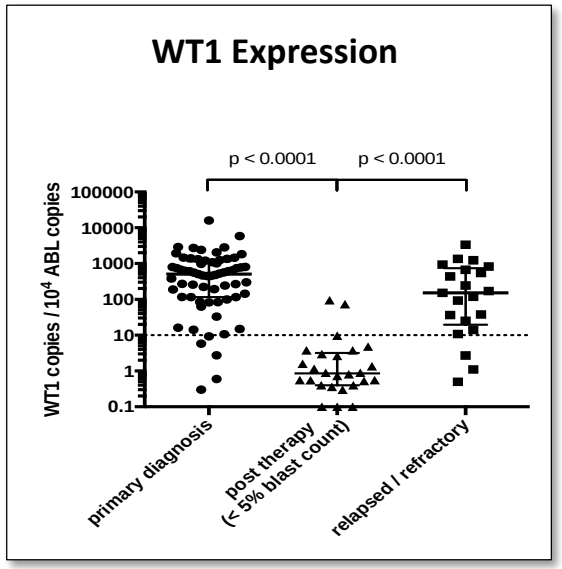
TCR-like binding of WT1-TCB to pMHC

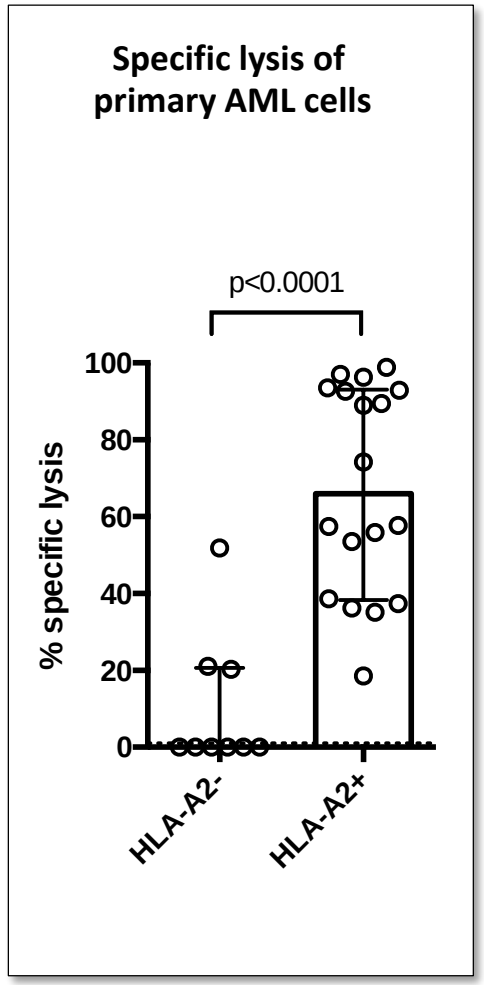


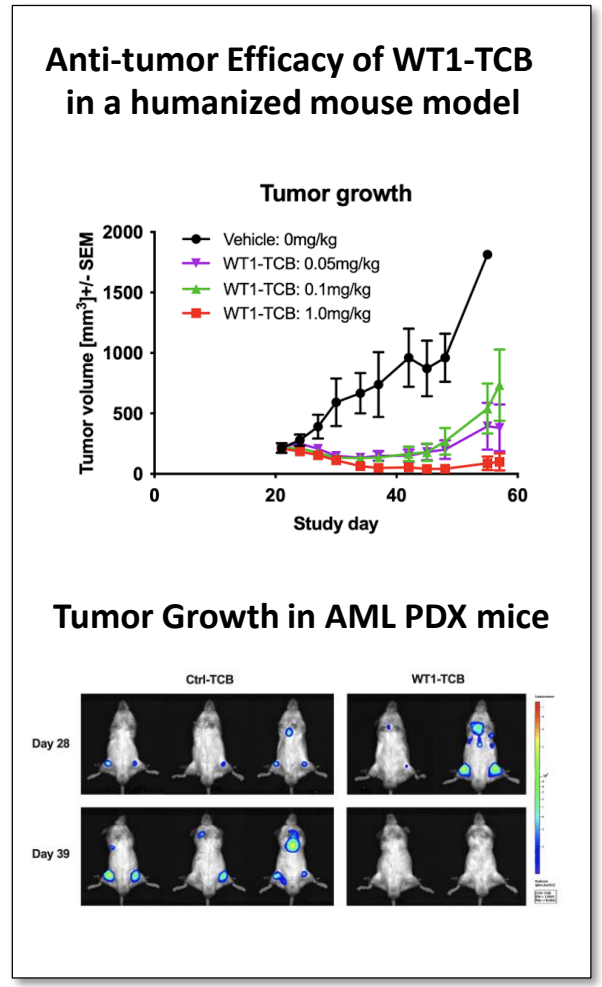
Augsberger C.*, Hänel G.* et al. Blood (2021)

Initiation of a Phase I trial in HLA-A2$^+$patients with r/r AML & MRD$^+$ (> 0.1%)









Currently recruiting into a Phase I clinical trial in r/r AML and also MRD$^+$ AML

Augsberger, Hänel et al, Subklewe, Blood 2021

Evolving Intracellular Target Antigens in AML: Neoantigens – AML specificity

Science

EMBARGOED UNTIL 11:00AM US ET, MONDAY 1 MARCH 2021

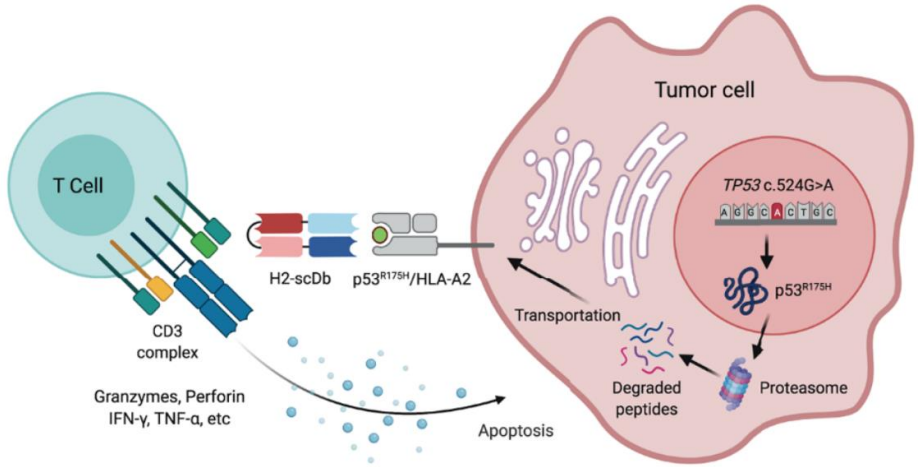
RESEARCH ARTICLES

Cite as: E. H. Hsiue *et al.*, *Science* 10.1126/science.abc8697 (2021).

Targeting a neoantigen derived from a common *TP53* mutation Using TCR Tg T cells or Bispecifics

Emily Han-Chung Hsiue[1,2,3*], Katharine M. Wright[2,4,5*], Jacqueline Douglass[1,2,3*], Michael S. Hwang[1,2,3], Brian J. Mog[1,2,3,6], Alexander H. Pearlman[1,2,3], Suman Paul[1,2,3,7], Sarah R. DiNapoli[1,2,3], Maximilian F. Konig[1,2,3,8], Qing Wang[1,2,9], Annika Schaefer[1,2,3], Michelle S. Miller[2,4,5†], Andrew D. Skora[1,2‡], P. Aitana Azurmendi[2,4,5], Michael B. Murphy[10], Qiang Liu[1,2,3], Evangeline Watson[1,2,3], Yana Li[4], Drew M. Pardoll[5,7], Chetan Bettegowda[1,3,11], Nickolas Papadopoulos[1,3,5,12], Kenneth W. Kinzler[1,3,5], Bert Vogelstein[1,2,3,5,12§], Sandra B. Gabelli[4,7,13§], Shibin Zhou[1,3,5§]

[1]Ludwig Center, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. [2]Howard Hughes Medical Institute, Chevy Chase, MD 20815, USA. [3]Lustgarten Pancreatic Cancer Research Laboratory, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. [4]Department of Biophysics and Biophysical Chemistry, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. [5]Bloomberg~Kimmel Institute for Cancer Immunotherapy, Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD 21287, USA. [6]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21218, USA. [7]Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA. [8]Division of Rheumatology, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21224, USA. [9]Complete Omics, Baltimore, MD 21227, USA. [10]Cytiva, Marlborough, MA 01752, USA. [11]Department of Neurosurgery, Johns Hopkins University School of Medicine, MD 21205, USA. [12]Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA. [13]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA.



JCI The Journal of Clinical Investigation

CBFB-MYH11 fusion neoantigen enables T cell recognition and killing of acute myeloid leukemia

Melinda A. Biernacki, … , Anthony Rongvaux, Marie Bleakley

J Clin Invest. 2020;130(10):5127-5141. https://doi.org/10.1172/JCI137723.

Research Article Immunology Oncology

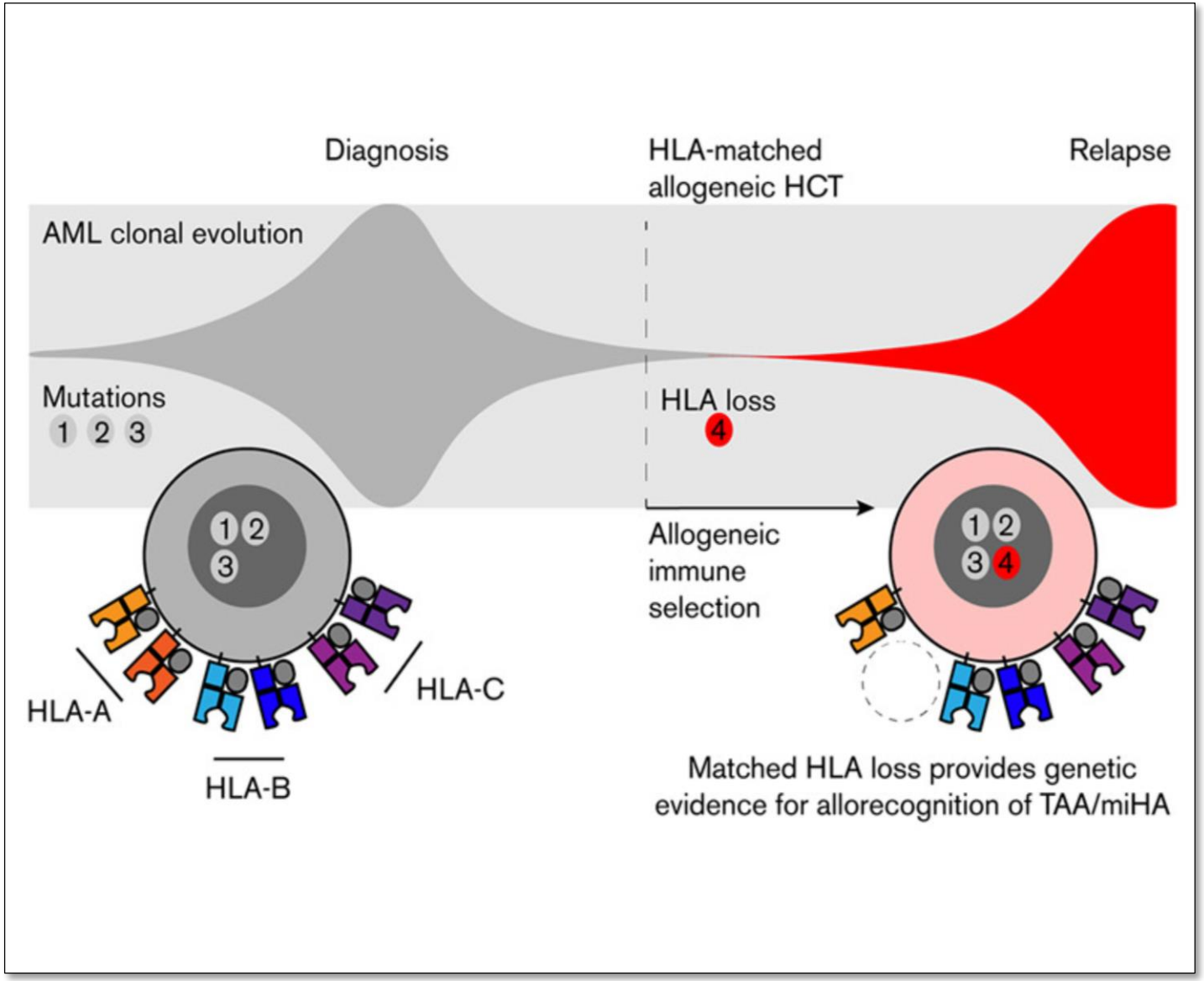
Proteins created from recurrent fusion genes like *CBFB-MYH11* are prevalent in acute myeloid leukemia (AML), often necessary for leukemogenesis, persistent throughout the disease course, and highly leukemia specific, making them attractive neoantigen targets for immunotherapy. A nonameric peptide derived from a prevalent CBFB-MYH11 fusion protein was found to be immunogenic in *HLA-B*40:01*$^+$ donors. High-avidity CD8$^+$ T cell clones isolated from healthy donors killed *CBFB-MYH11*$^+$ *HLA-B*40:01*$^+$ AML cell lines and primary human AML samples in vitro. CBFB-MYH11–specific T cells also controlled *CBFB-MYH11*$^+$ *HLA-B*40:01*$^+$ AML in vivo in a patient-derived murine xenograft model. High-avidity CBFB-MYH11 epitope–specific T cell receptors (TCRs) transduced into CD8$^+$ T cells conferred antileukemic activity in vitro. Our data indicate that the CBFB-MYH11 fusion neoantigen is naturally presented on AML blasts and enables T cell recognition and killing of AML. We provide proof of principle for immunologically targeting AML-initiating fusions and demonstrate that targeting neoantigens has clinical relevance even in low–mutational frequency cancers like fusion-driven AML. This work also represents a first critical step toward the development of TCR T cell immunotherapy targeting fusion gene–driven AML.

› Cancers (Basel). 2021 Oct 27;13(21):5390. doi: 10.3390/cancers13215390.

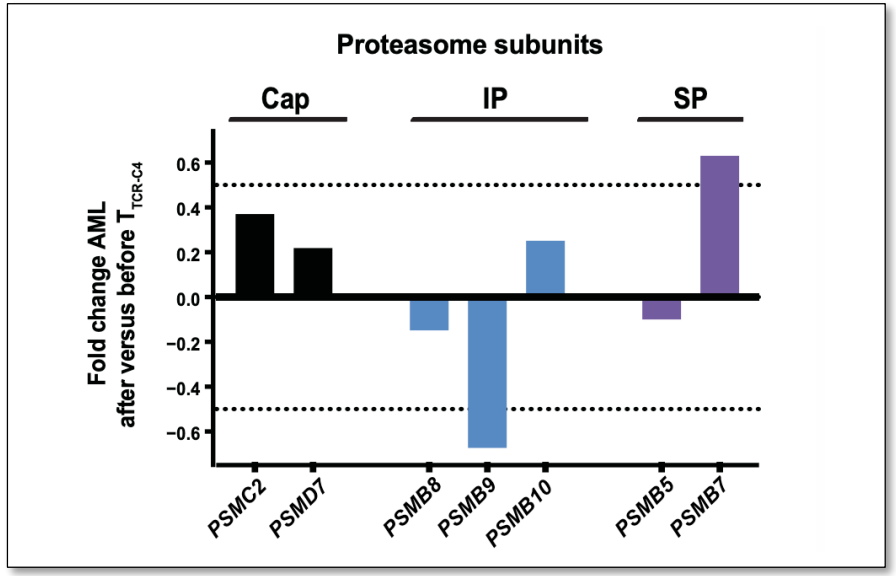
An HLA-A*11:01-Binding Neoantigen from Mutated NPM1 as Target for TCR Gene Therapy in AML

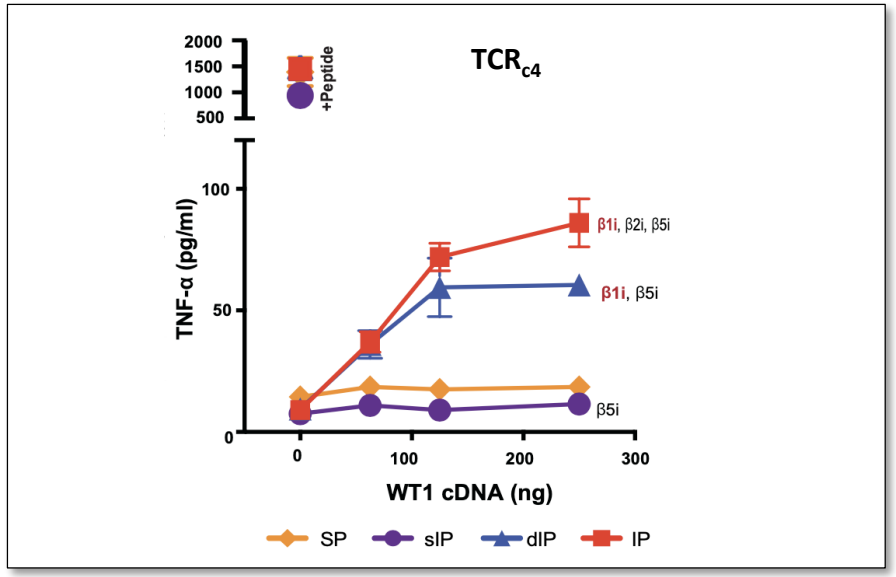
Dyantha I van der Lee [1], Georgia Koutsoumpli [1], Rogier M Reijmers [1], M Willy Honders [1], Rob C M de Jong [1], Dennis F G Remst [1], Tassilo L A Wachsmann [1], Renate S Hagedoorn [1], Kees L M C Franken [2], Michel G D Kester [1], Karl J Harber [1], Lisanne M Roelofsen [1], Annemiek M Schouten [1], Arend Mulder [2], Jan W Drijfhout [2], Hendrik Veelken [1], Peter A van Veelen [3], Mirjam H M Heemskerk [1], J H Frederik Falkenburg [1], Marieke Griffioen [1]

Immune Evasion by Antigen Escape unter Immunological Pressure



Jan et al, Blood Advances 2019



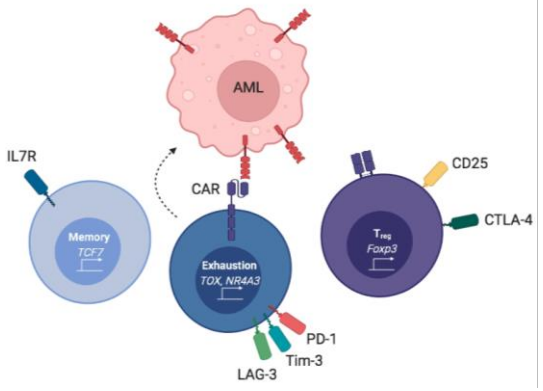


Lahman et al, Science Translational Medicine 2022

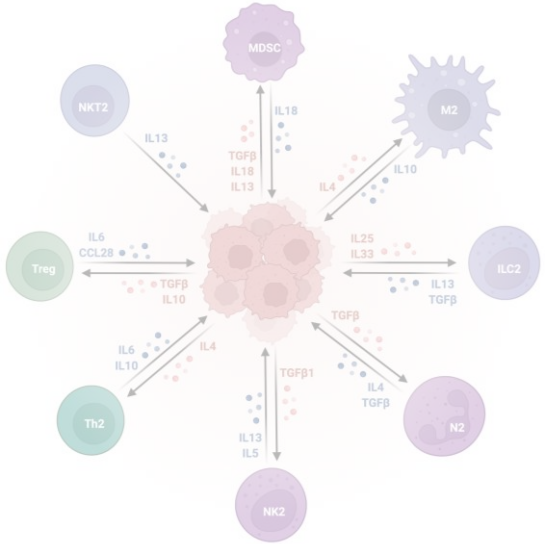
Challenges of T cell-based Immunotherapy in AML

Target Antigen Heterogeneity / Specificity

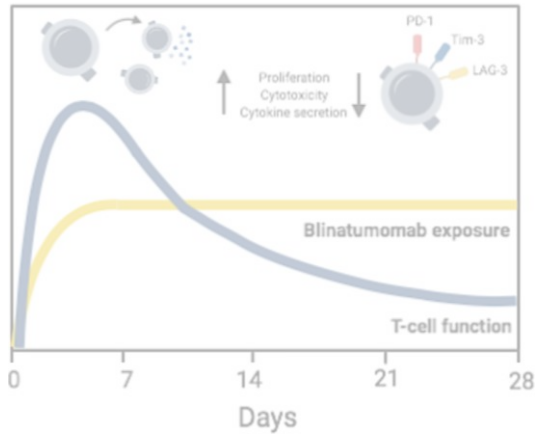
T-cell Subsets / T-cell Function



TME / BM Niche Inflammatory Signature



Schedule of Application / Trial Design



LYMPHOID NEOPLASIA

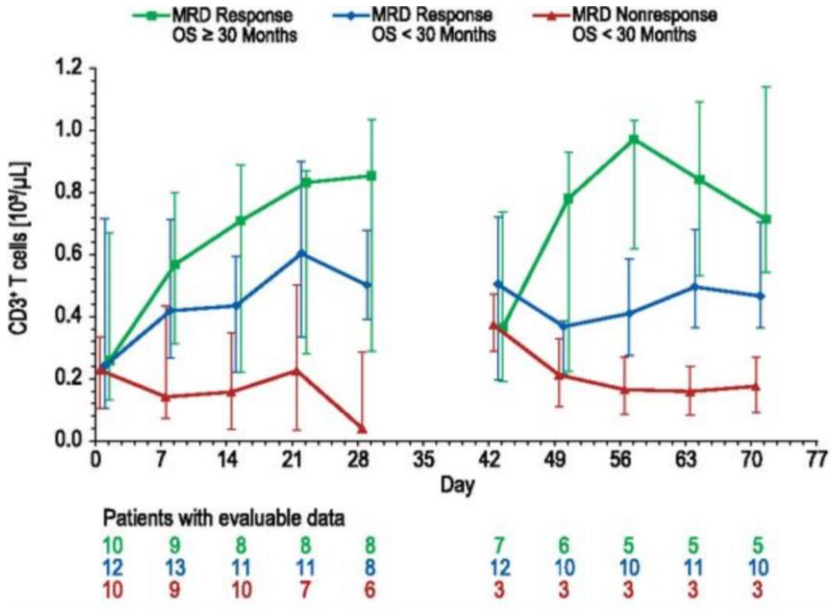
Long-term survival and T-cell kinetics in relapsed/refractory ALL patients who achieved MRD response after blinatumomab treatment

Gerhard Zugmaier,[1] Nicola Gökbuget,[2] Matthias Klinger,[1] Andreas Viardot,[3] Matthias Stelljes,[4] Svenja Neumann,[5] Heinz-A. Horst,[5] Reinhard Marks,[6] Christoph Faul,[7] Helmut Diedrich,[8] Albrecht Reichle,[9] Monika Brüggemann,[5] Chris Holland,[10] Margit Schmidt,[1] Hermann Einsele,[11] Ralf C. Bargou,[12] and Max S. Topp[11]

[1]Amgen Research (Munich), Munich, Germany; [2]Department of Medicine II, Goethe University Frankfurt, Frankfurt, Germany; [3]Department of Internal Medicine III, University Hospital Ulm, Ulm, Germany; [4]Department of Medicine A, University of Münster, Münster, Germany; [5]Department of Medicine II, Christian-Albrechts-Universität zu Kiel, Kiel, Germany; [6]Department of Medicine I, Albert-Ludwigs-Universität Frieburg, Freiburg, Germany; [7]Department of Medicine II, Eberhard Karls Universität Tübingen, Tübingen, Germany; [8]Department of Hematology and Oncology, Medizinische Hochschule Hannover, Hannover, Germany; [9]Department of Medicine III, University of Regensburg, Regensburg, Germany; [10]Amgen, Rockville, MD; and [11]Department of Medicine II and [12]Comprehensive Cancer Center Mainfranken, Universitätsklinikum Würzburg, Würzburg, Germany

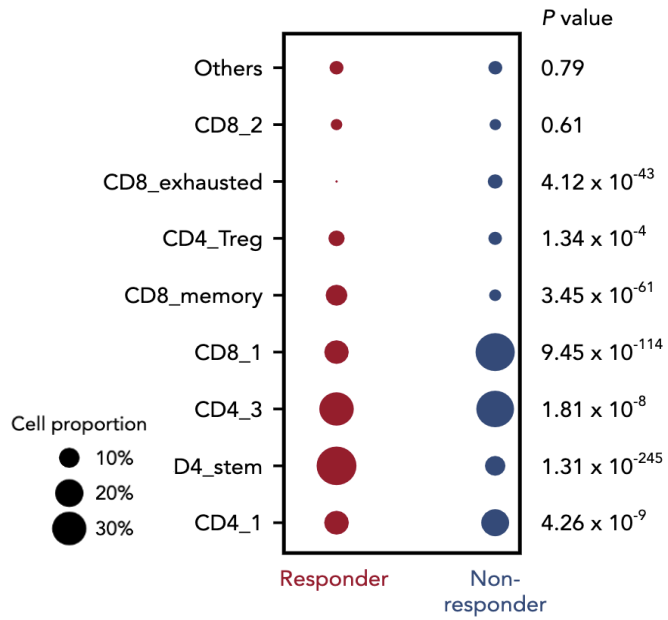
Key Points

- Ten of 36 patients (28%) achieved an OS ≥ 30 months in a blinatumomab study in relapsed/refractory acute lymphoblastic leukemia.
- Long-term survival may be associated with T-cell expansion, B-cell depletion, and a minimal residual disease response.



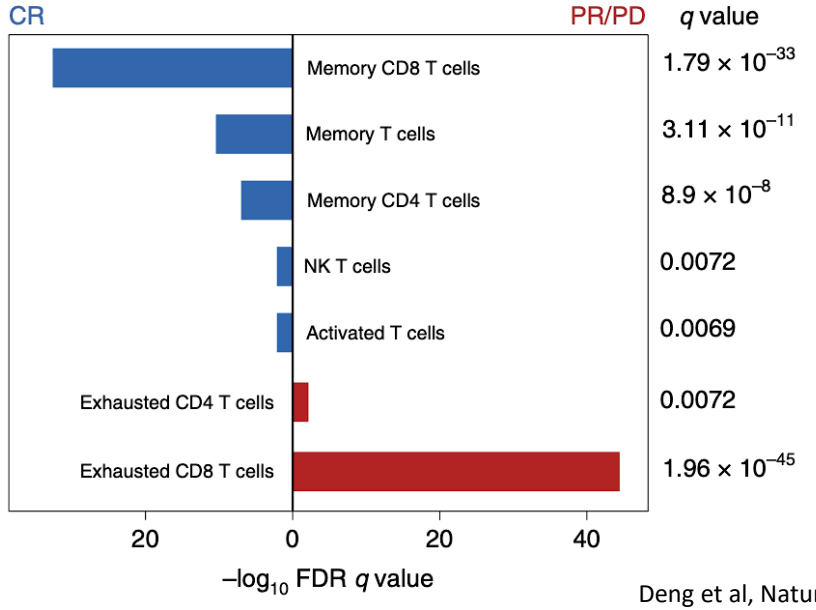
In BiTE & CART alike: T cell Fitness & Composition Determines Response Rate

Responders to Blinatumomab: Increase in naive and central memory T cells



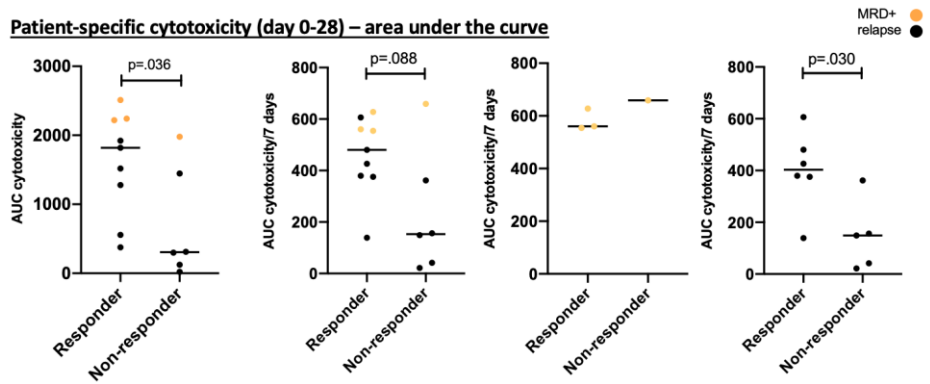
Zhao et al, Blood 2021

Responders to CD19 CAR T cells in DLBCL: memory CD4 & CD8 T cells



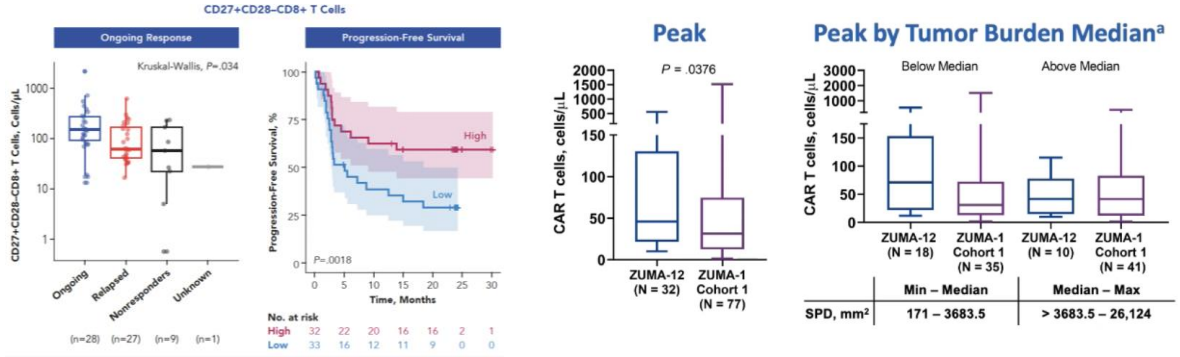
Deng et al, Nature Medicine 2020

Reduced *in vitro* CD19-BiTE-mediated Cytotoxicity in non-Responders



Bücklein et al, ASH 2019

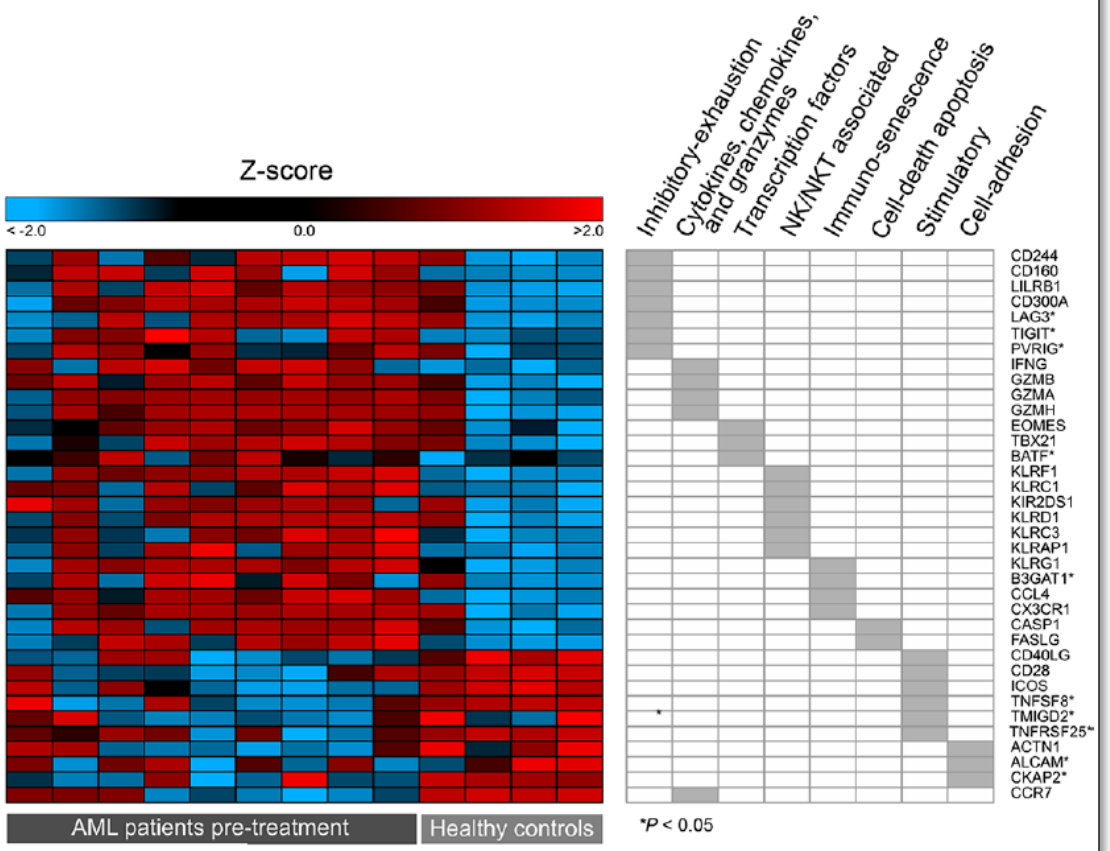
T cell subsets & T cell expansion correlate to response: ZUMA-1 immune profile and comparision of ZUMA 1 vs ZUMA 12 data



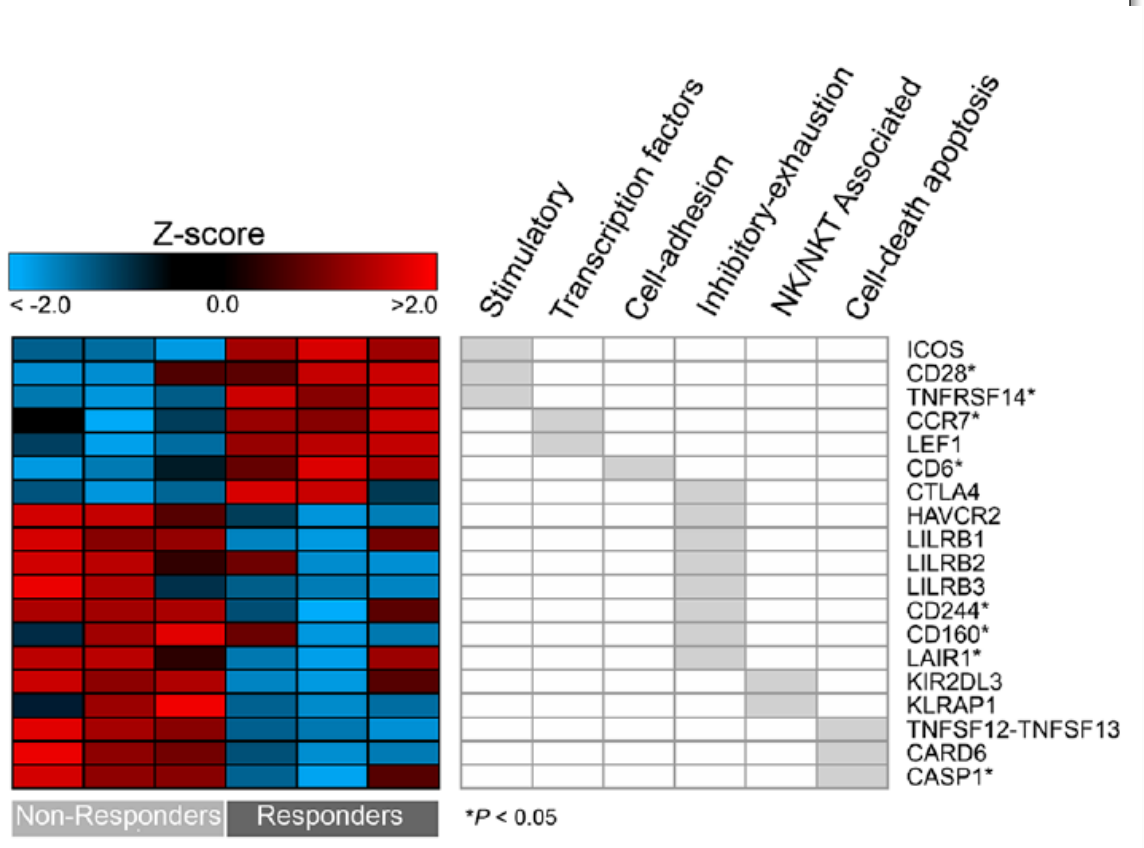
Chou et al, TCT 2022, Neelapu et al, ASH 2020

Signatures of CD8$^+$ T-cell Dysfunction

AML pts vs Healthy Controls



Responders vs Non-Responders

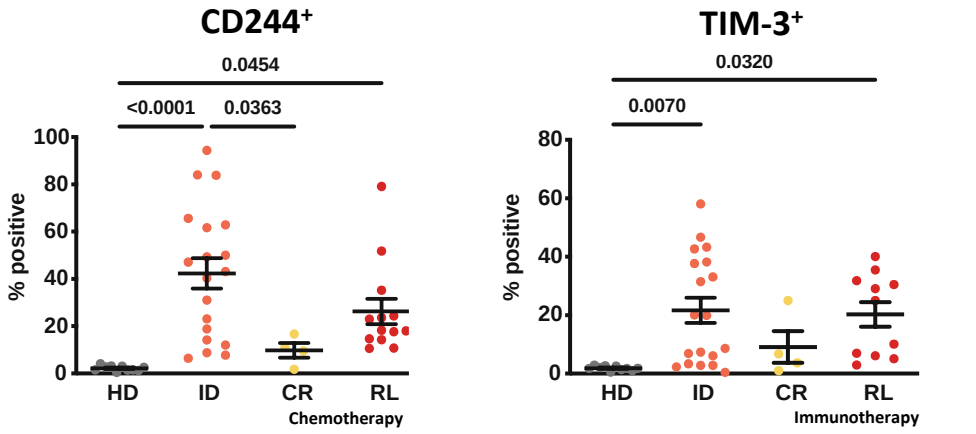


Knaus et al., JCI 2018

Characterization of T cells during AML Progression

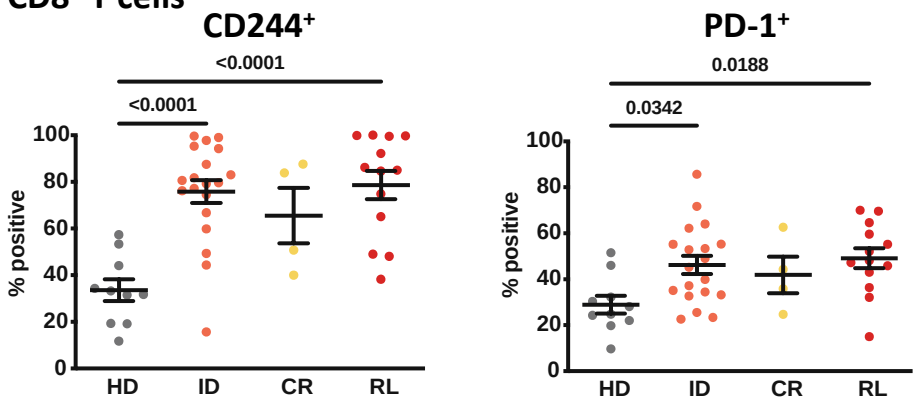
BM T cells Express Exhaustion Markers at ID, RL

CD4⁺ T cells

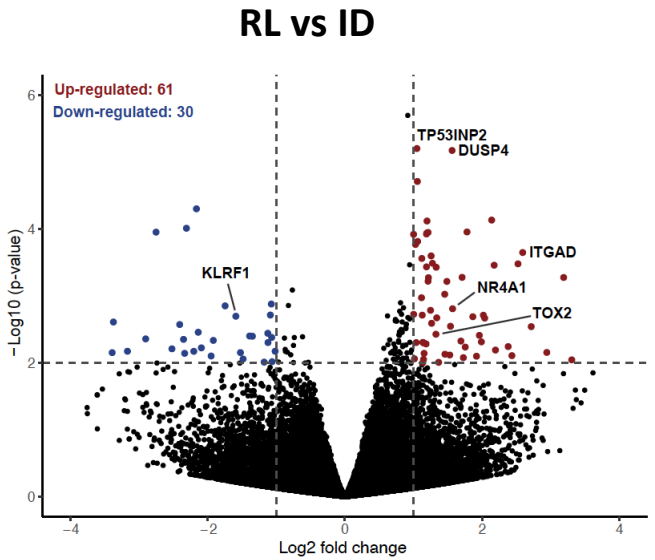


- RL vs ID: LAG3
- ID/RL vs HD: CD244, TIM-3

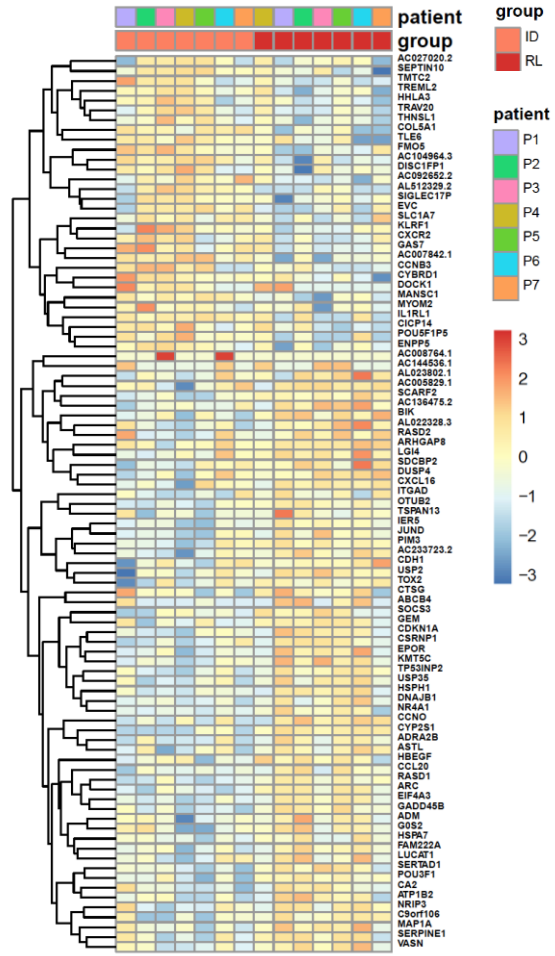
CD8⁺ T cells



Genes Related to T cells and Exhaustion are Upregulated at Time of RL Compared to ID

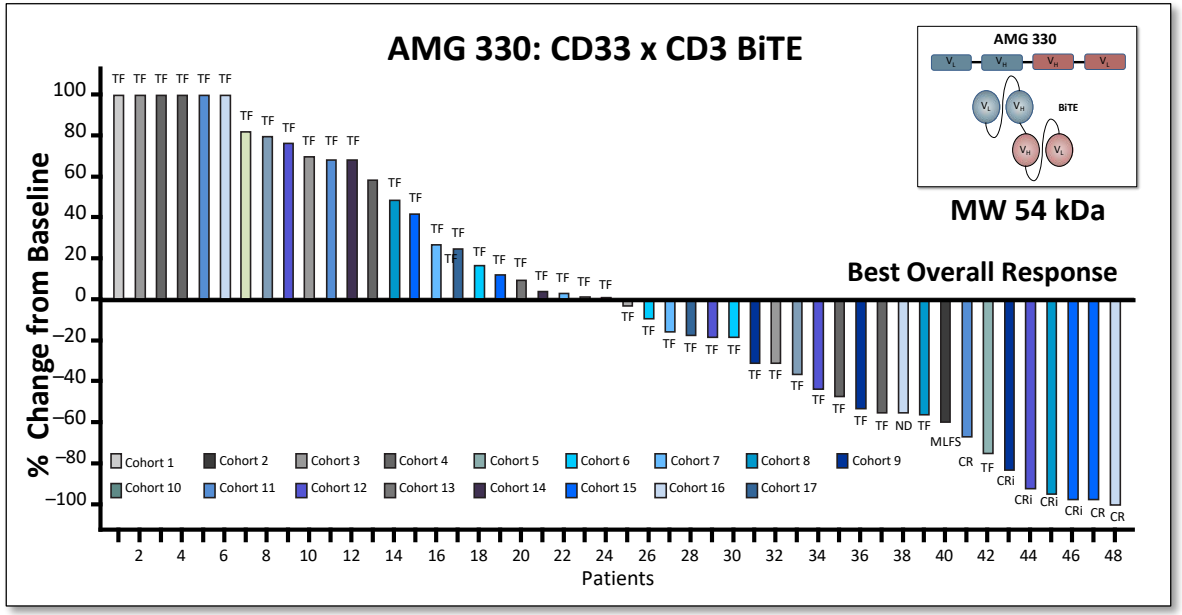


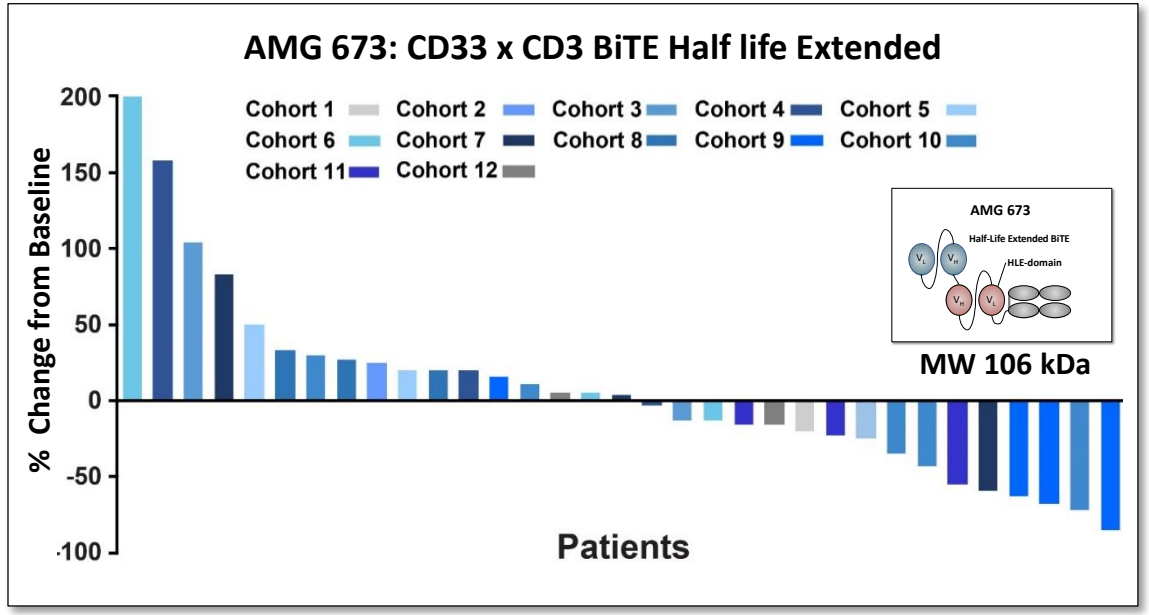
Log2 FC > 1 or < -1; p < 0.01



Kazerani et al, ASH 2021

Phase I Clinical Trials in r/r AML: CD33-BiTE & CD33-BITE-HLE: Response to Treatment





- **48/60 Pt: > 4 prior anti AML therapies;** 27/60 prior HST
- 41/60: > 25% blast count in the BM; 24/60 > 50%
- 8 patients responded to AMG 330 treatment: CR (n=3, cohorts 11, 15, and 16), CRi (n=4, cohorts 8, 9, 12, and 15) and MLFS (n=1, cohort 2) with 3 responders out of 14 treated patients (21%) in cohorts 15-17
- Lower leukemic burden & higher E:T ratio was associated with higher likelihood of response, higher AMG 330 Exposure in responders Response was observed after 1st cycle and sustained for a median 38.5 days (range of 14 –121 days) during the on-study period

- **25/38 patients ≥ 4 prior anti-AML therapies;** 7/38 prior HSCT
- Reduction in blasts was observed in 16/38 (42%) patients
  - ≥ 50% reduction in blasts was seen in 6 patients
  - One patient from cohort 9 achieved CRI, with 85% reduction in bone marrow blasts; 2 additional pts achieved CRh + Cri at target dose of 72 ug
- Reduction in blast numbers was observed in patients with higher exposure to AMG 673

Ravandi et al, ASCO 2020, Subklewe et al, ASH 2019

CD123 DART – Flotetuzumab: Phase I/II Study Design

Flotetuzumab Phase 1/2 Study Design

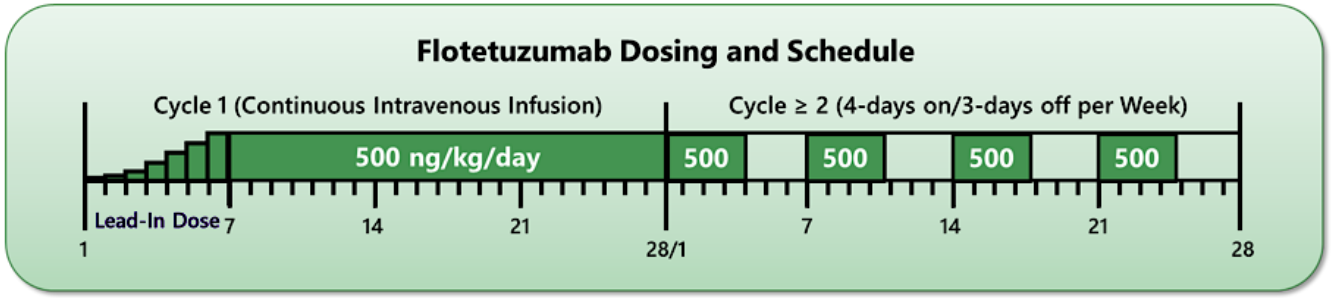
Expansion in primary induction failure & early relapsed AML patients

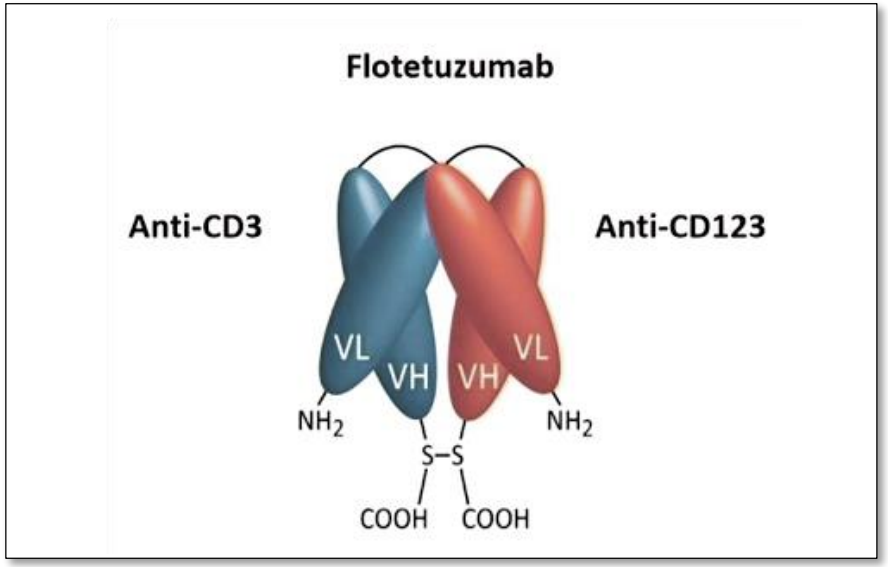
Key Entry Criteria (refractory AML population)

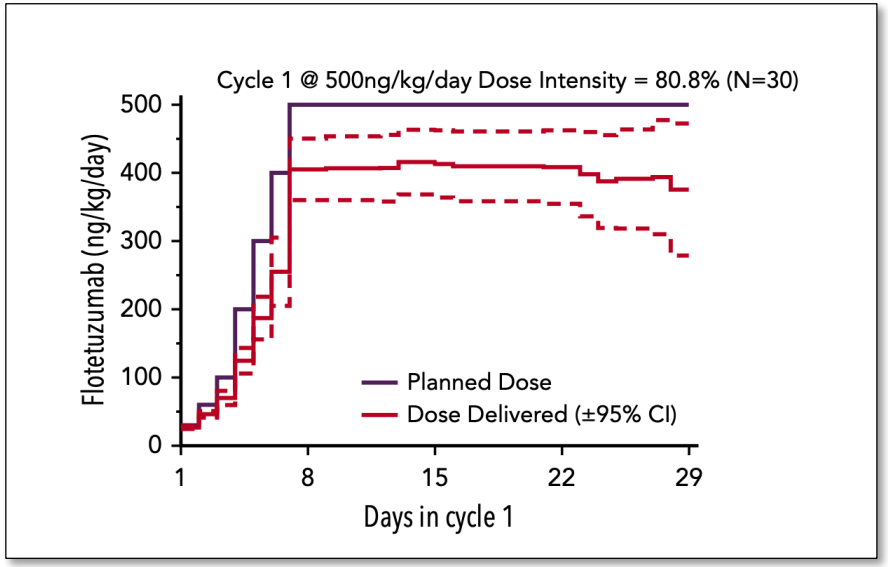
- Primary induction failure (PIF): refractory to 2 induction attempts
- Early relapse: First relapse with initial CR duration of 6 months or any prior unsuccessful salvage
- No prior allogeneic hematopoietic cell transplant

Study Objectives

- Safety and preliminary clinical activity
- Optimize delivery and supportive care
- Define PK, PD and PK/PD relationships

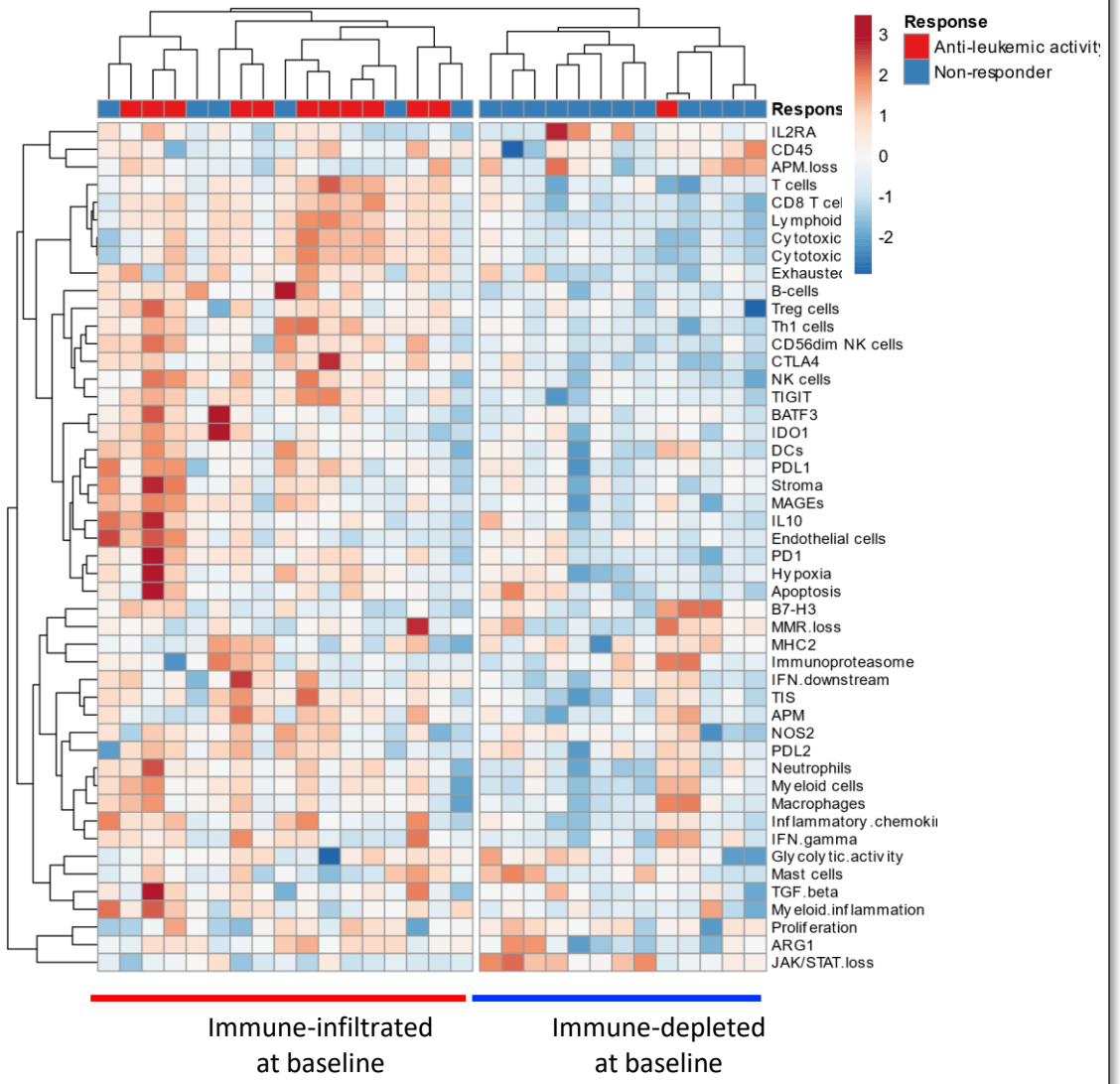






Uy et al, Blood 2021

Immune Infiltration and response to Flotetuzumab



**P<0.01; Mann Whitney *U* test for unpaired determinations

Immune:	Infiltrated (n=17)	Depleted (n=13)
CR	29.4% (5)	0
CRh	5.9% (1)	7.7% (1)
CRi	5.9% (1)	0
CR/CRh/CRi	41.2%	7.7%
% BM change (avg)	-48%	+37%

Vadakekolathu et al, Sci Transl Med. 2020; Vadakekolathu et al, Blood Advances 2020

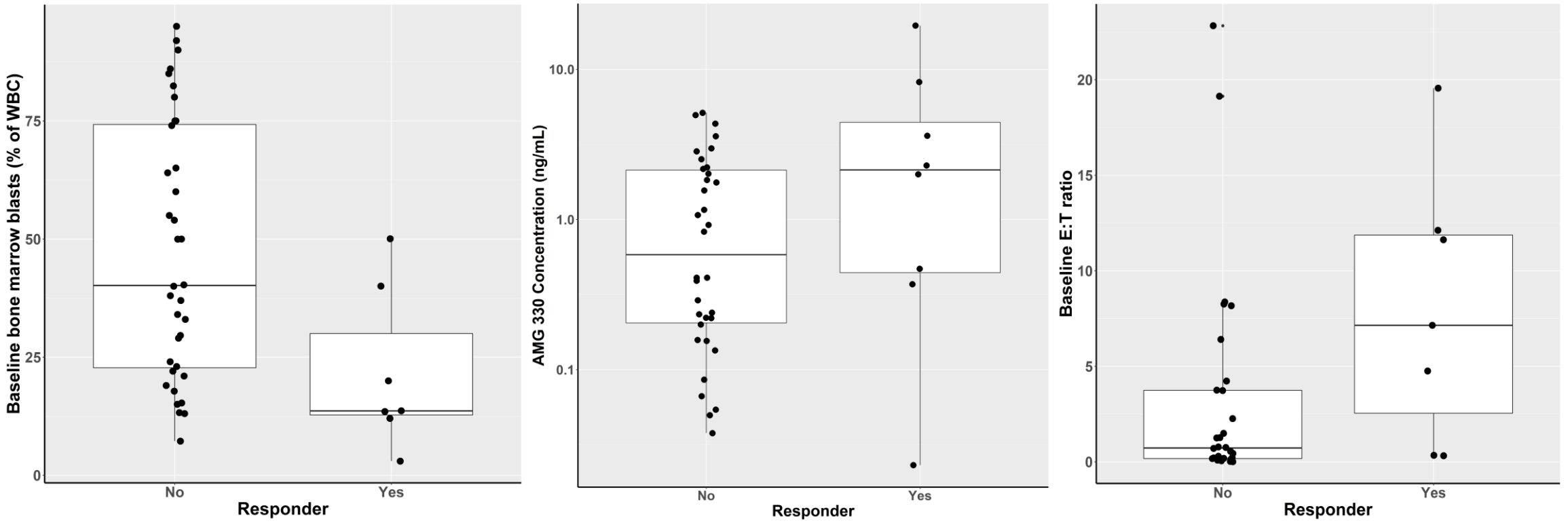
Clinical trials of Bispecifics in AML

Target, Construct	N	CR	CRS
CD123[4], **Flotetuzumab**	30	30%	100%
CD33[5], **AMG330**	55	19%	60%
CD33[6], **AMG673**	30	44 % withBlastreduction	50%
CD123[7], **XmAb14045**	104	14%	59%

Adapted from Allen et al, , Life 2021; 4: Uy et al, Blood 2021; 5: Ravandi et al, ASH 2019; 6: Subklewe et al, ASH 2019; 7: Ravandi et al, ASH 2019

AMG 673: Exposure-Baseline Patient Characteristics–Efficacy Relationships

Responses vs. baseline tumor burden, AMG 330 exposures, and baseline E:T ratio

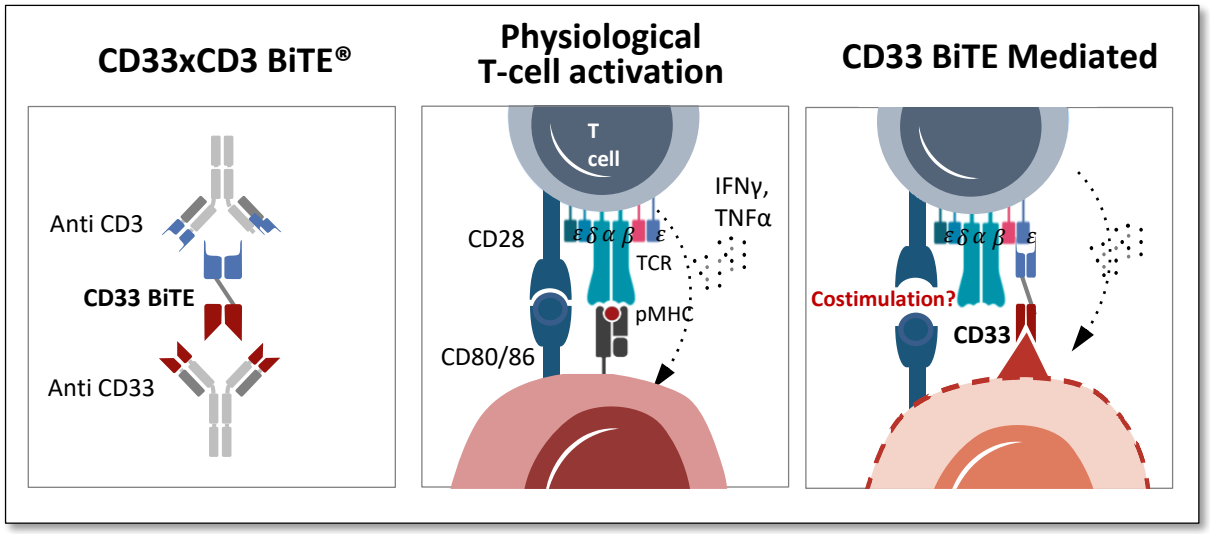


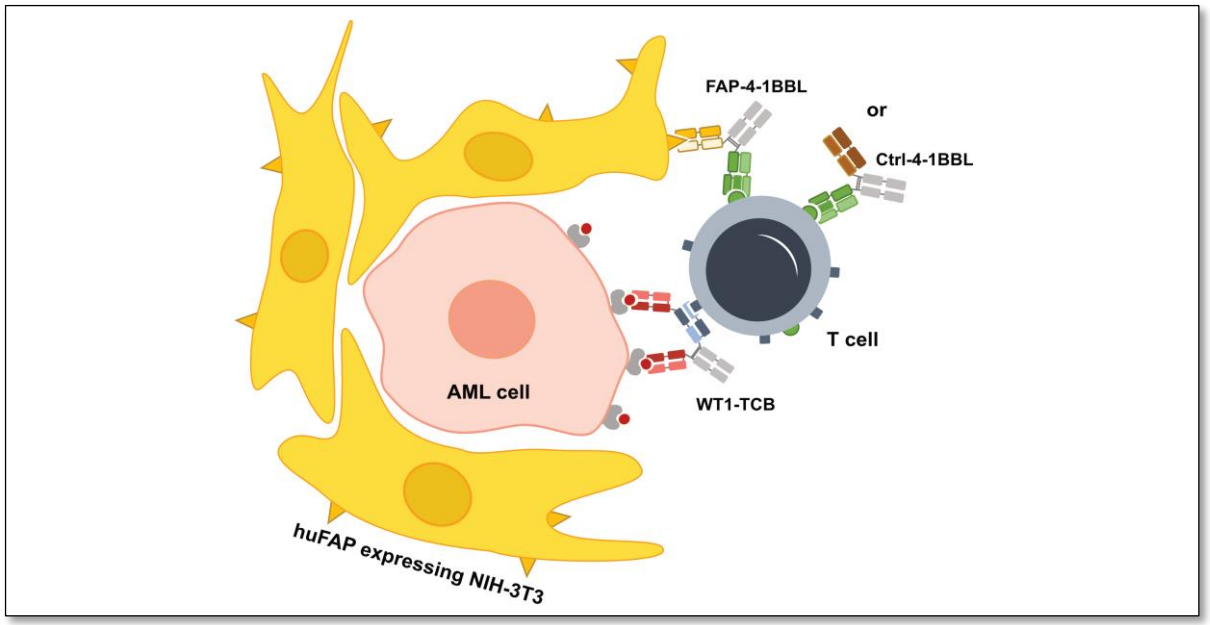
- **A trend towards better clinical responses was observed in patients with lower baseline leukemic burden in bone marrow, higher AMG 330 exposures, and higher baseline Effector (CD3): Target (blasts) cell ratio**

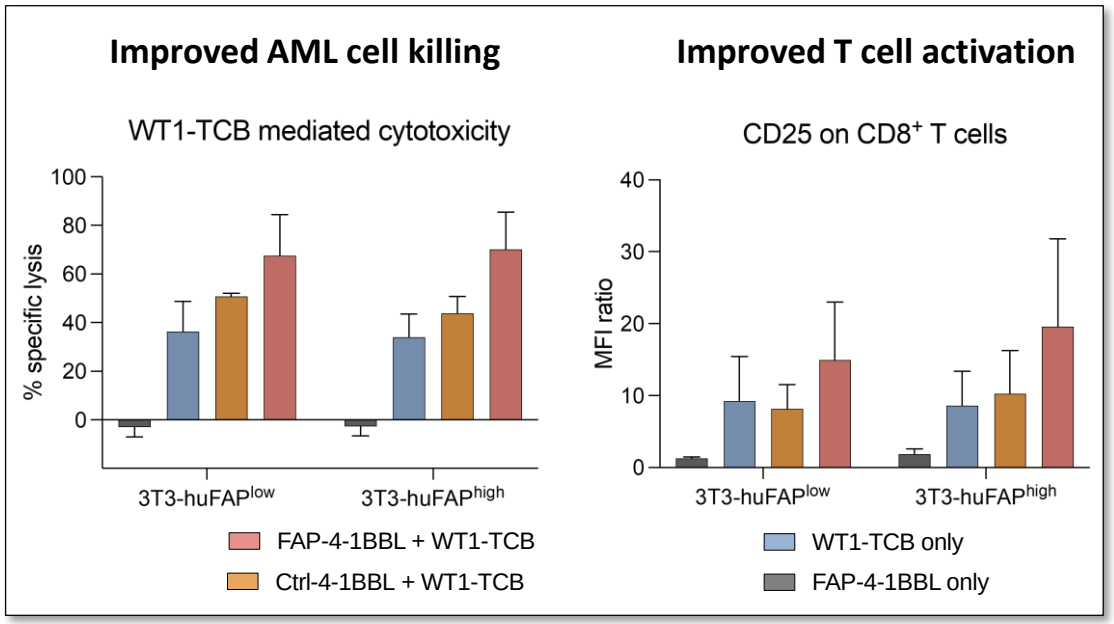
E:T, effector:target; WBC, white blood cells

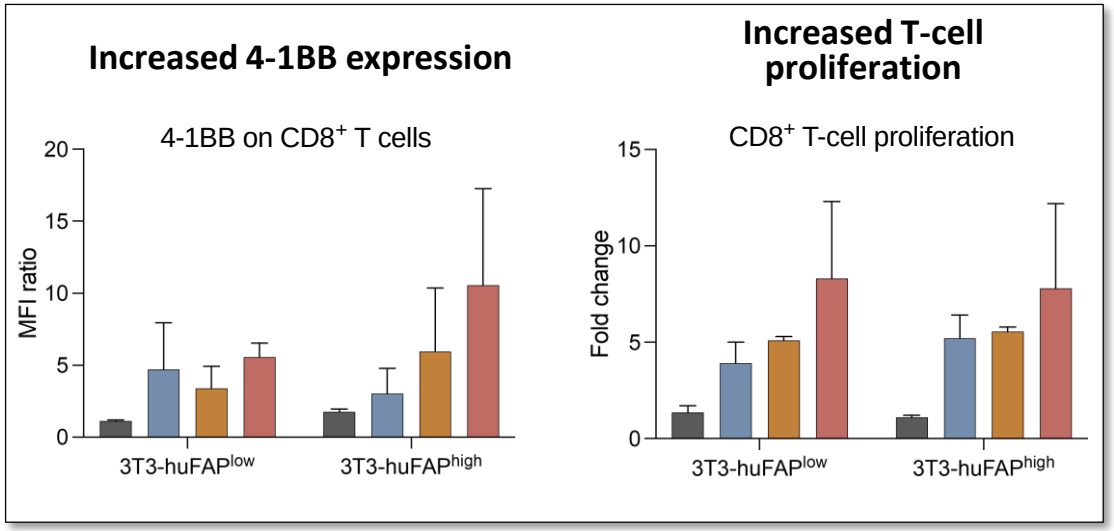
Subklewe, ASH 2019

Reversing T-cell Dysfunction: Providing Positive Costimulation by a FAP-4-1BBL biAb





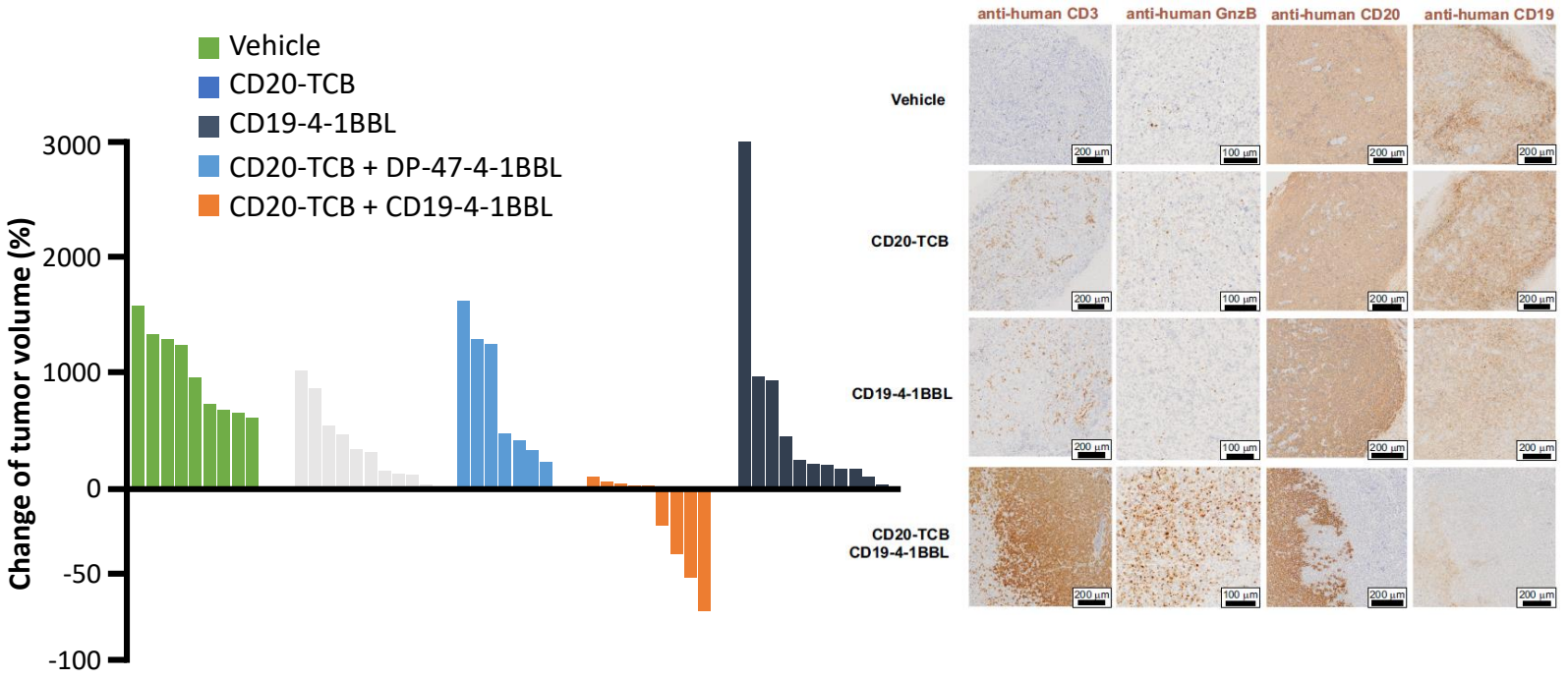




Hänel et al, ASH 2021

Combination of CD20-Bispecific + CD19-4-1BBL induces Complete Tumor Regression

Lymphoma Mouse Model (WSU-DLCL2): Read out of TV on Day 38



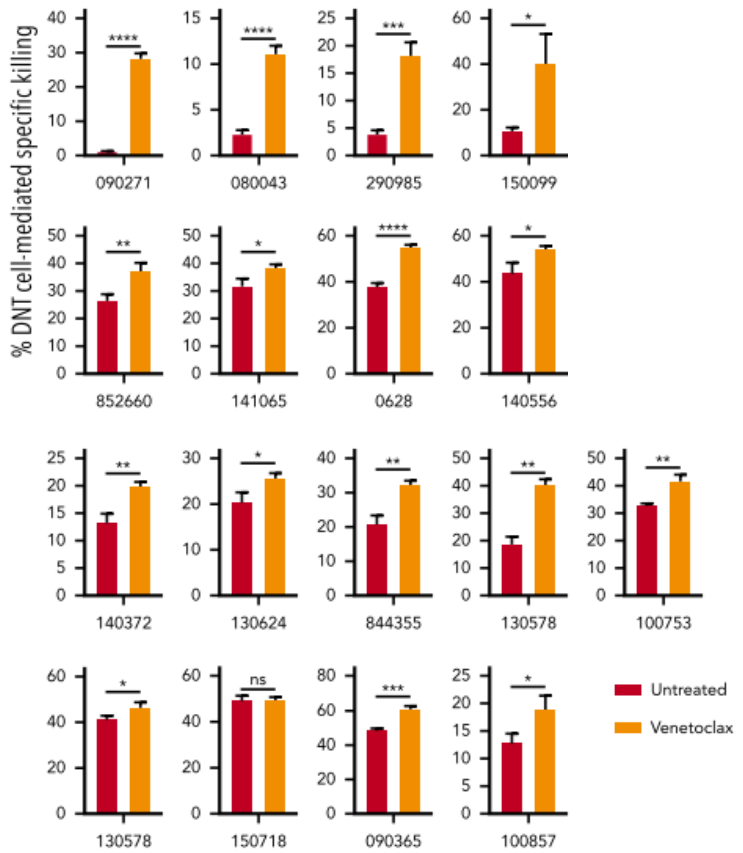
4-1BB agonism enhances T cell

- **Proliferation**
- **Cytotoxicity**
- **Cytokine secretion** (e.g IFNg, IL-2, TNFa, GM-CSF)
- **Th1 polarization**
- **Memory formation**
- **T cell survival** (anti-apoptosis)
- **Resistance to exhaustion**
- **Metabolic fitness**

Claus et al., Science Transl Med, 2019

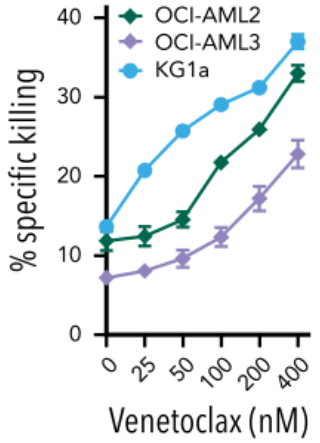
Venetoclax improves T-cell mediated cytotoxicity in AML

Venetoclax causes superior killing of primary AML cells by T cells

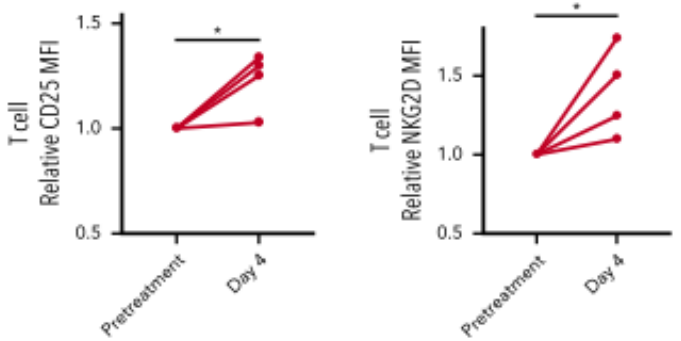


DNT: $CD3^+ CD4^- CD8^-$ double-negative T cells

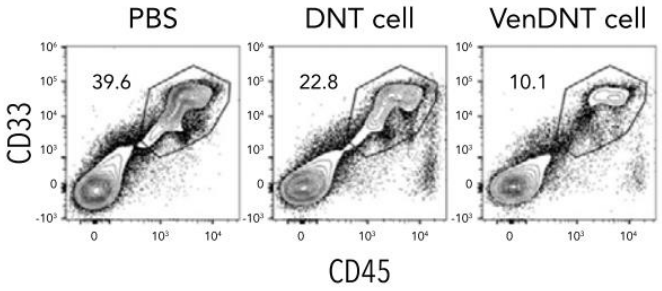
Improved AML cell killing by conventional T cells

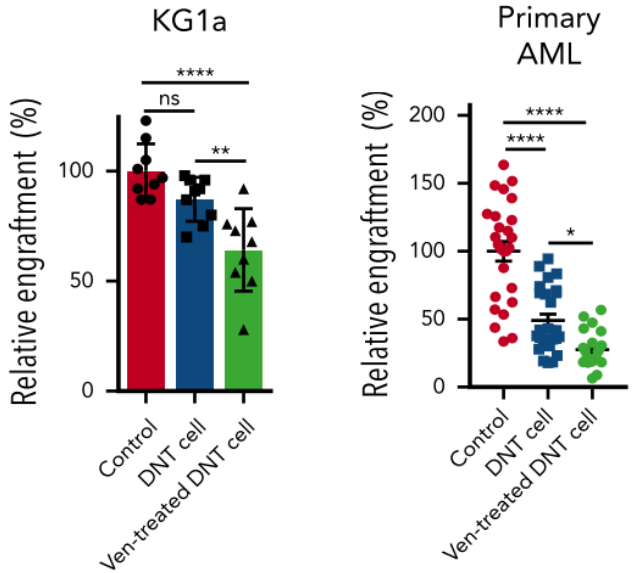


Venetoclax causes T-cell activation in patients



Reduction of AML burden *in vivo*



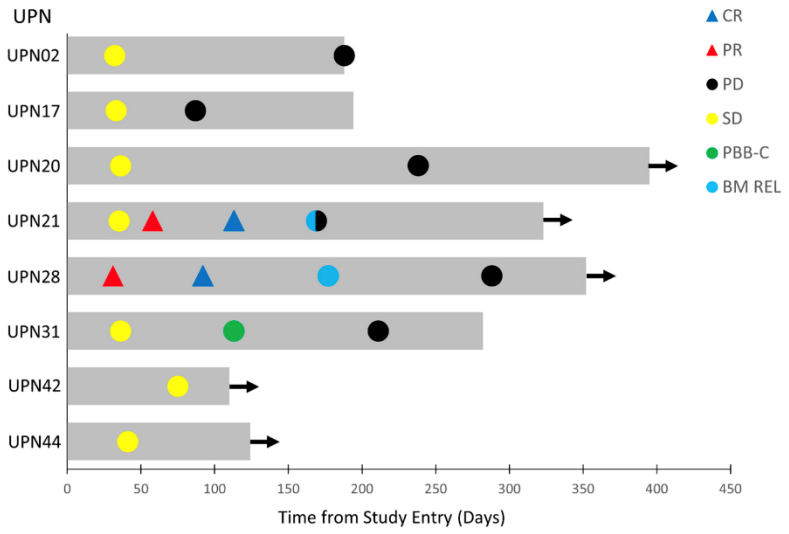


Lee et al. Blood 2021

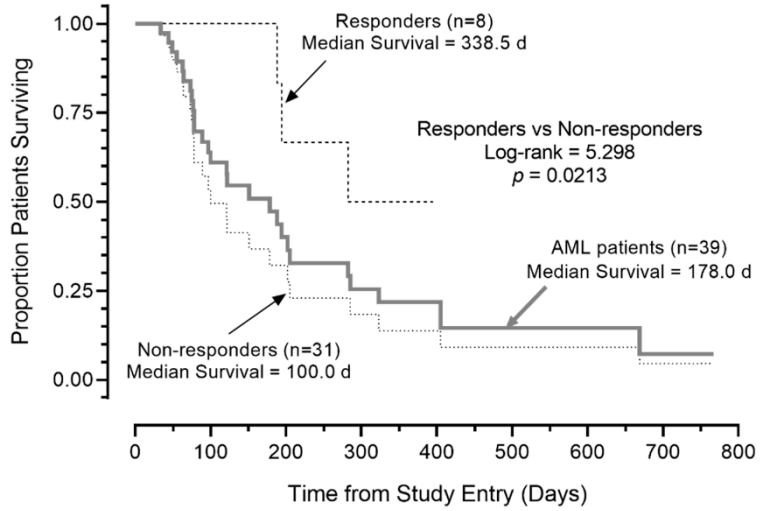
CD3 x CD123 BiAb + Ven/AZA in Pt with R/R AML or high Risk MDS

- The most common APVO436-related AEs were IRRs occurring in 13 (28.3%) patients and CRS occurring in 10 (21.7%) patients

Swimmer Plot of Best Overall Responses of the 8-Patient Favorable Response Population of R/R AML Patients. The onset and duration of SD, PR, CR, clearance of peripheral blasts (PBB-C), bone marrow relapse (BM REL) and onset of PD are indicated with specific symbols. Arrow: Alive.



Survival Outcome of AML Patients According to Response to APVO436. Depicted are the overall survival curves of the 8 patients favorable responses, 31 patients who did not respond, and all 39 patients combined. Favorable responses of CR, PR or SD≥3 months is associated with improved overall survival in R/R AML patients treated with APVO436 monotherapy.



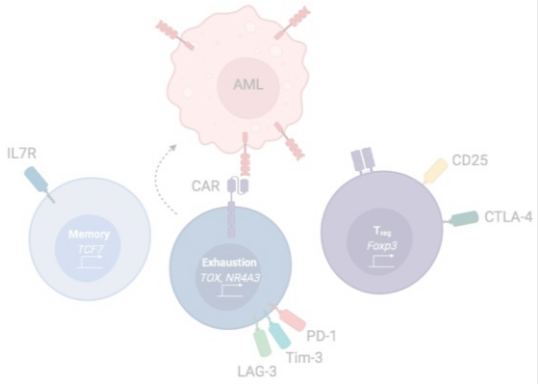
- In this trial a bivalent aCD123 x aCD3 bispecific was tested, kDA 161, given 1 x week i.v., in conjunction with chemo, AZA + Ven
- Safety profile better than in other early trials reported, not clear how CRS was mitigated
- In this trial 46 R/R AML pts included, of the 34 evaluable pts, 8 had SD, PR or CR, median OS of 300 d

Uckun et al., Cancers 2021

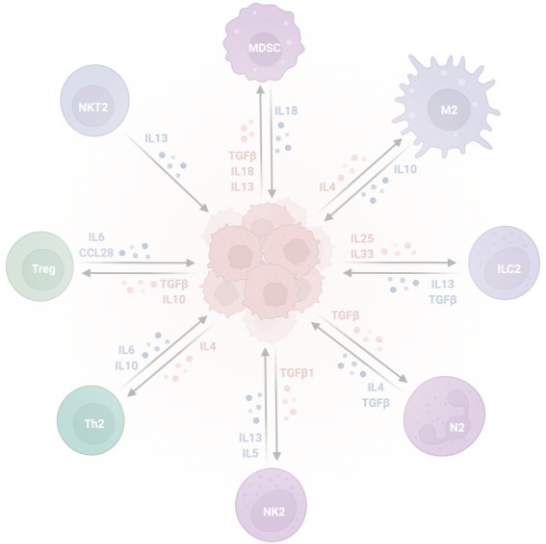
Challenges of T cell-based Immunotherapy in AML

Target Antigen Heterogeneity / Specificity

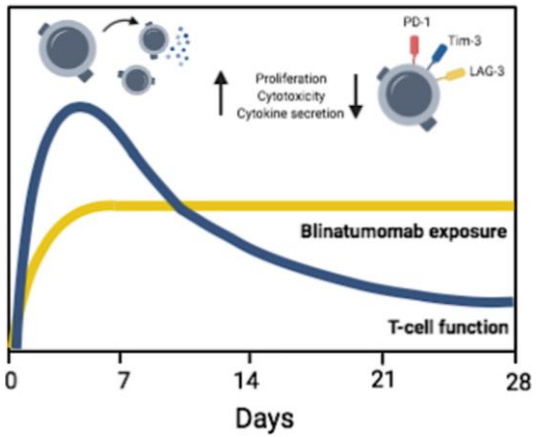
T-cell Subsets / T-cell Function



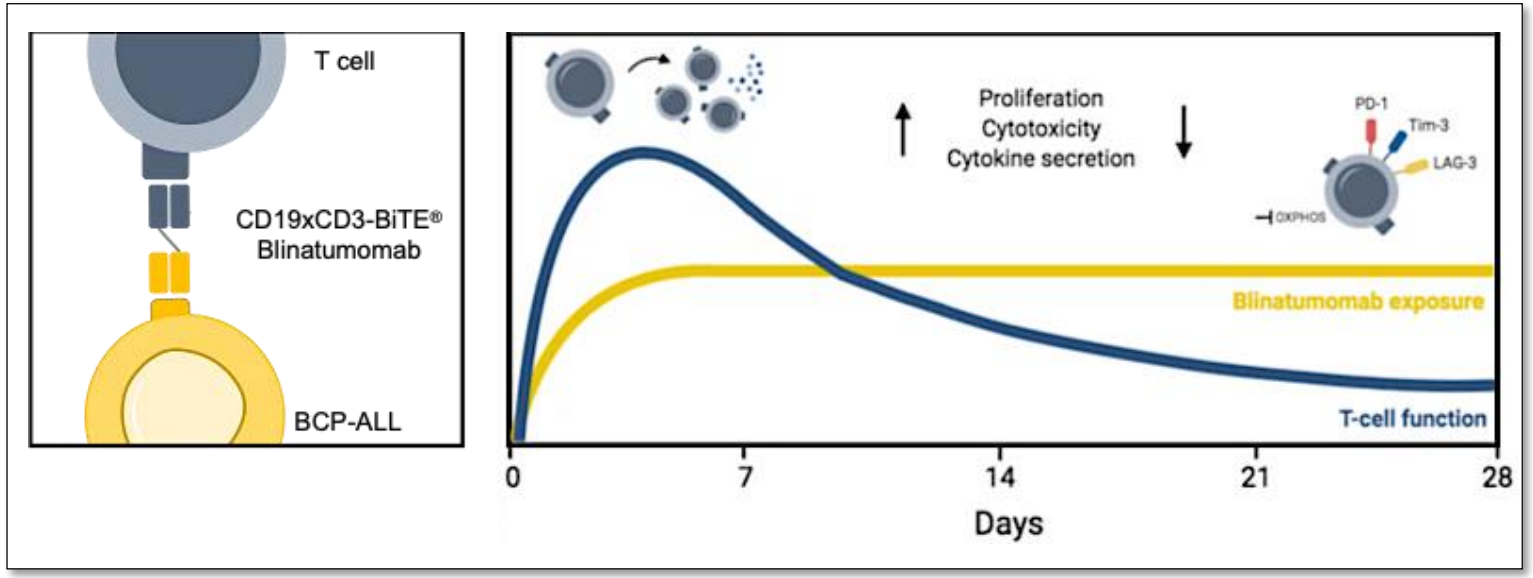
TME / BM Niche Inflammatory Signature



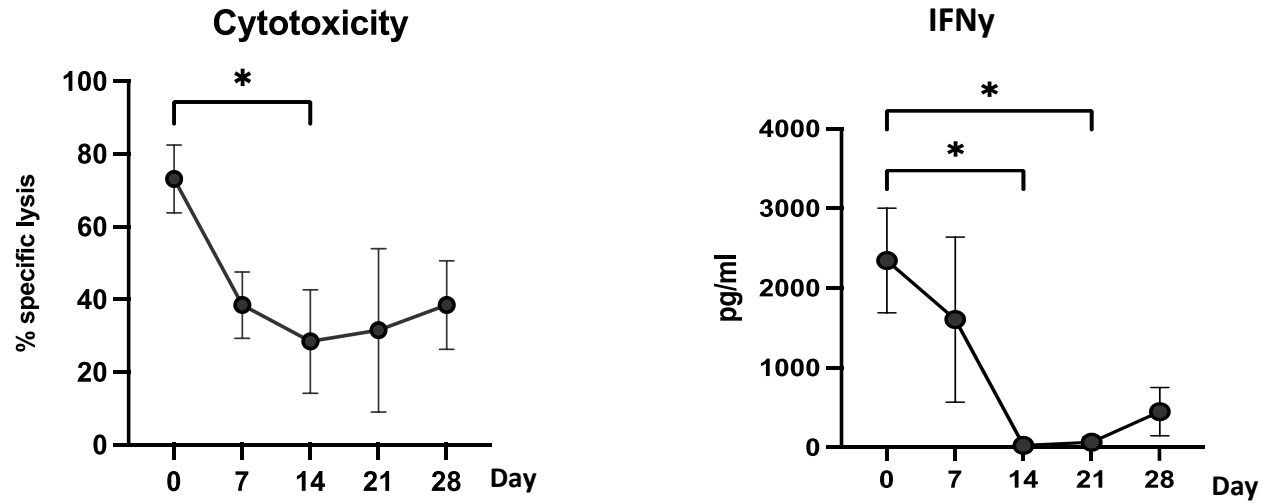
Schedule of Application / Trial Design



Continous Blinatumomab Exposure Induces T-cell Exhaustion

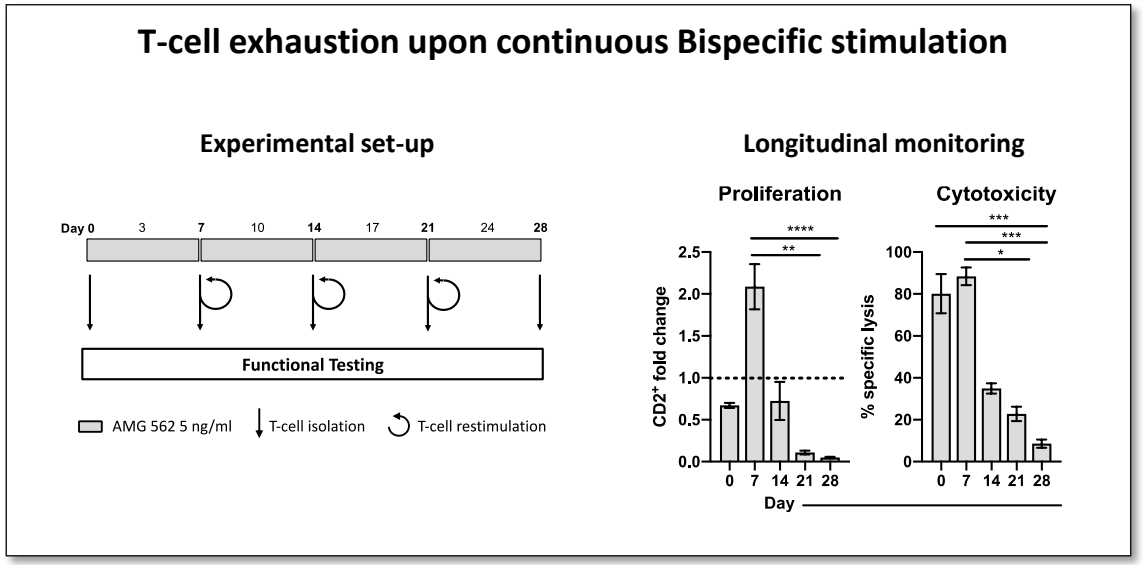


Immunmonitoring of ALL pt on Blin Tx (CD19 x CD3 BiTE)



Zieger et al, ASH 2021

Mimicking the Clinical Application in an *in vitro* model system: Continous BisAb Exposure

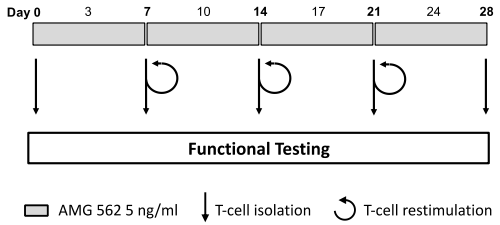


Zieger et al, ASH 2021

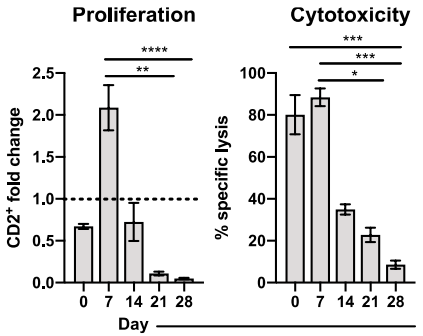
Treatment-Free Intervals Ameliorate T-cell Exhaustion Induced by Bispecifics

T-cell exhaustion upon continuous Bispecific stimulation

Experimental set-up

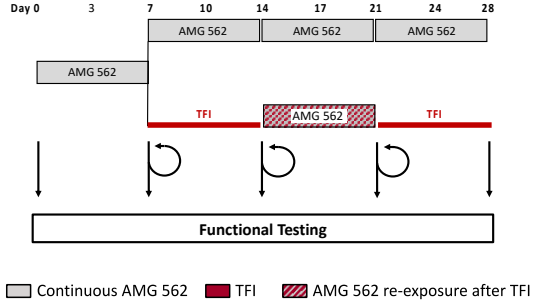


Longitudinal monitoring

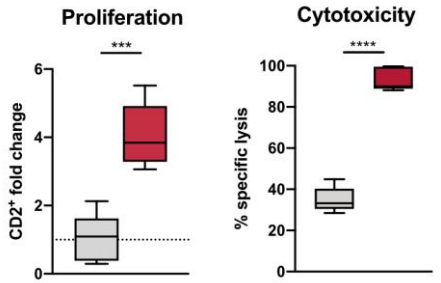


TFI ameliorate exhaustion & maintain T-cell function

Experimental set-up



Day 14

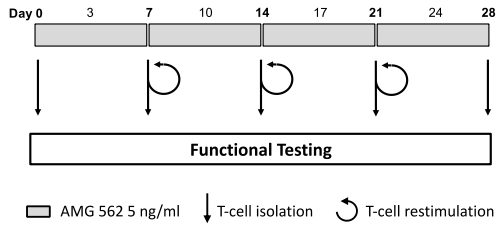


Zieger et al, ASH 2021

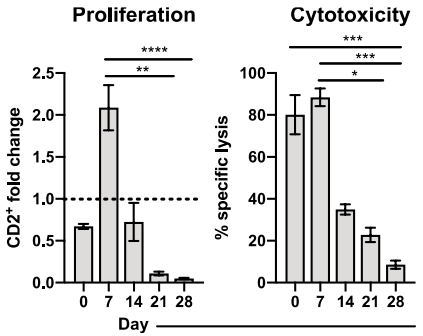
Treatment-Free Intervals Ameliorate T-cell Exhaustion Induced by Bispecifics

T-cell exhaustion upon continuous Bispecific stimulation

Experimental set-up

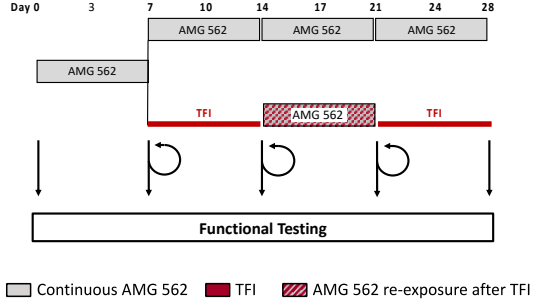


Longitudinal monitoring

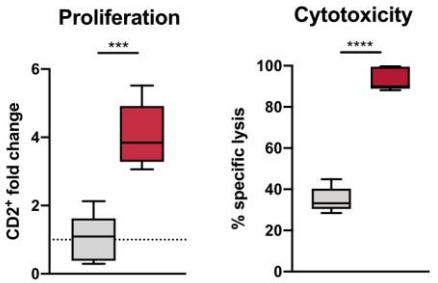


TFI ameliorate exhaustion & maintain T-cell function

Experimental set-up

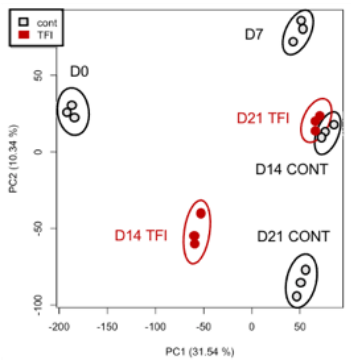


Day 14

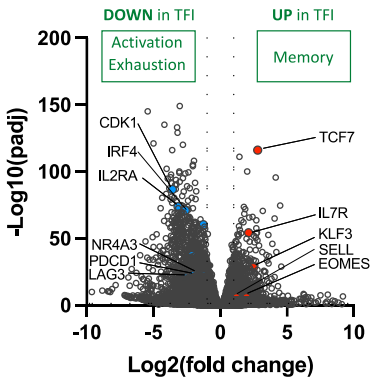


Treatment-Free Intervals induce transcriptional reprogramming

Principal component analysis

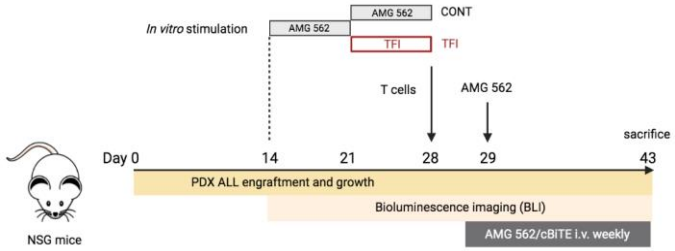


Day 14 TFI vs CONT

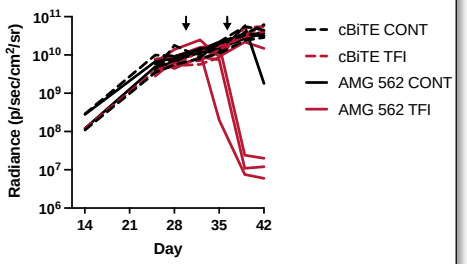


Treatment-Free Intervals preserve leukemia control *in vivo*

PDX ALL mouse model



ALL burden (Imaging)



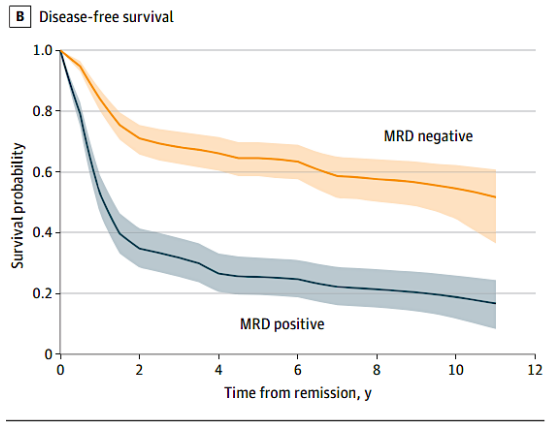
TFI=treatment-free interval

Zieger et al, ASH 2021

Comparison to Allogeneic Stem Cell Transplantation: also not successful in MRD & Relapse

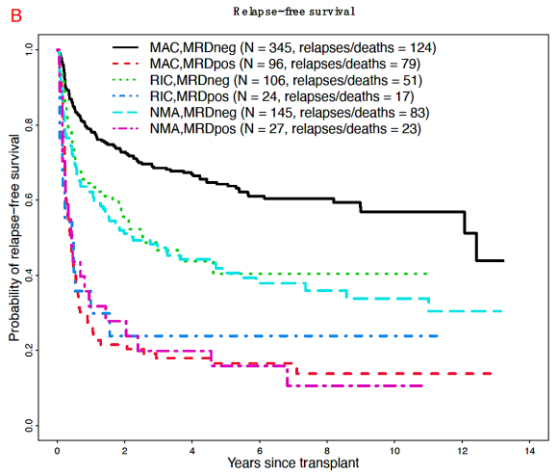
Majority of Clinical Trials of Bispecifics in R/R AML post > 3 prior treatment lines are prone to fail: dysfunctional T cells; immunosuppressive TME, high tumor burden

MRD pos. = worse Outcome



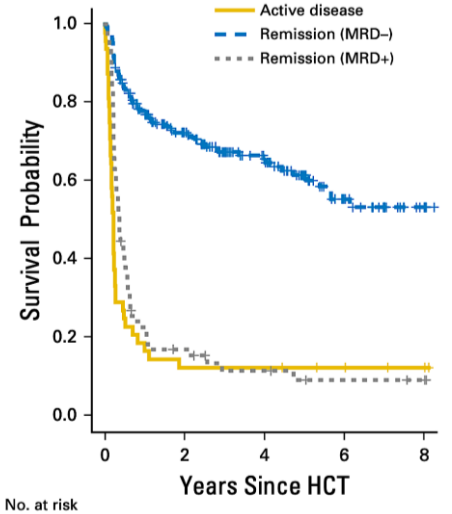
Short et al, JAMA Oncology 2020

Allo SCT: MRD pos. = worse Outcome



Morsink et al, Cancers 2020

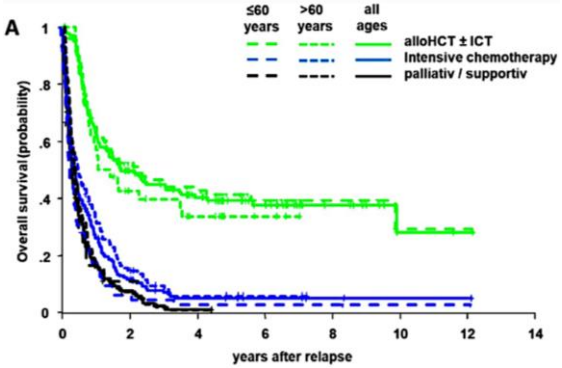
Similar outcome in pts MRD+ or in Relapse post allo SCT:



No. at risk					
Active disease	48	6	6	4	2
Remission (MRD–)	235	127	73	29	7
Remission (MRD+)	76	11	6	3	2

Araki et al, JCO 2016

Outcome in Relapse



	alloHCT ± prior ICT			Intensive chemotherapy (ICT)		
	n	OS %	median (months)	n	OS %	median (months)
all ages	151	39.3 (31.8 - 48.6) @5y	20.4	190	5.0 (2.5 - 9.9) @5y	4.8
age ≤60 years	107	41.6 (32.8 - 52.9) @5y	28.8	71	3.2 (.8 - 12.5) @5y	3.6
age >60 years	44	33.8 (21.7 - 52.5) @5y	16.8	119	6.0 (2.7 - 13.2) @5y	6.0
P-value (≤vs. >60 years)		0.3			<0.05	

	palliativ/supportiv			
	n	OS %	median (months)	P-value
all ages	155	1.2 (.2 - 7.7) @4y	3.6	<.001
age ≤60 years	21	11.3 (3.1 - 41.3) @2y	4.8	<.001
age >60 years	134	1.1 (.2 - 7.3) @4y	3.6	<.001
P-value (≤vs. >60 years)		0.9		

Heinicke et al, Annals of Hematology 2021

Acknowledgements

Gene Center Munich

Laboratory for Translational Cancer Immunology

Julian Benkel
Viktoria Blumenberg
Bettina Brauchle
Veit Bücklein
Jelena Demler
Gerulf Hänel
Maryam Kazerani
Sonja Lacher
Alexandra Leutbecher
Anetta Marcinek
Daniel Nixdorf
Simone Pentz
Kai Rejeski
Lisa Rohrbacher
Michael Ruzika
Sabine Sandner
Monika Sponheimer
Alexandra Stein
Benjamin Tast
Yingshuae Wang
Lis Winter
Jan Wulf
Nora Zieger

LMU KLINIKUM DER UNIVERSITÄT MÜNCHEN

Department of Medicine III – Oncology and Hematology

Michael v. Bergwelt
Friderieke Hildebrandt
Niklas Müller
Sebastian Theurich
Anna Reischer

Laboratory of Leukemia Dx

Karsten Spiekermann
Stephanie Schneider
Elke Habben
Bianca Kirschbaum
Aurelia von Orlikowski
Ewelina Zientara

dkfz. GERMAN CANCER RESEARCH CENTER IN THE HELMHOLTZ ASSOCIATION
50 Years – Research for A Life Without Cancer

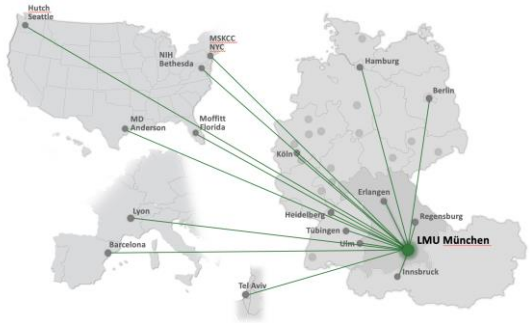
Christoph Stein-Thöringer

IMMP CSP MUNICH

LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN GENE CENTER MUNICH

Structural Molecular Biology

Karl-Peter Hopfner
Monika Herrmann
Nadja Fenn



LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN FACULTY OF BIOLOGY DEPARTMENT II HUMAN BIOLOGY & BIOIMAGING

Human Biology and Bioimaging

Heinrich Leonhardt
Heinrich Flaswinkel
Elisabeth Kremmer

Hospices Civils de Lyon
Emmanuel Bachy
Gilles Salles (MSKCC)
Pierre Sesques
Laurent Jallades

Moffitt Cancer Center
Michael Jain
Frederick Locke
Ariel Perez

Memorial Sloan Kettering Cancer Center

Center for Cell Engineering

Michel Sadelain
Sascha Haubner

University Hospital Tübingen
Wolfgang Bethge
Christoph Faul
Liv Jentzsch

University Hospital Erlangen
Andreas Mackensen
Dimitrios Mougiakakos

University Hospital Hamburg-Eppendorf
Francis Ayuketang
Boris Fehse
Carolina Berger

myT·Cell

dkfz. Deutsches Konsortium für Translationale Krebsforschung Kernzentrum Heidelberg

Roche

munich biotech m4 CLUSTER

GILEAD Advancing Therapeutics. Improving Lives.

MACS Miltenyi Biotec

AMGEN

morphosys

CRC TRR 338 LETSIMMUN

SFB 1243

WILHELM SANDER-STIFTUNG

Elitenetzwerk Bayern

DFG Deutsche Forschungsgemeinschaft

FLOW

Harmonize MRD FLOW HARMONIZATION