Pre-Clinical Activity of Allogeneic Anti-CD22 CAR-T Cells for the Treatment of B-Cell Acute Lymphoblastic Leukemia

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
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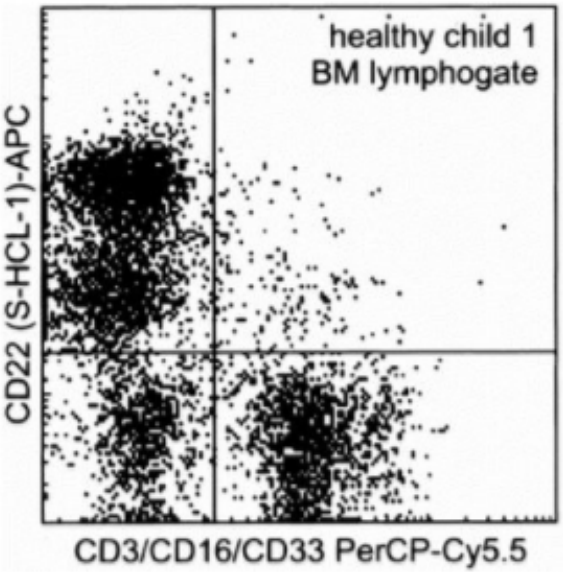
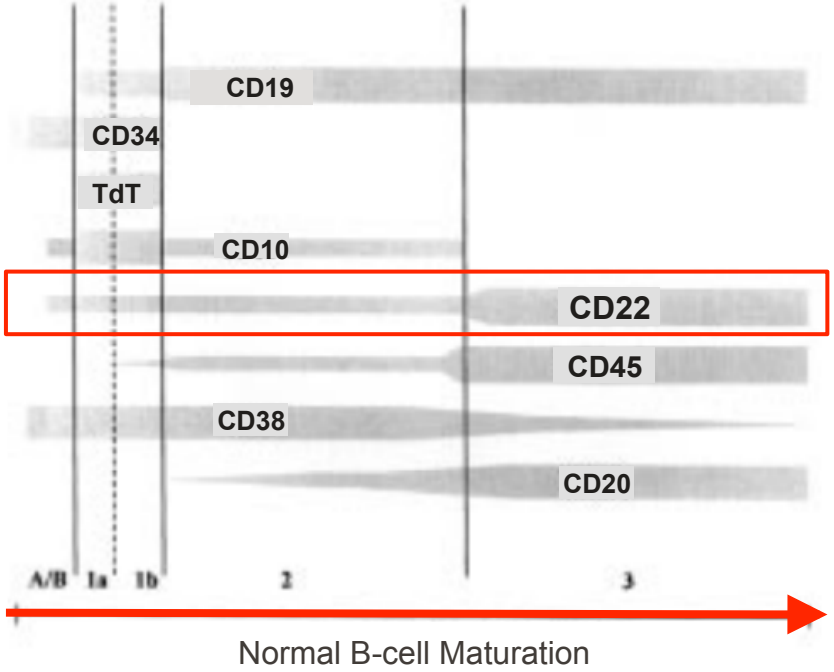
CD22 Surface Expression in Healthy B-cells

CD22 is a pan-B antigen which is usually negative in T, NK and granulomonocytic cells.

Differential fluorescence intensities (CD22dim and CD22bright) are found on precursor B-cells.



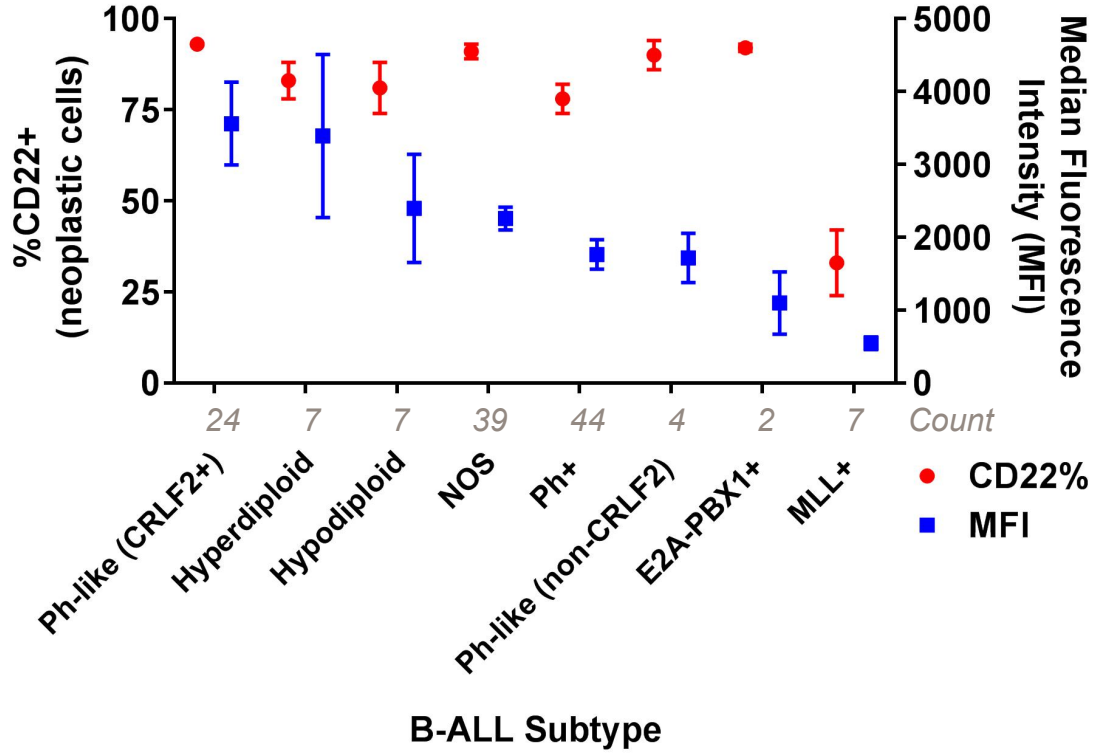
(T/NK/Myeloid cell markers)



Normal B-cell Maturation

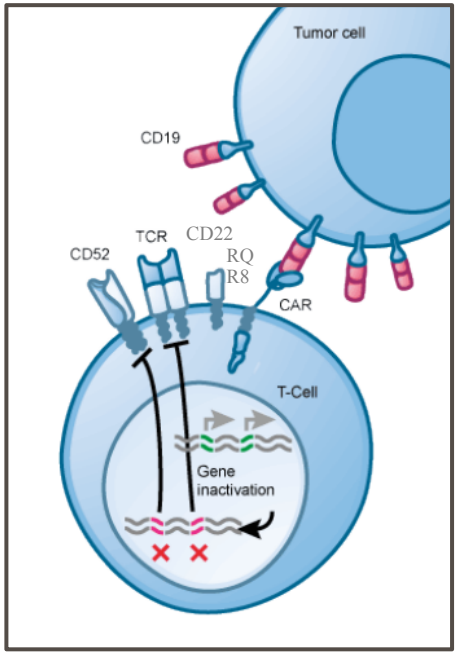
Lucio et al., 1999, Leukemia,
Noordzij et al., 2002, Ped. Res.

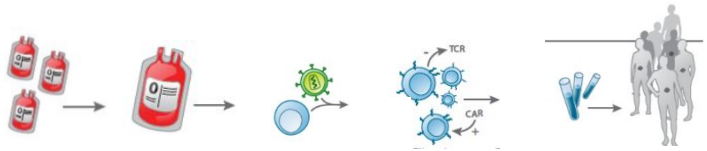
CD22 Surface Expression in B-ALL Subtypes



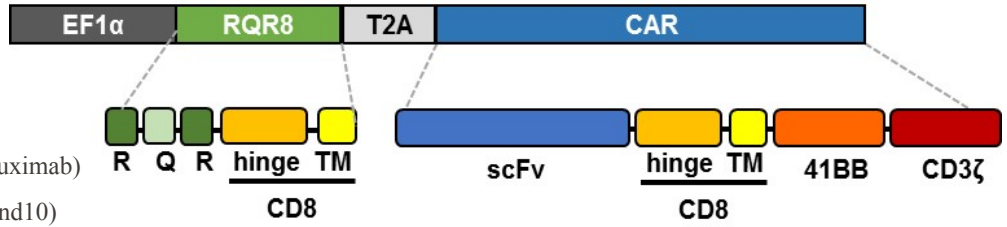
S Konoplev, S Wang et al (USCAP abstract), 2017, Hematopathology Dept, MD Anderson Cancer Center

UCART22 Product Description





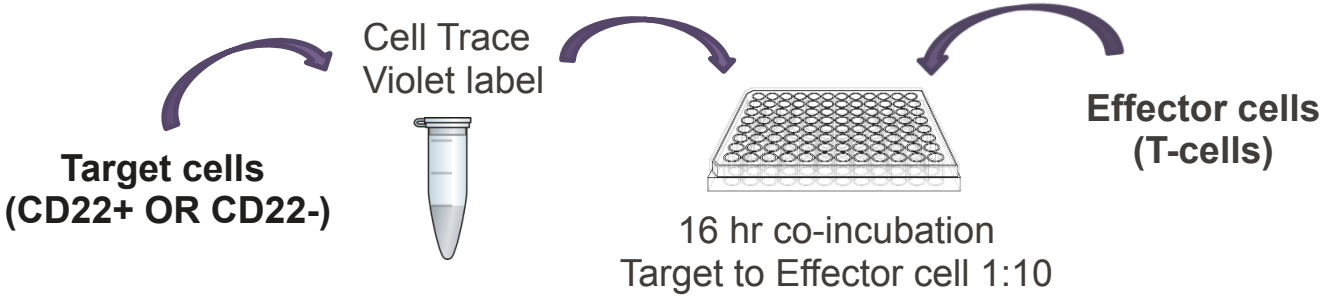
- anti-CD22 CAR expression to redirect T cells to tumor antigens
- RQR8 expression to confer susceptibility to rituximab
- TCR disruption to avoid GvHD
- CD52 disruption to confer resistance to the lympho-depleting agent Campath® (alemtuzumab)



R=CD20 mimotope (rituximab)

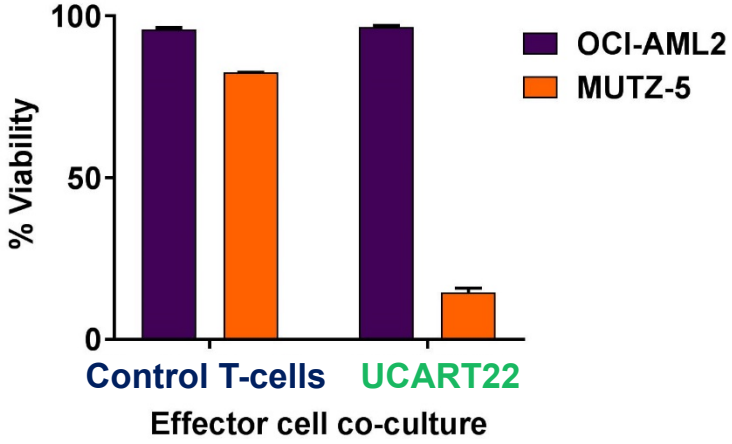
Q=CD34 epitope (QBEnd10)

In Vitro Specific Cell Lysis Methods

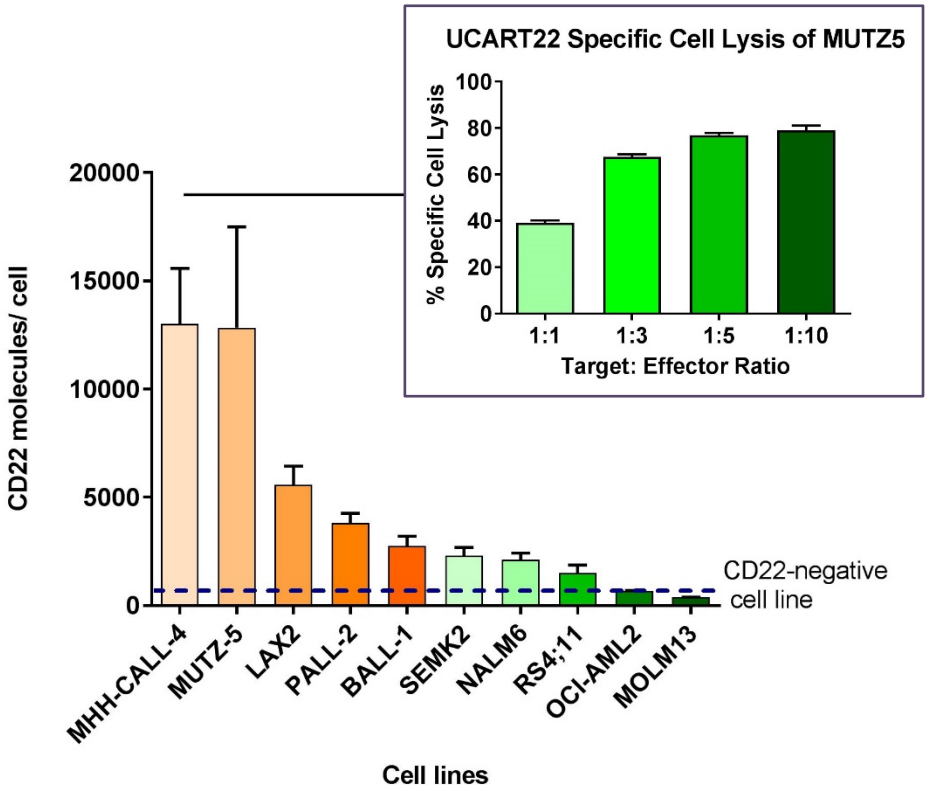


specific cell lysis=

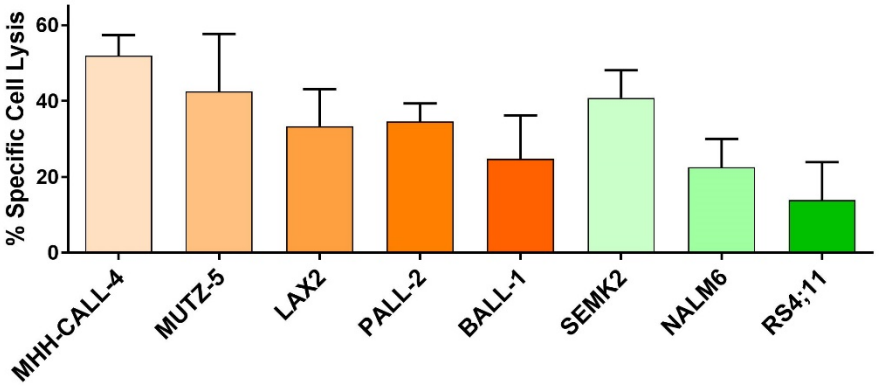
% lysis CD22+ B-ALL cells (UCART22/ Control T-cells)
% lysis CD22- AML cells (UCART22/Control T-cells)



UCART22 *In Vitro* Activity Against B-ALL Cell Lines



Strong correlation between CD22 molecules/cell and cell lysis, r^2=0.7077



B-ALL Patient Characteristics

ID	Origin sample	Age/ Sex	Cytogenetic Abnormalities	Mutations	Clinical Status	% Blasts	% CD22
Pt1	PB	24/M	CRLF2+ AND Ph+	JAK2-R683G, EZH2	Diagnosis	84	-
Pt2	PB	69/F	Ph-like (CRLF2+)	TP53	Diagnosis	17	92.3
Pt3	PB	29/M	Ph-like (CRLF2+)	No mutations	Relapse	32	58.7
Pt4	PB	21/M	Ph-like (IGH-CRLF2)	JAK2-R683S	Relapse	65	94.7
Pt5	PB	68/M	Other	TP53, IDH2	Diagnosis	69	25.7
Pt6	PB	81/M	Ph+	No mutations	Diagnosis	48	86.5
Pt7	PB	56/F	Ph+	No mutations	Diagnosis	68	90.2
Pt8	BM	51/M	t(2;8) and t(14;18)	No mutations	Relapse	96	98.3
Pt9	PB	21/M	Trisomy 4	No mutations	Diagnosis	60	92.0
Pt10	BM	69/F	Ph-like (CRLF2+)	NRAS, EZH2	Relapse	93	84.3
Pt11a	PB	55/F	Ph-like (CRLF2+)	No mutations	Diagnosis	75	89.75
Pt11b	BM	55/F	Ph-like (CRLF2+)	No mutations	Diagnosis	91	98.06
Pt12	PB	22/M	Ph+	No mutations	Diagnosis	79	47.2
Pt13	PB	33/M	t(4;11) MLL	TP53	Relapse	59	80.2
Pt14	PB	54/F	Ph+	No mutations	Diagnosis	23	83.8
Pt15	PB	68/M	Hypodiploid, Complex	No mutations	Diagnosis	67	90.9
Pt16	PB	70/M	Complex	TP53	Relapse	51	74.0
Pt17	BM	39/M	Ph-like	Not Done	Diagnosis	90	81.6
Pt18	BM	65/F	Ph-like (IGH-CRLF2)	IKZF1 deletion	Diagnosis	92	76.9
Pt19	BM	21/M	Ph-like (IGH-CRLF2) AND Ph+	CRLF2-F232C,ITPKB-P167R, ITPKB-S92SG PTPN11	Relapse	82.5	98.3

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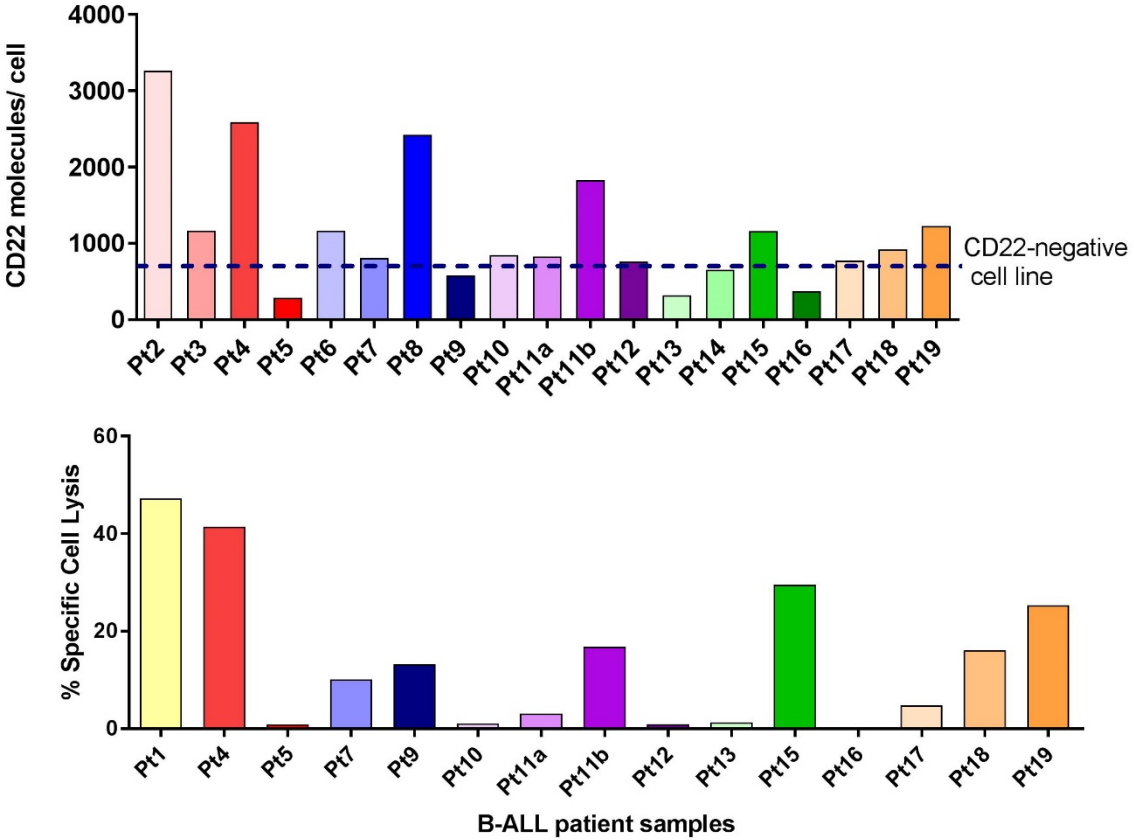
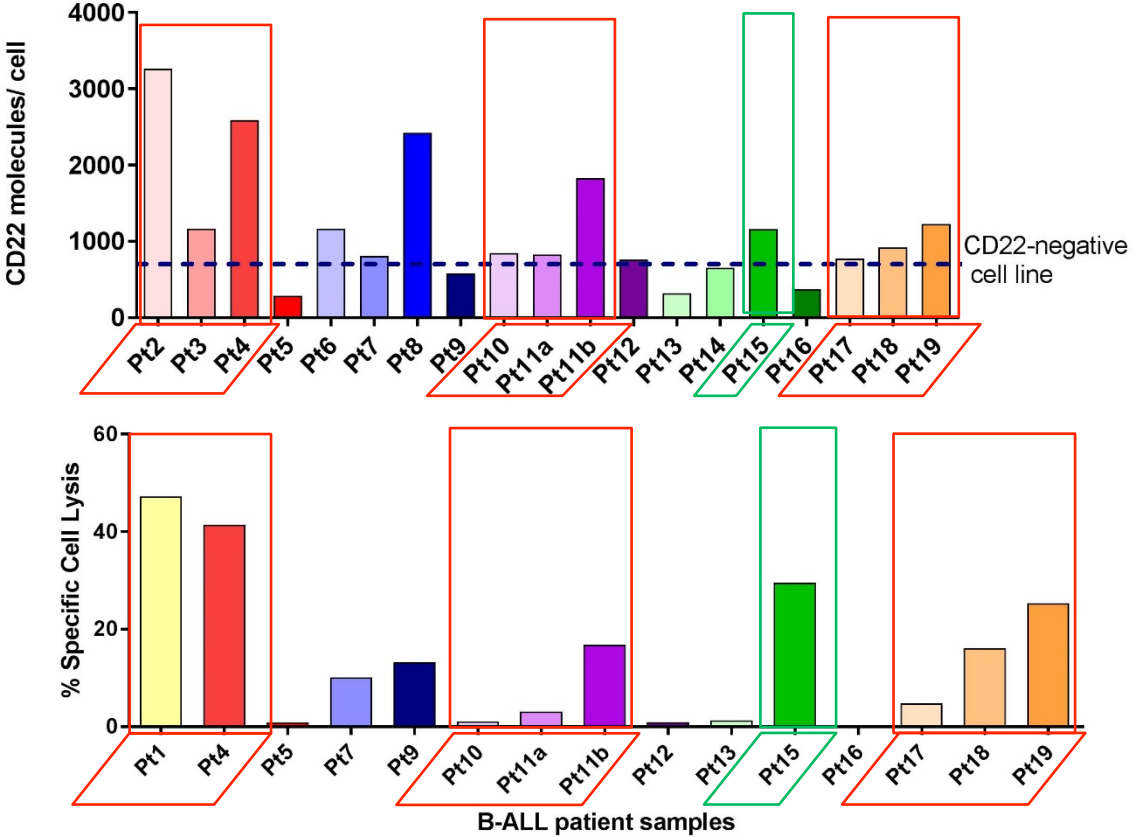
UCART22 *In Vitro* Activity Against B-ALL Patient Samples



Strong correlation between CD22 molecules/cell and cell lysis, r^2=0.693

UCART22 *In Vitro* Activity Against B-ALL Patient Samples

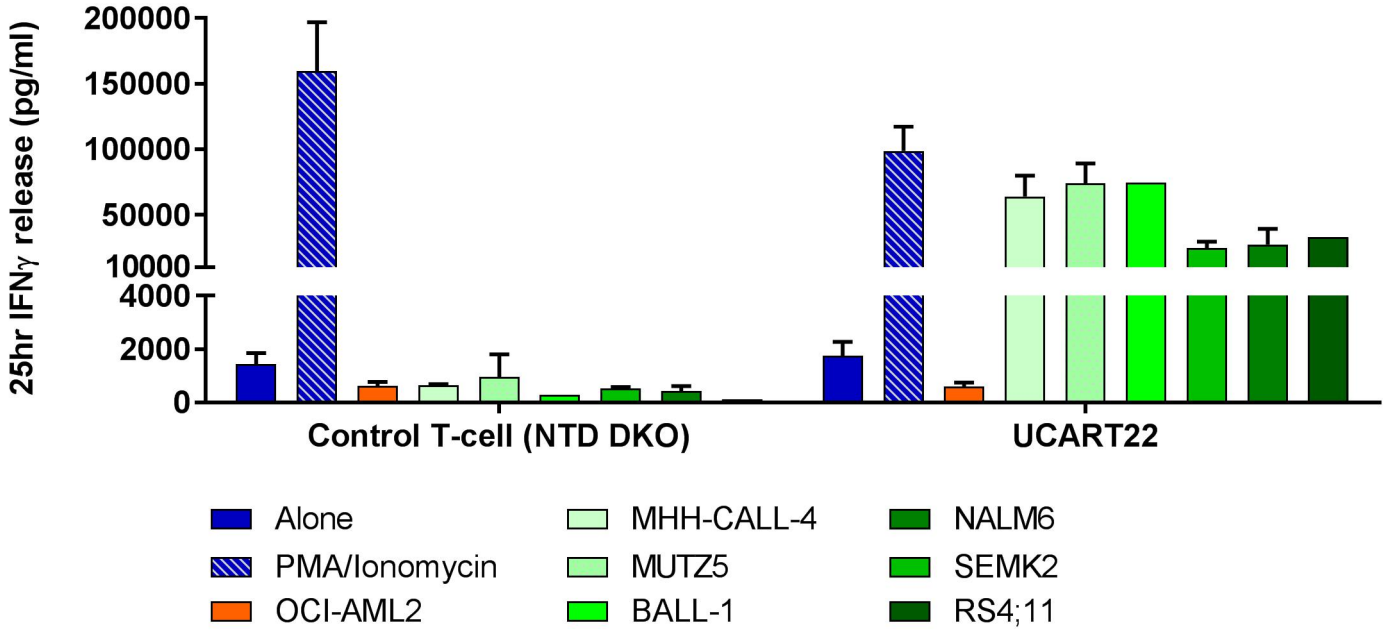


Strong correlation between CD22 molecules/cell and cell lysis, r^2=0.693

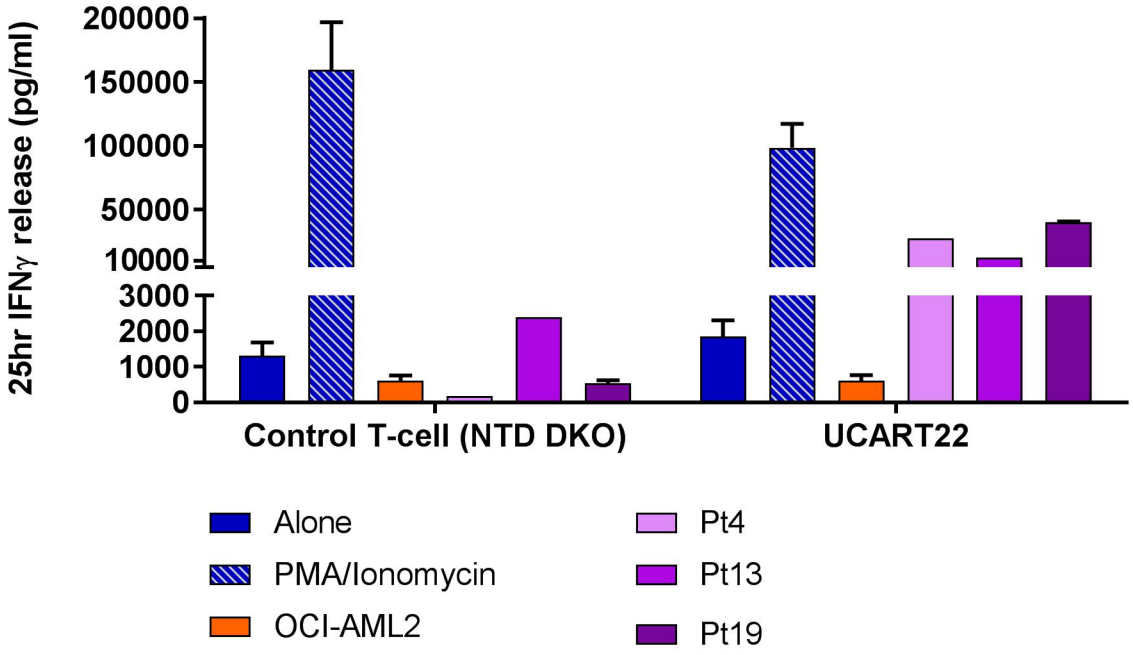
Ph-like and Hypodiploid subtypes accounted for the highest CD22 surface density and strongest cell lysis response.

UCART22 *In Vitro* Activity: Interferon-gamma Release

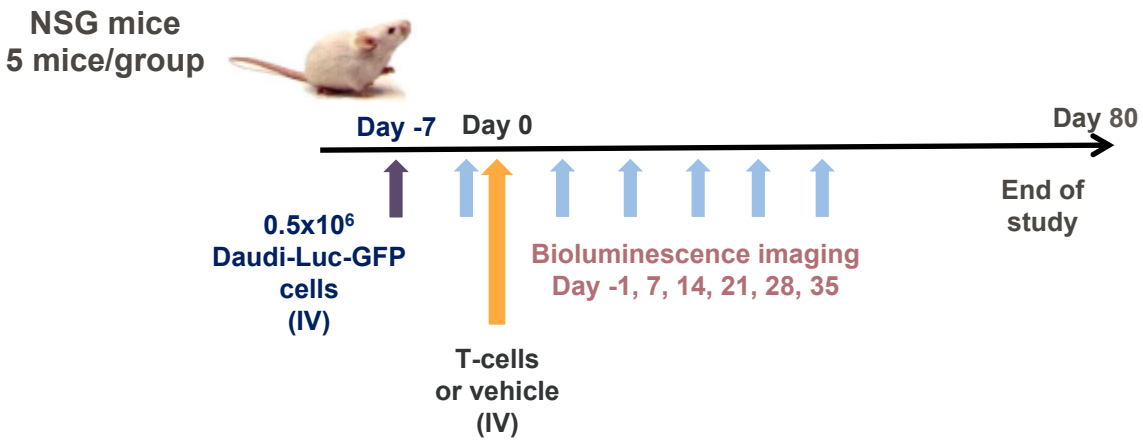
Bead-based immunoassay on secreted media of 25hr target and effector cell co-incubation.



UCART22 *In Vitro* Activity: Interferon-gamma Release



UCART22 *In Vivo* Activity Against Daudi Cells

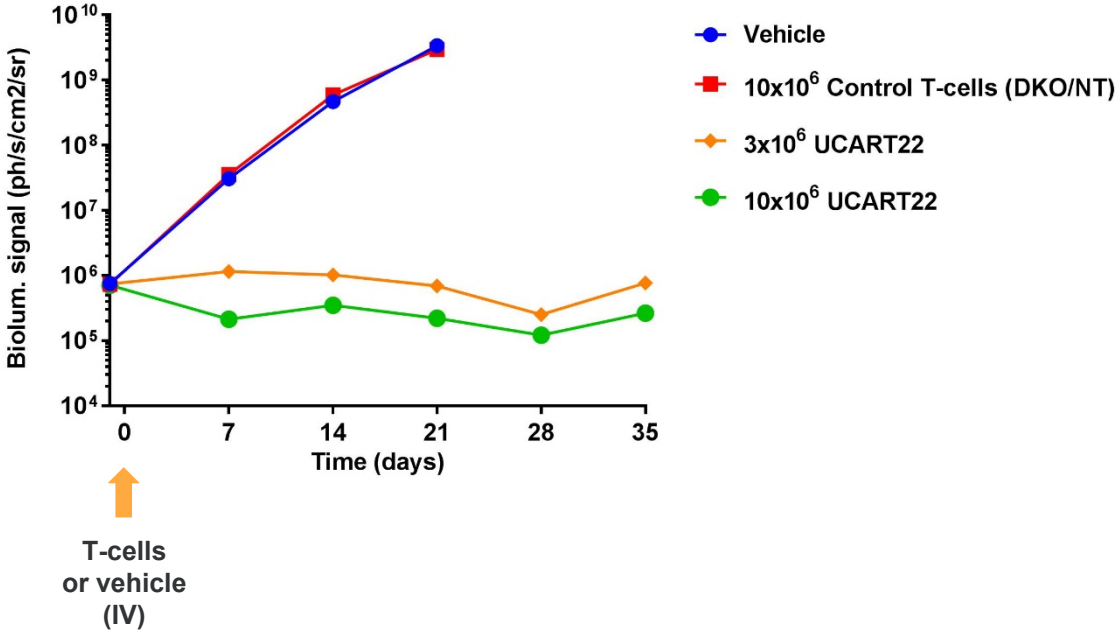


Daudi *in vivo* treatment schedule:

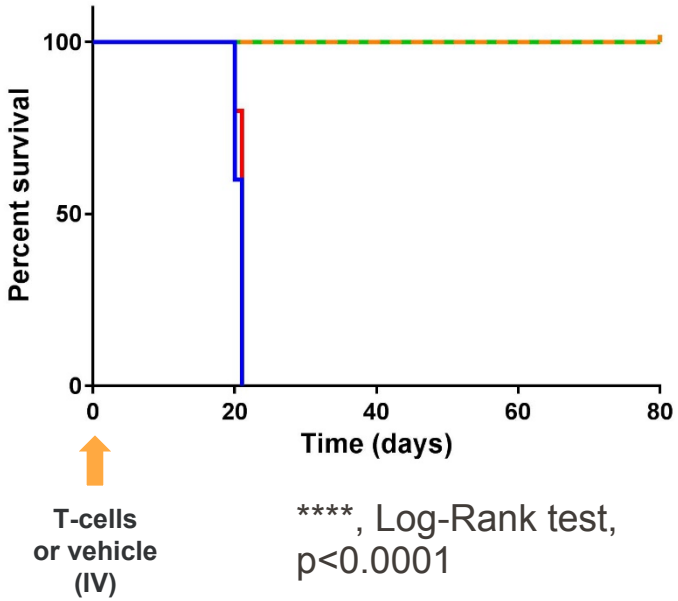
- Vehicle
- UCART22 (doses $3x10^6$ or $10x10^6$ cells)
- Control DKO/NTD (non transduced; TRAC and CD52 KO T-cells) (dose $10x10^6$ cells)

UCART22 *In Vivo* Activity Against Daudi Cells

Daudi Engraftment



Daudi Survival



****, Log-Rank test, p<0.0001

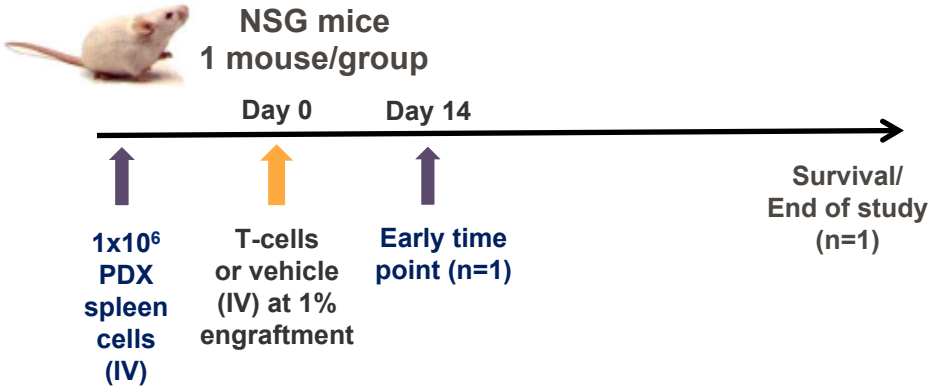
UCART22 *In Vivo* Activity Against B-ALL PDX Models

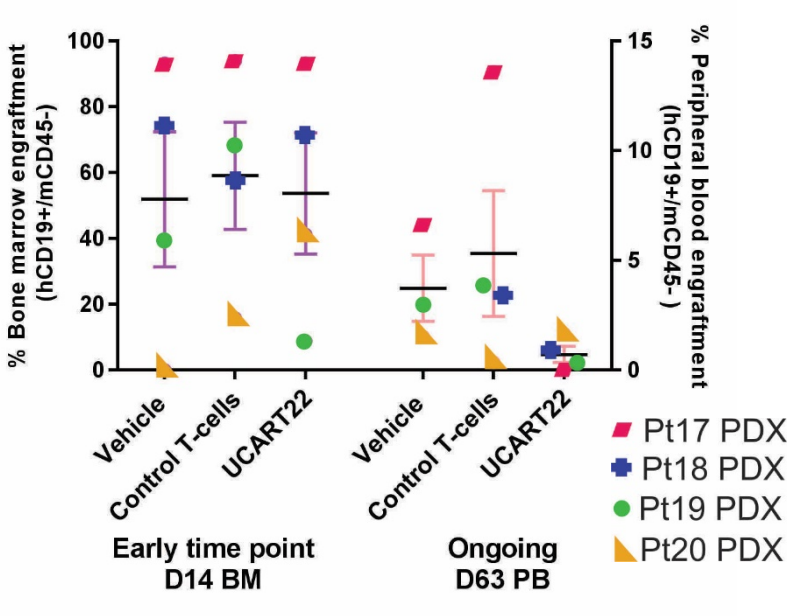
Ongoing expansion of tumor xenograft (PDX) models treated with UCART22 (1 mouse per group).

Provides pre-clinical data for a broad range of genetically distinct tumor xenografts.

Currently, 4 PDX models have been treated with:

- Vehicle
- UCART22 ($10x10^6$ cells)
- Control T-cells (DKO, NTD, $10x10^6$ cells).





Conclusion

- **CD22 is highly expressed on B-ALL cells and is unique to hematological cells. Both normal B-cells and B-ALL cells, while CD22+, show variable antigen site density.**
- **UCART22 is an off-the-shelf allogeneic CAR-T product capable of producing lysis in CD22+ target cells (both B-ALL cell lines and patient samples).**
- **Pre-clinical efficacy was greatest in cells with high surface expression of CD22, including Ph-like and hypodiploid subtypes.**
- **A phase 1 trial for UCART22 is planned for Q2 2018.**

Acknowledgements

MD Anderson Cancer Center:

Leukemia Dept

Marina Konopleva
Nitin Jain
Tianyu Cai
Elias Jabbour

Hematopathology

Sergej Konoplev
Marian Kersh
Jeff Jorgernsen
Sa Wang

Cellectis, SA and Cellectis, Inc:

Cécile Schiffer-Manniou
Stéphanie Filipe
Agnès Gouble
Roman Galetto
Julianne Smith

Collaborators:

Markus Muschen, COH, CA

Thank you!

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