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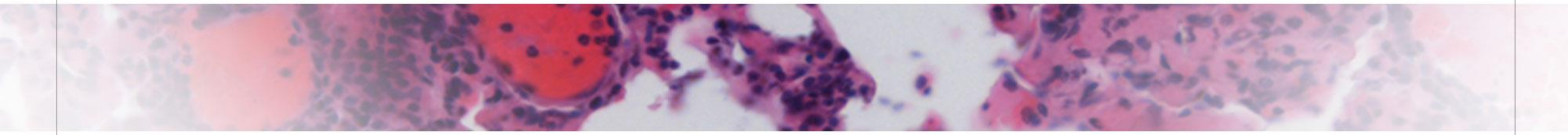

Phase 1/2 study of AUTO3, the first bicistronic chimeric antigen receptor (CAR) targeting CD19 and CD22, followed by an anti-PD1 in patients with relapsed/refractory (r/r) Diffuse Large B Cell Lymphoma (DLBCL): Results of Safety Cohorts of the ALEXANDER study

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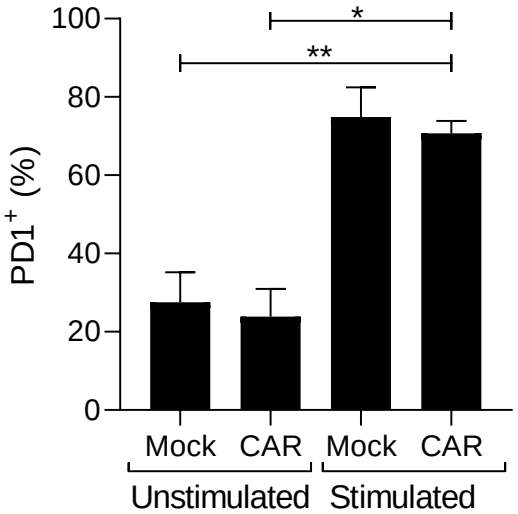
Improving CAR T Cell Immunotherapy In DLBCL

Dual Targeting CAR & Prevention of CAR T cell inhibition

- CD19 CARs are active in r/r DLBCL
- However unmet need remains with CD19 CAR T cell therapy
  - 29-37% durable CRR in DLBCL[1,2]
  - The potential causes for relapse include:
    - PD-L1 upregulation[3] which contributes to CAR T exhaustion
    - CD19 antigen loss[4]
  - Rate of severe (grade ≥3) cytokine release syndrome (CRS 13-22%) and neurotoxicity (NT 12-28%)[2,4]
- Simultaneous targeting of CD19 and CD22 may reduce the probability of relapse due to antigen loss
- PD1/PDL1 mediated CAR T cell inhibition may be prevented by adding pembrolizumab to the preconditioning regimen

Activated T-cells Upregulate PD1

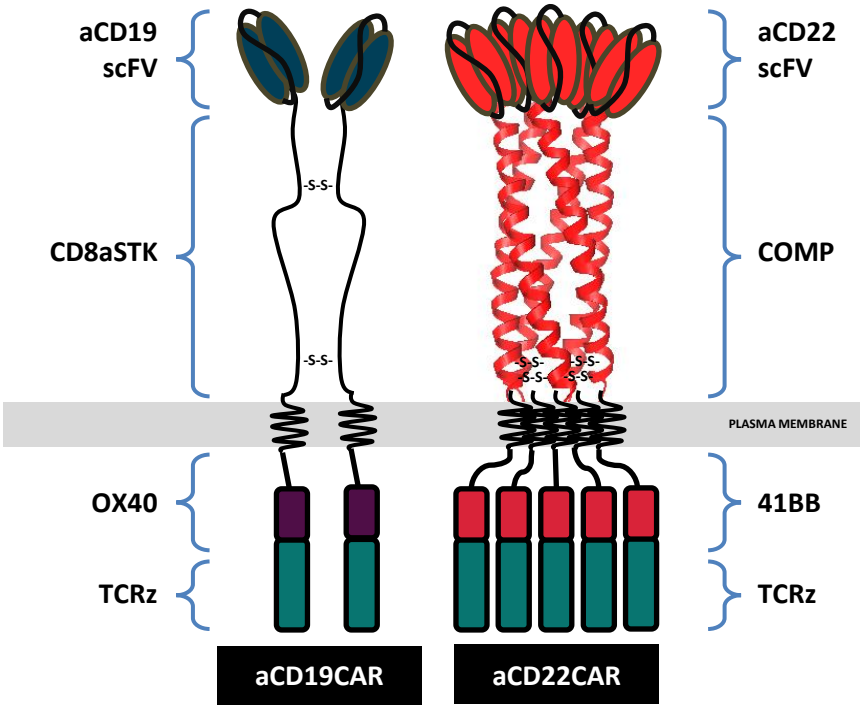


[1] Locke F et al Lancet Oncol 2019
[2] Schuster S et al NEJM 2019
[3] Neelapu S et al ASCO 2018
[4] Neelapu S et al NEJM 2017

AUTO3: First CD19 and CD22 Targeting Bicistronic CAR

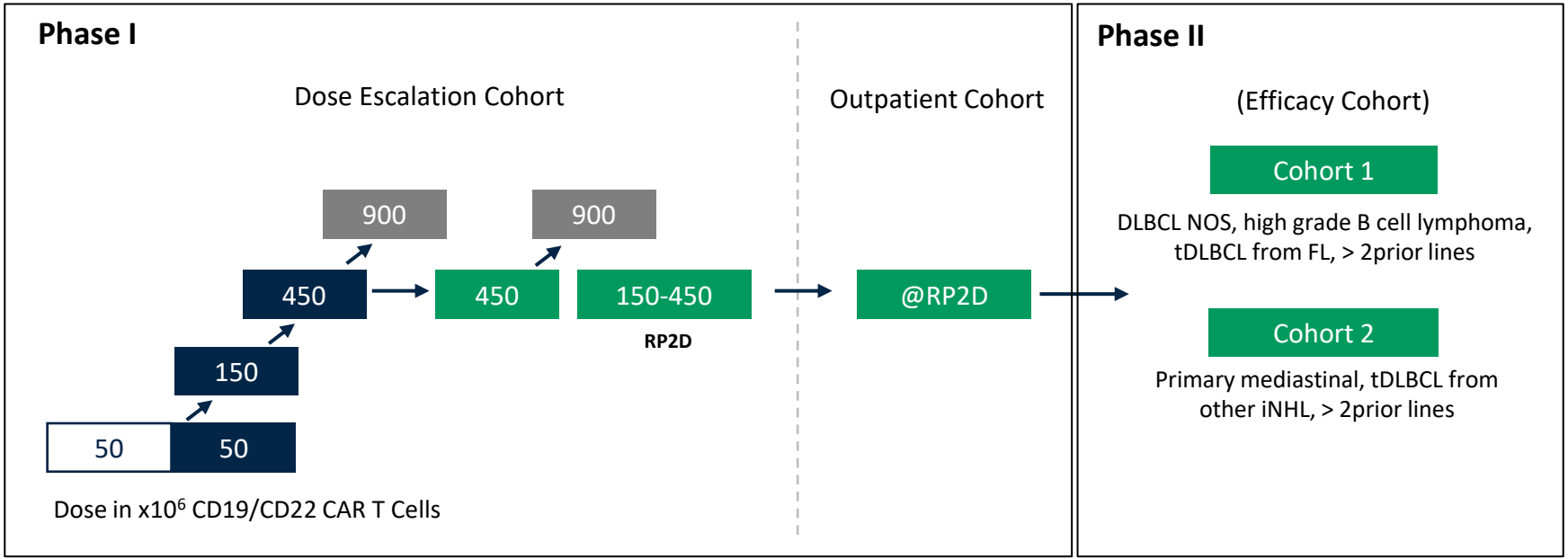
Gamma Retroviral-Based Vector with RD114 Pseudotype

- Dual antigen targeting
- Two independent CARs delivered in single retroviral vector
- Humanized binders
- CD22 CAR with novel pentameric spacer
- OX40/41BB costimulatory domains designed to improve persistence
- Independently target CD19 and CD22



Alexander Study Design

AUTO3-DB1, Single-Arm, Open-Label, Multi-Center, Phase 1/2 Study



Preconditioning: Flu/Cy

Flu/Cy + Pembro day 14 x 3 doses

Flu/Cy + Pembro day -1 x 1 dose

Phase 1 Outpatient Expansion Cohort

Inclusion / Exclusion

- Subjects who do not have caregiver support (in line with institutional outpatient transplant guidelines) for outpatient/ambulatory care setting.
- Subjects who are staying greater than 60 minutes (or whatever is permissible per institutional outpatient transplant guidelines) from the clinical trial site at the time of treatment.

Monitoring

- Monitored for at least 10 days in an outpatient/ambulatory care setting.
- During the 10 days following AUTO3 infusion, monitored at a minimum every 2 to 3 days. Recommended for the patient to have a daily verbal communication with qualified nurse/medical personnel (phone call).

Baseline Patient Characteristics: All Patients

Baseline Patient Characteristics		N=49
Age, median (min-max)		59 (27-83)
Gender, n	Male, Female	29, 20
Current Histology, n	DLBCL NOS	34 (69%)
	tDLBCL	11 (22%)
	High Grade B Cell Lymphoma	3 (6%)
	Primary Mediastinal Large B Cell Lymphoma	1 (2%)
Molecular Risk, n (%)	High Risk	27 (55%)
	- Triple HIT	-5
	- Double HIT	-14
	- Double Expressor	- 8
	No High Risk	13 (27%)
	Unknown/Not Done	9 (18%)
Disease Stage, n (%)	II	4 (8%)
	III	10 (20%)
	IV	35 (71%)
Relapsed/Refractory, n (%)	Refractory	11 (22%)
	Relapsed	14 (29%)
	Relapsed and Refractory	24 (49%)
No. Prior Therapies, median (min-max)		3 (1-11)
Prior ASCT, n (%)		15 (31%)
SPD, median (min-max)		18.5 cm (2.1 – 260.8)

ASCT: Autologous Stem Cell Transplant; tDLBCL: transformed DLBCL; IPI: International Prognostic Index

Data Cutoff Date: 30-Oct-2020

Treatment Emergent Adverse Events ≥ 25% and SAE ≥ 5%

AEs (Total N = 49)	All Grades n (%)	≥ Grades 3 n (%)
Neutropenia	29 (59%)	28 (57%)
Anaemia	25 (51%)	20 (41%)
Thrombocytopenia	23 (47%)	18 (37%)
Cytokine release syndrome	17 (35%)	1 (2%)
Fever	13 (27%)	0
Infections	13 (27%)	8 (16%)

SAEs (Total N = 49)	All Grades n (%)	≥ Grades 3 n (%)
Cytokine release syndrome	6 (12%)	1 (2%)
Fever	5 (10%)	0
Infections	4 (8%)	4 (8%)
Febrile neutropenia	3 (6%)	3 (6%)

- Majority of ≥ Grade 3 AEs are haematological
- Two patients had death possibly related to AUTO3. One in the setting of disease progression and multiorgan failure and other due to infection in a patient with secondary HLH.

Data Cutoff Date: 30-Oct-2020

Cytokine Release Syndrome (CRS)

Low rates of CRS

	Total (N=49)	50 x 10^6 AUTO3 (N=7)	150 x 10^6 AUTO3 (N=16)	300 x 10^6 AUTO3 (N=10)	450 x 10^6 AUTO3 (N=16)
All Grades	17 (35%)	1 (14%)	4 (25%)	2 (20%)	10 (63%)
Grade 1	10 (20%)	1 (14%)	2 (13%)	2 (20%)	5 (31%)
Grade 2	6 (12%)	0	1 (6%)	0	5 (31%)
≥ Grade 3	1 (2%)	0*	1 (6%)	0	0

* 1 patient who had no CRS with primary infusion, developed G3 CRS (severe hypoxia) with re-treatment 1 year later which happened in a setting of no CAR T expansion and significant disease burden in lung that had been treated with radiation

- No prophylactic measures of any kind
- Median time to CRS 2 days (1-36), Median duration 3 days (1-19)
- Eight patients received tocilizumab (16%)
- No patients received steroids

CRS grading as ASCT/ASBMT (Lee et al 2019)
Data Cutoff Date: 30-Oct-2020

Neurotoxicity (NT/ICANS)

Low rates of NT

	Total (N=49)	50 x 10^6 AUTO3 (N=7)	150 x 10^6 AUTO3 (N=16)	300 x 10^6 AUTO3 (N=10)	450 x 10^6 AUTO3 (N=16)
All Grades	3 (6%)	1 (14%)	2 (13%)	0	0
≥ Grade 3	2 (4%)	1 (14%)	1 (6%)	0	0

- No prophylactic measures of any kind
- No NT of any grade in patients that achieved CR
- All NT atypical in context of tumor progression with zero to minimal CART expansion in peripheral blood
  - **1st case of NT (G3):** Day 53. Duration 5 days (G2). The same symptoms of facial/muscle weakness occurred > 10 years ago without specific diagnosis. Resolved.
  - **2nd case of NT (G2):** Day 21. Duration 6 days. AMS associated with sepsis and narcotic. Resolved.
  - **3rd case of NT (G4):** Day 10. Encephalopathy associated with sepsis, hyponatremia, metabolic acidosis, and multiorgan failure. Patient died of disease progression and multiorgan failure

Data Cutoff Date: 30-Oct-2020

Efficacy - Best Overall Responses

Complete responses observed at all doses

	Total (N=49)	50 x 10^6 AUTO3 (N=7)	150 x 10^6 AUTO3 (N=16)	300 x 10^6 AUTO3 (N=10)	450 x 10^6 AUTO3 (N=16)
N Evaluable*	43	6	13	9	15
ORR	28 (65%)	4 (67%)	4 (31%)	7 (78%)	13 (87%)
CR	22 (51%)	2 (33%)	4 (31%)	5 (56%)	11 (73%)
PR	6 (14%)	2 (33%)	0	2 (22%)	2 (13%)

- Across all doses CRR of 51% (n=43)
- Doses ≥ 300 x 10^6, CRR of 62% (n=26)
- Doses ≥ 450 x 10^6, CRR of 73% (n=15)

*Evaluable = PET positive disease prior to start of pre-conditioning and infused at least 28 days prior to data cutoff date
Data Cutoff Date: 30-Oct-2020

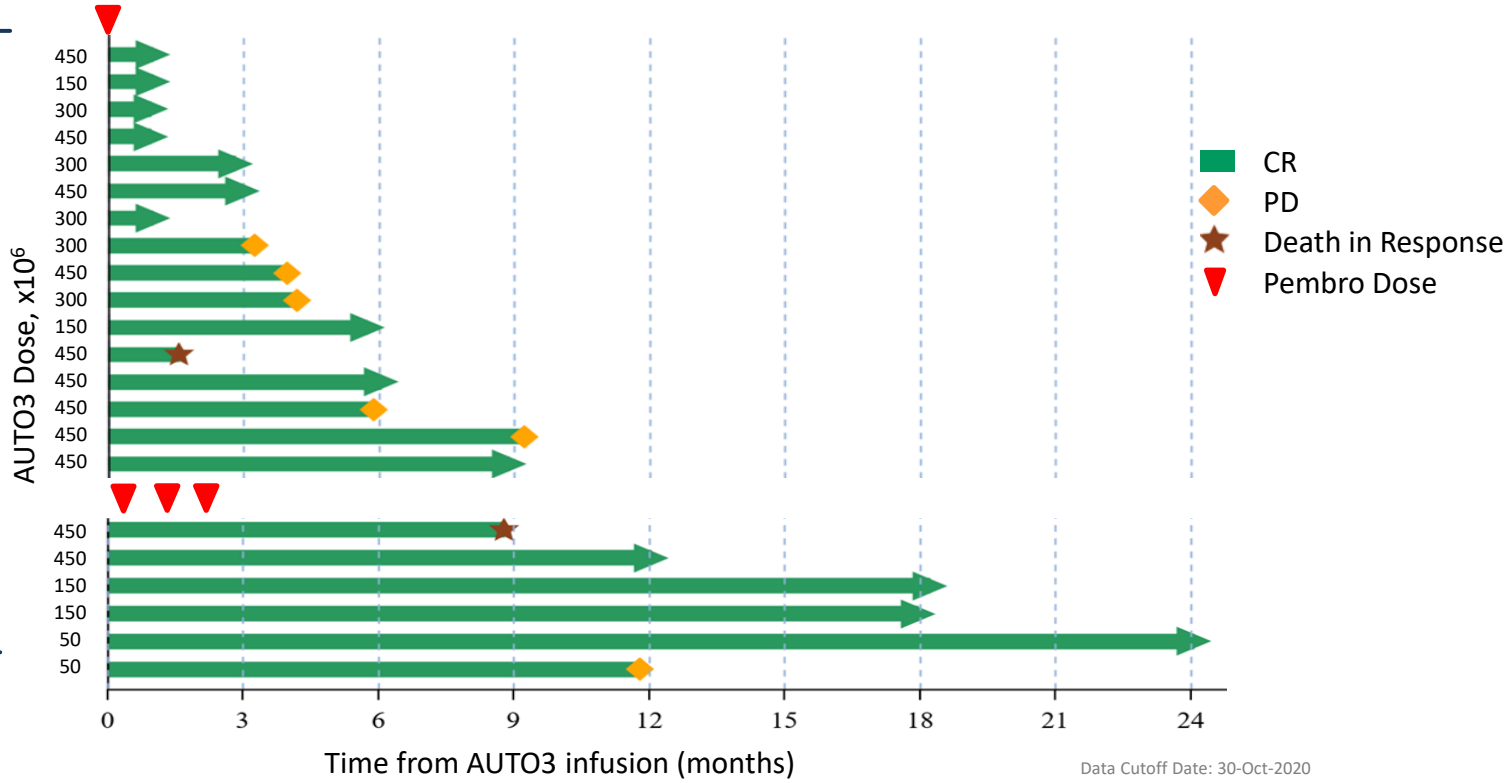
Disease Assessment of CR Patients

16/22 (73%) without progression, median follow up of 4 months

150-450x10^6
D-1 Pembro
1x Dose Pembro

50-450 x10^6
D14, D35, D56 Pembro
3x Doses Pembro

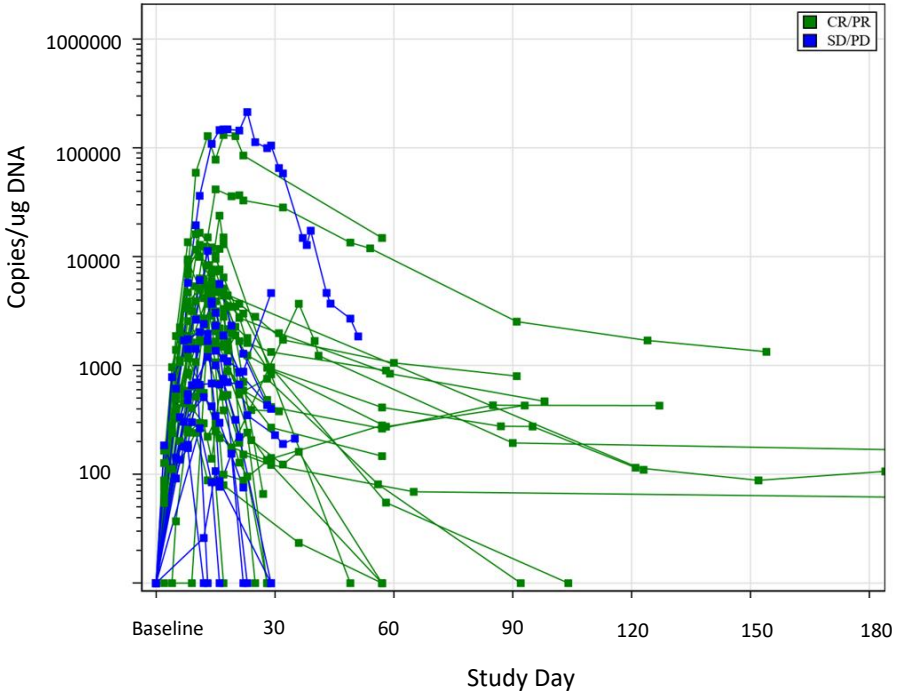
50 x10^6
No Pembro



Data Cutoff Date: 30-Oct-2020

Cellular Kinetics by Best Overall Response

CR/PR are associated with higher expansion and longer persistence



	CR/PR (N=28)	SD/PD (N=13)
Tmax (days) median (range)	11 (7 – 35)	12 (7 – 28)
Cmax (copies/ug) Geo-mean (CV%)	6129 (175)	1841 (722)
AUC0-28 (copies/ug day) Geo-mean (CV%)	54419 (199)	13731 (1275)

- Ongoing CAR-T persistency observed at ≥ 18 months

Evaluable = PET positive disease prior to start of pre-conditioning, infused at least 28 days prior to data cutoff date and with at least one sample providing evaluable cellular kinetic data
Data Cutoff Date: 30-Oct-2020

AUTO3 Healthcare Utilizations in Outpatient Cohort

Outpatient infusion of AUTO3 is feasible

	150-450 x10^6 AUTO3 D-1 pem Outpt (N=17)
AUTO3 infusion inpatient	4
AUTO3 infusion outpatient	13
Admission post AUTO3	5 (38%)
ICU admission	0

- 5 patients received AUTO3 outpatient but admitted (due to FN and CRS)
- Median duration of hospitalisation was 5 days (range 1-9 days)

Data Cutoff Date: 30-Oct-2020

Conclusions

Phase I Cohorts, ALEXANDER Study

- AUTO3 has a tolerable and best-in-class safety profile:
  - 35% CRS (2% ≥ Grade 3 CRS) with primary infusion
  - 6% NT/ICANs (4% ≥ Grade 3 NT/ICANs)
    - Patients that achieved CRs, where robust expansion was observed, no severe NT of any grade was seen
    - All three cases of NT in setting of disease progression, very minimal / undetectable CAR-T cells in peripheral blood and with confounding factors

- AUTO3 shows high rate of complete responses
  - Overall CRR of 51% (N=43)
  - Among patients receiving 450 x 10^6 AUTO3, CRR of 73% (N=15)
  - Ongoing CR observed beyond 24 months

- Outpatient administration is feasible with low admission rate (38%)

Acknowledgments

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SCRI: Austin St. Davids
SCRI: Denver CBCI
Washington University
University of Miami
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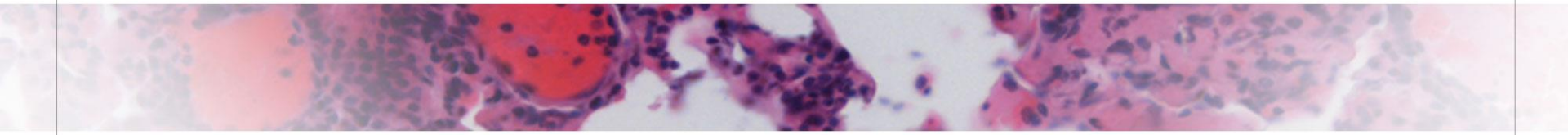

Thank you