European Hematology Association Data Update June 2022

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Agenda

- Welcome and Introduction: Dr. Christian Itin, CEO
- AUTO4 in T-Cell Lymphoma
  - Review of T Cell Lymphoma – Dr. Horwitz
  - AUTO4/5 introduction – Dr. Martin Pule, CSO
  - AUTO4 data – Dr. Kate Cwynarski
  - Next steps – Dr. Martin Pule, CSO
- Obe-cel life cycle management: Dr. Martin Pule, CSO
  - Obe-cel in NHL
  - Obe-cel in PCNSL
  - AUTO1/22 in pediatric ALL
- Summary: Dr. Christian Itin, CEO
- Q&A: Dr. Christian Itin, Dr. Martin Pule and Dr. Edgar Braendle

EHA EUROPEAN HEMATOLOGY ASSOCIATION

Dr. Christian Itin
Chief Executive Officer

Dr. Martin Pule
Chief Scientific Officer

Dr. Edgar Braendle
Chief Development Officer

Autolus

Autolus

Dr. Stephen Horwitz

Peripheral T-cell Lymphomas

Member and Attending Physician
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Cornell Medical College, Cornell University
Chair NCCN T-Cell and Cutaneous Lymphoma Guidelines Committee

Conflicts Of Interest

In the past 12, I have the following relationships:

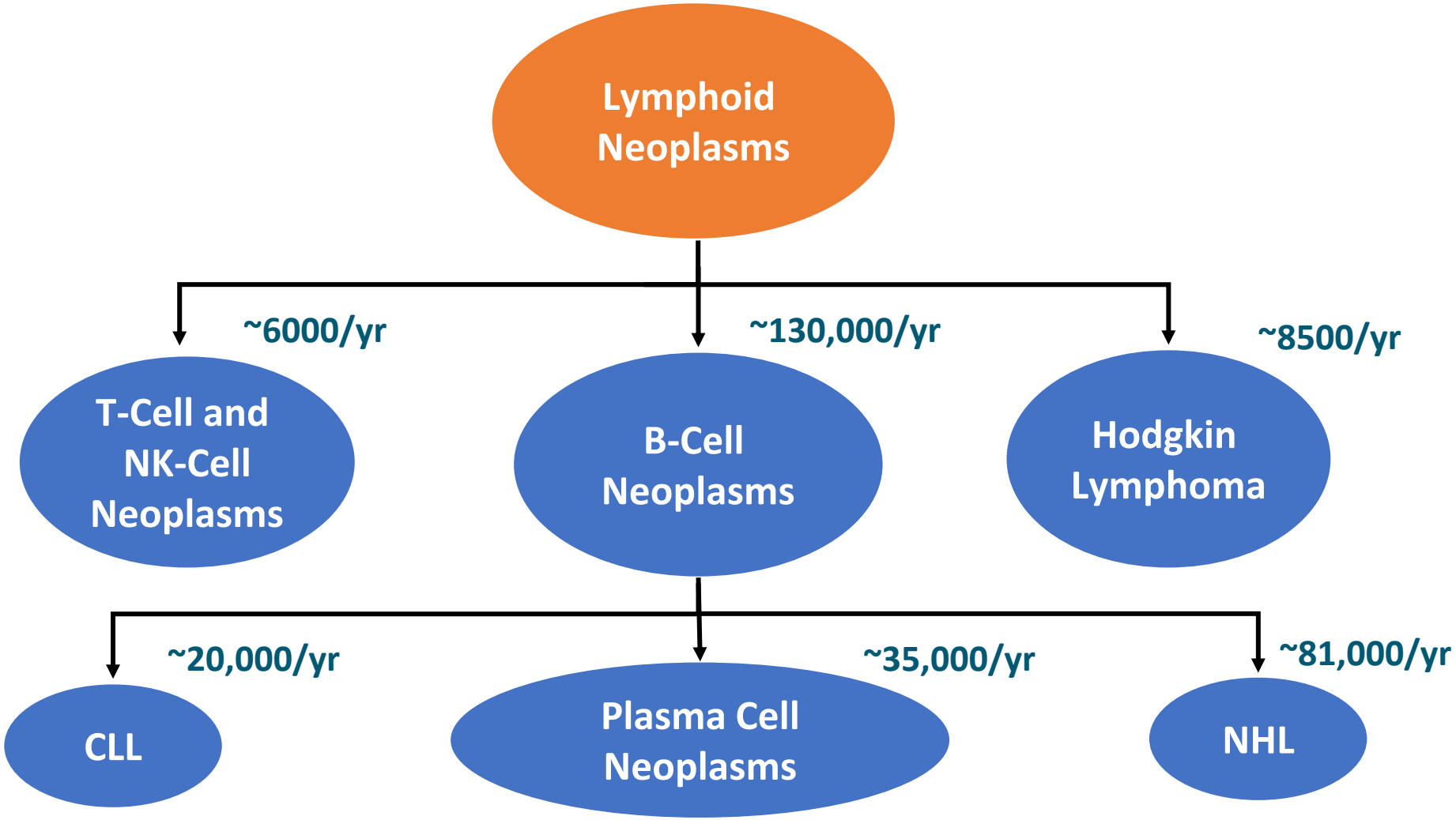
Consulting:
Acrotech Biopharma, Affimed, C4 Therapeutics, Kyowa Hakko Kirin, Myeloid Therapeutics, ONO Pharmaceuticals, Seattle Genetics, SecuraBio, Shoreline Biosciences, Inc. Takeda, Trillium Therapeutics, Tubulis

Research support: ADC Therapeutics, Affimed, C4 Therapeutics, Celgene, Daiichi Sankyo, Kyowa Hakko Kirin, Millennium /Takeda, Seattle Genetics, Trillium Therapeutics, and Verastem/SecuraBio

T-cell Lymphomas

- Background
- Upfront Chemotherapy Approaches
  - Dose Intensification
  - Patient Selection
  - Adding to a CHOP Backbone
- Therapies for Relapsed PTCL

T-Cell Lymphoma Is An Uncommon Non-Hodgkin Lymphoma Incidence in US



ACS. Cancer Facts and Figures 2022. Harris. JCO. 1999;17:3835.

"Heterogeneous and Poor Prognosis"

Leukemic
- T-cell PLL
- T-cell LGL leukemia
- *Chronic LPDs of NK cells*
- Aggressive NK-cell leukemia
- ATLL
- Systemic EBV+ T-cell lymphoma of childhood
- Hydroa vacciniforme-like lymphoproliferative disorder

Nodal
- PTCL-NOS
- AITL (angioimmunoblastic)
- *Follicular T-cell lymphoma*
- *Nodal PTCL with TFH phenotype*
- ALCL, ALK-positive
- ALCL, ALK-negative

Cutaneous
- MF/Sezary Syndrome
- Primary cut CD30+ LPD
- LyP, pcALCL
- Primary cut γδ TCL
- *Primary cut CD8+ aggressive epidermotropic cytotoxic TCL*
- *Primary cut acral CD8+ TCL*
- *Primary cut CD4+ small/medium T-cell LPD*

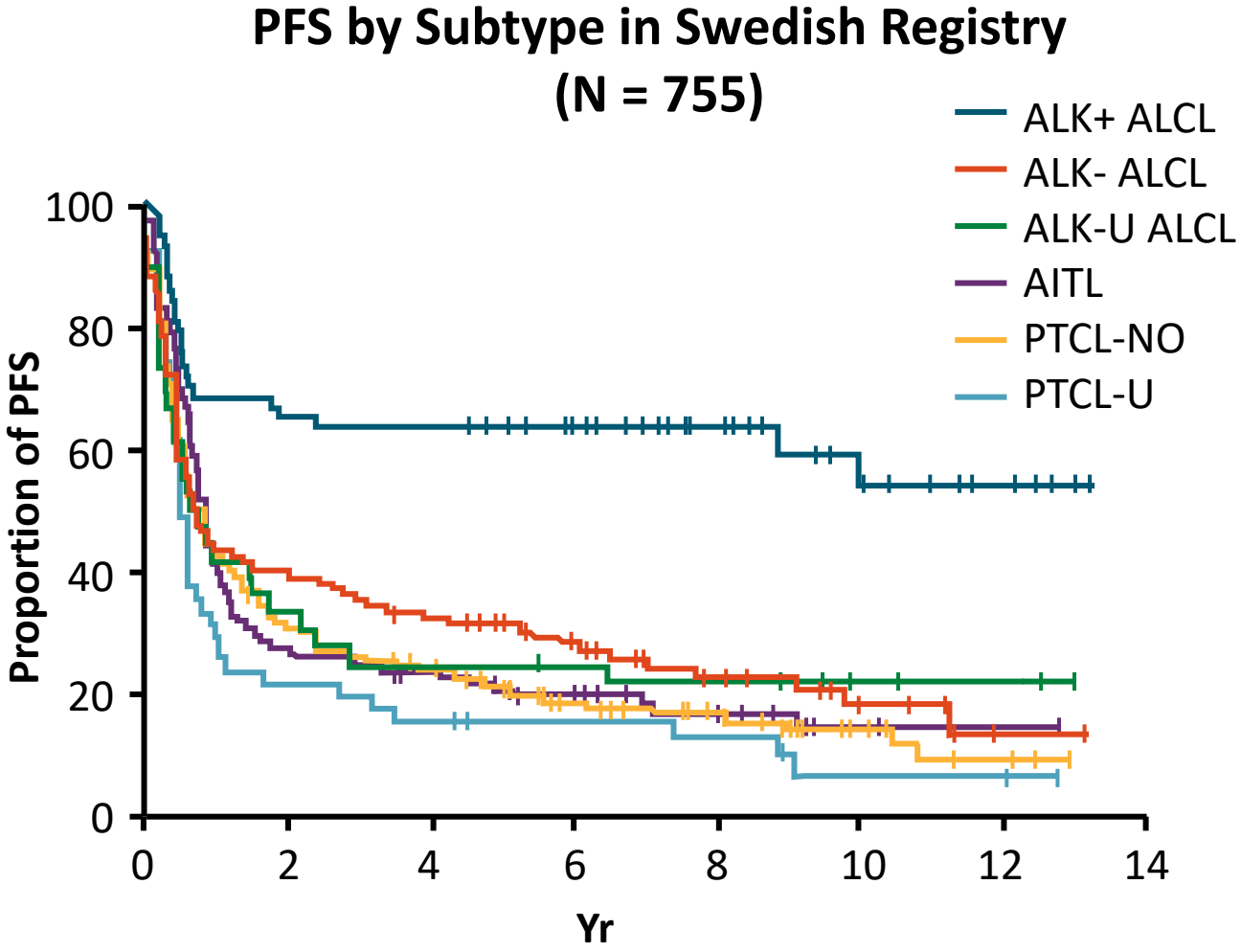
Extranodal
- Extranodal NK/TCL, nasal type
- Enteropathy-associated TCL
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- *Indolent T-cell proliferative disorder of the GI tract*
- Subcut. panniculitis-like TCL
- Hepatosplenic TCL
- *Breast implant-associated ALCL*

Most common Less common Rare

Swerdlow SH, et al. *Blood.* 2016;127:2375-2390.

Prognosis with Standard Therapy and Dose Intensification

Non-ALCL Subtypes Have Poor Outcomes With Standard CHOP-Like Regimens



Rate, %	AITL	PTCL NOS	EATL	TCL U
5-yr OS	31.6	28.1	20.4	24.6
5-yr PFS	20.4	21.3	17.6	15.1

Ellin. Blood. 2014; 124:1570.

Slide credit: clinicaloptions.com

PTCL Entities by Therapeutic Strategy (Chemotherapy)

CHOP based not recommended

- Extranodal NK/TCL, nasal type
- Hepatosplenic TCL
- T-cell PLL
- T-cell LGL leukemia
- MF/Sezary Syndrome
- Primary cutaneous CD_{30}+ LPD
- LyP, pcALCL
- Primary cutaneous acral CD8+ TCL
- Primary cutaneous CD_4+ small/medium T-cell LPD
- Indolent T-cell of the GI tract
- *Chronic LPDs of NK cells*
- Aggressive NK-cell leukemia
- ATLL
- Systemic EBV+ TCL f childhood
- Hydroa vacciniforme-like LPD

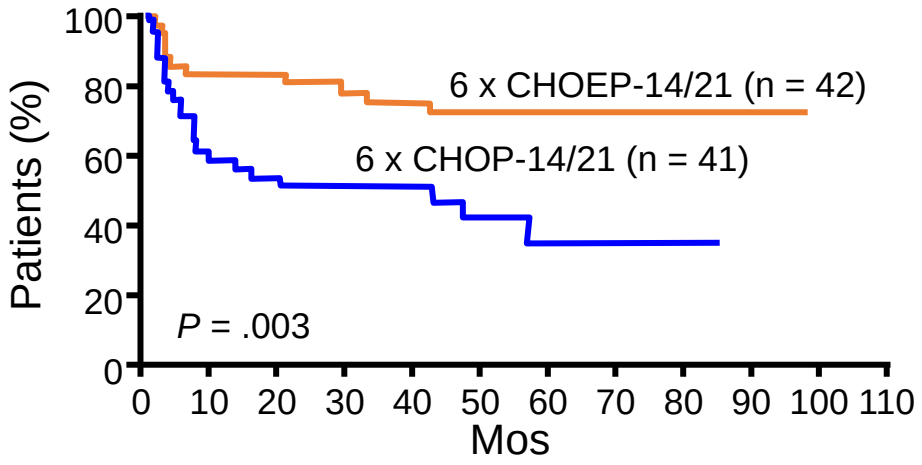
CHOP based therapy *Reasonable*

- PTCL-NOS
- AITL (angioimmunoblastic)
- Follicular T-cell lymphoma
- Nodal PTCL with TFH phenotype
- ALCL, ALK-positive
- ALCL, ALK-negative
- Enteropathy-associated TCL
- *Monomorphic epitheliotropic intestinal T-cell lymphoma*

Other- very limited data

- Primary cutaneous $\gamma\delta$ TCL
- Primary cutaneous CD8+ aggressive epidermotropic cytotoxic TCL
- Subcut. panniculitis-like TCL
- Breast implant-associated ALCL

Possible Improvement (and Toxicity) with Addition of Etoposide? German Prospective High-Grade NHL Studies



PTCL Subtype	n
ALCL, ALK+	78
ALCL, ALK-	113
PTCL-NOS	70
AITL	28
Other	31
Total	320

Schmitz N, et al. Blood. 2010;116:3418-3425.

Study B1: Patients 18-60 years of age[1]

Grade 3/4 AE, %	CHOP-21	CHOP-14	CHOEP-21	CHOEP-14	*P* Value
Leukocytopenia	34.1	33.6	73.6	72.5	< .001
Thrombocytopenia	2.4	1.2	7.0	22.2	< .001
Anemia	3.6	5.6	8.5	35.4	< .001
Infection	1.8	4.2	4.4	5.2	.390
Mucositis	2.9	3.0	1.6	6.9	.048

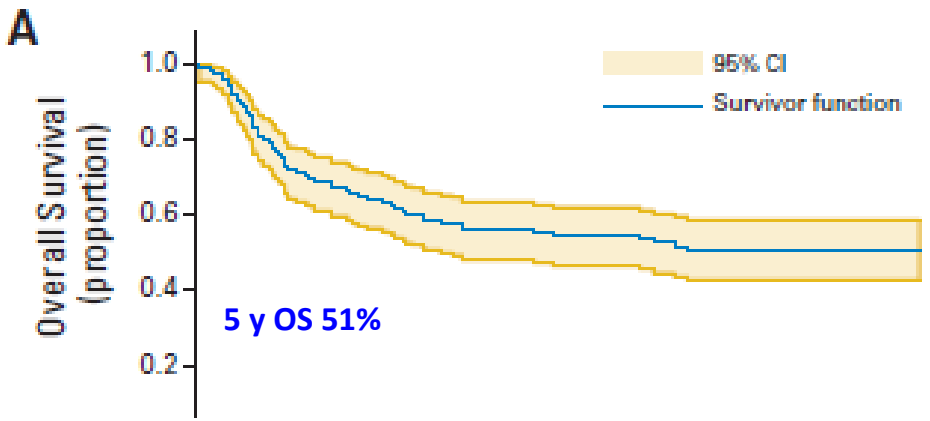
Study B2: Patients 61-75 years of age[2]

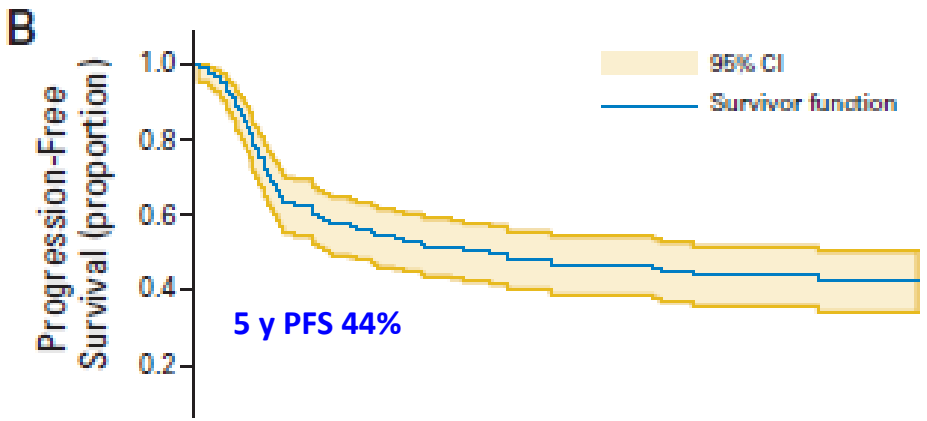
Grade 3/4 AE, %	CHOP-21	CHOP-14	CHOEP-21	CHOEP-14	*P* Value
Leukocytopenia	72.1	70.1	94.4	92.4	< .001
Thrombocytopenia	4.7	15.1	28.4	50.8	< .001
Anemia	12.5	19.5	28.7	45.1	< .001
Infection	8.0	10.6	13.2	24.1	< .001
Mucositis	0.0	7.1	4.9	14.3	< .001

1. Pfreundschuh. Blood. 2004;104:626. 2. Pfreundschuh. Blood. 2004;104:634.

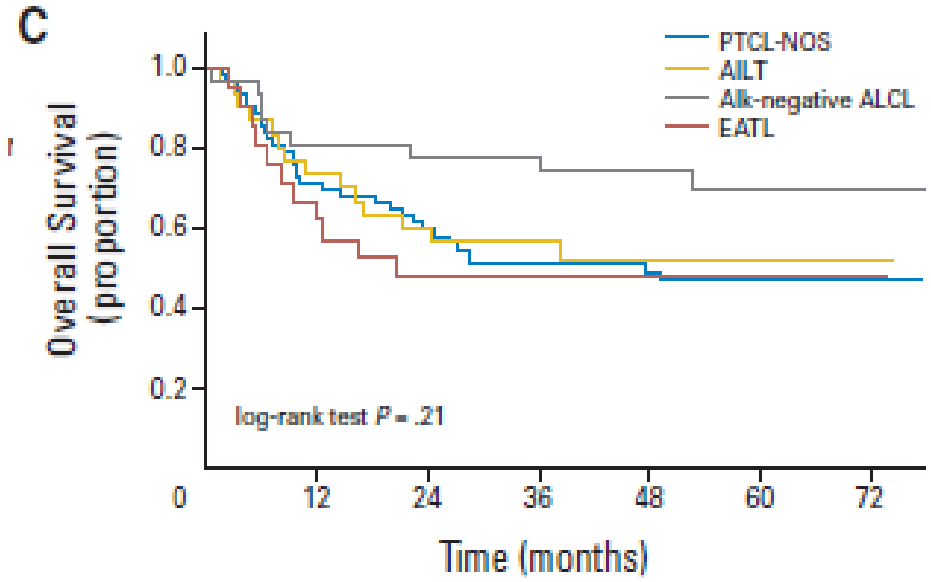
Upfront Transplant in PTCL

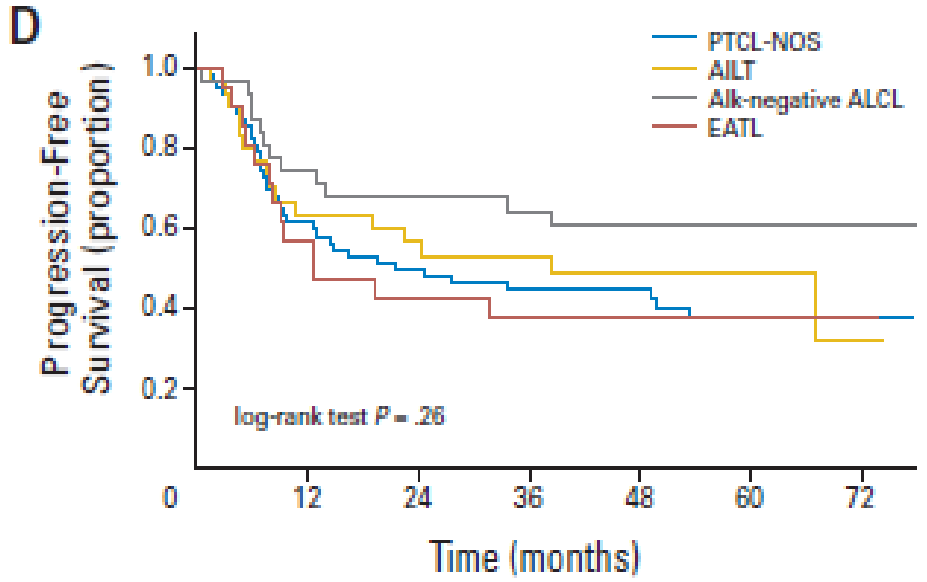
All patients





5 y OS by Subtype
ALK- 70%
AITL 49%
NOS 52%
EATL 48%





5 y PFS by Subtype
ALK- 61%
AITL 49%
NOS 38%
EATL 38%

d'Amore F et al. *J Clin Onc*. 2012;30:3093-3099.

Adding to a CHOP Backbone

ECHELON-2 Study Design (NCT01777152)

Key Eligibility Criteria
- Age ≥18 years
- CD30-expression (≥10% cells)
- Previously-untreated PTCL:
  - Systemic ALCL (sALCL)* including ALK(+) sALCL with IPI ≥2, ALK(-) sALCL
  - PTCL-NOS, AITL, ATLL, EATL, HSTCL

*targeting 75% (±5%) ALCL per EU regulatory commitment

Stratification Factors
- IPI score (0-1 vs. 2-3 vs. 4-5)
- Histologic subtype (ALK-positive sALCL vs. all other histologies)

R (1:1)

N=226

A+CHP
(A) brentuximab vedotin 1.8 mg/kg +
(C) cyclophosphamide 750 mg/m^2 +
(H) doxorubicin 50 mg/m^2 +
(P) prednisone 100 mg (Days 1-5)

+ placebo vincristine

Q3W for 6 to 8 cycles

N=226

CHOP
(C) cyclophosphamide 750 mg/m^2 +
(H) doxorubicin 50 mg/m^2 +
(O) vincristine 1.4 mg/m^2 +
(P) prednisone 100 mg (Days 1-5)

+ placebo brentuximab vedotin

Q3W for 6 to 8 cycles

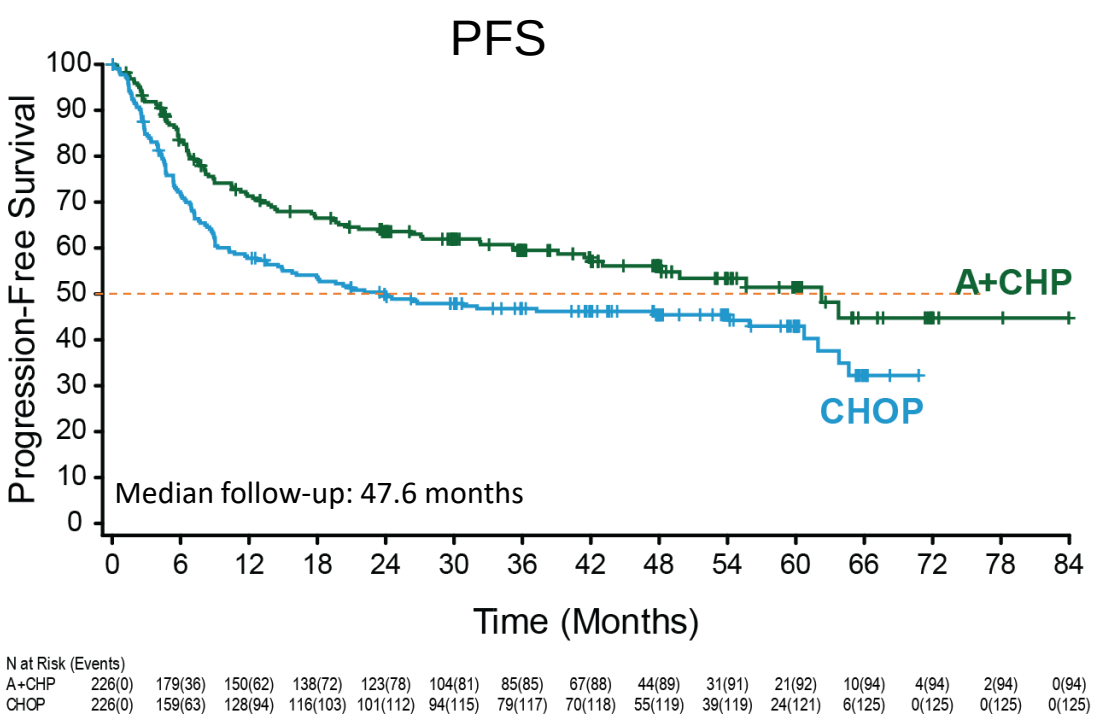
EOT PET

Primary Endpoint

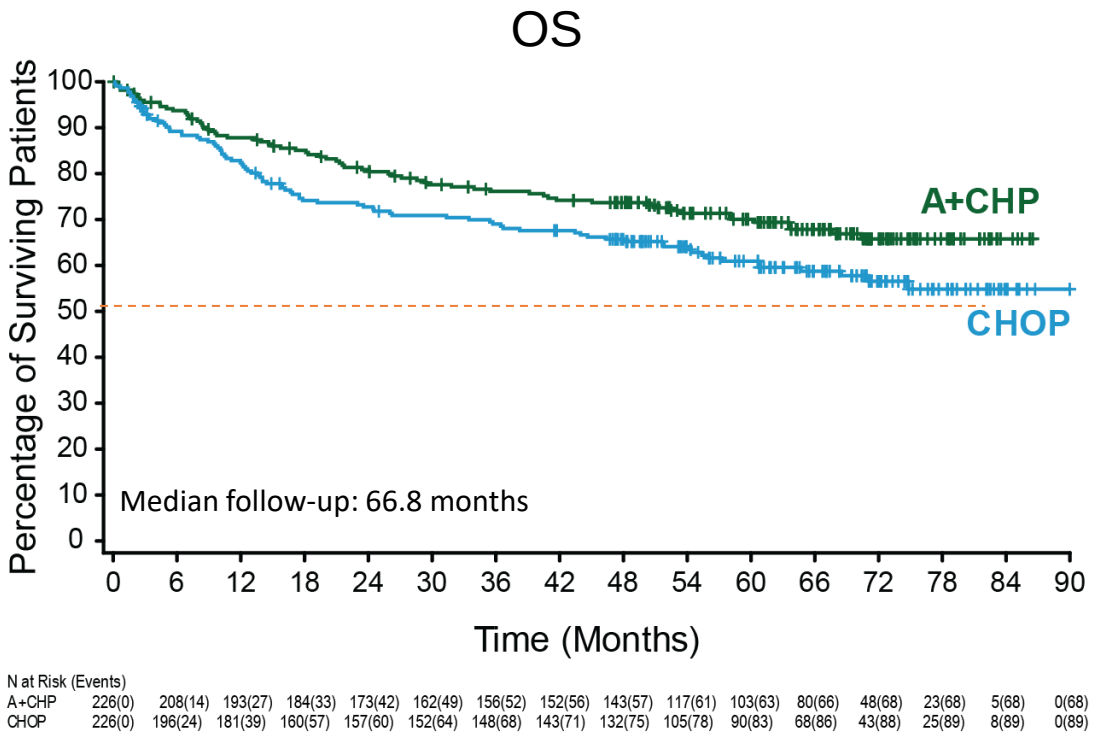
PFS per BICR, ASCT or RT consolidation not an event

Horwitz S et al. *Lancet.* 2019; 393:229-240.

Echelon-2 Trial 5-Year Results: PFS (INV Assessment) and OS



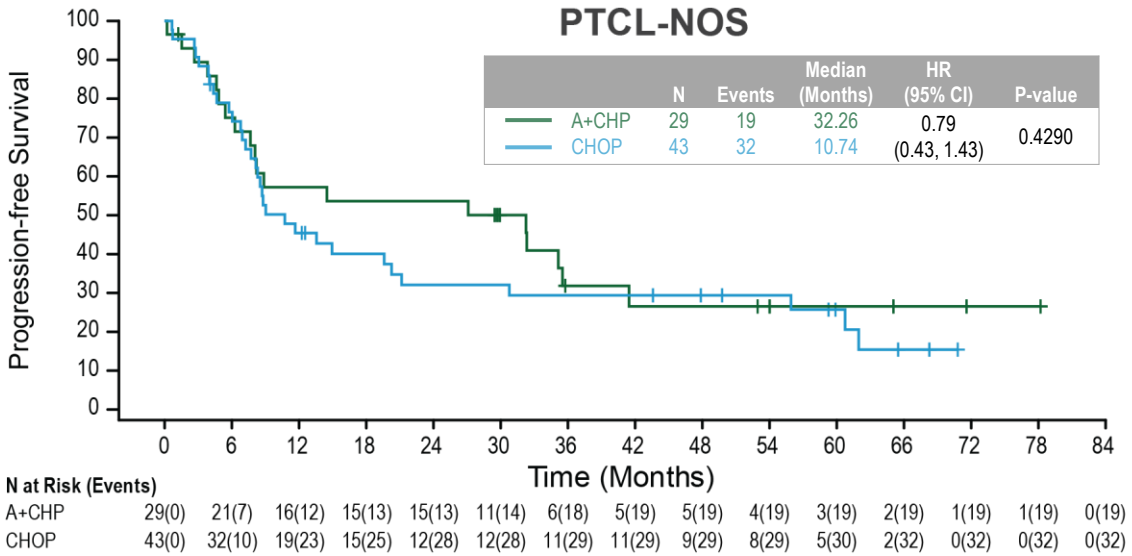
	N	Events	Medians (Months)	HR (95% CI)	p-value*
A+CHP	226	94	62.26	0.70 (0.53, 0.91)	0.0077
CHOP	226	125	23.75		



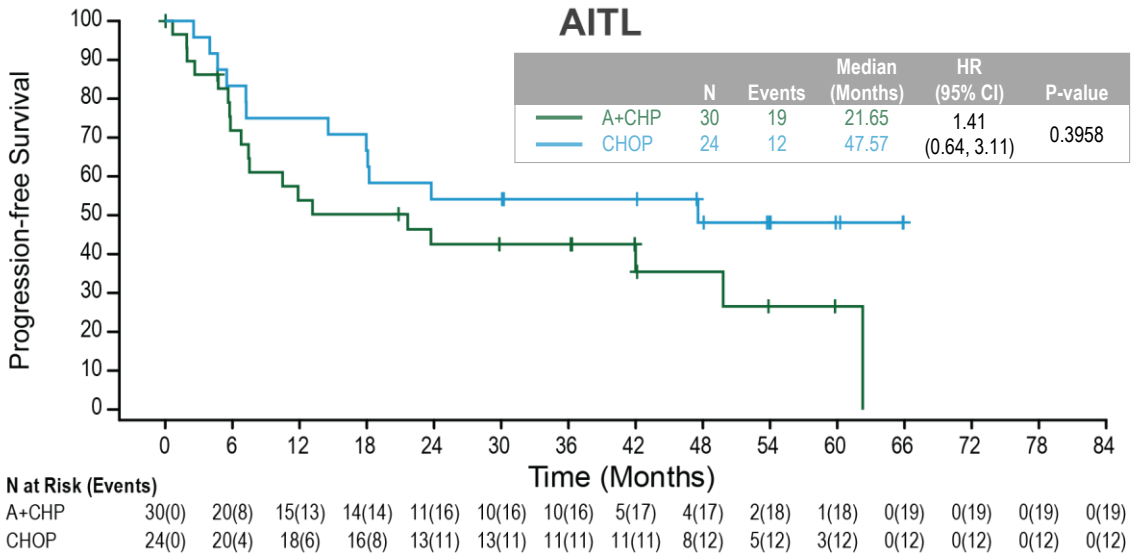
	N	Events	Medians (Months)	HR (95% CI)	p-value*
A+CHP	226	68	–	0.72 (0.53, 0.99)	0.0424
CHOP	226	89	–		

Horwitz et al ASH 2020 a1150

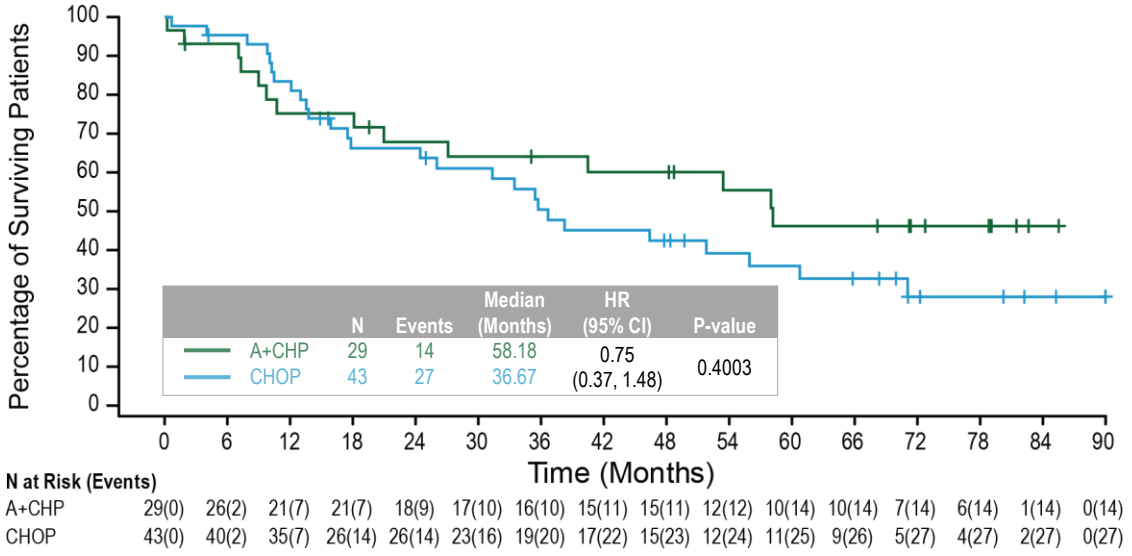
Summary of PFS and OS per Investigator (PTCL-NOS and AITL)



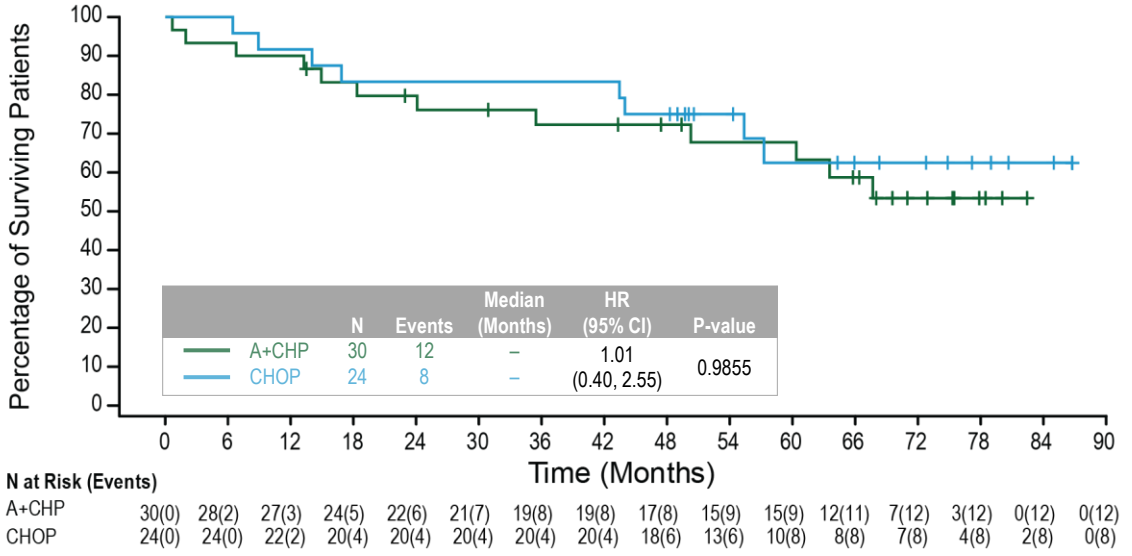
	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	29	19	32.26	0.79 (0.43, 1.43)	0.4290
CHOP	43	32	10.74		



	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	30	19	21.65	1.41 (0.64, 3.11)	0.3958
CHOP	24	12	47.57		



	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	29	14	58.18	0.75 (0.37, 1.48)	0.4003
CHOP	43	27	36.67		



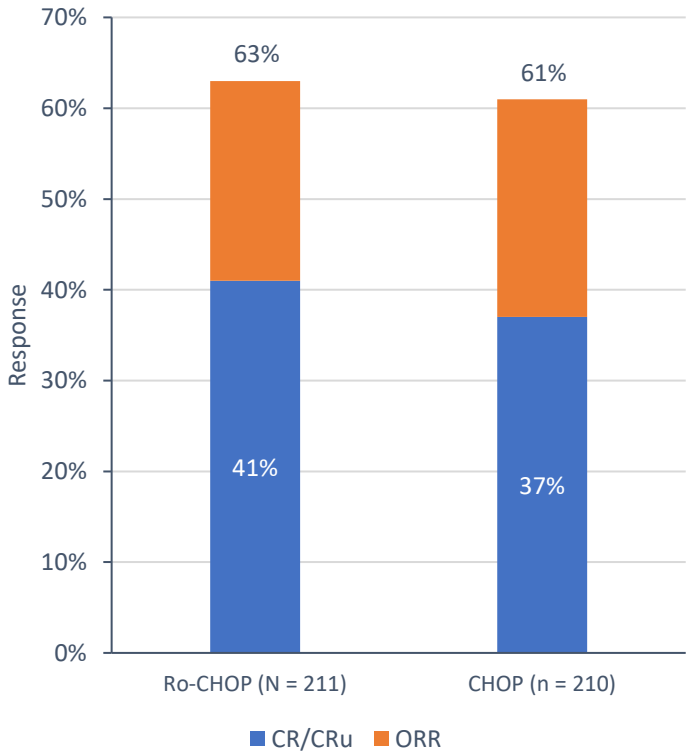
	N	Events	Median (Months)	HR (95% CI)	P-value
A+CHP	30	12	–	1.01 (0.40, 2.55)	0.9855
CHOP	24	8	–		

Horwitz et al ASH 2021 a1150

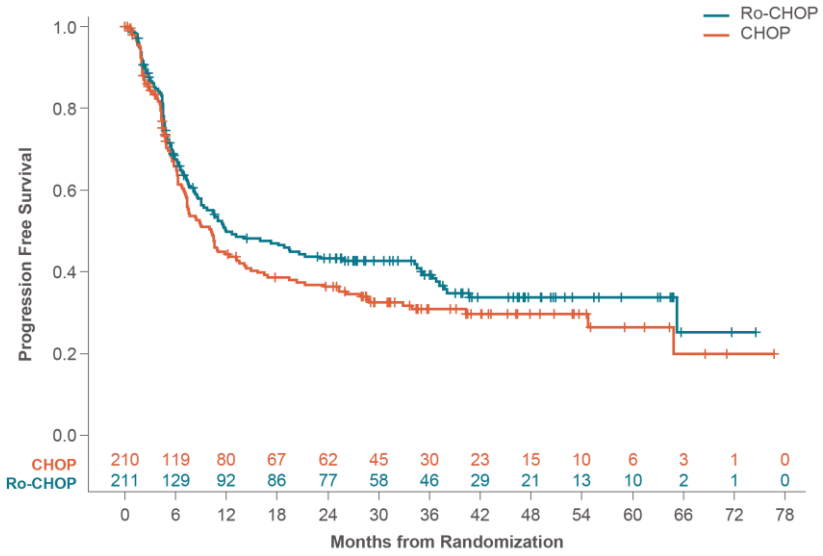
Romidepsin Plus CHOP vs CHOP in Previously Untreated PTCL

Efficacy

Ro-CHOP: Response at End of Treatment

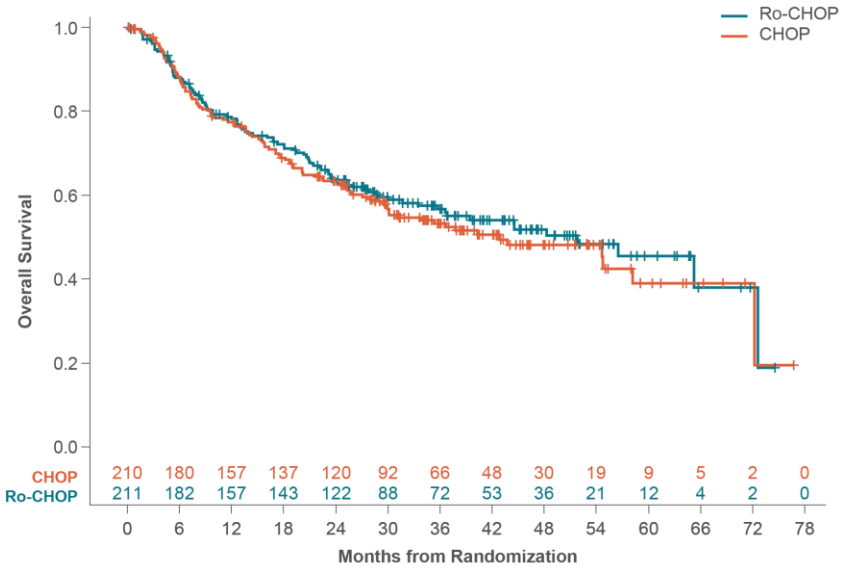


Ro-CHOP: PFS by independent RAC (ITT Population)*



	Ro-CHOP (n = 211)	CHOP (n = 210)
PFS, median (95% CI), mo	12.0 (9.0-25.8)	10.2 (7.4-13.2)
HR (95% CI)	0.81 (0.63-1.04)	
P value	0.096	

Ro-CHOP: OS (ITT Population)



	Ro-CHOP (n = 211)	CHOP (n = 210)
OS, median (95% CI), mo	51.8 (35.7-72.6)	42.9 (29.9-NR)
HR (95% CI)	0.90 (0.68-1.20)	
P value	0.477	

- Bachy E, et al. ASH 2020. Abstract 39.

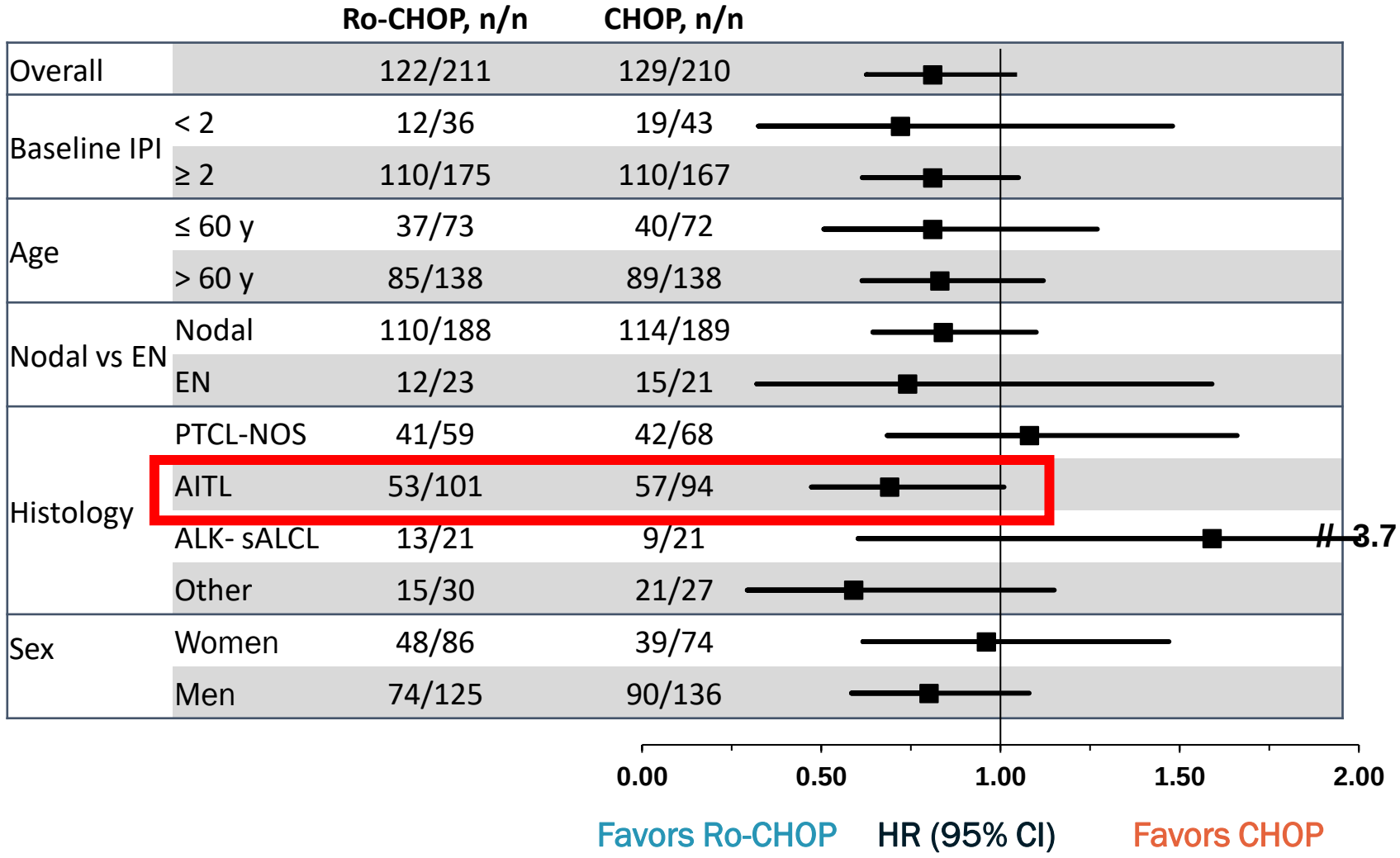
Ro-CHOP
Additional toxicity, Unselected patients

Dose Reductions and Interruptions

≥ 1 TEAE Dose Modification, n (%)	Ro-CHOP (n = 210)	CHOP (n = 208)
Romi red	77 (37)	NA
Romi interrupt	132 (63)	NA
Romi DC	17 (8)	NA
CHOP red	54 (26)	31 (15)
CHOP interrupt	75 (36)	42 (20)

Completed All 6 Cycles w/o Red or Inter, n (%)	Ro-CHOP (n = 210)	CHOP (n = 208)
Romi	62 (30)	NA
CHOP	112 (53)	125 (60)

Subgroup Analysis of PFS (ITT Population)



- Bachy E, et al. ASH 2020. Abstract 39.

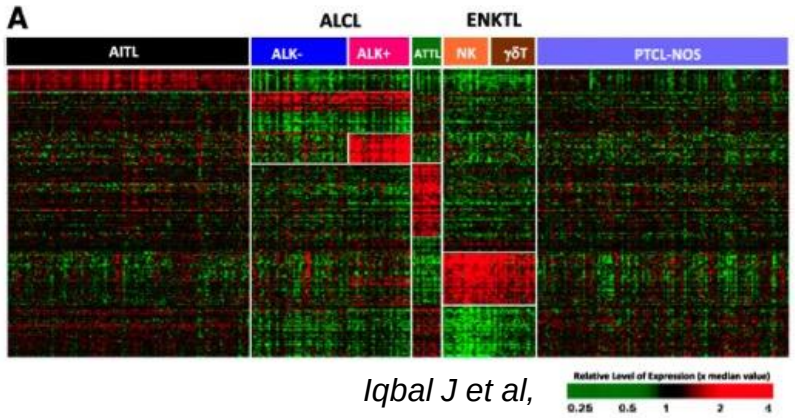
CHOP or CEOP + X: Do Subgroups Benefit From Targeted Therapy?

Novel Agent	Population	Outcome	Group With Benefit
Lenalidomide	AITL aged 60-80 yr	Complete metabolic response not improved*	Yes
Pralatrexate	PTCL-NOS, AITL, ALCL	PFS and OS not improved*	No
Romidepsin	PTCL (all subtypes)	PFS, ORR, OS not improved	No
Alemtuzumab	PTCL age 61-80 yr	Increased response rates, OS not improved	No
Brentuximab vedotin	70% ALCL, other PTCL	Improved PFS and OS	ALCL
Azacitidine	PTCL-TFH (81%)	Produced sustained remission; positive	PTCL-TFH

*Compared with historic controls.

Lemonnier. Blood Adv. 2021;5:539. Advani. Br J Haematol. 2016;172:535. Bachy. JCO 2022;40:242. Wulf. Leukemia 2021;35:143. Horwitz. Lancet. 2019; 393:229. Ruan. ASH 2021. Abstr 138.

PTCL genetics and molecular pathogenesis



Iqbal J et al,

Deregulated pathways

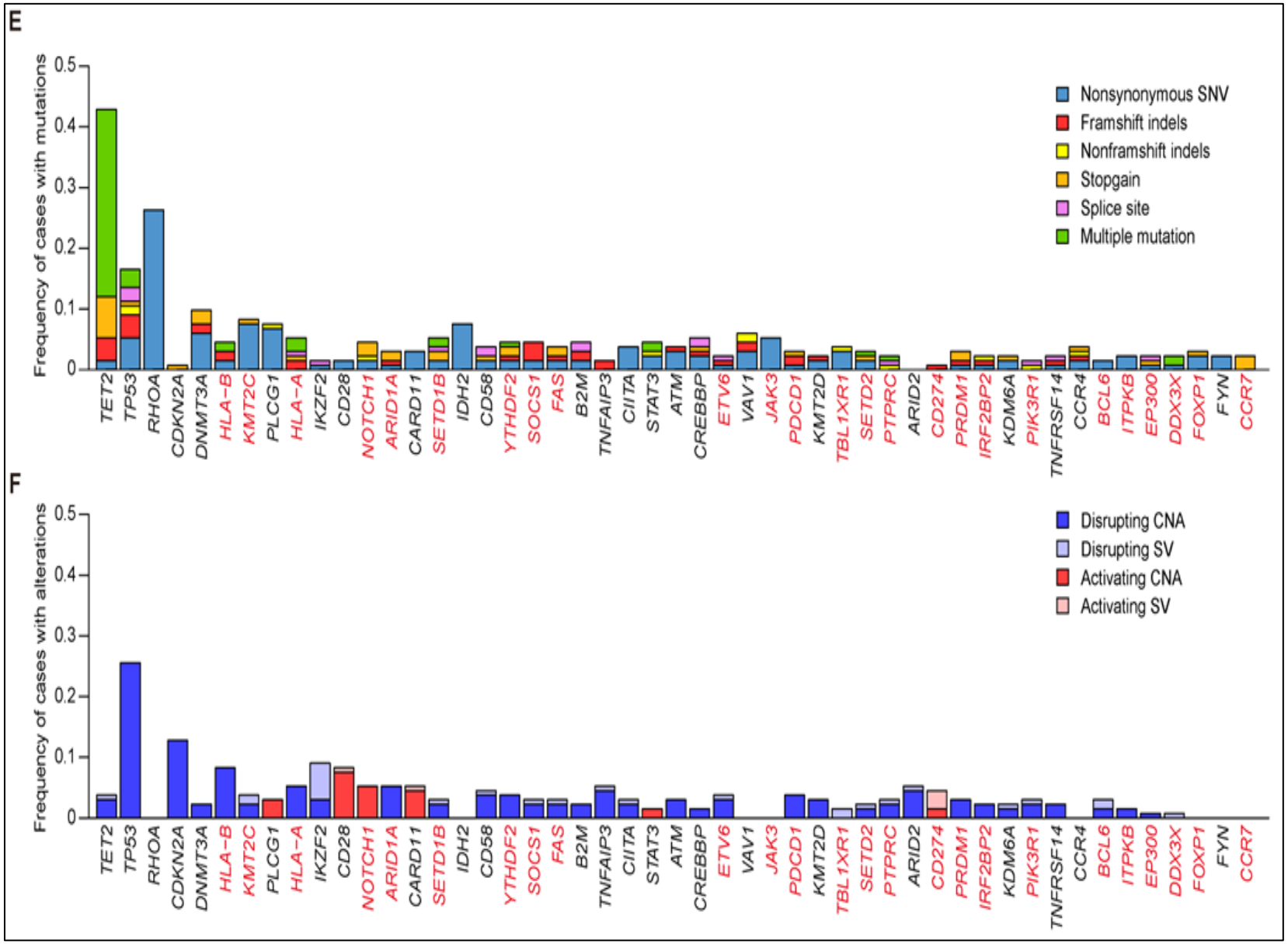
- Epigenetics
- TCR signaling
- JAK/STAT pathway
- Immune evasion
- Cell cycle

- **Gene expression signatures correlate with subtypes**
- **Heterogeneous landscape of somatic mutations**
  - Few highly recurrent mutations, a few variants characteristic of certain entities (RHOA G17V-AITL)
  - A higher number of genes mutated at low frequency
- **Genomic imbalances:**
  - Gene expression deregulation and mutation-induced activation or inactivation
- **Novel gene fusions**
  - Several gene partners, activation (or inactivation) of the gene
  - Overall low frequency
  - *ALK-1,DUSP22, VAV1, TP63, TYK2, ROS1, JAK2, CD28-ICOS, CD28-CTLA4, CARD11-PIK3R3*

Courtesy of and modified from L. de Leval

Genetic Profiling of PTCL-NOS

- N=133 PTCL cases
- 80% carried ≥1 mutation
- 52% had ≥1 CNA/SV
- 49 “recurrently” altered genes (found in ≥ 3 cases)
- But only 10 were affected in more ≥5% of the cases



Watatani Y, et al. *Leukemia,* 2019;134(24):2159-2170

Adding to a CHOP backbone in untreated PTCL

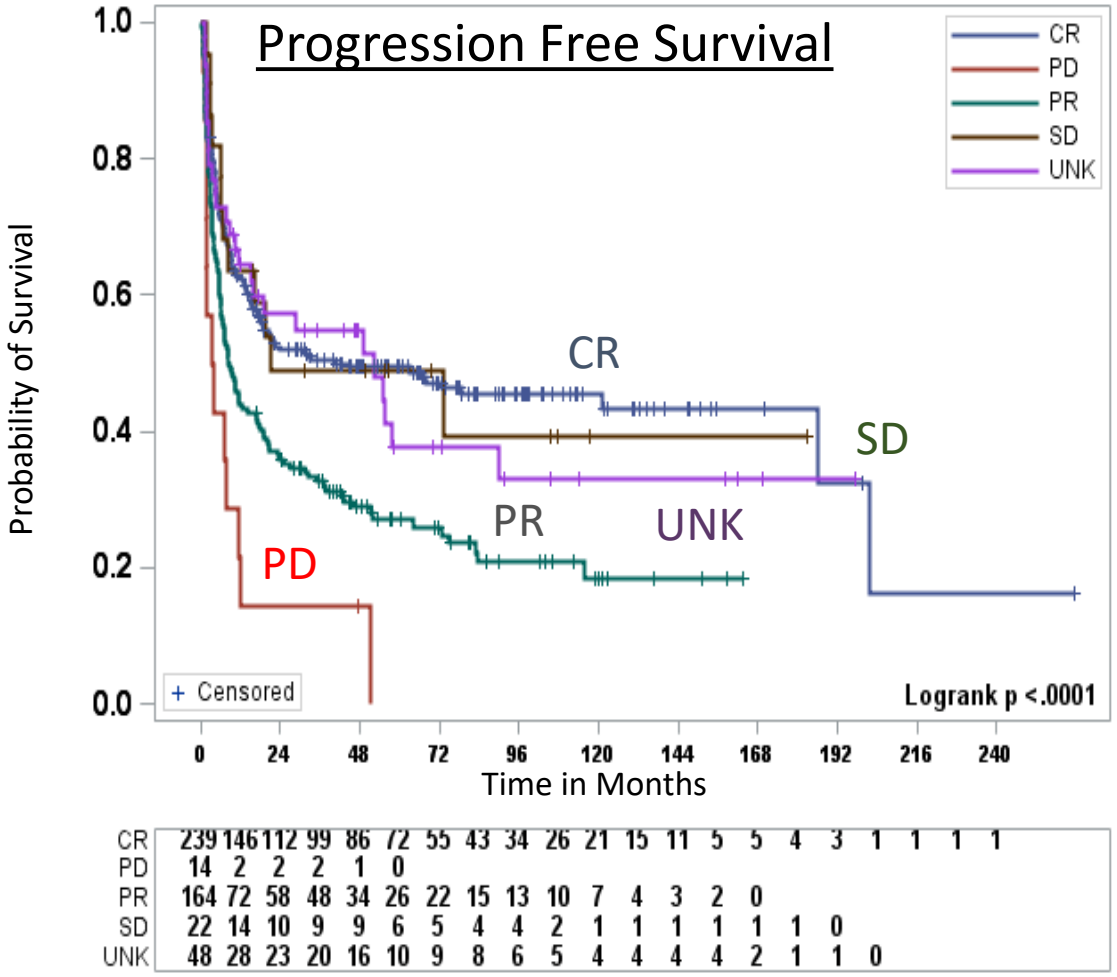
- ALCL
  - BV-CHP-Overall survival benefit
  - *standard of care*

- PTCL-NOS, AITL
    - CD30 expressing -Subset size precludes statistical conclusions
    - BV and/or Etoposide -*might* add to CHOP (Schmitz et al Blood 2010; Herrera et al ASH 2021)
    - Imperfect datasets
    - Other agents no clear benefit
      - Inadequate efficacy
      - One size fits all for a heterogenous group
      - Increased toxicity
  - Limited to no data in other less common subtypes

  - Adding an active drug to *CHOP* AND Enriching for those most likely to benefit AND no significant increase in toxicity-can be successful-but this is hard

Relapsed T-cell Lymphoma

Allogeneic SCT can be Curative: Depth of Remission at Time of Transplant Matters



Response	N	Median PFS in months (95% CI)	Median OS in months (95% CI)
CR	**239**	**44.6** (17.9-201.5)	**154.2** (72.8-201.5)
PR	**164**	**8.5** (6.1-16.6)	**31.3** (16.8-64.2)
SD	**22**	**21.0** (6.0- NR)	**12.4** (12.5-NR)
PD	**14**	**3.5** (1.5-11.2)	**8.9** (2.3-51.4)

Responses were based on the treating physician determination (CT or PET/CT)

Mehta-Shah, N et al. ASH 2020 a41

"Standard" Agents in R/R PTCL

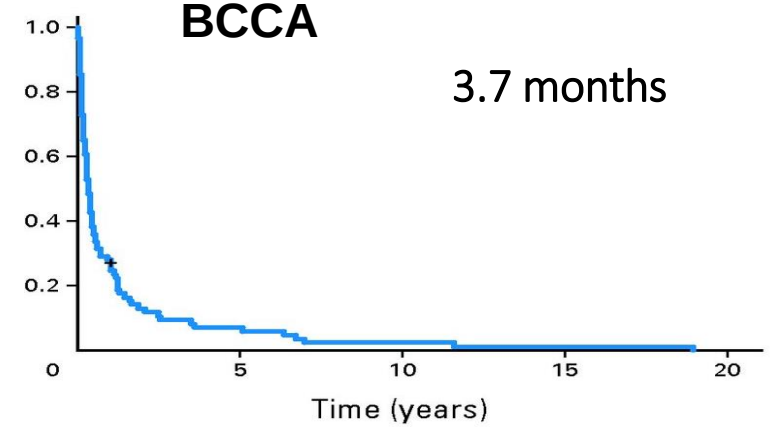
Agent	Mechanism	Response	Median DOR (m)
belinostat	HDAC inhibitor	ORR: 25.8% CR: 10.8%	13.6
brentuximab vedotin	CD30 ADC	ALCL: ORR: 86% CR: 57% PTCL/AITL: ORR: 41% CR: 24%	25.6 7.6
pralatrexate	DHFR inhibitor	ORR: 29% CR: 10%	10
Romidepsin*	HDAC inhibitor	ORR: 25-38% CR: 15-18%	8.9 – 17

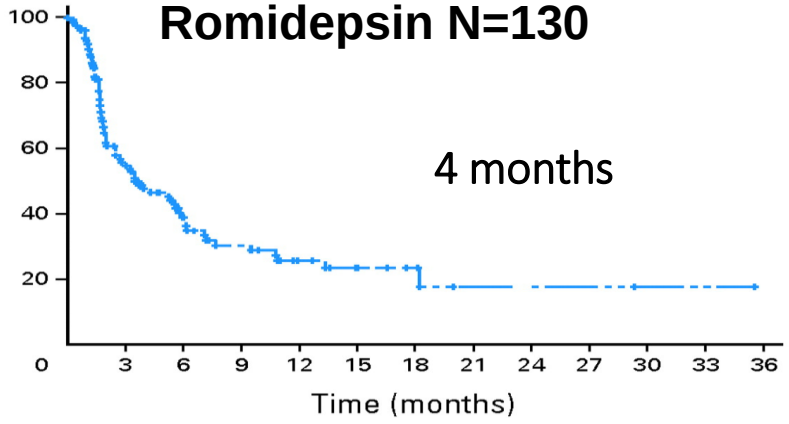
*Accelerated approval withdrawn by Bristol Myers Squibb

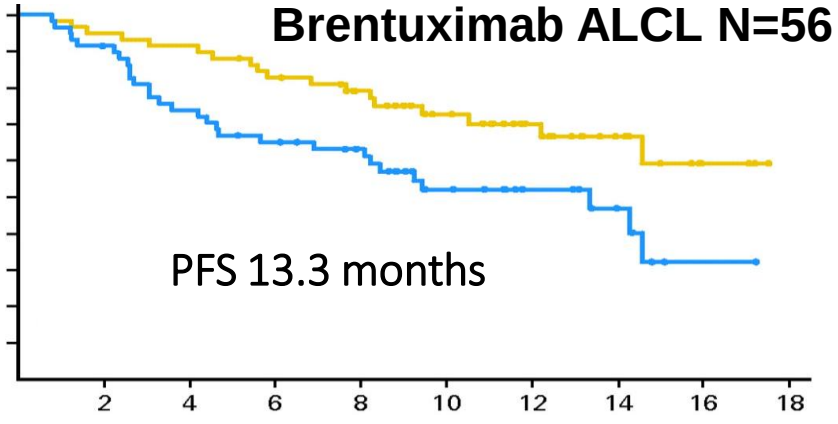
(O'Connor et al., JCO 2015; Pro et al., JCO 2012; Horwitz et al., Blood 2014; O'Connor et al., JCO 2011; Piekarz et al., Blood 2011; Coiffier et al., JCO 2012; Brammer et al., ASH 2021: Poster 2456)

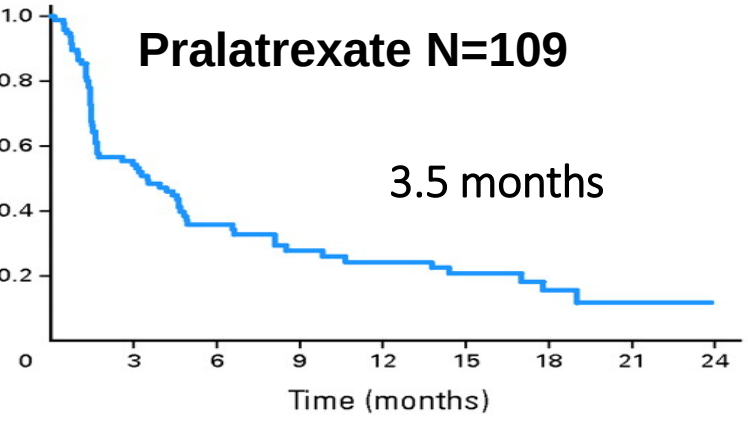
*

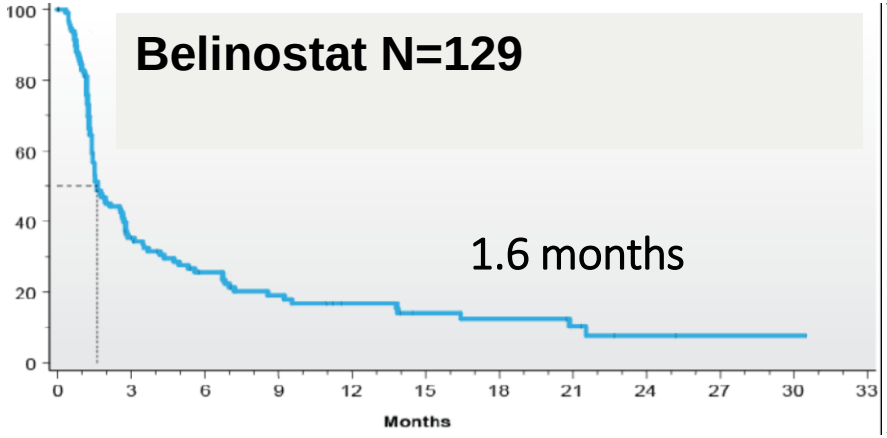
Progression Free Survival: Relapsed/Refractory PTCL

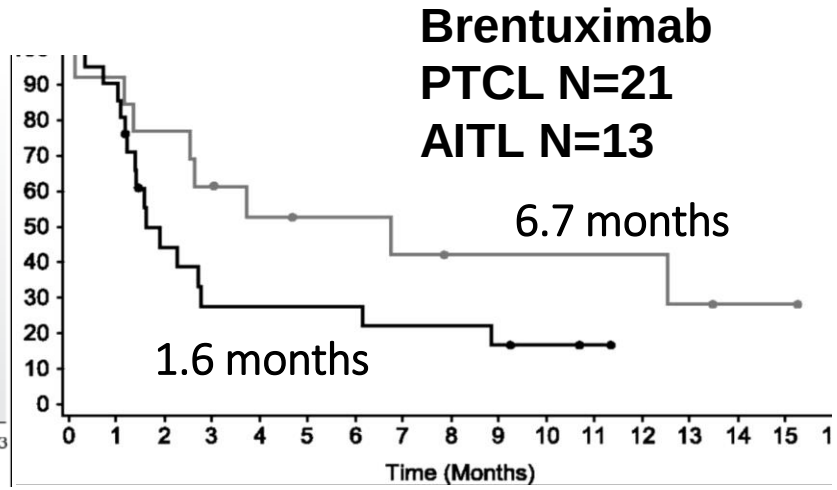












Mak V et al. JCO 2013;31:1970-1976, O’ Connor OA, et al. *J Clin Oncol*. 2011;29:1182-1189,Coiffier B, et al. *J Clin Oncol*. 2012;30 :631-636, O’Connor OA et al ASCO 2013, Pro B, et al. J Clin Oncol. 2012;30:2190-2196, Horwitz S M et al. Blood 2014;123:3095-3100

Other Emerging Therapies in PTCL

- Jak inhibitors
- Pi3K inhibitors-Duvelisib
- EZH 1/2 inhibitors-Valemetostat
- Immune Therapies-very early
  - Bispecifics
    - CD16/CD30 (NCT04101331)
    - PD-1-CD3 (NCT05079282)
  - Anti-CD47 antibody (magrolimab) + mogamulizumab: (NCT04541017)
  - CD5.CART T-cell: phase I ongoing (NCT03081910)
  - Allogeneic anti-CD70 CAR T-cells (CTX130): (NCT04502446)
  - CD30 CAR T-cells co-expressing CCR4: (NCT03602157)

Peripheral T-cell lymphoma - first-line treatment and beyond

- PTCL remains heterogeneous and poor prognosis, however:
  - Cures for some with combination chemotherapy
    - Majority do not respond or relapse after initial therapy
    - Many subtypes no standard approach
  - Remains high unmet need
- Attempts to incorporate into combination/upfront/curative therapy
    - Active agents
    - Enriched population + minimize toxicity
    - Subtype specific strategies: Disease subtypes, molecular subtypes, other
- Newer Approaches
  - Epigenetic therapies, signaling targets, immune therapy
  - Need more therapies, More effective therapies

Autolus

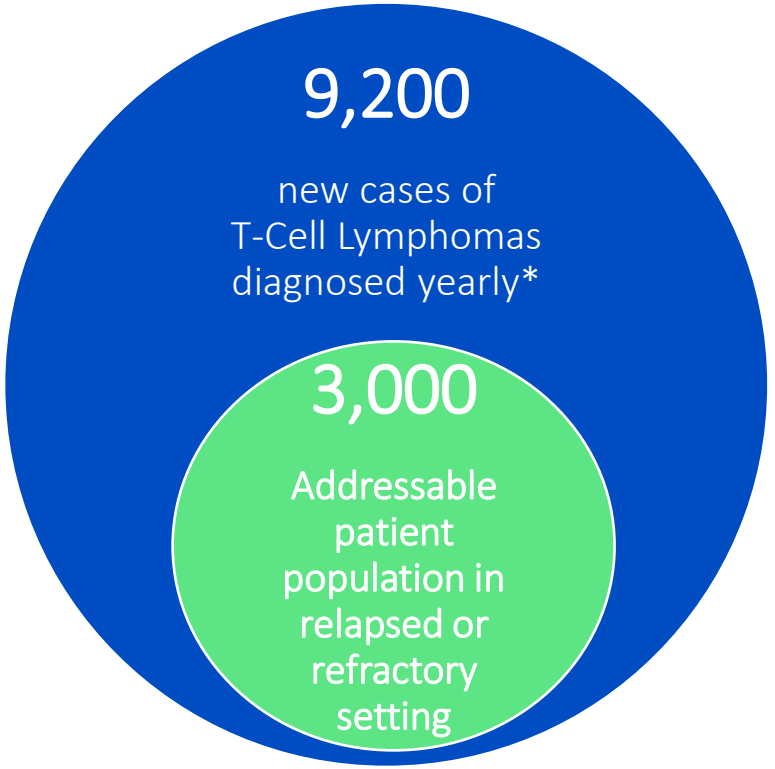
Dr. Martin Pule

Introduction to AUTO4 and AUTO5

AUTO4 and AUTO5 for Peripheral T-Cell Lymphoma

T-Cell Lymphoma is an aggressive disease with a very poor prognosis

- A large portion of T-Cell Lymphoma patients are refractory/relapse following first-line treatment (68%)[3]
- Standard of care is variable and often based on high-dose chemotherapy and stem cell transplants:
  - Median 5 yrs OS: 32% [1]
- Relapsed/refractory patients have a worse prognosis
  - Median PFS approximately 3 months/ Median OS < 6 months [2,3]
- Brentuximab survival benefit restricted to CD30 positive ALCL subtype[4]
  - approx. 12% of total PTCL patient population[4,5]
- T cell lymphoma has not benefited from advances in immunotherapy
  - Pan T-cell depletion highly toxic; few/no tumor-specific antigen targets



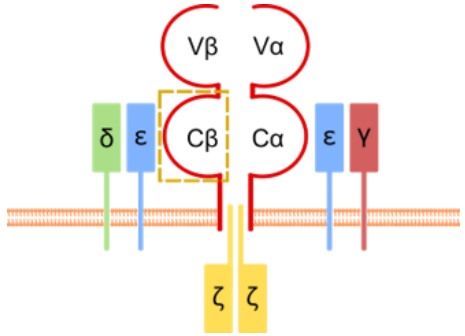
*Japan, US and EU5 (DRG Epidemiology Data)

[1] Weisenburger et al., Blood 2011; [2]Mak et al, JCO 2013; [3]Bellei M et al, Haematologica 2018, [4]Horwitz et al, Lancet, 2019, [5]Vose et al., JCO 2008

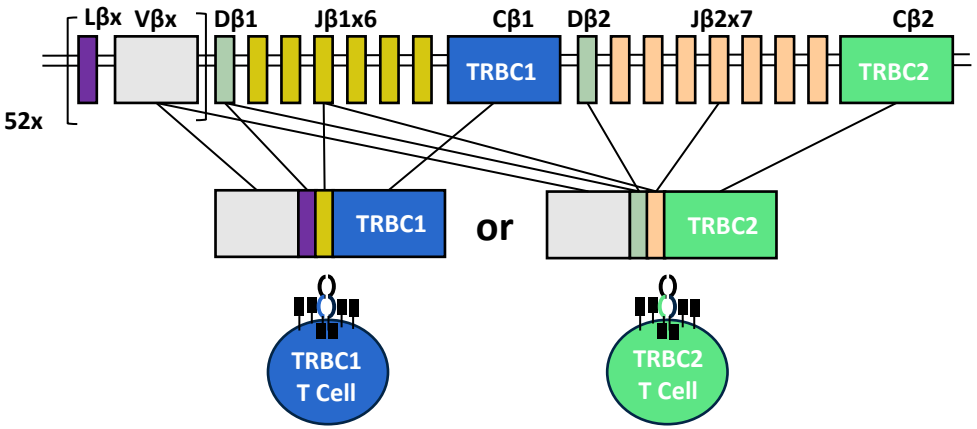
Mature T cells express either TRBC1 or TRBC2

T-Cell Lymphomas are also clonal and express either TRBC1 or TRBC2

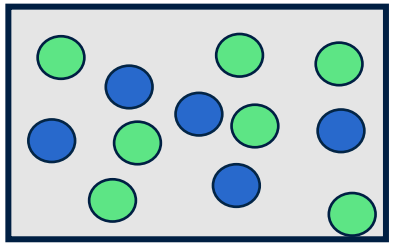
Structure of the T Cell Receptor or TCR



Duplication of β chain constant region gene



Healthy T Cells

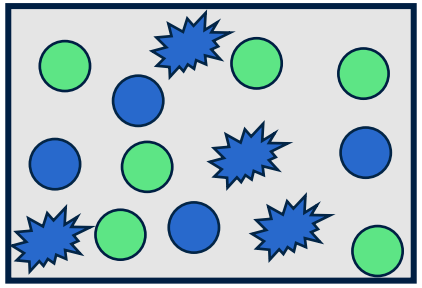


Contain mixture of

TRBC1+ cells

TRBC2+ cells

TRBC1+ T cell lymphoma

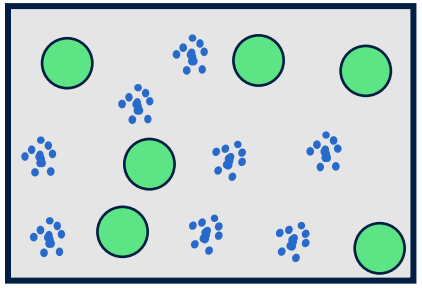


TRBC1+ tumour cell

TRBC1 CAR

TRBC2+ normal T cells retained

(immunity maintained)

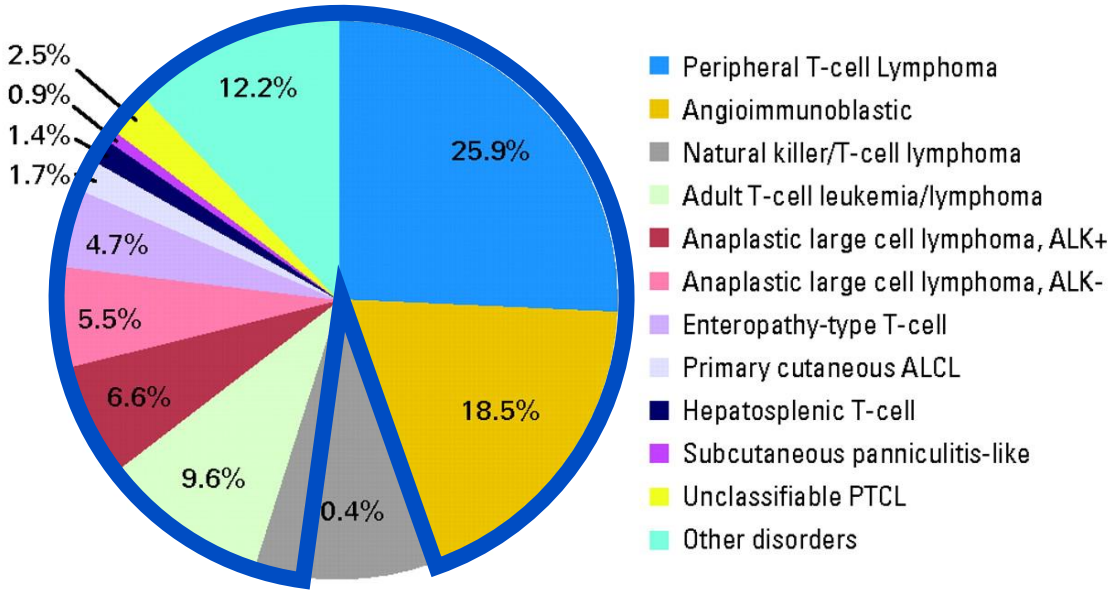


TRBC1+ cells killed
(tumour & healthy)

Maciocia et al., Nature Medicine, 2017

TRBC1/TRBC2 targeting approach applicable to 95% of TCL subtypes

Distribution of cases by subtype



Subtypes that are TRBC1 or TRBC2 positive

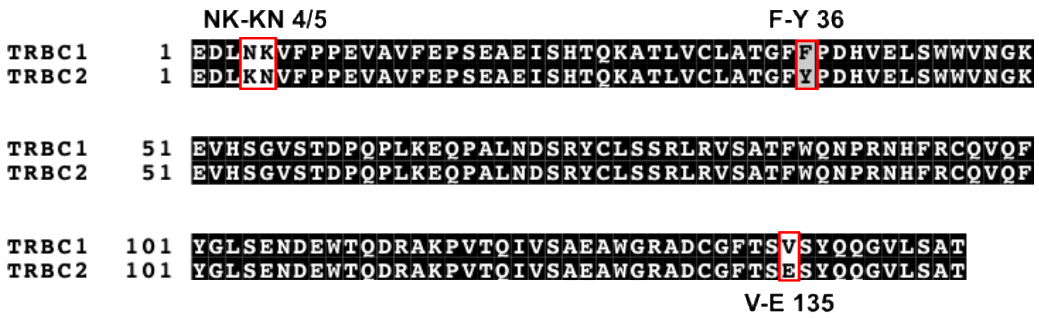
- High and homogeneous expression of TRBC1 or TRBC2 is seen in the majority of TCL subsets - 95% of cases
- TRBC1 and TRBC2 will not be expressed in NK cell lymphomas or rare gamma delta t-cell lymphomas
- Other potential TCL targets:
  - Highly restricted in their expression
  - High and homogenous expression of CD30 is restricted to ALCL subset - 12% of cases
  - Widely expressed on normal T cells and therefore come with a significant risk of toxicities

Source: International T-Cell Lymphoma Project published in Journal of Clinical Oncology 2008 264124-4130

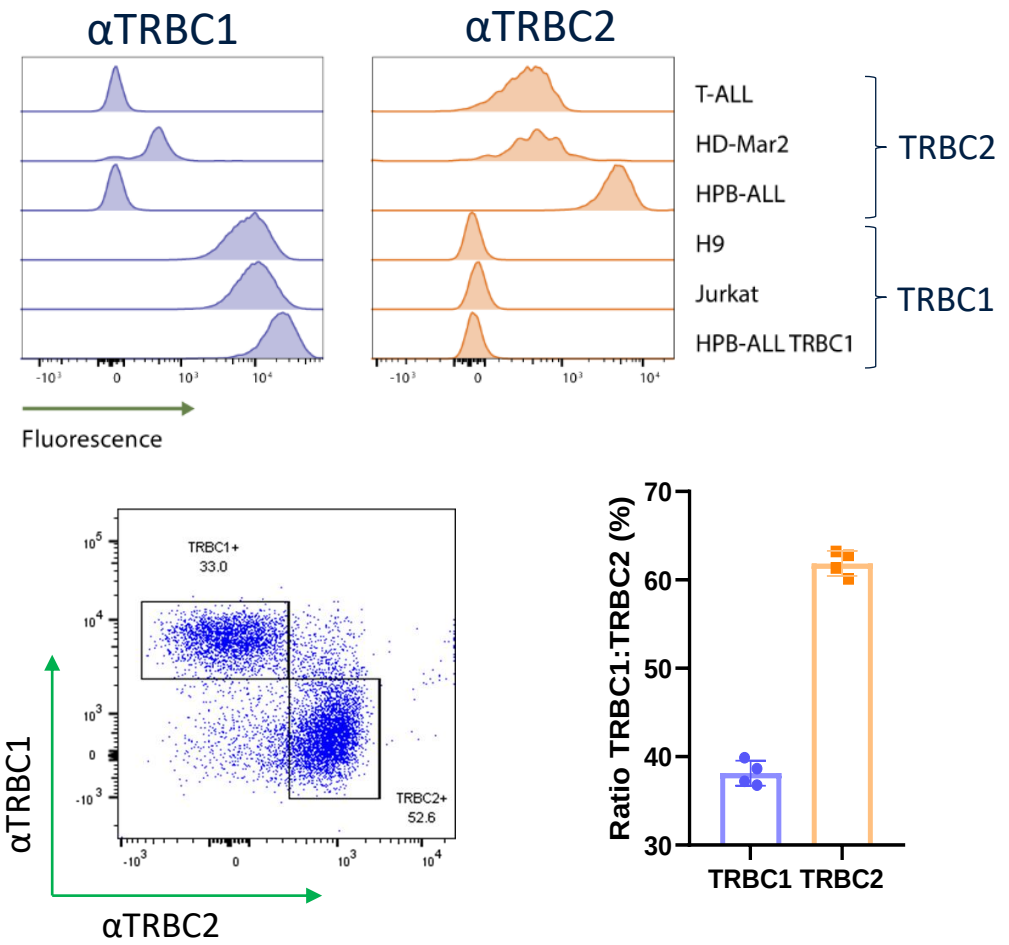
Development of TRBC1 and TRBC2 selective antibodies

TRBC1 and TRBC2 proteins are very similar

Our antibodies are designed to selective target the NK-KN inversion at position 4/5



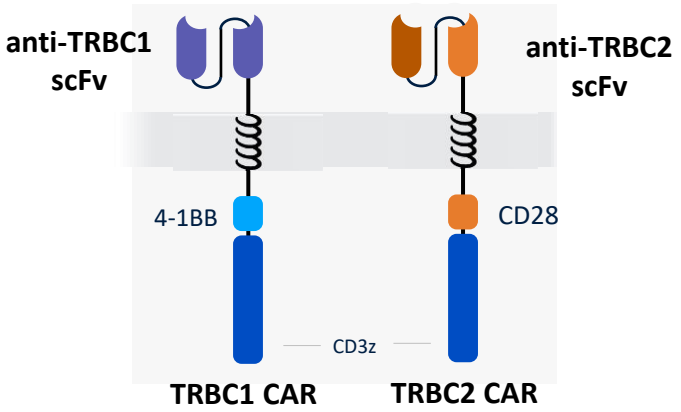
TRBC1 and TRBC2 discrimination on tumour cell lines and in healthy peripheral blood T cells

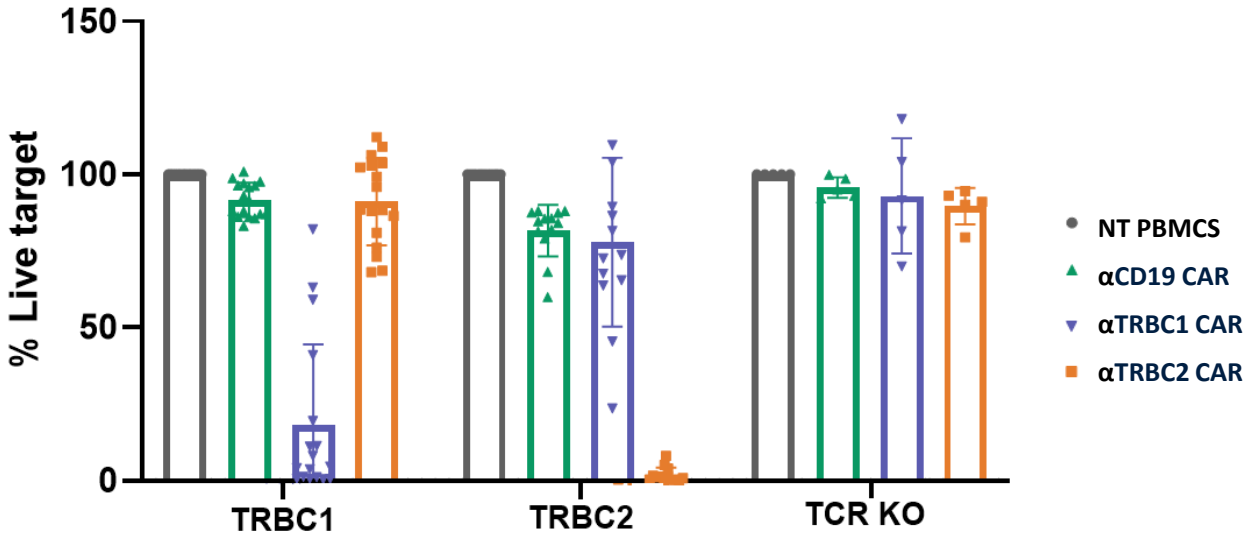


Maciocia et al., Nature Medicine, 2017 and Ferrari et al., in press 2022

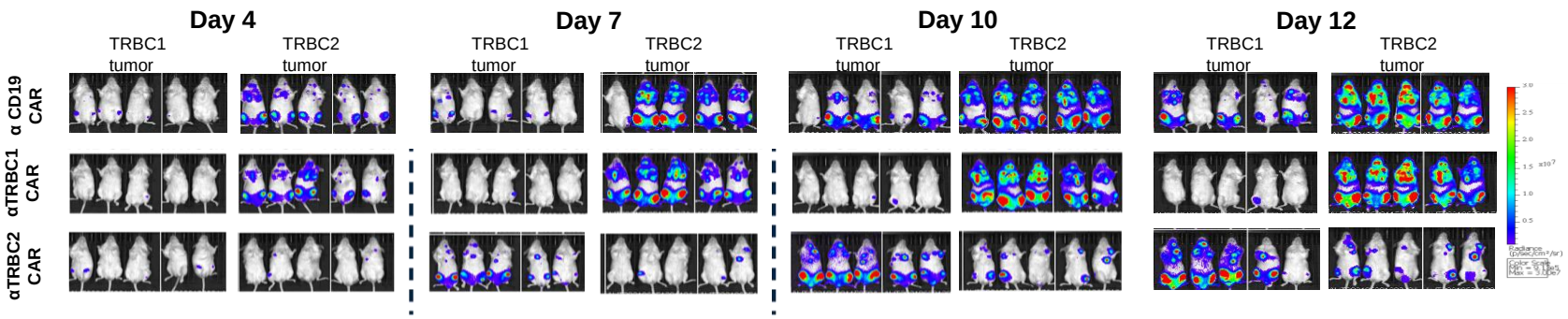
Development of αTRBC1 and αTRBC2 CAR T cells

Demonstration of in vitro and in vivo selectivity and activity against TRBC1 and TRBC2 target cells





1:16 E:T ratio, 72h timepoint, n = 17 for TRBC1 and TRBC2+ targets, n = 5 for TCR KO targets



Ferrari et al., In Press 2022

Three key elements to address T-Cell Lymphomas

Multiple approaches de-risked for development

Companion Diagnostic

Stratify into TRBC1 + and TRBC2 + lymphoma

> ~40% of T-Cell Lymphomas are TRBC1+

AUTO4 – TRBC1+ TCL

AUTO5 – TRBC2+ TCL

> ~60% of T-Cell Lymphomas are TRBC2+

Current Development Milestone

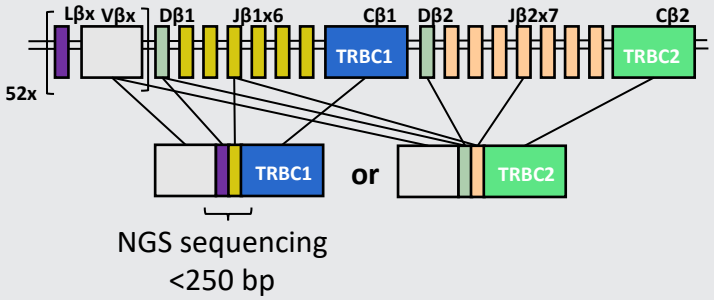
Phase 1 dose escalation

Candidate selected

Companion Diagnostic

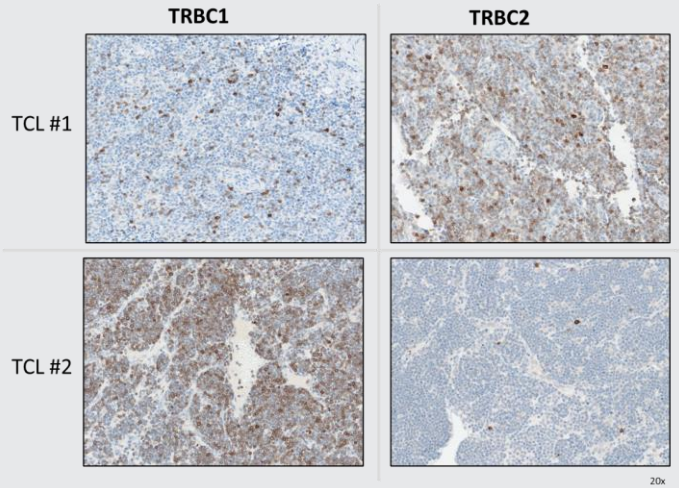
Multiple approaches de-risked for development

Next Generation Sequencing



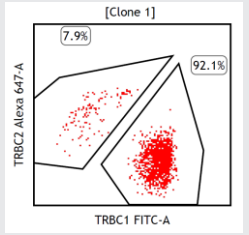
T cell clonality NGS assay currently used in AUTO4 Phase 1

Immunohistochemistry

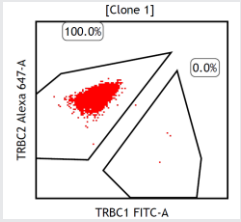


FFPE specific antibodies can discriminate between TRBC1 and TRBC2 patient tumors

Flow Cytometry



TRBC1 positive T-cell Prolymphocytic Leukemia



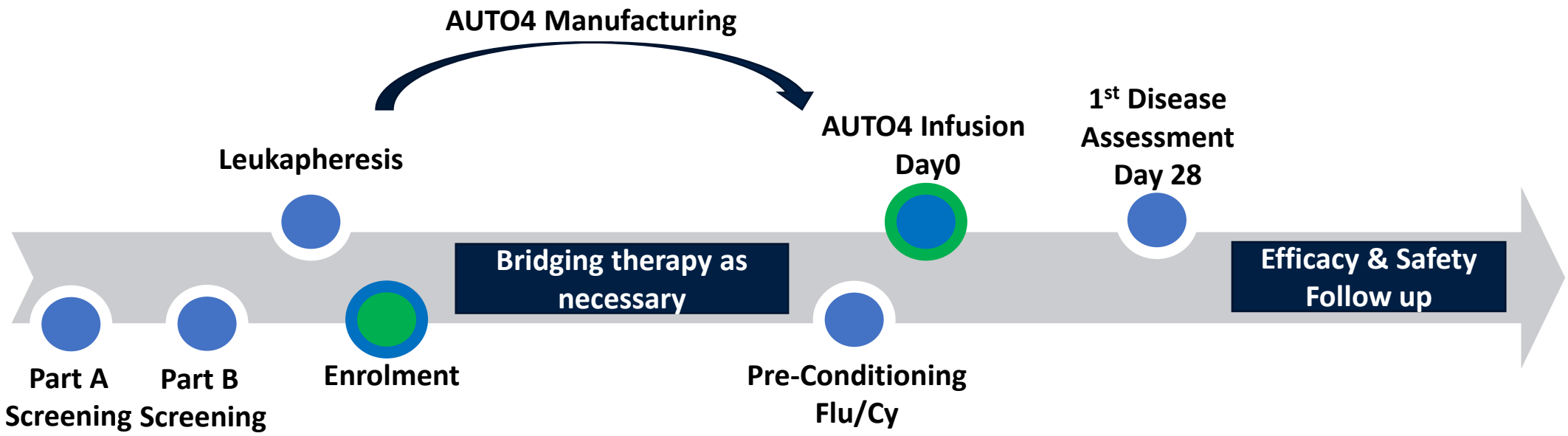
TRBC2 positive small Sezary cell cutaneous T-Cell Lymphoma

Flow specific antibodies can discriminate between TRBC1 and TRBC2 in patient tumors

Dr. Kate Cwynarski

Phase 1/2 Study of AUTO4 in r/r TRBC1 Positive Peripheral T-cell Lymphomas

Study design



- Part A: Lymphoma tissue screening for TRBC1 or TRBC2 expression using NGS
- Part B: Study screening for patients determined to have TRBC1+ Lymphoma

Baseline Characteristics

AUTO4 findings / clinical data

	Total (N=10)
Age, median (range)	55 (34 – 63)
Median prior lines of treatment (range)	3 (1 – 5)
Stage of Lymphoma at screening • I/II • III/IV	 2 (20%) 8 (80%)
Lymphoma Subtype, n (%) • Peripheral T-cell lymphoma NOS • Anaplastic large cell lymphoma, ALK-negative • Angioimmunoblastic T cell lymphoma (AITL)	 5 (50%) 1 (10%) 4 (40%)
Prior Autologous Stem Cell Transplant, n (%)	3 (30%)
ECOG 0/1, n (%)	3 (30%), 7 (70%)
Bridging therapy YES, n (%)	7 (70%)

Data Cut-off: 26 April 2022

Key Safety Data

AUTO4 findings / clinical data

	Cohort 1 $25x10^6$ cells (N = 3)	Cohort 2 $75x10^6$ cells (N = 2)	Cohort 3 $225x10^6$ cells (N = 1)	Cohort 4 $450x10^6$ cells (N = 4)	Total (N = 10)
Dose Limiting Toxicity (DLT)	0	0	0	0	0
Grade 3 or 4 TEAE within 60 days	3 (100%)	2 (100%)	1 (100%)	4 (100%)	10 (100%)
Neutropenia	3 (100%)	2 (100%)	0	3 (75%)	8 (80%)
Infections and Infestations	0	0	0	0	0
Serious TEAE	2 (67%)	0	0	2 (50%)	4 (40%)
Any grade CRS	0	0	0	4 (100%)	4 (40%)
Grade 3 CRS	0	0	0	1 (25%)	1 (10%)
Any grade ICANS	0	0	0	0	0

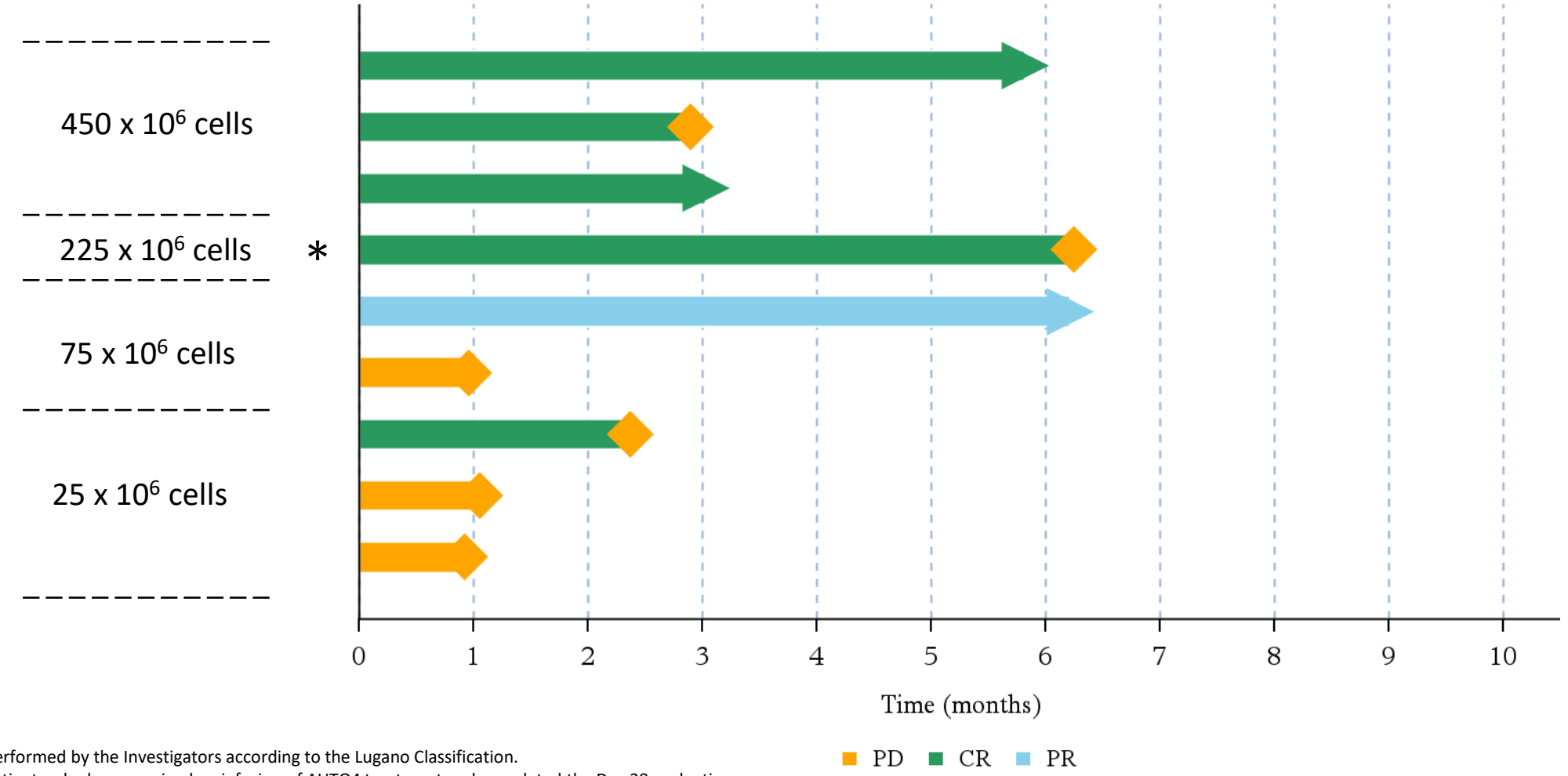
Safety set is all infused (n=10)

TEAE - **Treatment-emergent adverse events;** CRS - cytokine release syndrome; ICANS - Immune Effect Cell-Associated Neurotoxicity Syndrome

Data Cutoff: 26 April 2022

Initial data encouraging

All patients treated at highest dose level had a complete metabolic response

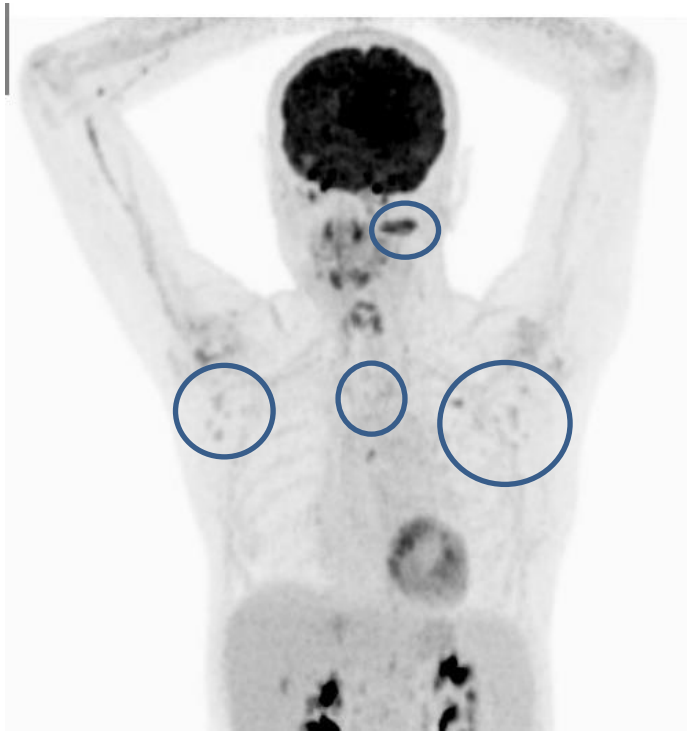


Efficacy assessments were performed by the Investigators according to the Lugano Classification.
† Evaluable Set consists of patients who have received an infusion of AUTO4 treatment and completed the Day 28 evaluation.
All patients had relapsed/refractory disease at time of Part B screening and enrolment.
* Patient was PET-negative at the start of pre-conditioning therapy.

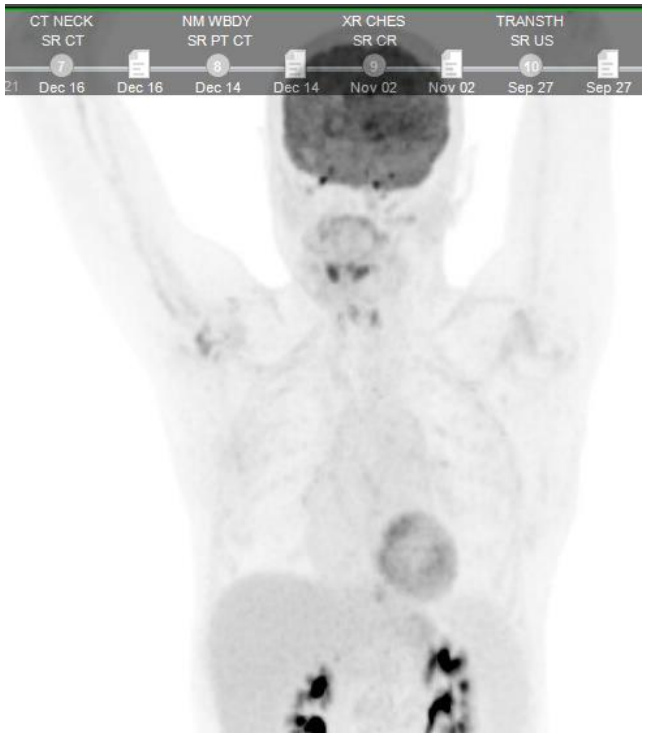
Data Cut off: 26 April 2022

PET scans for patient given 450 x 10^6 CAR T cells

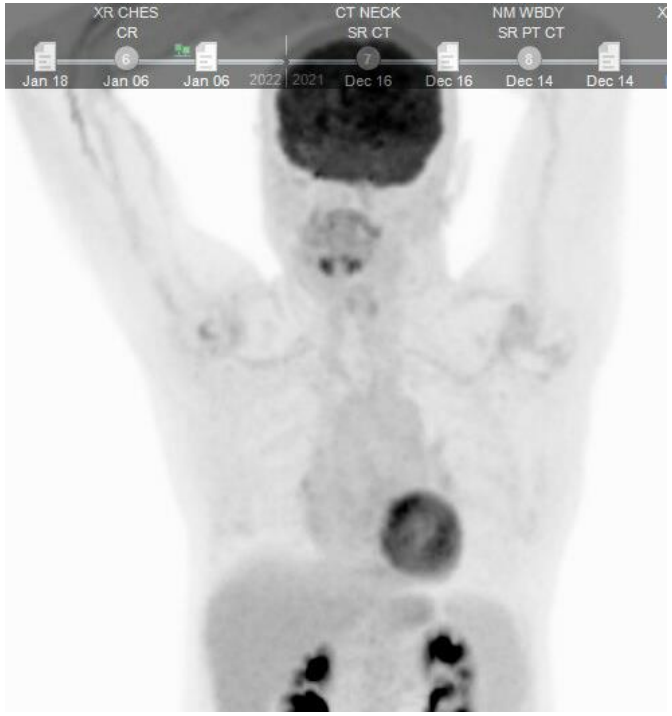
Patient refractory to prior therapies achieved a metabolic complete response



Baseline



Day 28 post-infusion

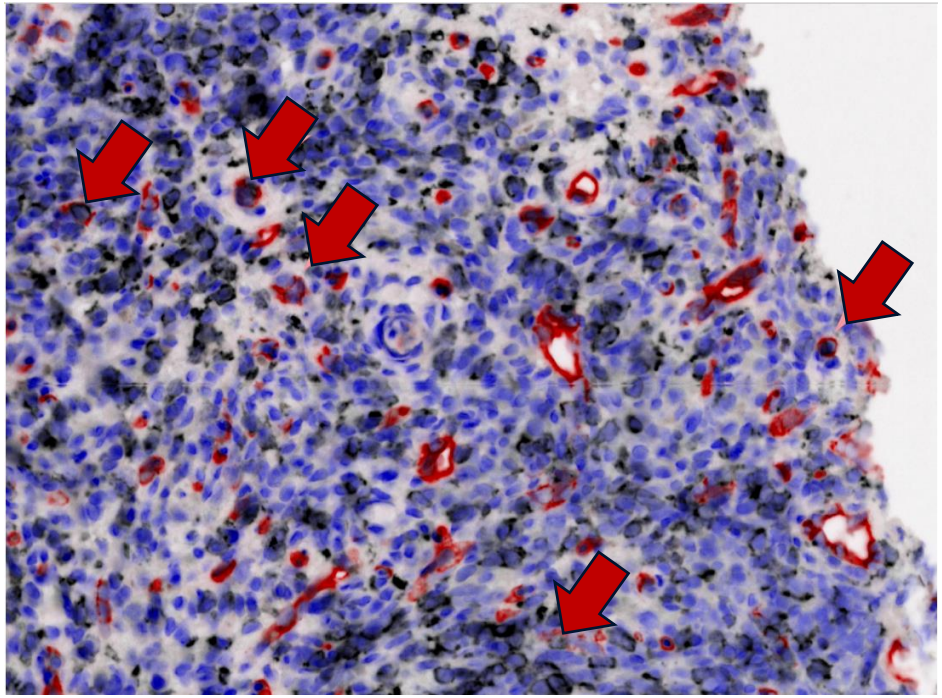


3 months post-infusion

Data Cutoff: 26 April 2022

CAR T cells detected in lymph node but not in peripheral blood

- CAR T cells detected in a lymph node biopsy of a patient who achieved complete remission
  - Approx 2% nucleated cells in lymph node are CAR T cells (n=1)[1]
- No CAR T expansion detected by PCR or flow in peripheral blood



Double staining for CAR T cell (red) and CD3 (black) x40 IHC view (deconvoluted)[1]

CAR T cell – double stained for CAR and CD3

[1]Professor Teresa Marafioti, personal communication

Data Cutoff: 26 April 2022

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AUTO4 Summary and Next Steps

AUTO4 summary and next steps

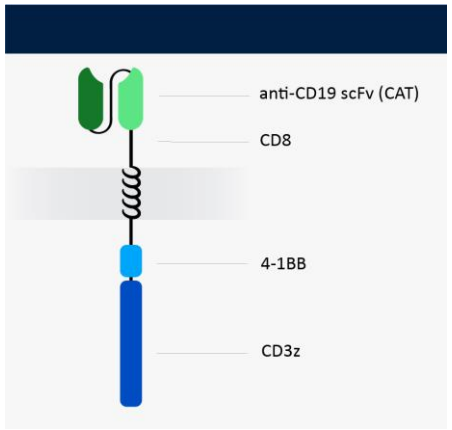
- AUTO4 treatment generally well tolerated
- Early efficacy is encouraging, particularly with all patients responding at higher dose levels
- CAR T-cells detected in lymph node but no expansion observed in peripheral blood
- Study ongoing, with additional patients due to be treated to define recommended Phase 2 dose

Autolus

Dr. Martin Pule

obe-cel life cycle management

obe-cel has a unique mechanism of action



CD19 binder with fast off-rate

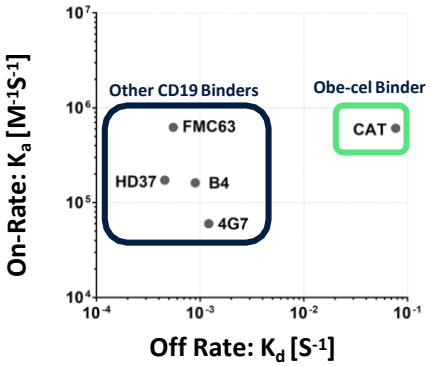
- **Improved potency, reduced toxicity**

Avoids over-activation of CAR T cells
-> Reduced toxicities

Increased CAR T peak expansion
-> Improved persistence

Avoids exhaustion of CAR T cells
-> Improved engraftment
-> Improved persistence

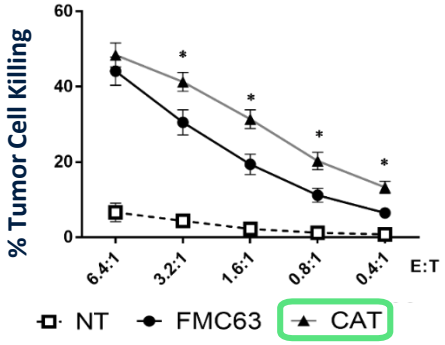
- **Fast off-rate**

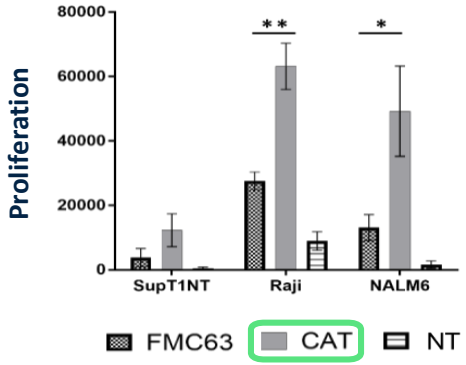


obe-cel has a shorter half-life of interaction compared to binders used in approved products

- obe-cel = 9.8 seconds
- Kymriah® = 21 minutes

- **Enhanced cytotoxicity and proliferation**





Ghorashian et al. *Nature Medicine* 2019

Capitalising on the unique profile of obe-cel

- Clinical data supports differentiated product profile
  - High degree of activity and persistence -> drives long term outcomes
  - Potential best-in-class safety profile -> will drive adoption of obe-cel in all clinical settings
  - Initial NHL data is consistent with this profile

- Solid foundation for onward development

PRODUCT	INDICATION	TARGET	STUDY NAME	PHASE
obe-cel	Adult ALL	CD19	FELIX	Pivotal
obe-cel	B-NHL & CLL	CD19	ALLCAR19*	Phase 1
obe-cel	Primary CNS Lymphoma	CD19	CAROUSEL*	Phase 1
AUTO1/22	Pediatric ALL	CD19 & CD22	CARPALL*	Phase 1

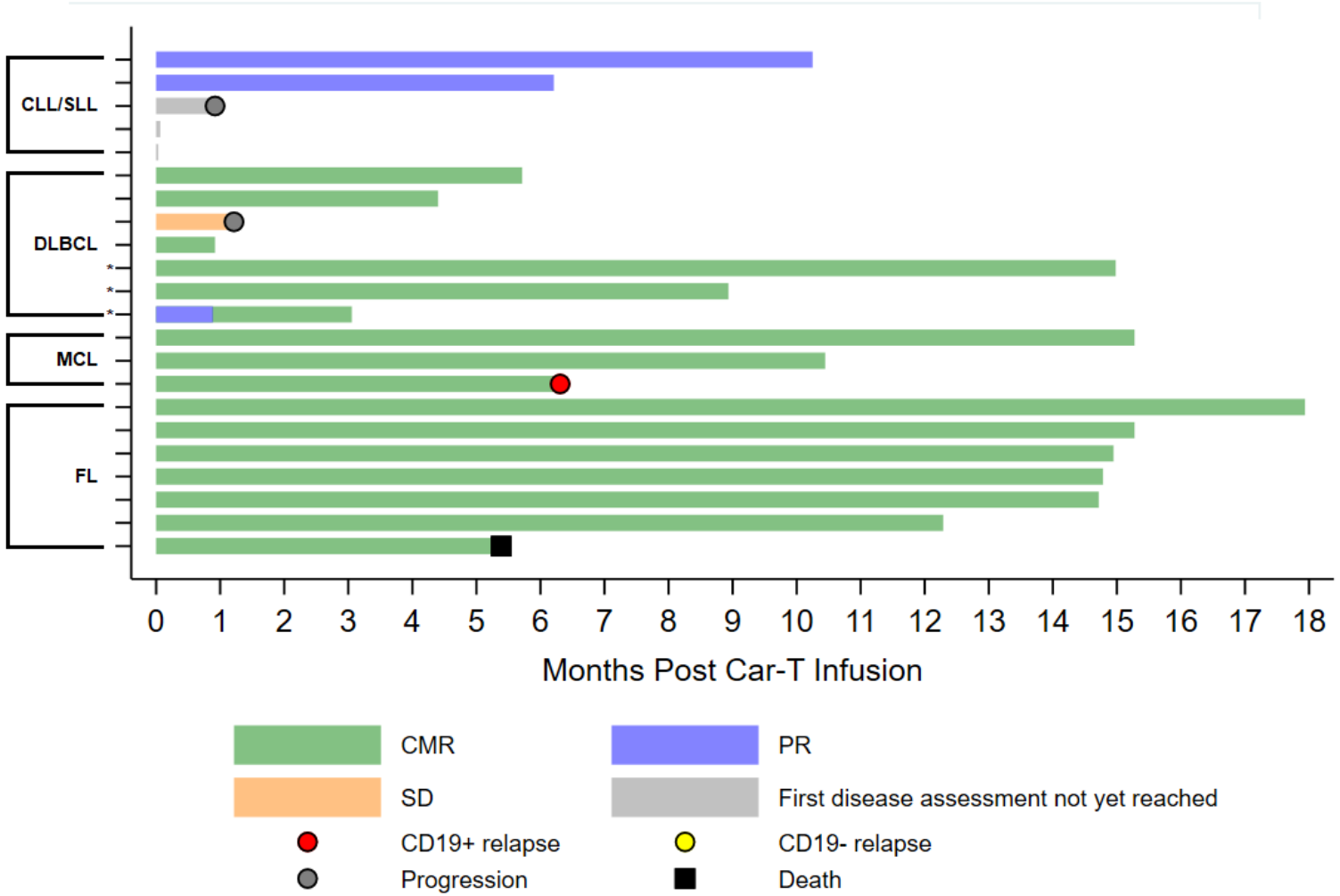
B Cell Malignancies

* Collaboration with UCL

obe-cel shows encouraging efficacy and duration of response in NHL/CLL

Long term persistence drives durable outcomes

	N (%)
Follicular Lymphoma	
CR + PR	7 (100%)
CR	7 (100%)
	1 death in CR from Covid19
DLBCL	
CR + PR	6 (84%)
CR	6 (84%)
SD	1
	1 PD at day 37
MCL	
CR + PR	3 (100%)
CR	3 (100%)
	1 relapse at 6 months
CLL/SLL	
CR + PR	2 PR (67%) (BM MRD-neg.)
PD	1
Pending	2



Median (Range) Follow-Up Time:

- FL/DLBCL: 9.2 Months (Range 1.9-19.1)
- MCL/CLL: 8.9 Months (Range 0.0-19.7)

DLBCL* = transformed follicular lymphoma

Data Cut-off: 12-May-2022

Primary CNS Lymphoma: favorable tolerability profile

- No grade high grade CRS was observed using IV or intraventricular obe-cel administration
- 2 cases of grade 3 ICANS were reported following IV infusion
  - 1 patient improved with steroids / toci
  - 1 patient had several neurological deficits consistent with progressive disease and didn't respond to steroids / toci
- 2 patients died from progressive PCNSL

Adverse Events of Special Interest

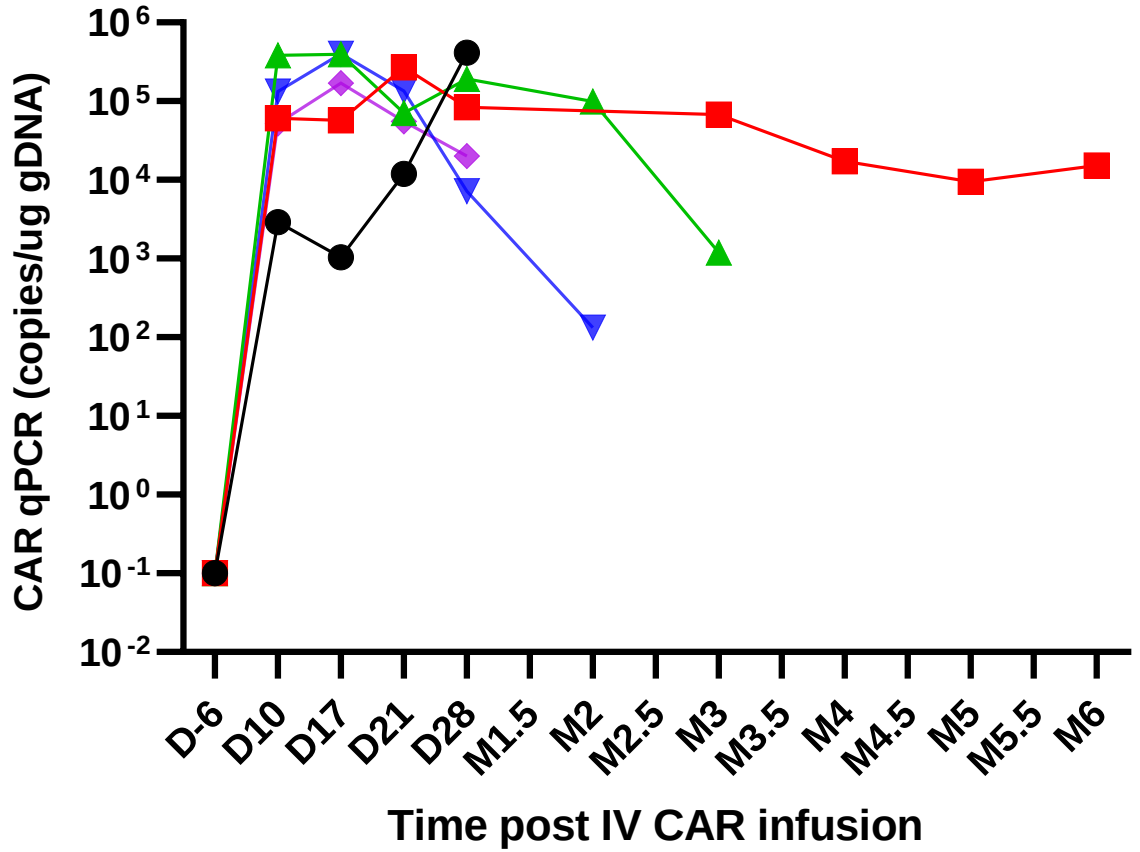
Event N = 6 patients	All Grades n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
CRS*	6	2	4**	0	0
ICANS	3	1	0	2	0

*CRS grading by grading by ASTCT consensus criteria, Lee et al 2019
**Grade 2 CRS in 3 patients with IV AUTO1 and 1 patient with I-VEN AUTO1

Data Cut-off: 12-May-2022

obe-cel shows excellent T cell expansion and engraftment

Persistence of obe-cel demonstrated by qPCR



- Persistence in all treated patients at last follow-up

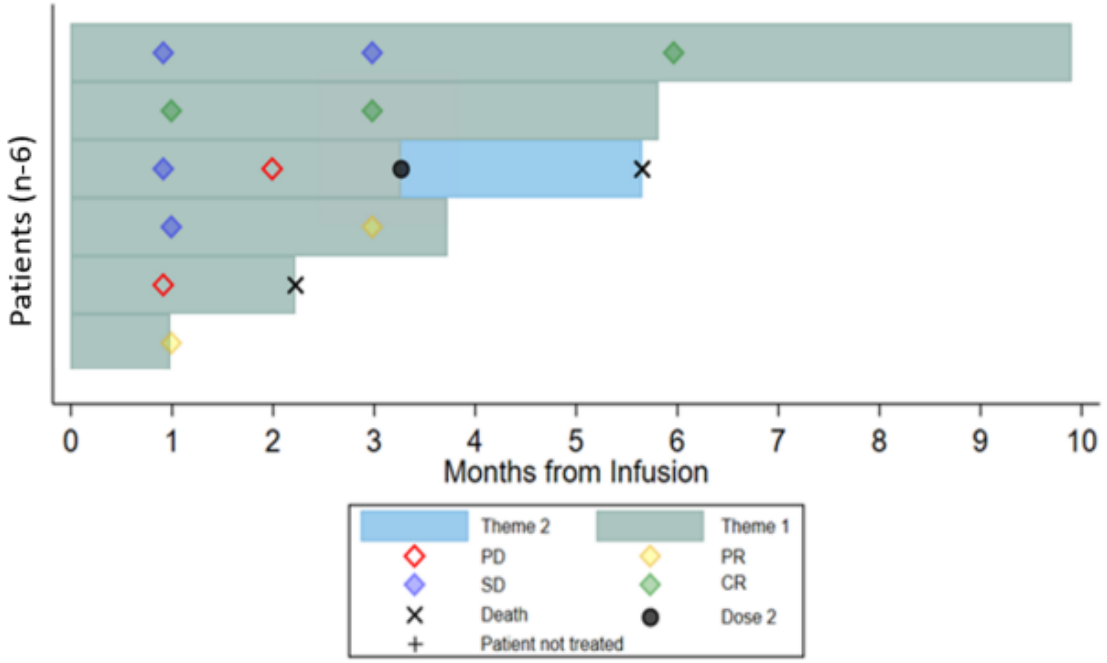
CAR, chimeric antigen receptor; VCN, vector copy number; qPCR, quantitative polymerase chain reaction

Data Cut-off: 12-May-2022

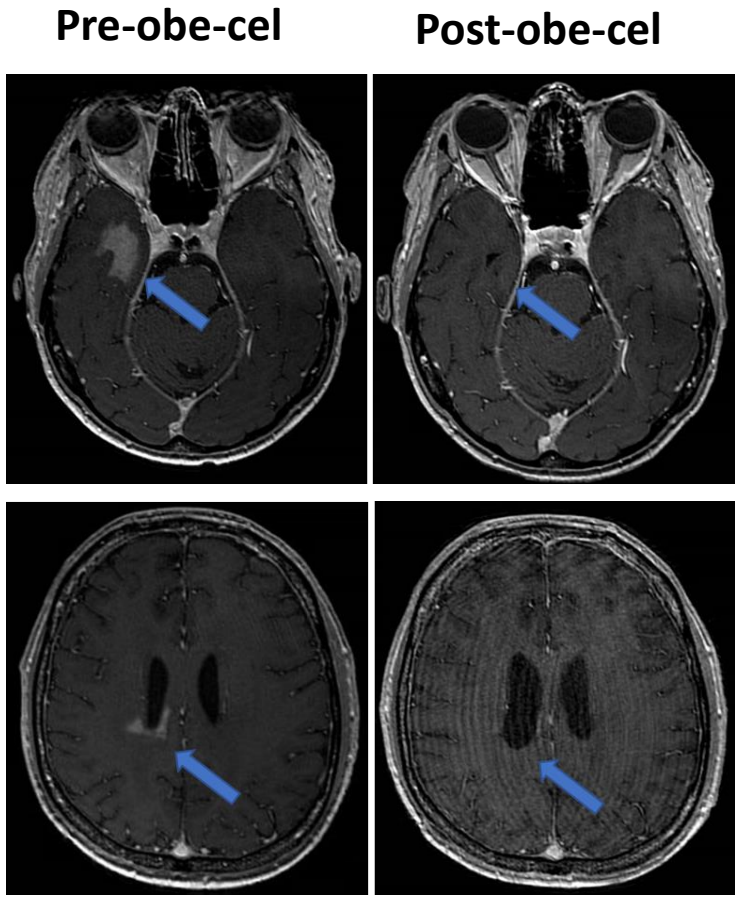
obe-cel shows encouraging initial efficacy and durability in PCNSL

Overall response rate was 4/6 (67%) and these patients are without disease progression at last follow up

	N (%)
CR + PR	4 (67%)
CR	2 (33%) (1 SD -> CR)
PR	2 (33%) (1 SD -> PR)



Median Follow-Up Time: 4.7 Months (Range 1-10)



Disease assessment by MRI imaging

Data Cut-off: 12-May-2022

Summary and next steps for obe-cel

Building a franchise through broad applicability

- ✓ Favorable and consistent safety profile demonstrated across all indications
- ✓ Of patients evaluable for efficacy across MCL, DLBCL, FL and CLL the ORR was 18/20 (90%)
- ✓ In the B-NHL cohorts, the CRR was 16/17 (94%)
- ✓ In the CLL cohort a best response of a PR was achieved in 2/3 patients, notably both achieved MRD-negativity in their marrow and both remain in PR at 10 and 6 months respectively
- ✓ Of the responding MCL, DLBCL, FL and CLL patients, 17/18 (94%) are without disease progression at last follow-up
- ✓ Encouraging initial data in PCNSL with 4/6 patients (2 CR and 2 PR) in ongoing responses at last follow up

Next steps…

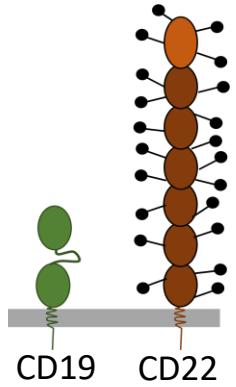
- Longer follow-up and enrolment of additional MCL, FL, DLBCL and CLL/SLL patients is ongoing

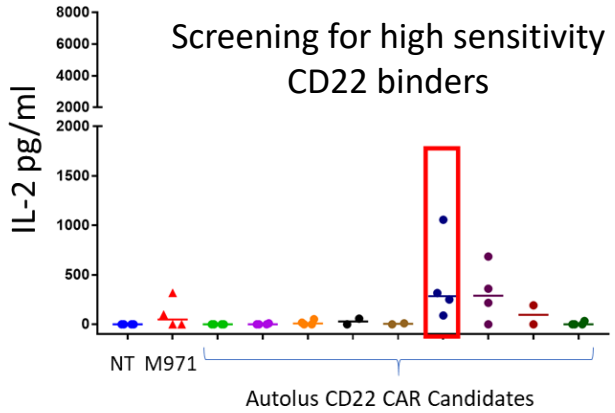
AUTO1/22: Pediatric Acute Lymphoblastic Leukemia

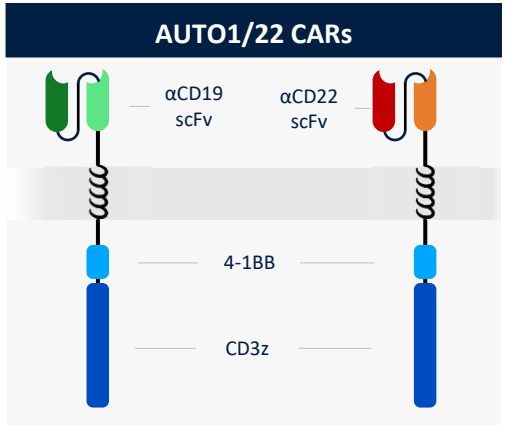
CD19 negative antigen escape is a common cause of treatment failure

CARPALL Study	
n	14
CR Rate	86%
EFS 12m	52% (95% CI, 16% to 72%)
No. of CD19 negative relapses	5/6
CRS ≥ G3	0%

- obe-cel (AUTO1) in r/r pALL is highly active and has a favourable safety profile - CARPALL study[1,2]
- Medical need in pALL is to minimize rates of antigen-loss–driven relapses and improve long-term outcomes – points to need for a dual targeting CAR T







AUTO1/22 is a next generation program that builds on obe-cel and adds a highly potent CD22 CAR, capable of targeting low levels of CD22

- AUTO1/22 is being evaluated in Phase 1 in r/r paediatric patients

(1) NCT02443831 (2) Ghorashian et al., Nat Med 2019 (3) Shah et al., JCO 2020, Spiegel et al., Nat Med 2021

AUTO1/22 in pediatric Acute Lymphoblastic Leukemia

Patient characteristics

Total Median age at registration	n=11 (%) 12 yrs (range = 3.7-20.5)
Indication	
Post SCT relapse	**6 (55%, 3 isolated extramedullary)**
1st relapse	2 (18%)
2nd relapse	8 (73%)
>2nd relapse	1 (9%)
Median number of lines of prior Rx	**3 (range 2-6)**
Prior Inotuzumab/Blinatumomab	6 (55%)
Prior CD19 CAR T cell therapy	4 (36%)
CD19-ve disease	3 (27%)
BM status pre-lymphodepletion	
Morphological relapse (>5% blasts)	4 (36% + 1 NE with 6% mol MRD)
MRD 2-5%	1 (9%)
MRD 10^{-2}-10^{-5}	3 (27%)
MRD negative	2 (18%)

None eligible for Kymriah (4 previous Kymriah, 5 EM disease, 3 CD19-ve component at enrolment)

Data Cutoff: 27-May-2022

AUTO1/22 in pediatric Acute Lymphoblastic Leukemia

Product characteristics

- Reproducible generation of products balanced in CD19 vs CD22 CAR
- Products have predominantly central memory and stem cell memory phenotype
- AUTO1/22 shows excellent T cell expansion and engraftment in patients

Safety Data

- AUTO1/22 shows favourable safety profile in patients
  - with no severe CRS, and one Grade 4 ICANS with atypical features

Criteria	N=11 N (%)
CRS Maximum Grade (ASTCT)	
Grade 1	4 (36%)
Grade 2	6 (55%)
Grade 3-4	0
ICANS Maximum Grade (ASTCT)	
Grade 1	4 (36%)
Grade 2	1 (9%)
Grade 3	0
Grade 4 (MRI leukoencephalopathy)	1 (9%)

Data Cut-off: 27-May-2022

AUTO1/22 in pediatric Acute Lymphoblastic Leukemia

Efficacy data

Total	N=11
Molecular MRD neg CR/Cri by d60	9 (82%)
Disease progression	2 (18%)
Events in responders	3
Emergence of molecular MRD	1
CD19+/CD22+ relapse	2

- No antigen-ve relapse was seen in responding patients
- At median follow up of 8.7 months, 6 of 9 responding patients were in MRD-ve complete response (1-12 mo)

Data Cut-off: 27-May-2022

Phase 1 study in r/r pALL ongoing

Initial data presented at EHA, June 2022

- ✓ CD19/CD22 targeting CAR T cells generated by co-transduction show robust expansion and persistence
- ✓ Favorable safety profile demonstrated, with no severe CRS
- ✓ Demonstration of efficacy of CD22 CAR
- ✓ Early efficacy in a heavily pre-treated cohort with 9/11 (82%) MRD negative CR rate
- ✓ To date with limited follow-up we have not observed antigen negative relapse

Next steps…

- Longer follow-up data H2 2022

Autolus

Dr. Christian Itin

Summary

Autolus poised for potential value inflection

obe-cel potential pivotal data in adult ALL in 2022

- obe-cel
  - FELIX Phase 2 study in adult ALL ongoing; initial data expected in H2 2022 and full data in H1 2023
  - Evaluation in r/r B-NHL and CLL ongoing
  - Evaluation in Primary CNS Lymphoma ongoing

- AUTO1/22
  - AUTO1/22 Phase 1 (CARPALL) study in pediatric ALL ongoing
  - Longer term follow-up data in H2 2022

- AUTO4 /AUTO5
  - AUTO4 Phase 1 (LibrA T1) study in Peripheral T-Cell Lymphoma ongoing

- Pipeline transitioning to Phase 1 in 2022
  - AUTO8 Phase 1 study has started
  - AUTO6NG in Neuroblastoma – start Phase 1 H2 2022

Q&A