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UPDATES ON T-CELL LYMPHOMA

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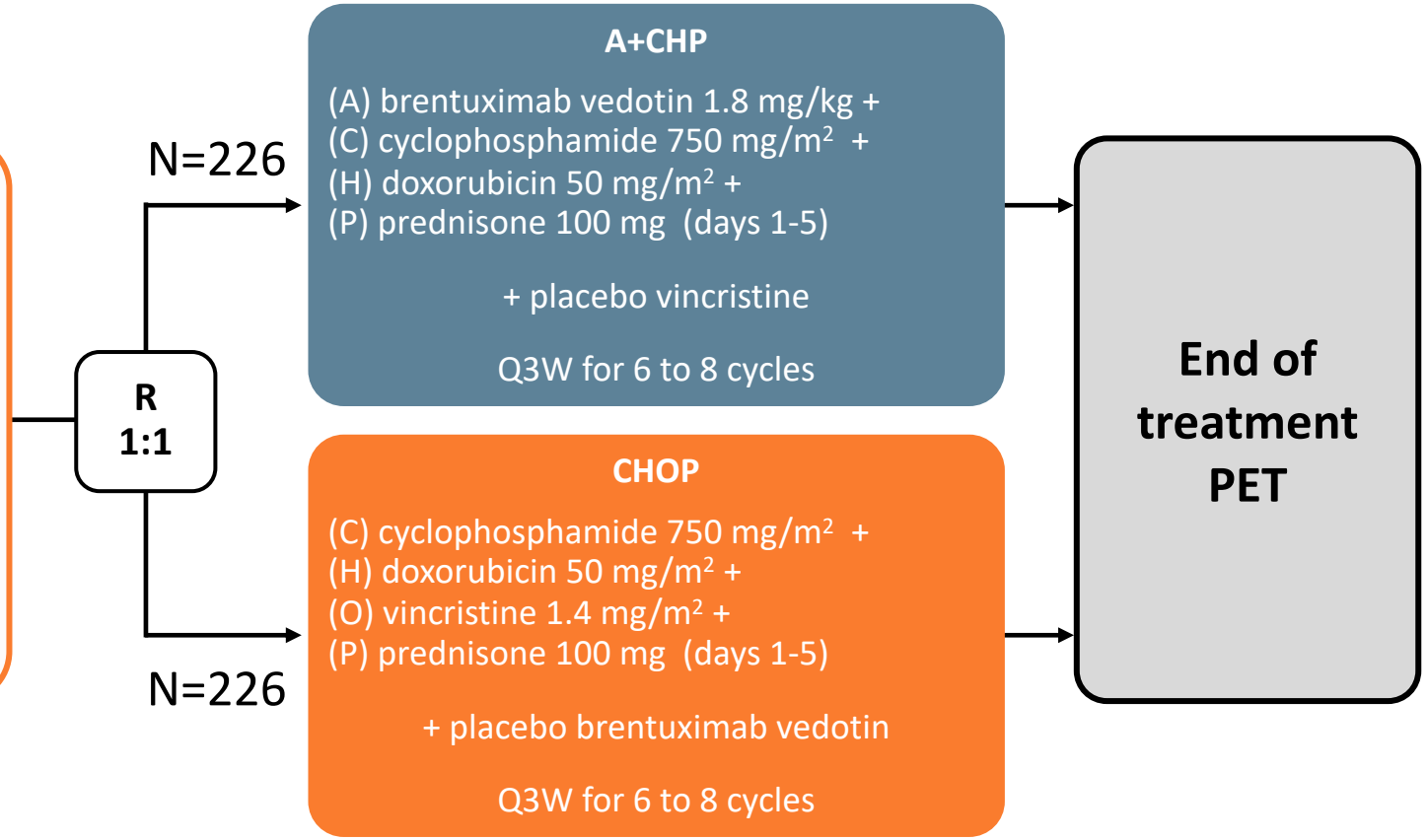
FRONT-LINE SETTING

ECHELON-2 (NCT01777152)
STUDY DESIGN

Key eligibility criteria

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



Stratification Factors:

- IPI score (0-1 vs. 2-3 vs. 4-5)
- Histologic subtype (ALK+ systemic ALCL vs. other histologies)

Per investigator discretion:

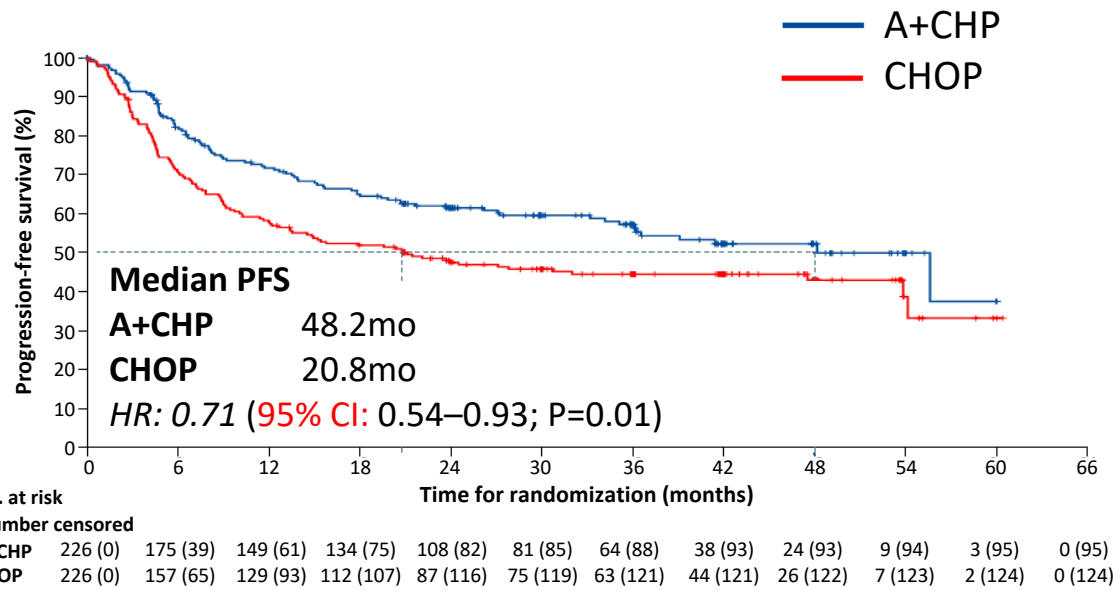
GCSF primary prophylaxis, consolidative radiotherapy and stem-cell transplantation

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; ATLL, adult T-cell leukaemia/lymphoma; CD, cluster of differentiation; EATL, enteropathy-associated T-cell lymphoma; GCSF, granulocyte-colony stimulating factor; HSTCL, hepatosplenic T-cell lymphoma; IPI, International Prognostic Index; NOS, not otherwise specified; PET, positron emission tomography; PTCL, peripheral T-cell lymphoma; Q3W, once every 3 weeks; R, randomisation

Horwitz S, et al. Lancet. 2019; 393:229-40

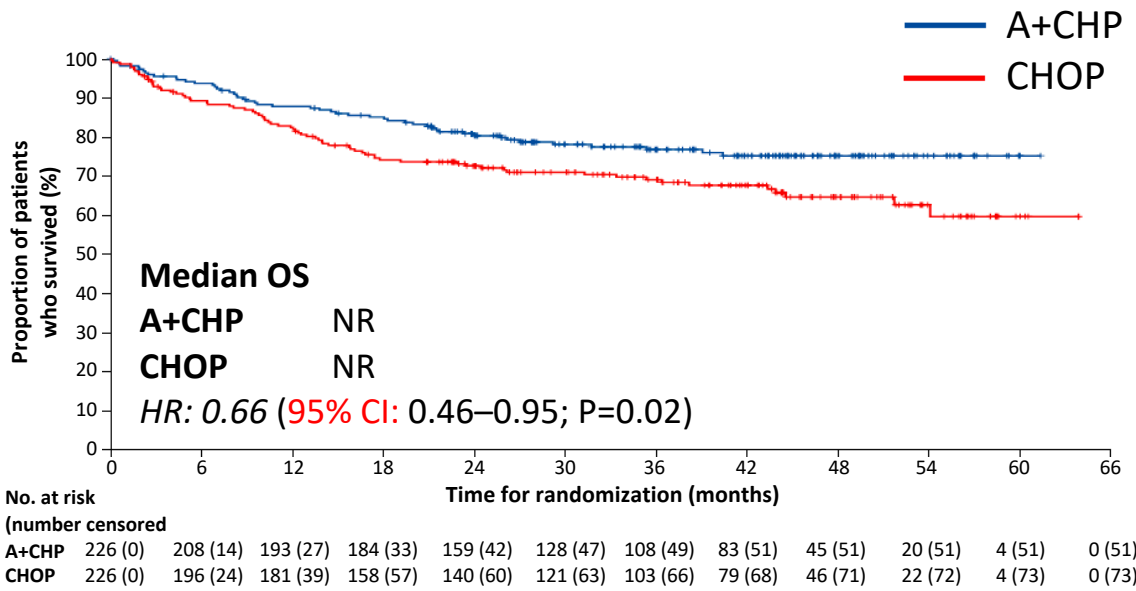
ECHELON-2
SURVIVAL CURVES

PROGRESSION-FREE SURVIVAL



No. at risk (number censored)												
A+CHP	226 (0)	175 (39)	149 (61)	134 (75)	108 (82)	81 (85)	64 (88)	38 (93)	24 (93)	9 (94)	3 (95)	0 (95)
CHOP	226 (0)	157 (65)	129 (93)	112 (107)	87 (116)	75 (119)	63 (121)	44 (121)	26 (122)	7 (123)	2 (124)	0 (124)

OVERALL SURVIVAL



No. at risk (number censored)												
A+CHP	226 (0)	208 (14)	193 (27)	184 (33)	159 (42)	128 (47)	108 (49)	83 (51)	45 (51)	20 (51)	4 (51)	0 (51)
CHOP	226 (0)	196 (24)	181 (39)	158 (57)	140 (60)	121 (63)	103 (66)	79 (68)	46 (71)	22 (72)	4 (73)	0 (73)

A+CHP, brentuximab vedotin, cyclophosphamide, doxorubicin, prednisone; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CI, confidence interval; HR, hazard ratio; NR, not reached; OS, overall survival; PFS, progression-free survival

Horwitz S, et al. Lancet. 2019; 393:229-40

ECHELON-2
SUMMARY AND IMPLICATIONS FOR CLINICAL PRACTICE

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ECHELON-2 supports brentuximab vedotin + CHP as the new standard of care for ALCL

Toxicities compared to CHOP were generally comparable

brentuximab + CHP is also an option for all non-ALCL CD30+ T-cell lymphomas (CD30 expression ≥1% on IHC)

- Whether it is superior to other regimens in that setting is less clear

The role of consolidative transplant after brentuximab vedotin + CHP is unclear

ALCL, anaplastic large-cell lymphoma; CD, cluster of differentiation; CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone; CHP, cyclophosphamide, doxorubicin, prednisone; IHC, immunohistochemistry

Horwitz S, et al. Lancet. 2019; 393:229-40

RELAPSED/REFRACTORY SETTING

IN RELAPSED T-CELL LYMPHOMA OUTCOMES ARE LARGELY UNCHANGED OVER THE LAST DECADES

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New strategies

Novel biological agents targeting deregulated pathways, such as:

- PI3K inhibitors
- JAK/STAT inhibitors
- Hypomethylating agents
- Farnesyltransferase inhibitors
- ITK inhibitors

Immunotherapy:

- PD-1/PD-L1 inhibitors
- CAR T-cell therapy

Combination regimens, such as:

- duvelisib + romidepsin
- durvalumab + romidepsin / azacitidine
- romidepsin + pralatrexate

CAR, chimeric antigen receptor; ITK, interleukin-2-inducible T-cell kinase; JAK, Janus kinase; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PI3K, phosphoinositide 3-kinase; STAT, signal transducer and activator of transcription proteins

PHASE 2 STUDY OF CERDULATINIB IN T-CELL LYMPHOMA

BEST OVERALL RESPONSE BY PTCL SUBTYPE

Response	AITL / TFH	PTCL-NOS	PTCL-Other	Total
N	27	11	26	64
Overall response rate	**14 (52)**	**0**	**8 (31)**	**22 (34)**
Complete response	10 (37)	0	4 (15)	14 (22)
Partial response	4 (15)	0	4 (15)	8 (12)
Stable disease	4 (15)	3 (27)	6 (23)	13 (55)
Duration of response (months), [range]	9+ [1–20]	–	5 [1–12]	8 [1–20]

- N includes all patients enrolled (including patients discontinued prior to evaluation)
- Responses in "Other" include:
  - Complete responses in ALCL, ATLL, HSTCL, LGL
  - Partial responses in ATLL, CD8+ epidermotropic cytotoxic T-cell lymphoma, cGDTCL, NK T-cell lymphoma

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ATLL, adult T-cell leukaemia/lymphoma; CD, cluster of differentiation; cGDTCL, primary cutaneous gamma-delta T-cell lymphoma; HSTCL, hepatosplenic T-cell lymphoma; LGL, large granular leukaemia; NK, natural killer; NOS, not otherwise specified; PTCL, peripheral T-cell lymphoma; TFH, T follicular helper cells

Horwitz SM, et al. Blood. 2019; 134(Supplement_1):466

DUVELISIB IN T-CELL LYMPHOMA

MONOTHERAPY[1]

	Total	Duvelisib dose (mg, BID), n (%)		
		60	75	100
Peripheral T-cell lymphoma, n	16	2	13	1
Overall response rate, n (%)	8 (50)	1 (50)	7 (54)	0
Complete response	3 (19)	1 (50)	2 (15)	0
Partial response	5 (31)	1 (50)	2 (15)	0
Median PFS, months (95% CI)	4.4 (0.7-NE)			

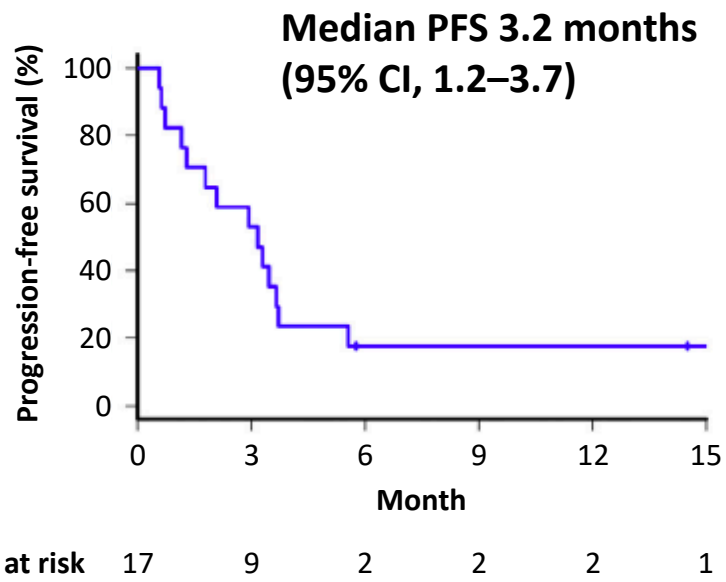
COMBINATION WITH ROMIDEPSIN[2]

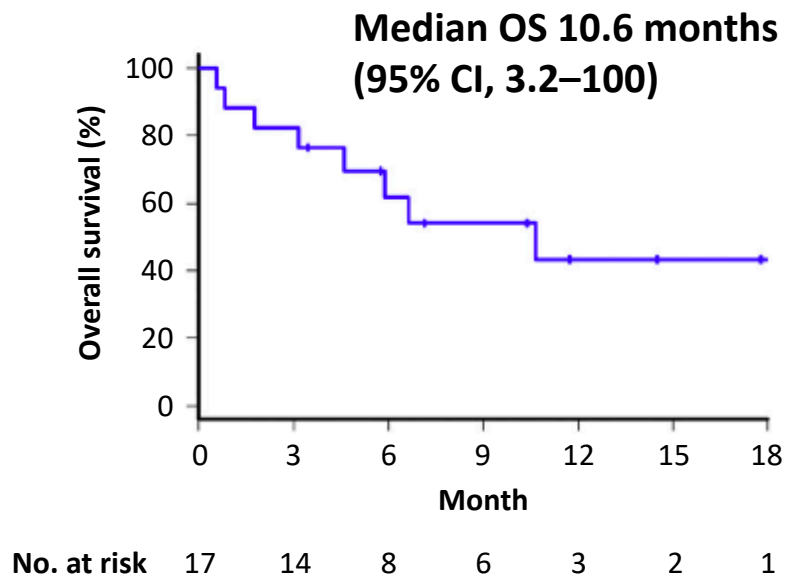
- Overall response rate: 55%
- Complete response rate: 24%
- Median PFS: 6 months

BID, twice a day; CI, confidence interval; PFS, progression-free survival

1. Flinn IW, et al. Blood. 2018; 131:877-887; 2. Horwitz SM, et al. Blood. 2018; 132(supplement_1):683

EFFICACY OF PEMBROLIZUMAB IN RELAPSED/REFRACTORY T-CELL LYMPHOMA





The trial was **stopped early** based on a preplanned **futility** analysis (<50% of patients free of progression at 3 months).

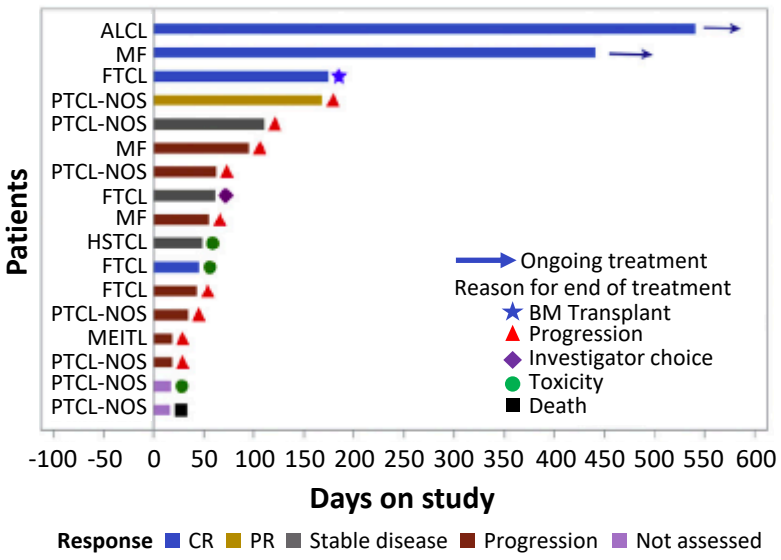
CI, confidence interval; OS, overall survival; PFS, progression-free survival

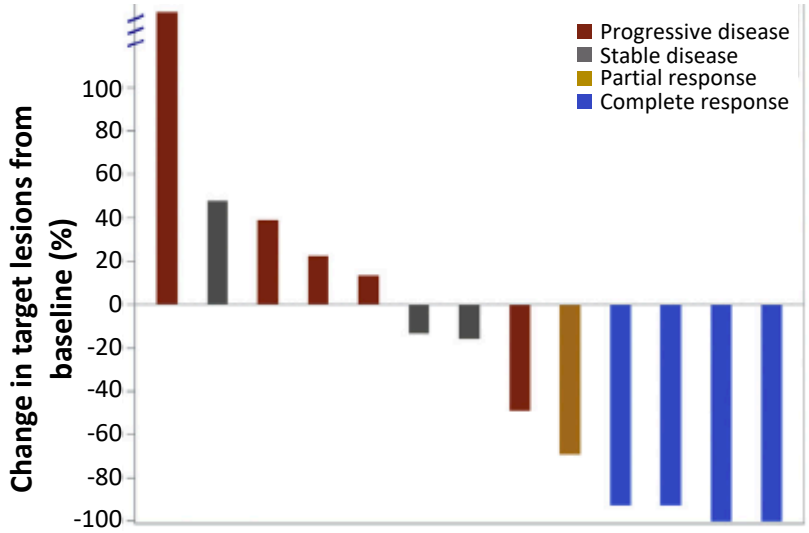
Barta SK, et al. Clin Lymphoma Myeloma Leuk. 2019; 19:356-64.e3

EFFICACY OF PEMBROLIZUMAB IN RELAPSED/REFRACTORY T-CELL LYMPHOMA

RESPONSE RATE (IN EVALUABLE PATIENTS)

- **Overall response rate: 33%**
  (5/15; 95% CI, 9–57%)
- **Complete response rate: 27%**
  (4/15; 95% CI, 4–49%)
- **Median duration of response: 2.9 months**
  (95% CI, 0–10.1)
  - However, two patients who responded were censored early (toxicity; HCT) and two remained in remission >15 months





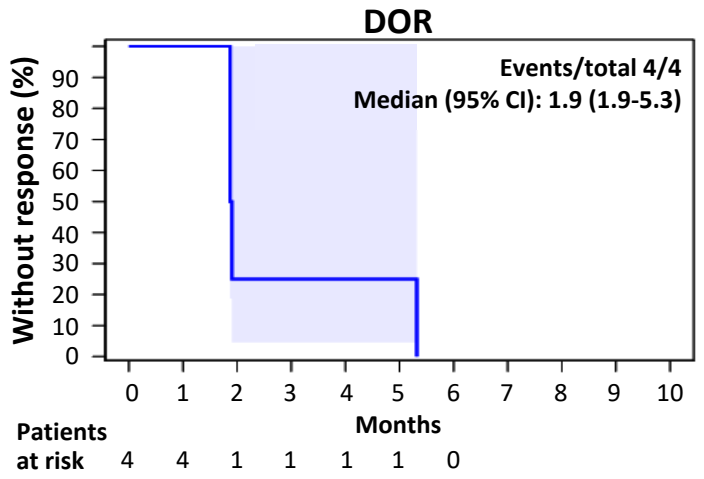
ALCL, anaplastic large-cell lymphoma; BM, bone marrow; CI, confidence interval; CR, complete response; FTCL, follicular T-cell lymphoma; HCT, hematopoietic cell transplantation; HSTCL, hepatosplenic T-cell lymphoma; MEITL, monomorphic epitheliotropic intestinal T-cell lymphoma; MF, mycosis fungoides; NOS, not otherwise specified; PR, partial response; PTCL, peripheral T-cell lymphoma

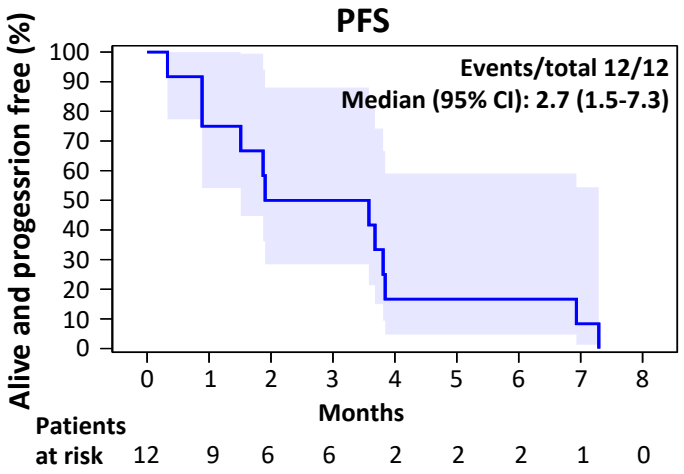
Barta SK, et al. Clin Lymphoma Myeloma Leuk. 2019; 19:356-64.e3

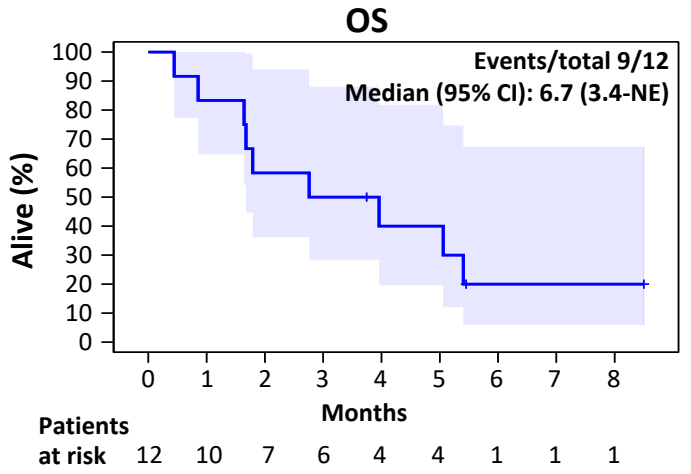
PROSPECTIVE PHASE 2 TRIAL OF NIVOLUMAB IN RELAPSED/REFRACTORY T-CELL LYMPHOMA

Baseline characteristics	Total N=12
Median age, years (range)	65 (35–75)
Male gender, n (%)	6 (50)
ECOG performance score, n (%)	
0	7 (58)
1	4 (33)
2	1 (8)
Median prior lines of therapy, n (range)	2 (1–6)
Prior ASCT, n (%)	6 (50)
T-cell lymphoma subtype, n (%)	
AITL	6 (50)
PTCL-NOS	3 (25)
ALCL, ALK negative	1 (8)
EATL	1 (8)
Hepatosplenic gamma-delta T-cell lymphoma	1 (8)
Ann Arbor stage, III/IV n (%)	12 (100)
Extranodal involvement, n (%)	11 (92)

Response	Total N=12
Overall response rate, n (%) (95% CI)	4 (33) (12.3–63.7)
Complete Response:	1 ALK-ALCL 1 AITL
Partial Response:	1 PTCL-NOS 1 EATL







Modified slide courtesy of Nora Bennani

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large-cell lymphoma; ALK, anaplastic lymphoma kinase; ASCT, autologous stem-cell transplant; CI, confidence interval; DOR, duration of response; EATL, enteropathy-associated T-cell lymphoma; NE, not evaluable; NOS, not otherwise specified; OS, overall survival; PFS, progression-free survival; PTCL, peripheral T-cell lymphoma

Bennani NN, et al. Blood. 2019; 134(Supplement_1):467

CLINICAL OUTCOMES OF CD5 CAR T-CELLS IN RELAPSED/REFRACTORY CD5+ T-CELL MALIGNANCIES

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LYMPHOMA
ORR: 50%

	Dose-level 1 ($1 \times 10^7/m^2$		Dose-level 2 ($5 \times 10^7/m^2$)			
Disease type	CTCL/ Sezary	AITL	AITL	PTCL	PTCL	PTCL
Best clinical response	PD	CR	MR→CR	PD	CR	PD
Bridge to allo-SCT	–	No	Yes	–	No	–
Duration of response	–	7 months	9 months	–	7 months	–
Outcome at last follow-up	Deceased	**Alive in CR**	**Alive in CR**	Deceased	**Alive in CR**	Deceased

LEUKEMIA
ORR: 20%

	Dose-level 1 ($1 \times 10^7/m^2$	Dose-level 2 ($5 \times 10^7/m^2$)			
Best clinical response	NR	NR	CR	PD	PD
Bridge to allo-SCT	–	–	No	–	–
Duration of response	–	–	6 weeks	-	–
Outcome at last follow-up	Deceased	Deceased	Deceased	**Alive in CR**	Deceased

AITL, angioimmunoblastic T-cell lymphoma; CD, cluster of differentiation; CR, complete response; CTCL, cutaneous T-cell lymphoma; MR, mixed response; NR, no response; ORR, objective response; PD, progressive disease; PTCL, peripheral T-cell lymphoma; SCT, stem-cell transplant

Hill LC, et al. Blood. 2019; 134(Supplement_1):199

SUMMARY

In the **frontline setting**, brentuximab vedotin + CHP is the new standard of care for ALCL

Although outcomes for **relapsed T-cell lymphoma** have been largely unchanged over the last decades, potential novel treatment options include:

- Novel biological agents targeting deregulated pathways
- Immunotherapy
- Combination regimens

ALCL, anaplastic large-cell lymphoma; CHP, cyclophosphamide, doxorubicin, prednisone

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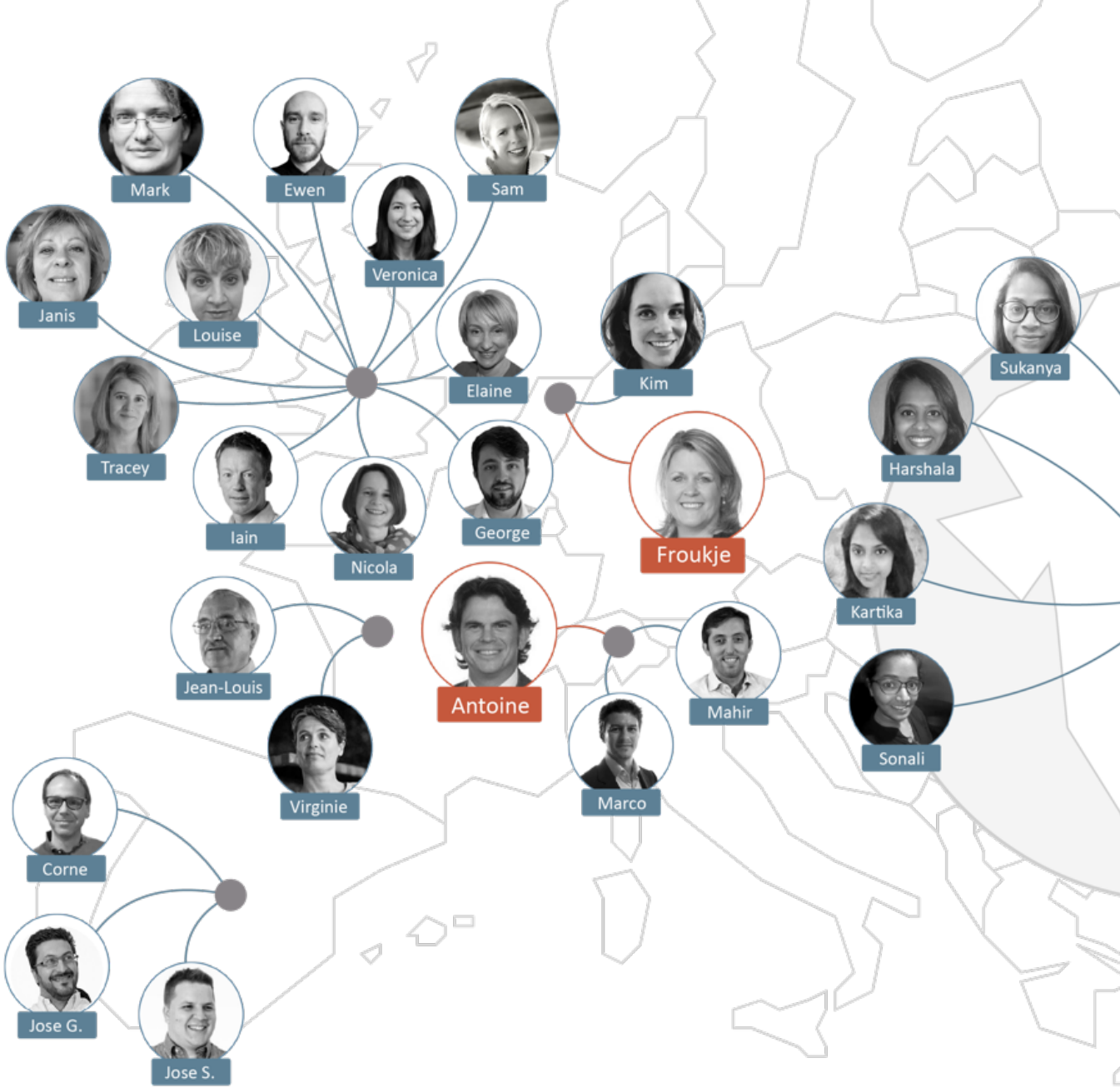

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