Systemic ALCL treated in routine clinical practice: survival outcomes following first-line chemotherapy from an international multicentre cohort study

Nicolas Martinez-Calle[1], Amy A Kirkwood[2], Maxine Lamb[3], Alex Smith[3], Jahanzaib Khwaja[4], Kate Manos[5], Caroline Shrubsole[6], Nicola Gray[7], Katharine Lewis[8], Ann Tivey[9], Mark Bishton[1], Eliza Hawkes[10], Matthew J Ahearne[11], Wendy Osborne[6], Graham P. Collins[7], Timothy Illidge[12], Kim M. Linton[9], Kate Cwynarski[4], Cathy Burton[13], Christopher P Fox[1]

1.Nottingham University Hospitals NHS Trust, Nottingham, UK; 2.CRUK and UCL Cancer Trials Centre, UCL Cancer Institute, London UK; 3.Haematological Malignancy Research Network, University of York, Leeds, UK; 4.University College of London Hospitals, NHS Foundation Trust, London, UK; 5.Austin Health, Heidelberg, Australia; 6.Newcastle upon Tyne Hospitals NHS Foundation trust, Newcastle, UK; 7.Oxford University Hospitals NHS Foundation Trust, Oxford, UK; 8.Sir Charles Gairdner Hospital, Perth, Australia; 9.The Christie, NHS Foundation Trust, Manchester, UK; 10.Olivia Newton-John Cancer Research Institute, Austin, Australia; 11.University Hospitals of Leicester NHS Trust, UK; 12.Faculty of Biology, Medicine and Health The University of Manchester; 13.Leeds Teaching Hospitals NHS Trust, Leeds, UK.

INTRODUCTION

- Brentuximab vedotin (BV) is FDA approved in combination with CHP as first-line (1L) treatment for CD30+ T-cell lymphoma. 34% reduction in risk of death compared to CHOP (70% ALCL on BV cohort) [5]
- CHOP-based regimens are traditionally accepted 1L regimens for ALCL with or without consolidative autologous stem cell transplant (ASCT) [1-2].
- 40-65% of patients relapse following 1L therapy, for which BV has established efficacy [3-4].
- We investigated outcomes of unselected patients with ALCL treated in routine clinical practice as a benchmark cohort, prior to the widespread adoption of BV into 1L regimens.

METHODS

- Consecutively diagnosed patients with systemic ALCL
- 8 UK and Australian centres **(n=214)**, retrospective data collection
- Diagnosis **(Dec 2004-July 2019)**
- Patients **≥16 years**
- Treatment allocation by clinician choice, best supportive care (BSC) included.
- Post-mortem diagnoses and patients treated on clinical trials (n=17) were excluded.
- Outcome variables: Time to treatment failure and overall survival (**TTF, OS) following 1L** treatment. Additional outcome measures included frequency of **ASCT** and **PFS/OS of BV for r/r ALCL**.

RESULTS

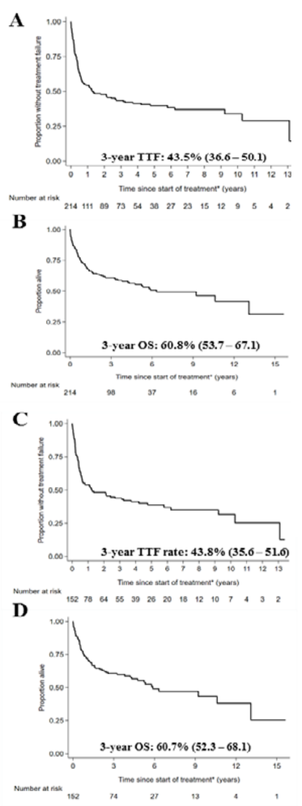

Figure 1. Outcomes of ALCL-treated cohort. TTF and OS KM curves of complete cohort (A-B) and CHOP-treated cohort (C-D).

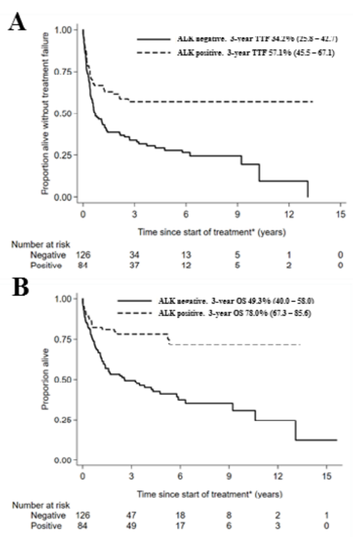

Figure 2. TTF and OS KM curves stratified by ALK status

Table 2. Responses to 1L treatment and outcome of ALCL and CHOP-treated cohort	ALCL cohort N=198*	CHOP cohort N=152
Response at EOI [ITT], n(%)		
CR	102 (53)	71 (47)
PR	34 (18)	27 (18)
SD/PD	39 (20)	33 (23)
Died/PD before assessment	18 (9)	18 (12)
Missing	5	1
Time to treatment Failure		
3-year TTF, % (95% CI)	45.4 (38.2—52.4)	43.8 (35.6—51.6)
Median, months (95% CI)	25 (12.8—50.5)	15 (7.4—39)
Overall Survival		
3-year OS, % (95% CI)	64 (56.8—70.6)	60.7 (52.3—68.1)
Median, months (95% CI)	110 (60.8—NR)	70.5 (50.7—157)

ALCL: Anaplastic large-cell lymphoma. * Based on patients treated with curative intent (Excluding RT only)

Tables 3A and 3B. Staging and response evaluation by PET

Table 3A. Concordance between PET and CT at diagnosis

PET STAGING Number of patients	CT STAGING Number of patients I	II	III	IV
I	6	1	0	1
II	5	7	1	2
III	0	1	6	1
IV	1	2	1	18

Table 3B. Response assessment by PET

PET RESPONSE Number of patients (% of PET response)	PFS events: No event	PD/Death event
CR (Deauville 1-2)	41 (71)	17 (29)
≤ PR (Deauville 3-5)	6 (18)	27 (82)

Table 4. Baseline risk factors for TTF and OS in CHOP-treated cohort (n=152)

	Time to Treatment Failure			Overall Survival		
	Events/N	HR (95% CI)	p	Events/N	HR (95% CI)	P value
Alk status						
Positive	28/67	0.4 (0.3 - 0.7)	<0.001	16/67	0.3 (0.2 – 0.6)	< 0.001
Negative	64/82	Ref		53/82	Ref	
IPI score						
0-2	43/92	Ref	< 0.001	27/92	Ref	< 0.001
3+	44/52	2.8 (1.8 – 4.2)		39/52	4.5 (2.7 – 7.4)	
PIT score						
0-1	33/74	Ref	< 0.001	22/74	Ref	< 0.001
2+	46/54	2.9 (1.9 – 4.6)		39/54	4.0 (2.4 – 6.8)	

TTF: Time to treatment failure; OS: Overall survival.

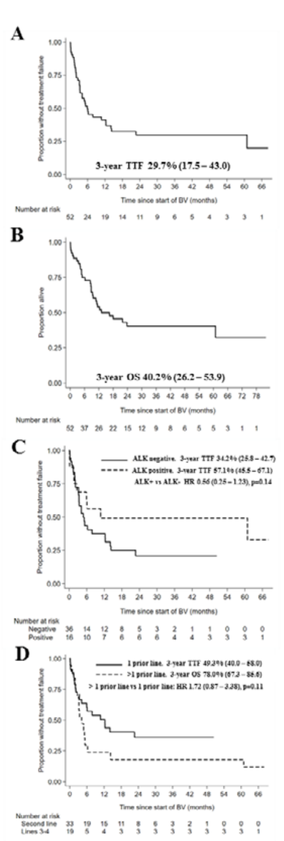

Figure 3. Outcomes BV at relapse on our ALCL cohort. TTF and OS KM curves (A-B). TTF stratified by ALK status (C) and number of prior lines of therapy (D).

Table 1. Demographic characteristics of patients

	All patients N=214	CHOP cohort N=152	ECHELON-2 CHOP cohort¶ N=226
Age, median(range)	52.0(16.0- 93.0)	52.0(17.0- 85.0)	58(18.0- 83.0)
Male, N (%)	135 (63.1)	94 (61.8)	151 (67)
ECOG, N (%)			
0-1	129 (66.5)	94 (68.1)	179 (79)
2	30 (15.5)	23 (16.7)	47 (21)
≥3	35 (18.1)	21 (15.2)	0
Missing	20	14	0
ALK Positive, N (%)	83 (39.5)	66 (44.3)	49 (22)
Missing	4	3	0
B symptoms, N (%)	109 (54.2)	77 (52.4)	N/A
Missing	13	5	
BM involvement, N (%)	14 (8.9)	11 (9.0)	N/A
Missing	57	30	
Stage*, N(%)			
I	22 (11.1)	17 (11.6)	9 (4)
II	49 (24.7)	38 (26.0)	37 (16)
III	32 (16.2)	24 (16.4)	67 (30)
IV	95 (48.0)	67 (45.9)	113 (50)
Missing	16	6	
≥2 extra nodal sites, N (%)	57 (27.8)	42 (28.4)	N/A
Missing	9	4	
High LDH, N (%)	95 (54.0)	64 (49.6)	N/A
Missing	38	23	
IPI score, grouped, N (%)±			
Low: 0-2	119 (60.7)	92 (63.9)	126 (56)
High: 3+	77 (39.3)	52 (36.1)	100 (44)
Missing	18	8	6
PIT score, grouped, N (%)±			
Low: 0-1	95 (54.6)	74 (57.8)	N/A
High: 2+	79 (45.4)	54 (42.2)	N/A
Missing	40	24	

¶ For comparison; * Stage is based on CT imaging and when available on PET/CT imaging; ± Missing scores grouped if definitely low or high regardless of missing values.

CONCLUSIONS

- Large unselected cohort of ALCL treated in routine clinical practice.
- Survival outcomes of CHOP-treated inferior to E2 control arm despite baseline characteristics (age, ALK-status, stage). 18% of patients had ECOG ≥3 (E2 exclusion criterion).
- ALK status remains the strongest prognostic variable for outcomes.
- A minority of pts received intensified regimens and only 9.4% underwent ASCT.
- IPI and PIT scores had equivalent prognostic value
- Outcomes of r/r ALCL after single-agent BV were inferior compared to the pivotal Phase 2 data.[3]

REFERENCES

1. *Blood. 2010;116(18):3418-25.*
2. *Br J Haematol. 2011;153(4):451-85*
3. *Blood. 2017;130(25):2709-2717.*
4. Crit Rev Oncol Hematol. 2015;95(3):359-69
5. Lancet. 2019;393(10168):229-240.

CONTACT INFORMATION
Nicolas Martinez-Calle; nmartinezc@unav.es

BSH2020 PO-091-A
Lymphoma/CLL
Nicolas Martinez-Calle
Poster presented at: British Society for Haematology
PosterSessionOnline.com