Outcome of NK/T-Cell Lymphoma – Retrospective Analysis from a Tertiary Care Cancer Center

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Background

- Extranodal NK-T Cell lymphoma(ENKTL) is a rare aggressive non-hodgkins lymphoma(NHL) commonly seen in Asian countries and latin American countries
- Limited stage ENKTL is treated with combined modality of radiotherapy and chemotherapy and advanced stage is treated with predominantly chemotherapy
- Conventional chemotherapy regimes used in NHL – CHOP and CHOP like regimes have dismal outcomes
- Use of L-Asparaginase based chemotherapy has resulted in improved outcomes, however evidence for the same comes for phase II and retrospective trials
- Outcomes with various L-asparaginase protocols in the real world setting is scarce
- We are presenting the retraospective analysis of 78 patients across a decade treated in a single centre in India, to ascertain the efficacy of these protocols in the real world setting

Objectives

- To evaluate the outcome of patients with extra-nodal NK T cell lymphoma treated in a tertiary cancer care center in India from 2012 to 2021.

Materials and methods

We included consecutive denovo and partially treated patients greater than 15 years of age who had a confirmed histopathological diagnosis of ENKTL and were treated in Tata Memorial Centre, a tertiary cancer center in India between May 2010 till December 2021

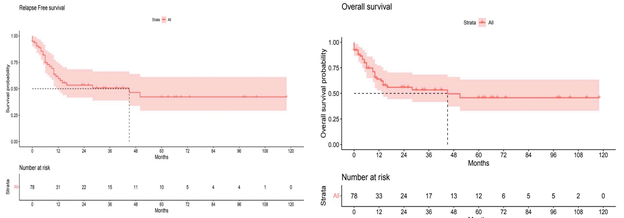
Chemotherapy regimens used

Total number of patients	78	Number of cycles
Pre-treatment details	Treatment naive – 63 Treated from outside – 15	
Prior treatment details (Number of patients)	CHOP – 11 CHOEP – 2 ICE – 1 Non-lymphoma treatment – 1	
Treatment at our centre	SMILE	6 cycles – 28 5 cycles – 5 4 cycles – 7 3 cycles – 5 2 cycles – 1 1 cycle – 4
	CHOP	4 cycles – 1
	LVP	3 cycles – 3 4 cycles – 2
	GDP	2 cycles – 1 1 cycle – 1
	GELOX	6 cycles – 1 4 cycles – 1 3 cycles – 1
	ICE	6 cycles – 1
	ddGDP	6 cycles – 2 3 cycles – 2

Results

Parameter	Overall population	Lugano Stage I/II	Lugano Stage III/IV
Total patients	78	44	30
Age	Median age 40 years (IQR: 32 – 49 years)	Mean – 42.2 (IQR: 34 – 50.5 years) Age >60 years: 2(4.6%)	Mean – 35.77 (IQR: 29.7 – 47.2 years) Age >60 years: 2(6.6%)
Sex	Male – 56 (71.8%) Female – 22 (28.2%)	Male – 29(65.9%) Female – 15(34.1%)	Male – 25(83.3%) Female – 5(16.7%)
No. of comorbidity	None – 54 (69.2%) 1 – 15 (19%) 2 – 7(9%) NA – 2(2.6%)	None – 27 (61.4 %) 1 – 12 (27.2%) 2 – 5(11.4%) NA – 2(2.6%)	None – 25(83.3%) 1 – 3(10%) 2 – 1(3.3%) NA – 1(3.3%)
Presenting symptoms	Nasal swelling – 42.3% Nasal blockade – 20.5% Nasal discharge – 16.6% Symptoms at non-nasal site – 12.8% Epistaxis – 9% Dysphagia – 9% Ulcer in the oral cavity – 9% Voice change – 4% Proptosis – 2.6%	Nasal swelling – 45.5% Nasal blockade – 52.2% Nasal discharge – 25.3% Epistaxis – 15.7% Dysphagia – 11.4% Ulcer in the oral cavity – 4.6% Voice change – 4.6% Proptosis – 2.3%	Nasal swelling – 40% Nasal blockade – 21.3% Symptoms at non-nasal site – 23.3% Nasal discharge – 13.4% Epistaxis – 6.7% Dysphagia – 3.3% Ulcer in the oral cavity – 3.3% Voice change – 3.3% Proptosis – 3.3%
Disease type	Nasal – 62(79.5%) Non-Nasal – 15 (19.2%)	Nasal – 41(93.2%) Non-Nasal – 3 (6.8%)	Nasal – 23(76.7%) Non-Nasal – 7 (23.3%)
B Symptoms	Present – 35(44.9%)	Present – 17(38.6%)	Present – 17(56.7%)
ECOG performance status	0 – 5(6.4%) 1 – 56(71.8%) 2 – 13(16.7%) 3 – 2(2.6%) NA – 2(2.6%)	0 – 4(9.1%) 1 – 34 (77.3%) 2 – 4 (9.1%) 3 – 1(2.3%) NA – 1(2.3%)	0 – 1(3.3%) 1 – 20(66.7%) 2 – 8 (26.7%) 3 – 1(3.3%)
Baseline Hemoglobin	Mean 10.71 Median 11.55 IQR 9.67 – 12.9 Hb >8 – 70 (89.7%)	Mean 10.99 Median 11.6 IQR 9.8– 13.05 Hb >8 – 39(88.6%)	Mean 10.66 Median 11.15 IQR 9.53 – 12.5 Hb >8 – 28(93.3%)
Baseline creatinine	Mean – 0.85 Median 0.84 IQR – 0.7 – 1 Creatinine >1.3 – 5(6.4%)	Mean – 0.83 Median 0.80 IQR – 0.7 – 1 Creatinine >1.3 – 1(2.3%)	Mean – 0.90 Median 0.90 IQR – 0.7 – 1.01 Creatinine >1.3 – 4(13.3%)
Baseline albumin	Mean – 3.51 Median 3.8 IQR – 3.3 – 4.3 Alb <=3– 20(25.6%)	Mean – 3.62 Median 3.85 IQR – 3.4 – 4.4 Alb <=3– 9(20.4%)	Mean – 3.45 Median – 3.80 IQR – 3.08 – 4.1 Alb <=3– 12(40%)
Baseline LDH	Mean – 257 Median 213 IQR – 145 – 301 LDH>ULN – 47(60%)	Mean – 219 Median 196 IQR – 141 - 253 LDH>ULN – 26(59.1%)	Mean – 330 Median 297.5 IQR – 150 – 432 LDH>ULN – 19(63.3%)
Bone marrow involvement	7 (9.2%)*	Not involved	7(23.3%)*
CSF involvement	1 (1.3%)**	None'	1(3.3%)**
Regional node involvement	Yes – 47(60.3%) No – 27 (34.6%)	Yes – 20(45.5%) No – 23(52.3%)	Yes – 27(90%) No – 3(10%)
Distant node involvement	Yes – 22(28%) No – 52 (66.7%)	Yes – 1(2.3%) No – 42(95.5%)	Yes – 21(70%) No – 9(30%)
>1 EN sites	28(33%)	None	20(66.7%)
Bulky disease at presentation	18(23%)	10(22.7%)	8(26.7%)
Lugano staging	Stage I – 22(28%) Stage II – 21(26.9%) Stage III – 1(1.3%) Stage IV – 26(33.3%) Not available – 4(5.1%)	Stage I -22(50%) Stage II – 22(50%)	Stage III – 1(3.3%) Stage IV – 29(96.7%)
AJCC Staging(13)	T1 – 17(21.8%) T2 – 15(19.2%) T3 – 20(25.6%) T4a – 8(10.3%) T4b – 4(5.1%) Not available – 3(3.8%) Not applicable – 11(14.1%)	T1 – 12(27.3%) T2 – 9(20.5%) T3 – 12(27.3%) T4a – 4(9.1%) T4b – 3(6.8%) Not applicable – 4(9.1%)	T1 – 3(10%) T2 – 6(20%) T3 – 8(26.7%) T4a – 4(13.3%) T4b – 1(3.3%) Not available – 1(3.3%) Not applicable – 7(23.3%)
CSWOG Staging(14)	Stage I – 11(14.1%) Stage II – 12(15.4%) Stage III – 21(26.9%) Stage IV – 20(25.6%) Not available – 3(3.8%) Not applicable – 11(14.1%)	Stage I – 10(22.7%) Stage II – 12(27%) Stage III – 19(40.9%) Stage IV – 0 Not applicable – 4(9.1%)	Stage III – 2(6.7%) Stage IV – 20(66.7%) Not available – 1(3.3%) Not applicable – 7(23.3%)
IPI Score	Low (0-1) – 39 (50%) Low intermediate(2) – 9(11.5%) High intermediate (3) – 19 (24.4%) High (4-5) – 3(3.8%)	Low (0-1) – 27 (64.1%) Low intermediate(2) – 3(6.8%)	Low (0-1) – 2(6.7%) Low intermediate(2) – 6(20%) High intermediate (3) - 19(63.3%) High (4-5) – 3(10%)
PINK Score	Low(0) – 33(42.3%) Intermediate (1) – 7(21.8%) High (2-4) – 2(529.5%)	Low(0) – 33(75%) Intermediate (1) – 10(22.7%)	Low(0) – 0 Intermediate (1) – 7(23.3%) High (2-4) – 23(76.6%)
Korean Score	Low(0) – 7(9%) Low intermediate(1) – 14(17.9%) High intermediate(2) – 22(28.2%) High(3-4) – 27(34.6%)	Low(0) – 7(15.9%) Low intermediate(1) – 14(31.8%) High intermediate(2) – 14(31.8%) High(3-4) – 9(11.4%)	Low(0) – 0 Low intermediate(1) – 0 High intermediate(2) – 8(26.7%) High(3-4) – 22 (73.3%)
PIT Score	Low(0) – 15(19.3%) Low intermediate(1) – 38(48.7%) High intermediate(2) – 13(16.7%) High(3-4) – 4(5.2%)	Low(0) – 12(27.3%) Low intermediate(1) – 23(50%) High intermediate(2) – 5(11.4%) High(3-4) – 1(2.3%)	Low(0) – 3(10%) Low intermediate(1) – 16(53.3%) High intermediate(2) – 8(26.7%) High(3-4) – 2(6.6%)
HLH anytime during the clinical presentation	4(5.1%)	2(4.5%)	2(6.7%)
Type of clinical presentation	Treatment naive – 62(79.5%) Outside treated – 15(19.2%)	Treatment naive – 38(86.4%) Outside treated – 6(13.6%)	Treatment naive – 21(70%) Outside treated – 8(26.7%)
Baseline EBV DNA detection	Detected – 2***	Not available	Detected – 2***
Immunohistochemistry	CD3+VE – 74(94.9%) CD56+VE – 62(79.5%) EBVLMP1 – 18/46.7%## EBERISH – 7/17.7%##	CD3+VE – 42(95.5%) CD56+VE – 30(81.1%) EBVLMP1 – 10(22.7%)# EBERISH – 3(75%)#	CD3+VE – 29(96.7%) CD56+VE – 22(73.3%) EBVLMP1 – 8(26.7%)# EBERISH – 4(80%)#

Results



Treatment subgroups(n)	ORR/CR	RFS	OS
Overall population(78)	71.8%/62.8%	Median – 45 months(95%CI: 12-NE months)	Median – 45 months(95%CI: 14 – NE)
Lugano Stage I/II(44)	79.5%/68.2%	Median – Not reached At 45 months – 50.1% (95% CI:26.1 – 74.1%)	Median – Not reached At 45 months – 62.3%(95%CI: 42.9%-81.7%)
Lugano Stage III/IV(30)	66.7%/60%	Median – 10 months (95% CI: 0.3 – 19.61 months)	Median – 11 months (95% CI: 4.3 – 17.6 months)
SMILE Chemotherapy(52)	80.8%/73.3%	Median – 50 months (95%CI: 16 – NE months)	Median – not reached At 3 years – 59.2% (95%CI: 45.2 – 77.4%) At 5 years – 54.3%(95%CI: 39.5 – 74.6%)
Non-SMILE Chemotherapy(26)	53.8%/42.3%	Median – 9 months (95%CI: 3.5 – 14.4 months)	Median – 10 months (95% CI. 3.6 – 16.3 months)
L-Asparaginase based chemotherapy(SMILE +Non-SMILE) (66)	81.8%/71.2%	Median – 50 months (95%CI: 14 – NE months)	Median – not reached At 3 years – 58.2% (95%CI: 45.4 – 74.6%) At 5 years – 53.3%(95%CI: 39.4 – 72.1%)
L-Asparaginase based chemo(Non SMILE alone) (15)	86.7%/66.7%	Median – 10 months (95% CI: 8.5 – 11.46 months)	Median – not reached At 2 years – 55.6% (95%CI: 31.1% - 99.7%)
Therapy with RT(43)	90.7%/81.4%	Median – 50 months (95%CI: NE – NE) At 3 years – 63.1% (95%CI: 49.2 – 80.7%) At 5 years – 49%(95%CI: 32 – 75%)	Median – not reached At 3 years – 70.4% (95%CI: 57 – 87%) At 5 years – 57.6%(95%CI: 40.6 – 81.7%)

Univariate analysis showed that PINK score of 2 or 3 or 4, use of alternative protocols (apart from SMILE), use of non-L-asparaginase containing protocol, omitting RT in the treatment protocol and non achievement of CR was associated with poorer outcome(RFS and OS)

Multivariate analysis showed that PINK score of 2 or 3 or 4, omitting RT, and non-achievement of CR was associated with poorer outcome(RFS and OS)

Discussion

- Use of SMILE chemotherapy resulted in superior survival in comparison to non-SMILE chemotherapy
- However, by multivariate analysis, baseline PINK score of 0 or 1, incorporation of RT and achievement of CR resulted in better survival
- Overall outcomes are inferior to trial data in view of inclusion of patients with poor PS(2 or 3), non-uniform application of RT and use of SMILE/L-asparaginase based protocol.
- Only 3 patients, received ddGDP, hence comparison between SMILE and ddGDP will not be possible in this analysis.

Conclusions

- Multimodality treatment consisting of L-asparaginase based chemotherapy(preferably SMILE chemotherapy) along with incorporation of RT resulted in better survival
- However, baseline risk factors(PINK score), achievement of CR and incorporation of RT impacts the outcome significantly
- Future trials must aim to identify the optimal regimen for treatment of this rather rare NHL.

References

1. Kwong YL, Kim WS, Lim ST, Kim SJ, Tang T, Tse E, et al. SMILE for natural killer/T-cell lymphoma: analysisof safety and efficacy from the Asia Lymphoma Study Group. Blood. 2012 Oct 11;120(15):2973-80
2. Li X, Cui Y, Sun Z, Zhang L, Li L, Wang X, et al. DDGP versus SMILE in Newly Diagnosed Advanced Natural Killer/T-Cell Lymphoma: A Randomized Controlled, Multicenter, Open-label Study in China. Clin Cancer Res Off J Am Assoc Cancer Res. 2016 Nov 1;22(21):5223–8.
3. Yamaguchi M, Kwong YL, Kim WS, Maeda Y, Hashimoto C, Suh C, et al. Phase II Study of SMILE Chemotherapy for Newly Diagnosed Stage IV, Relapsed, or Refractory Extranodal Natural Killer (NK)/T-Cell Lymphoma, Nasal Type: The NK-Cell Tumor Study Group Study. J Clin Oncol. 2011 Nov 20;29(33):4410–6
4. Allen PB, Lechowicz MJ. Management of NK/T-Cell Lymphoma, Nasal Type. J Oncol Pract. 2019 Oct;15(10):513–20

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