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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Predicting Toxicities in Older Adults with Non-Hodgkin Lymphoma (NHL) Receiving Systemic Chemotherapy: A Prospective Geriatric Assessment (GA) Study

Pallawi Torka[1], *Esther Drill, DrPH*[2], *Nivetha Ganesan*[3], *Mayan Oliveros*[4], *Alexander P. Boardman*[5], *Philip Caron, MD*[6], *Kevin A. David, MD*[7], *Zachary D. Epstein-Peterson, MD*[6], *Lorenzo Falchi, MD*[8], *Paola Ghione, MD MSEpi*[3], *Steven M. Horwitz, MD*[3], *Andrew M. Intlekofer, MDDPhil*[6], *William Johnson*[3], *Anita Kumar, MD*[9], *Jennifer Kimberly Lue, MD*[6], *Alison Moskowitz, MD*[3], *Ariela Noy, MD*[7], *Colette Owens, MD*[6], *Maria Lia Palomba, MD*[7], *Robert Stuver, MD*[3], *Santosha A Vardhana, MD PhD*[7], *Andrew D. Zelenetz, MD PhD*[6], *Gilles Salles, MD PhD*[7], *Paul A. Hamlin, MD*[6]

[1]Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, Montvale, NJ
[2]Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY
[3]Memorial Sloan Kettering Cancer Center, New York, NY
[4]Memorial Sloan Kettering Cancer Center, New York
[5]Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY
[6]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
[7]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York
[8]Department of Medicine, Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY
[9]Lymphoma Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, Short Hills, NJ

Background

Sixty percent of newly diagnosed NHL patients (pts) are ≥60 years (yrs) old and have significantly worse relapse-free and overall survival (OS) than their younger counterparts. Toxicity (tox) is more common in older adults (OA), and those who experience it derive less benefit from treatment. Use of reduced intensity treatment regimens can minimize tox but might also lead to poorer outcomes due to reduced disease control. Prospective identification of pts at greatest risk of toxic events may allow tailored dose reductions in those vulnerable individuals and mark them for closer monitoring during therapy. Currently, no validated instrument exists to predict tox in OA with NHL. We conducted a prospective study to determine if a geriatric assessment (GA) or its component measures predict tox in OA with NHL and determine if changes in GA during and after treatment correlate with tox.

Methods

Pts ≥ 60 yrs with confirmed diagnoses of NHL starting a new chemotherapy regimen (chemo) were included. GA was performed: 1) prior to pre-phase therapy in those who received it, 2) prior to initiation of the new chemo, 3) within 7 days prior to each cycle (up to 6), 4) 1 month (+/- 10 days) after completing therapy. GA instruments included MOS physical health subscale for ADLs, OARS subscale for IADLs, self-reported KPS, no. of falls, Timed up and go (TUG) test, Physical Health Section (subscale of OARS) for comorbidities, Mental Health Inventory-17 for psychological state, Blessed Orientation Memory Concentration Test for cognition, MOS social activity survey, MOS social support survey, % weight loss and Mini Nutritional Assessment (MNA) for nutrition and polypharmacy. Data regarding: 1) hematologic Tox ≥ Grade 4, and non-hematologic tox ≥ Grade 3, 2) hospitalization, 3) dose delay or reduction due to tox, and 4) discontinuation of chemo due to tox were collected at each visit.

Therapeutic regimens were at the discretion of the physician, characterized as curative intent or palliative. The primary outcome events were severe tox (STox) defined as any of the following: 1) Hospitalization during or within 30 days following chemotherapy, 2) Dose delay or reduction to a dose intensity ≤80% of the planned dose intensity, 3) Discontinuation of chemo due to tox, 4) Death. Secondary tox endpoints were Grade 3 or higher non-hematologic tox and Grade 4 or higher hematologic tox.

Results

A total of 194 pts were enrolled, one pt was missing baseline data, but was included in endpoint analysis. Median age was 75 yrs (IQR 68-81 yrs), 42% were women, majority had diffuse large B cell lymphoma (72%), and majority had advanced stage

disease (75%). All pts with DLBCL were treated with curative intent. The most common regimen was R-CHOP (71%). Median ADL score was 85 (IQR 46-95) and median IADL score was 14 (IQR 13-14). The median TUG time was 10 seconds (sec) (IQR 8-14 sec), and 29% pts had an abnormal TUG test (defined as ≥ 12 sec). Majority of pts (56%) had a normal nutritional status based on MNA score ≥ 24 (Table 1).

STox occurred in 57% pts, 25% had grade 3+ non-hematologic tox and 38% had grade 4+ hematologic tox. The 2-year OS was 83% (CI 78%, 89%) and 5-year OS was 78% (CI 71%, 84%) (Figure 1).

Pts experiencing STox were older (76 vs 72 yrs, p=0.007), had a lower ADL score (80 vs 90, p=0.014), and lower patient reported KPS (80 vs 90, p<0.001). Pts with an abnormal TUG at baseline had higher incidence of STox vs those with normal TUG (72% vs 51%, p=0.01). Pts with aggressive lymphoma and high aaIPI were more likely to experience STox than those with indolent lymphoma (80% vs 69%, p=0.07) and low aaIPI (58% vs 43%, p=0.09) though these differences did not reach statistical significance. 18 out of the 22 pts on R-EPOCH had STox events (82% vs 54% of patients on other treatments, p = 0.012). Conversely, 52% of the 137 patients on R-CHOP had STox events vs 70% of patients on other treatments (p=0.023). Analyses evaluating the correlation between dynamic changes in GA prior to each cycle and toxicities are currently underway.

Conclusions

Several components of GA such as low ADL score, self-reported KPS and abnormal TUG are associated with severe treatment related toxicity in OA with NHL receiving systemic chemo. In particular, the TUG test is objective and easy to administer, and an abnormal TUG time should be routinely incorporated in treatment decision making for these pts.

Disclosures Torka: *Genentech:* Consultancy; *Genmab:* Consultancy; *ADC Therapeutics:* Consultancy; *TG Therapeutics:* Consultancy; *Seagen:* Consultancy; *Lilly USA:* Consultancy. **Epstein-Peterson:** *Amgen:* Research Funding; *Viracta:* Research Funding; *Kymera:* Research Funding; *OncLive:* Honoraria; *WebMD:* Honoraria. **Falchi:** *Genentech:* Consultancy, Other: Advisory Board, Research Funding; *Roche:* Consultancy, Research Funding; *Abbvie:* Consultancy, Other: Advisory Board, Research Funding; *ADC Therapeutics:* Other: Advisory Board; *AstraZeneca:* Consultancy; *Seagen:* Other: Advisory Board; *Genmab:* Consultancy, Research Funding. **Ghione:** *AstraZeneca Pharmaceuticals:* Consultancy; *Kyowa Hakko Kirin:* Consultancy; *Secura Bio:* Consultancy; *Kite, A Gilead Company:* Research Funding. **Horwitz:** *Abcuro Inc.:* Consultancy; *ONO Pharmaceuticals:* Consultancy; *Trillium Therapeutics:* Consultancy, Research Funding; *Kyowa Hakko Kirin:* Consultancy, Research Funding; *SecuraBio:* Consultancy; *Cimieo Therapeutics:* Consultancy; *Shoreline Biosciences, Inc.:* Consultancy; *Takeda:* Consultancy, Research Funding; *Celgene:* Research Funding; *Affimed:* Research Funding; *ADC Therapeutics:* Research Funding; *Yingli Pharma Limited:* Consultancy; *Tubulis:* Consultancy; *Daiichi Sankyo:* Consultancy, Research Funding; *Auxilius Pharma:* Consultancy; *Crispr Therapeutics:* Research Funding; *Millenium:* Research Funding; *Seattle Genetics:* Research Funding; *Verastem/SecuraBio:* Research Funding. **Johnson:** *Myeloid Therapeutics:* Consultancy. **Kumar:** *Genentech:* Consultancy, Research Funding; *Adaptive Biotechnologies:* Research Funding; *Beigene:* Research Funding; *Kite Pharma:* Consultancy; *Loxo/Lily Oncology:* Consultancy, Research Funding; *Janssen:* Consultancy; *Celgene:* Research Funding; *BridgeBio:* Current equity holder in publicly-traded company; *Seattle Genetics:* Research Funding; *Pharmacyclics:* Research Funding; *Astra Zeneca:* Consultancy, Research Funding; *Abbvie Pharmaceuticals:* Research Funding. **Lue:** *OncLive:* Consultancy; *Merck:* Consultancy. **Moskowitz:** *Seattle Genetics:* Honoraria, Research Funding; *Merck:* Honoraria, Research Funding; *Incyte:* Research Funding; *Bristol-Myers Squibb:* Research Funding; *Beigene:* Research Funding; *ADC Therapeutics:* Research Funding. **Palomba:** *Pluto Immunotherapeutics:* Honoraria; *Seres Therapeutics:* Honoraria, Patents & Royalties; *Novartis:* Honoraria; *Ceramedix:* Honoraria; *MustangBio:* Honoraria; *GarudaTherapeutics:* Honoraria; *Rheos:* Honoraria; *Smart Immune:* Honoraria; *Thymofox:* Honoraria; *BMS:* Honoraria; *Cellectar:* Honoraria; *Juno:* Honoraria, Patents & Royalties; *Kite:* Honoraria; *Synthekine:* Honoraria. **Vardhana:** *Immunai:* Consultancy; *Koch Disruptive Technologies:* Consultancy. **Zelenetz:** *Lymphoma Research Foundation:* Membership on an entity's Board of Directors or advisory committees; *AstraZeneca:* Consultancy, Honoraria; *Pharmacyclics:* Consultancy, Honoraria; *Janssen Pharmaceuticals:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria; *Abbvie:* Research Funding; *MEI Pharma Inc:* Consultancy, Honoraria, Research Funding; *BeiGene:* Consultancy, Honoraria, Research Funding; *None other than mutual funds (401K):* Current equity holder in publicly-traded company; *Gilead:* Consultancy, Honoraria; *F. Hoffmann-La Roche Ltd:* Consultancy, Honoraria, Research Funding; *SAB:* Membership on an entity's Board of Directors or advisory committees. **Salles:** *Novartis:* Consultancy; *Molecular Partners:* Consultancy; *Nordic Nanovector:* Consultancy; *ATB Therapeutics:* Consultancy; *BMS/Celgene:* Consultancy; *AbbVie:* Consultancy, Honoraria; *Genentech, Inc./F. Hoffmann-La Roche Ltd:* Consultancy, Research Funding; *Genmab:* Consultancy; *Ipsen:* Consultancy, Research Funding; *Janssen:* Consultancy, Research Funding; *Incyte:* Consultancy; *BeiGene:* Consultancy; *Nurix:* Consultancy; *Orna:* Consultancy; *Merck:* Consultancy, Honoraria; *Kite/Gilead:* Consultancy; *Loxo/Lilly:* Consultancy; *Debiopharm:* Consultancy; *Owkin:* Current holder of *stock options* in a privately-held company; *EPIZYME:* Consultancy. **Hamlin:** *ADC Therapeutics:* Consultancy.

Figure 1. Overall survival in older adults with NHL receiving systemic chemotherapy

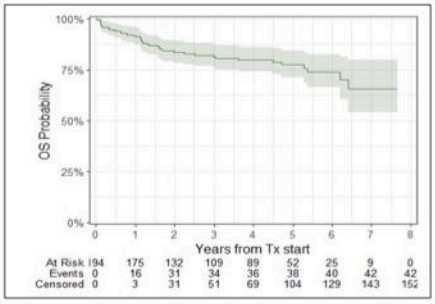

Table 1. General characteristics and geriatric assessment of the study population at baseline and associations with primary endpoint (hospitalization, dose delay or reduction, treatment discontinuation and death)

Characteristic	Overall, N = 193[1]	No, N = 83[1]	Yes, N = 110[1]	p-value[2]
Age (years), median (IQR)	75 (68, 81)	72 (66, 79)	76 (71, 82)	**0.007**
Sex (female)	82 (42%)	35 (42%)	47 (43%)	>0.9
NHL histology				0.3
DLBCL	136 (72%)	55 (66%)	81 (76%)	
FL	27 (14%)	16 (19%)	11 (10%)	
MCL	13 (6.9%)	8 (9.6%)	5 (4.7%)	
MZL	7 (3.7%)	2 (2.4%)	5 (4.7%)	
AITL	4 (2.1%)	1 (1.2%)	3 (2.8%)	
Richter's/SLL	2 (1.1%)	1 (1.2%)	1 (0.9%)	
Stage				0.3
1/2	45 (25%)	23 (28%)	22 (22%)	
3/4	138 (75%)	58 (72%)	80 (78%)	
Age-adjusted IPI				0.088
Low/Low-intermediate	64 (48%)	31 (57%)	33 (42%)	
High-intermediate/High	68 (52%)	23 (43%)	45 (58%)	
Chemotherapy regimen				0.061
R-mini-CHOP	7 (3.6%)	3 (3.6%)	4 (3.6%)	
R-CHOP	137 (71%)	66 (80%)	71 (65%)	
R-bendamustine	18 (9.3%)	8 (9.6%)	10 (9.1%)	
R-EPOCH	22 (11%)	4 (4.8%)	18 (16%)	
Others	9 (4.7%)	2 (2.4%)	7 (6.4%)	
Prephase therapy				0.4
Yes	35 (18%)	13 (16%)	22 (20%)	
No	158 (82%)	70 (84%)	88 (80%)	
ADL score	85 (46, 95)	90 (70, 100)	80 (45, 95)	**0.014**
IADL score	14 (13, 14)	14 (14, 14)	14 (12, 14)	**0.020**
Patient rated KPS	90 (80, 90)	90 (80, 90)	80 (70, 90)	**<0.001**
TUG >= 12 sec				**0.010**
Yes	53 (29%)	15 (19%)	38 (37%)	
No	130 (71%)	64 (81%)	66 (63%)	
BMI	27.0 (24.8, 30.6)	27.0 (25.2, 30.9)	27.0 (24.7, 30.0)	0.7
Mini nutritional assessment (MNA)	24.5 (21.5, 27.0)	25.0 (22.5, 27.1)	24.0 (20.5, 26.5)	0.062

[1]Median (IQR); n (%)
[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Figure 1

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