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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Treatment Intensity and Outcomes in Elderly Patients with DLBCL Receiving First Line Therapy

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Background:
One-third of patients (pts) with newly diagnosed DLBCL are 70 and older. Although a standard of care for first-line (1L) DLBCL is anthracycline-based chemoimmunotherapy with R-CHOP, in elderly DLBCL pts treatment approaches vary and outcomes of these are poorly understood. In this study, we aimed to evaluate long-term outcomes among elderly pts with DLBCL across 1L regimens with a focus on those who received reduced dose (RD) R-CHOP, standard dose (SD) R-CHOP, and non-anthracycline alternative regimens (AR).

Methods:
We evaluated a cohort of pts from the Flatiron Health electronic health record (EHR)-derived, de-identified database with DLBCL diagnosis (dx) after 1/1/2011, age 70 or greater at dx, and with no evidence of prior indolent lymphoma or other malignancy within 2 years of 1L therapy. RD R-CHOP was defined as <80% SD doxorubicin or cyclophosphamide. Time-to-event analysis was performed with the Kaplan-Meier method and differences were evaluated using the log rank test. Real world overall survival (rwOS) was defined as the interval, in months (mos), from DLBCL dx to death or last follow-up. Real world progression free survival (rwPFS) was defined as the interval, in mos, from initiation of 1L therapy to progression, death, or last follow-up. Multiple imputation was performed (m = 50). Multivariate Cox regression analysis (MVA) was conducted within each imputed dataset and pooled. MVA was additionally performed across age strata.

Results:
There were 434 pts included in the complete cohort. Eighty-six percent (N=372) received 1L therapy and 62 pts (14%) had no therapy documented. Among treated pts, 47% were female, median age was 79 (IQR 75-82), and median CCI score 7 (IQR 6-9). Twenty-six percent and 47% had limited and advanced stage at dx, respectively; stage was unknown in 27%. Cell of origin was germinal center (GCB), non-GCB, and unknown in 34%, 24%, and 43%, respectively. Forty-eight percent of pts (N=212) received R-CHOP as 1L. Best real world response (rwR), defined as either complete response (CR) or partial response (PR) to 1L, was 89.0%, 89.5%, and 81.6% (p = 0.20) in pts who received SD R-CHOP, RD R-CHOP, and AR, respectively. CR rates were 78.0%, 58.1%, and 60.2% (p = 0.008) among these cohorts, respectively. Median rwOS and rwPFS among all treated pts was 39.0 mos (32.4-47.3) and 15.2 mos (12.3-23.4), respectively. Among patients who received SD R-CHOP, RD R-CHOP, and AR, median age (IQR) was 72 (71-77), 81 (79-83), and 80 (77-81), respectively (p<0.001). Median Charlson comorbidity index (CCI) score (IQR) was 6 (5-8), 8 (6-9), and 7 (6-9) across these groups, respectively (p<0.001). SD R-CHOP was associated with better rwPFS and rwOS in the entire treated cohort. Real world OS and rwPFS were 95.6 mos (67.0-NE) and 77.3 mos (40.3-NE) for SD R-CHOP, 37.6 mos (27.9-NE) and 15.8 mos (11.9-35.8) RD R-CHOP, and 25.7 mos (16.0-32.6) and 9.6 mos (8.1-12.0) for AR, respectively. When stratifying by age, pts 70-79 years had PFS of 77.3 mos (41.2-NE), 22.4 mos (9.86-NE), and 11.0 mos (8.6-23.4) with SD R-CHOP, RD R-CHOP, and AR, respectively (p <0.0001), whereas pts >=80 had PFS 6.14 mos (4.21-NE), 14.7

mos (8.87-NE), and 7.3 mos (4.47-12.0) with these regimens (p=0.03). In Cox regression MVA, CCI was associated with rwPFS in pts >=80 (HR 1.18, p=0.004). High-risk IPI score was associated with rwPFS (HR 2.13, p=0.05) and rwOS (HR 2.51, p=0.033), but only in pts age 70-79. When stratifying by age and adjusting for comorbidities, IPI, and MYC alteration, treatment with RD R-CHOP and AR were associated with inferior rwPFS and rwOS compared to SD R-CHOP among pts age 70-79, however, there was no association between treatment intensity and outcome among pts >=80 (Table).

Conclusions:

This study represents one of the largest real-world studies evaluating contemporary outcomes among elderly pts with DLBCL receiving 1L therapy. In MVA, SD R-CHOP is significantly associated with improved rwPFS and rwOS compared to RD-RCHOP and AR, but only among pts aged 70-79. There was no effect of treatment intensity or regimen on either rwPFS or rwOS among pts aged >=80. Other covariates significantly associated with outcome included CCI among pts >=80 and high-risk IPI in pts 70-79. These results suggest that pts aged 70-79 should receive SD R-CHOP whenever feasible, but that treatment intensity is not the primary determinant of outcomes among pts aged >=80. CCI should be part of routine evaluation in elderly DLBCL pts.

Disclosures Narkhede: *Genentech, Inc. / F. Hoffmann-La Roche Ltd:* Speakers Bureau; *Genentech, Inc. / F. Hoffmann-La Roche Ltd, ADC Therapeutics, KITE, Abbvie:* Honoraria; *Genentech, Inc. / F. Hoffmann-La Roche Ltd, Gilead, T.G Therapeutics, Kite, Beigene, EUSA, ADC Therapeutics, Adaptive:* Research Funding. **Frosch:** *Abbvie:* Research Funding; *Seagen:* Membership on an entity's Board of Directors or advisory committees; *AstraZenica:* Research Funding; *Roche:* Research Funding. **Chong:** *MJH Healthcare Holdings, LLC:* Honoraria; *Genentech:* Research Funding; *Abbvie:* Research Funding; *Novartis:* Honoraria; *BMS:* Honoraria; *Beigene:* Honoraria. **Isufi:** *Incyte:* Consultancy; *Abbvie:* Consultancy; *Genmab:* Consultancy; *ADC Therapeutics:* Consultancy; *Gilead:* Consultancy, Current equity holder in publicly-traded company; *Beam Therpauetics:* Consultancy. **Awan:** *Pharmacyclics LLC, an AbbVie Company.:* Other: Contracted Research; *Janssen, Gilead, Kite pharmaceuticals, Karyopharm, MEI Pharma, Verastem, Incyte, Johnson and Johnson, Merck, Epizyme, Loxo Oncology, Adaptive Biotechnologies, Genmab:* Other: Consulting Agreements; *AstraZeneca Pharmaceuticals LP:* Other: Advisory Committee; *AbbVie Inc, ADC Therapeutics, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol-Myers Squibb Company, Cardinal Health, Caribou Biosciences Inc, Celgene Corporation, Cellectar Biosciences Inc, DAVA Oncology, Epizyme Inc, Genentech, a member of the Roche:* Other: Consulting Agreements. **Chavez:** *Epizyme:* Speakers Bureau; *Cellectar:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Beigene:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *Astra Zeneca:* Research Funding; *ADC Therapeutics:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Adaptive:* Research Funding; *Genmab:* Honoraria; *Karyopharm:* Membership on an entity's Board of Directors or advisory committees; *Kite/Gilead:* Membership on an entity's Board of Directors or advisory committees; *Lilly:* Honoraria; *Merck:* Research Funding; *Morphosys:* Speakers Bureau; *Novartis:* Membership on an entity's Board of Directors or advisory committees.

Table 1: Multivariable Cox regression of covariate association with outcome in 1L treatment of DLBCL, stratified by age

	Complete Cohort (n=372)		Age 70-79 (n=223)		Age ≥ 80 (n=149)	
Variables	**HR (95% CI)**	**p value**	**HR (95% CI)**	**p value**	**HR (95% CI)**	**p value**
Real world PFS						
Age	1.03 (0.99-1.08)	0.13	-	-	-	-
CCI score	1.07 (1.00-1.16)	0.05	1.02 (0.93-1.13)	0.65	**1.18 (1.06-1.32)**	**0.00**
High risk IPI (vs low risk)	**1.85 (1.02-3.33)**	**0.04**	**2.13 (0.98-4.65)**	**0.05**	1.49 (0.57-3.87)	0.41
Abnormal LDH	1.28 (0.87-1.88)	0.15	1.35 (0.79-2.30)	0.26	1.28 (0.74-2.22)	0.36
BCL2 rearrangement	1.41 (0.90-2.22)	0.13	1.88 (0.97-3.63)	0.06	1.08 (0.59-1.95)	0.80
MYC rearrangement	1.63 (0.92-2.90)	0.09	1.71 (0.74-3.96)	0.20	1.47 (0.75-2.90)	0.26
Treatment Category (vs SD R-CHOP)						
Reduced dose RCHOP (1L therapy)	1.37 (0.84-2.24)	0.21	**1.81 (1.00-3.31)**	**0.05**	0.87 (0.34-2.22)	0.76
Other therapies	**1.93 (1.24-3.03)**	**<0.01**	**2.48 (1.47-4.18)**	**<0.001**	1.26 (0.50-3.18)	0.62
Real world OS						
Age	1.04 (0.99-1.09)	0.09	-	-	-	-
CCI score	1.06 (0.99-1.15)	0.08	1.04 (0.95-1.15)	0.36	1.12 (0.99-1.26)	0.08
High risk IPI (vs low risk)	**2.36 (1.17-4.76**	**0.02**	**2.51 (1.08-5.85)**	**0.03**	2.21 (0.50-9.79)	0.29
Abnormal LDH	1.11 (0.71-1.76)	0.64	1.07 (0.54-2.13)	0.84	1.24 (0.66-2.35)	0.48
MYC rearrangement	**2.19 (1.06-4.54)**	**0.04**	2.02 (0.72-5.69)	0.17	2.12 (0.92-4.89)	0.07
Treatment Category (vs SD R-CHOP)						
Reduced dose RCHOP (1L therapy)	1.57 (0.91-2.73	0.10	**2.13 (1.14-3.98)**	**0.02**	1.26 (0.40-3.98)	0.69
Other therapies	**2.24 (1.36-3.71)**	**<0.01**	**2.55 (1.48-4.40)**	**<0.01**	2.14 (0.69-6.60)	0.18

*CCI, Charlson comorbidity index; IPI, international prognostic index; LDH, lactate dehydrogenase; SD, standard dose

Figure 1

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