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ORAL ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Identification and Clinical Characterization of CNS Relapse in DLBCL Patients across 19 Prospective Phase 2 and 3 Trials - a GLA/ DSHNHL and LYSA Collaboration

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Introduction: Depending on clinical and molecular risk factors, CNS relapse occurs in 1-15% of DLBCL patients (pts) and is associated with dismal outcomes. Despite its important role in further improving DLBCL therapy, a comprehensive and large-scale characterization of secondary CNS relapse remains challenging.

Methods: We conducteda retrospective analysis of 7775 pts treated within 19 prospective German and French phase 2/3 trials to identify and characterize DLBCL pts with progression or relapse in the CNS. Pts with histology different from DLBCL (subtypes), not treated with anti-CD20 antibody, or displaying CNS involvement at diagnosis were excluded from the analysis.
Results: Among 5289 eligible pts, 159 (3%) experienced progression or relapse in the CNS. Median age at diagnosis was 62 years (range: 19-80 years), 47% of pts were female. In 91% of all cases, reference pathology confirmed the diagnosis of DLBCL. At diagnosis, 28 pts (18%), 62 pts (39%), and 69 pts (43%) had a low (0-1 point), intermediate, and high CNS IPI (4-6 points), respectively. 133 pts received front-line therapy with R/O-CHOP, 19 pts with R-(Mega)CHOEP, and 7 pts with R/O-ACVBP. Following first-line therapy, 54% of pts achieved a CR/CRu. For 131 pts (82%), CNS progress/ relapse represented the first PFS event. Prior to the CNS event, salvage therapy was administered to 30 pts, including 11 pts treated with HDT/ASCT and one pt receiving allogeneic SCT.
For 70 out of 158 pts (44%), CNS involvement was classified as intracerebral, 31% showed meningeal, and 3% intraspinal lymphoma involvement. In 22% of pts, CNS involvement was classified as combined including 5 cases with eye involvement. The CNS event occurred as progression without prior CR/ CRu of disease in 61 out of 159 pts (38%). For 155 pts it could be specified that 25% had an isolated progress in the CNS while 12% showed both CNS and concomitant systemic progress. 35% of pts showed an isolated CNS relapse while 28% suffered from a combined relapse.
82% of all CNS events occurred within the first two years after randomization while 29 pts (18%) experienced a late CNS event after 24 months. Notably, 46% of pts with low CNS IPI developed a late CNS event compared to 9% with high CNS IPI at diagnosis (Fisher exact, $p<0.001$). During the course of disease, 138 pts (87%) showed extranodal lymphoma involvement outside the CNS. The most frequently involved extranodal sites were bone (34%), gastro-intestinal tract (21%), soft-tissue (21%), kidney/ adrenal gland (20%), lung (19%), and liver (18%).
In general, pts with CNS event had poor outcomes with a median OS of 3.4 months (95% CI 2.9-4.2) and a 2-year OS of only 15% (10-22%). While sex and initial (CNS) IPI had no impact on OS, we observed significantly worse OS for pts older than 70 years at diagnosis (log rank, $p<0.001$). OS was poor regardless of the site of CNS manifestation. Pts with isolated CNS disease demonstrated significantly better OS than pts with concomitant systemic involvement ($p=0.023$). Pts with CNS events occurring later than 24 months from randomization did not show improved OS compared to pts with early relapse/ progression ($p=0.19$).
Treatment categories were reported for 150 pts. 95 pts received immunochemotherapy (IC), 30 pts in combination with radiotherapy (RT). More precisely, 69 pts received salvage therapies containing systemic MTX and 22 pts underwent consolidation with HDT/ASCT (73% of which had thiotepa-based conditioning regimens). Three pts received allogeneic SCT for consolidation. 28 pts were treated with RT alone (+/- intrathecal therapy (IT)). 27 pts received only IT, corticosteroids, or no treatment. Pts consolidated with HDT/ ASCT or allogeneic SCT had superior outcomes with a 3-year OS of 36% (20%-66%) compared to 18% (7.5%-44%) for pts receiving IC and RT, and to 9.7% (3.9%-24%) and 9.5% (2.8-32%) for pts treated with IC or RT alone, respectively (**Fig. 1**). Overall, pts achieving a CR after CNS event (38/159, 24%) showed a 3-year OS of 52% (37-73%).
Conclusions: This large study including more than 5000 DLBCL pts all treated on prospective clinical trials highlights the unmet medical need to improve the outcome of DLBCL pts suffering from CNS relapse. About one third of pts who underwent transplantation showed long-term survival in contrast to all other pts displaying very dismal outcomes. Novel strategies including targeted therapies and CAR T cells will have to challenge the survival rates reported here.

Disclosures Renaud: *Janssen:* Honoraria; *Takeda:* Honoraria. **Poeschel:** *Gilead:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: travel expenses, congress support; *BeiGene:* Membership on an entity's Board of Directors or advisory committees; *Swedish Orphan Biovitrum GmbH:* Membership on an entity's Board of Directors or advisory committees; *PentixaPharm GmbH:* Membership on an entity's Board of Directors or advisory committees; *Amgen:* Other: travel expenses, congress support; *Abbvie:* Other: travel expenses, congress support; *Genmab:* Consultancy; *Roche:* Other: travel expenses, congress support; *Janssen-Cilag:* Consultancy; *EUSA Pharma:* Consultancy; *Bristol-Myers Squibb:* Consultancy, Membership on an entity's Board of Directors or advisory committees, Other: travel expenses, congress support; *AstraZeneca:* Honoraria; *Lilly:* Membership on an entity's Board of Directors or advisory committees. **Recher:** *Jazz Pharamceuticals:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Astellas:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Abbvie:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *BMS:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *Iqvia:* Research Funding; *Novartis:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Servier:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Held:** *Janssen:* Consultancy, Honoraria; *Bristol-Myers Squibb:* Consultancy, Honoraria, Research Funding; *Amgen:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *MSD:* Consultancy, Honoraria. **Casasnovas:** *Abbvie:* Consultancy, Honoraria; *ADC Therapeutics:* Consultancy, Honoraria; *AMGEN:* Consultancy, Honoraria; *Astra Zeneca:* Consultancy, Honoraria; *BEIGENE:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *GILEAD/KITE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *MSD:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *ROCHE:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding; *TAKEDA:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Research Funding. **Tilly:** *ADC Therapeutics:* Membership on an entity's Board of Directors or advisory committees; *BMS:* Membership on an entity's Board

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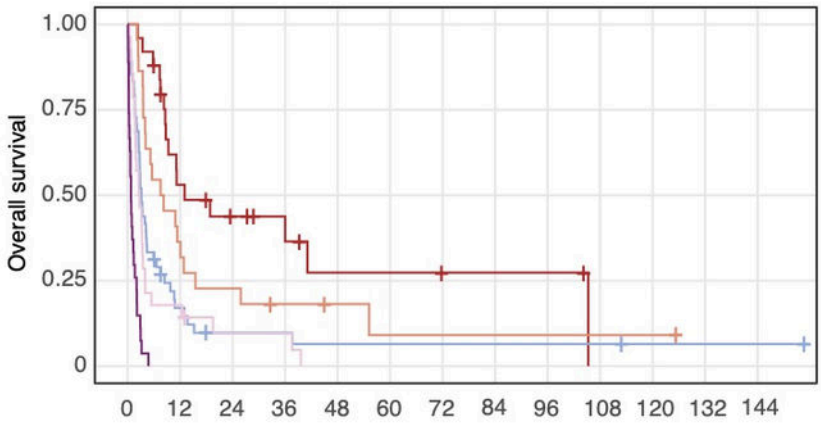

Treatment for CNS event													
HDT/ASCT or AlloSCT	25	12	8	6	3	3	2	2	2	0	0	0	0
Chemo+RT	22	8	5	3	2	1	1	1	1	1	1	0	0
Chemo alone	48	7	3	3	2	2	2	2	2	2	1	1	1
RT alone	28	5	2	2	0	0	0	0	0	0	0	0	0
Palliative care	27	0	0	0	0	0	0	0	0	0	0	0	0

Figure 1

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