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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Do the Control Cohorts of Phase III Randomized Trials Reflect the Real-World Results of DLBCL Patients?

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Background

Development of innovative therapeutical strategies is essential to improve survival of patients (pts) with diffuse large B-cell lymphoma (DLBCL), and control cohort selection in clinical trials should reflect real-world (RW) outcomes of pts. The ongoing frontMIND trial (NCT04824092) testing tafasitamab + lenalidomide + R-CHOP vs. R-CHOP alone targets at pts with high-risk DLBCL including short diagnosis-to-treatment interval (DTI). The GOYA and POLARIX trials have been published already, and based on results of the latter study, polatuzumab vedotin was approved in the 1 st line therapy of all DLBCL patients treated up to now with R-CHOP. The aim of this analysis was to compare outcomes of pts who fulfill the main inclusion/exclusion criteria (IC/EC) for the frontMIND, GOYA, and POLARIX trials in a daily practice with assumed and observed outcomes of control cohorts of these trials, as well as to establish proportion of DLBCL pts not fitting the trial population criteria.

Methods

Between 2010-2021, a total of 3875 pts with de novo systemic DLBCL or high-grade B-cell lymphoma (HG B-NHL) with available data and follow-up were identified in the CLSG lymphoma registry NiHiL (NCT03199066). All pts treated by R-CHOP entered the analysis as unselected RW cohort. Subsequent subgroup selection of pts was based on the main IC/EC: frontMIND (PS ECOG 0-2, age 18-80 years (y); IPI 3-5 in pts > 60 y or aaIPI 2-3 in pts ≤ 60 y; DTI, ≤ 28 days), GOYA (PS ECOG 0-2, age ≥ 18 y, IPI 2-5, IPI 1 in pts ≤ 60 y, IPI 0 in pts with bulky), and POLARIX trial (PS ECOG 0-2, age 18-80 y, IPI 2-5; **Figure**). Primary endpoint was PFS, secondary endpoint OS. We have performed a comparison of survival of the unselected RW cohort versus

RW-selected IC/EC subgroups, and numeric comparison of survival of the RW pts versus assumed/observed survival of R-CHOP-treated control cohorts of frontMIND, GOYA and POLARIX trials.

Results

The unselected RW R-CHOP-treated pts ($n = 2612$; 67% of all DLBCL pts; median age 66 y) were diagnosed with advanced clinical stage (aCS) in 57%, PS ECOG ≥ 2 in 26%, elevated LDH in 61%, IPI 3-5 in 48%, and AA IPI 2-3 of pts ≤ 60 y of age in 41%. Median DTI was 30 days with DTI ≤ 28 days observed in 45% of cases. Majority of pts (79%) received ≥ 6 cycles of R-CHOP. The ORR was 85% (CR rate 74%). With median follow-up time of 6.5 y, PFS was 75% at 2 y and 71% at 3 y, and OS 81% at 2 y and 78% at 3 y (**Table**).

RW-frontMIND accounts for 23%, RW-POLARIX 59%, and RW-GOYA subgroup for 71% of all R-CHOP-treated pts ($n = 2612$). Pts in RW-frontMIND ($n = 608$; median age 66 y) presented with higher-risk features, i.e., IPI 3-5 in 97%, aCS in 92%, PS ECOG 2 in 39%, and elevated LDH in 90%. Median DTI was 18 days. 77% of pts received all intended ≥ 6 cycles of R-CHOP. The ORR was 80% with CR rate 66%.

With a median follow-up of 6.0 y, survival of RW-frontMIND cohort was shorter (3-y PFS 61% and 3-y OS 69%) in comparison to the unselected R-CHOP cohort ($n = 2612$; 3-y PFS 71%, $P < 0.001$; 3-y OS 78%, $P < 0.001$) as well as to RW-GOYA ($n = 1853$; 3-y PFS 69%, $P < 0.001$; 3-y OS 77%, $P < 0.001$) and RW-POLARIX cohorts ($n = 1544$; 2-y PFS 71% and 3-y PFS 66%, $P = 0.013$; 2-y OS 79%, $P = 0.058$). Similarly, survival of RW-POLARIX was shorter when compared with unselected RW cohort (PFS $P = 0.0002$; OS $P = 0.008$) and RW-GOYA (PFS $P = 0.019$, OS $P = 0.013$). The survival of RW-GOYA didn't differ when compared with unselected RW cohort (PFS $P = 0.2058$; OS $P = 0.4732$).

RW cohorts showed numerically improved outcomes than the assumed PFS in control arms of all 3 trials with crude difference of 9% for GOYA, and 4% for both POLARIX and frontMIND trials. When compared the RW cohorts with observed outcomes, the difference was only 2% for GOYA and 1% for POLARIX control arms.

Conclusion

Survival of pts with DLBCL in a daily practice gradually decreases from unselected R-CHOP-treated cohort, toward pts selected by IC/EC of GOYA, POLARIX, and finally, frontMIND trial, in concordance with increasingly stringent eligibility criteria of the trials. On the other hand, selection process leads to decrease of relevant cohort's size; i.e., out of all RW R-CHOP-treated pts GOYA is relevant for 71%, POLARIX for 59% and frontMIND only for 23% of RW pts. Although there is a trend to underestimate the assumed survival of GOYA and POLARIX control cohorts, the observed survival of control arms of these trials is in concordance with our RW data.

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Figure. Flow chart.

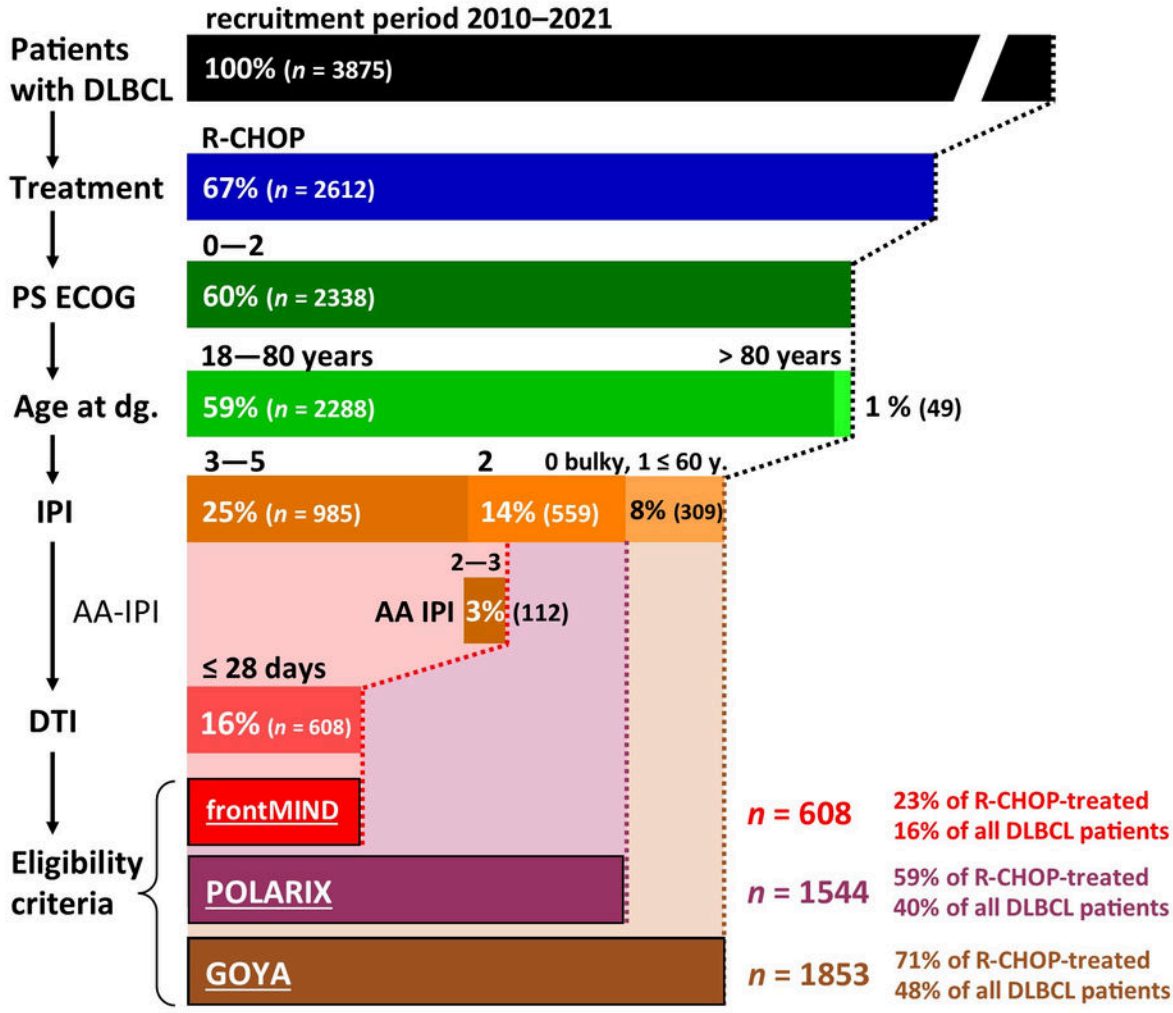

Table. Survival of pts with DLBCL treated by R-CHOP (*n* = 2612) and those fulfilling main IC/EC of frontMIND (*n* = 608), POLARIX (*n* = 1544) and GOYA trials (*n* = 1853) versus expected and observed survival of control cohorts treated by R-CHOP in the respective trials.

Trial	*Survival timepoints*	Progression-free survival (R-CHOP)				Overall survival (R-CHOP)			
		Clinical trial		RW	RW	Clinical trial		RW	RW
		Expected	Observed	IC/EC	unselected	Expected	Observed	IC/EC	unselected
GOYA	3 years	60%	67%	69%	71%	---	81%	77%	78%
POLARIX	2 years	62% *	70%	71% **	75%	---	89%	79%	81%
frontMIND	3 years	57%	---	61%	71%	63%	---	69%	78%

* at 3 years, ** 66% at 3 years

Figure 1

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