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POSTER ABSTRACTS

705.CELLULAR IMMUNOTHERAPIES: LATE PHASE AND COMMERCIALLY AVAILABLE THERAPIES

Relinf Registry-Based Analysis Shows Overall Survival Improvement with New Therapies for Relapsed or Refractory Large B-Cell Lymphoma: A Study from the Geltamo Group

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Introduction: Several new therapeutic agents have been approved in recent years for the treatment of relapsed/refractory (R/R) Large B cell lymphoma (LBCL) (diffuse large B cell lymphoma [DLBCL] and high-grade B cell lymphomas [HGBCL]), such as new monoclonal antibodies (MA), bispecific antibodies (BA) and CAR-T cell therapy. The objective of our study was to evaluate the epidemiology and the use of these new therapies (NT) in Spain and to analyze the impact on survival.
Methods: We present a multicenter retrospective study based on the GELTAMO (Spanish lymphoma group) RELINF platform. From 60 centers actively registering on the platform, 17 university hospitals accepted to participate, and 5 of them were CAR-T therapy providers. Participating centers completed a short questionnaire on disease relapse and the use of new drugs in their registered patients. The histologies included were DLBCL, HGBCL not otherwise specified (NOS), and double hit (DH).
Results: From 3270 patients with ABCL registered, 2853 patients were included in the present analysis; 738 patients experienced R/R disease, 492 (67%) were refractory or had early relapse (up to 1 year from the first line), and 246 (33%) late relapses, half of them (54%) during the second year. In both early and late relapse groups, about a third of patients were older than 80 years. Early relapses were significantly higher in double/triple hit HGL (34%) and T-cell-rich DLBCL (29%) compared to DLBCL or HGL NOS (16%) ($p<0.001$). The median number of lines among relapsed patients was 2 (1-10). 236 patients received NT, with the following distribution: CAR-T, n=144, BA, n=68, polatuzumab-based, n=92, and tafasitamab-lenalidomide, n=14. Most patients who received only 2 lines (n=376) were treated with conventional treatments, although 11 patients (3%) received CAR-T, 11 (3%) BM, 15 (4%) polatuzumab-based, and 5 (1%) tafasitamab-lenalidomide. Among 354 patients who received more than

2 lines of treatment, 130 (37%) received CAR-T cell therapy, 75 (21%) polatuzumab, 9 (2%) tafasitamab-lenalidomide, 55 (15%) BA, and 160 (45%) of these patients did not receive any NT. In the overall series, with a median follow-up of 49 months (95%CI: 47-51), median progression-free survival (PFS) was 54 months (95%CI: 48-61), and median overall survival (OS) was 82 months (95%CI: 74-90). Considering only the R/R patients, with a median follow-up of 40 months since the first relapse, the median OS2 (mOS2) was 16.8 (IC95%: 14.5-19) months. Survival analysis is shown in **Table 1**. The mOS2 for the early relapse group was 13.5 (95%CI: 11.5-15.5) months vs 31.1 (95%CI: 22.5-39.8) months for late relapses. Median OS2 for relapsed patients treated with NT was 31.1 months (95%CI: 22.5-39.7) compared with 11.9 months (95%CI: 9.2-14.6) for the group of standard treatment ($p<0.001$)) **(Figure 1)**. Interestingly, OS2 was longer in patients treated in CAR-T provider centers than in non-CAR-T centers, in both early relapse group (mOS: 18.3 months [95%CI: 14.1-22.5] vs. 8.6 months [95%CI: 6.2-11]: $p<0.001$) and late relapse group (37.9 months [95%CI: 24.2-51.5] vs. 18.7 months [95%CI: 13.9-23.4], $p=0.001$). This difference was not found when we evaluated high complexity institutions (those that perform allogeneic transplant) vs. those that are no. In multivariate analysis, early relapse (HR 1.68, 95%CI 1.37-2.06, $p<0.001$), age over 65 years (HR 1.91, 95%CI: 1.23-2.98, $p=0.004$), treatment with CAR-T cell therapy (HR 0.68, 95%CI: 0.51-0.90, $p=0.007$) and treatment in a CAR-T cell provider center (HR 0.7, 95%CI: 0.58-0.85, $p<0.001$) independently influenced OS2.

Conclusions: Our real-world analysis confirms the negative impact on OS of factors like age or early relapse in patients with R/R LBCL. According to our results, the introduction in recent years of NT has markedly improved OS, especially CAR-T cell therapy.

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	Median OS2 (CI95%)	p
Sex:		0.72
- Male	16 (13-20)	
- Female	18 (15-21)	
Age:		<0.001
- <40	31 (17-45)	
- 40-64	26 (18-34)	
- 65-74	14 (10-19)	
- >74	8 (6-10)	
Diagnosis:		0.23
- DLBCL	18 (15-20)	
- DLBCL T-cell rich	26 (12-41)	
- HGL NOS	20 (12-28)	
- HGL doble/triple hit	8 (4-11)	
Type of relapse:		<0.001
- Late relapse	31 (22-40)	
- Early relapse	13 (11-15)	
Treatment lines:		0.018
- 0-2	11 (6-16)	
- >2	19 (16-22)	
CAR-T center:		<0.001
- Yes	24.7 (18.1-31.3)	
- No	11.3 (8.9-13.7)	
New immunotherapies at relapse:		
- No	12 (9-15)	
- CAR-T	37 (31-44)	<0.001
- BA	23 (17-29)	0.024

Table 1. Univariate analysis of overall survival, since first relapse

Figure 1