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ORAL ABSTRACTS

731.AUTOLOGOUS TRANSPLANTATION: CLINICAL AND EPIDEMIOLOGICAL

Autologous Stem Cell Transplantation Remains a Curative Option As Second Line Treatment for Patients with Relapsed/Refractory Large B Cell Lymphoma: Spanish Multicenter Geth-TC/Geltamo Study

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Introduction:
High dose therapy and Autologous Stem Cell Transplantation (ASCT) has remained the treatment of choice for transplant-eligible patients with relapsed/refractory (R/R) large B cell lymphoma (LBCL) and chemosensitive disease. Recently, CART

therapy has been approved in second line for patients with primary refractory disease or early relapse (<1 year of first-line therapy) and the current role of ASCT has been questioned. However, several studies have shown that despite early failure of first line, patients with chemosensitive disease after salvage therapy can be cured with ASCT consolidation. Our objective was to analyze the efficacy of ASCT in patients with R/R LBCL after a long-term follow up and try to define the optimal role of ASCT.

Patients and methods:

We performed a retrospective multicenter study based on GETH-TC database of ASCT. We included patients from centers of GETH-TC/GELTAMO with R/R LBCL who underwent ASCT from January 2010 to December 2021. All the patients received rituximab and anthracycline-based frontline therapy. Diffuse LBCL NOS, high-grade B-cell lymphoma double/triple hit and NOS, primary mediastinal, transformed follicular lymphoma (tFL) and other less frequent LBCL subtypes were included. Plasmablastic and primary central nervous system lymphoma were excluded. Patients who underwent ASCT in first CR were also excluded except patients with tFL who had received previous anthracycline-based frontline therapy for the indolent lymphoma. The primary endpoints were progression-free survival (PFS) and overall survival (OS) in the overall series and according to different prognostic factors, including disease status at ASCT. Disease status was defined as complete remission (CR), partial response (PR) and refractory disease (stable disease or progression) assessed by PET/CT.

Results:

Seven-hundred and ninety-one patients fulfilled the inclusion criteria. Patients characteristics are summarized in **Table 1**. After a median follow-up of 74 months (95%CI 68-81), 65% of the patients were alive and 84% of them free of disease. Six-year-PFS and OS were 51% (95%CI 47-54) and 63% (95%CI 60-67), respectively. Non-relapse mortality at 1 year was 9% (95%CI 7-11). The main causes of death were progression in 161 (58%), ASCT-related toxicity in 18 (6%) and other causes in 98 (35%). PFS was significantly influenced by age at ASCT, treatment lines prior to ASCT and disease status at ASCT (p<0.01). OS was influenced by age at diagnosis, R-IPI at diagnosis, age at ASCT, treatment lines prior to ASCT and disease status at ASCT (p<0.01). In the multivariate analysis, age >60 years at ASCT [HR 1.31 (95%IC: 1.06-1.62), p=0.011], ASCT as $\geq 3^{th}$ line [HR 1.81 (95%IC: 1.42-2.31), p<0.001] and PR versus CR at ASCT [HR 1.46 (95%IC: 1.18-1.81), p<0.001] were the only independent variables influencing PFS, **Figure 1**. Age >60 years at ASCT [HR 1.62 (95%IC: 1.24-2.12), p<0.001], ASCT as $\geq 3^{th}$ line [HR 1.77 (95%IC: 1.32-2.37), p<0.001] and PR versus CR at ASCT [HR 1.58 (95%IC: 1.22-2.05), p<0.001] were the only independent variables for OS. From 307 (39%) patients who relapsed after ASCT, 59 received CART therapy (median PFS 8.9 months) and 69 allo-SCT (median PFS 10.8 months).

Refractory disease or early relapse did not significantly influenced survival. Analyzing this population separately (n=477), disease status at ASCT (PR versus CR) and ASCT as $\geq 3^{th}$ line were the only independent variables for both PFS [HR 1.46 (95%IC: 1.11-1.92), p=0.007; HR 1.79 (95%IC: 1.32-2.43), p<0.001, respectively] and OS [HR 1.92 (95%IC: 1.38-2.67), p<0.001; HR 1.91 (95%IC: 1.35-2.69), p<0.001, respectively].

Conclusions:

To our knowledge, this is the largest series analyzing the efficacy of ASCT in patients with R/R LBCL after rituximab-containing frontline therapy. Our results indicate that ASCT is a curative option for patients with chemosensitive disease (especially in CR after salvage), regardless of the timing of relapse after frontline treatment. These data support that ASCT could be considered in patients with primary refractory or early relapse, provided the disease is sensitive to salvage therapy.

Disclosures Martínez: *Novartis:* Honoraria, Research Funding. **Caballero:** *BMS:* Honoraria; *Gilead:* Honoraria; *Novartis:* Honoraria. **Bastos-Oreiro:** *Kite-Gilead:* Honoraria, Other: travel. **Mussetti:** *BMS, Jazz Pharaceuticals:* Consultancy; *Gilead:* Research Funding; *Takeda:* Honoraria. **Sureda Balari:** *Astra Zeneca:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *BMS/Celgene:* Consultancy, Honoraria, Research Funding; *Pierre Fabre:* Consultancy, Honoraria; *Kite:* Consultancy, Honoraria; *Jannsen:* Consultancy, Honoraria; *Sanofi:* Consultancy, Honoraria; *GenMab:* Consultancy, Honoraria; *Takeda:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *MSD:* Consultancy, Honoraria. **Martín García-Sancho:** *Sobi:* Consultancy, Honoraria; *Eusa Pharma:* Honoraria; *Takeda:* Honoraria; *Incyte:* Consultancy; *Lilly:* Consultancy; *ADC Therapeutics America:* Consultancy; *Miltenyi:* Consultancy; *Janssen:* Honoraria; *Gilead / Kite:* Consultancy, Honoraria; *Novartis:* Consultancy; *Kyowa Kirin:* Consultancy; *BMS/Celgene:* Consultancy, Honoraria; *Roche:* Consultancy, Honoraria; *Abbvie:* Consultancy; *Ideogen:* Consultancy.

Table 1: Patients characteristics	N (791)
Median age at diagnosis (range)	54 (17-74)
Median age at ASCT (range)	56 (18-76)
Gender (M/F) (%)	450 (57%) / 341 (43%)
Diagnosis:	
- DLBCL NOS	540 (68%)
- HGBCL DH/TH	32 (4%)
- HGBCL NOS	27 (3%)
- PMLBL	55 (7%)
- DLBCL transformed	76 (10%)
- DLBCL grey zone	18 (2%)
- DLBCL T-cell rich	20 (2%)
- Other	8 (1%)
- Missing	15 (2%)
Ann Arbor stage at diagnosis:	
- I-II	168 (21%)
- III-I	606 (77%)
- Missing	17 (2%)
B-symptoms at diagnosis:	
- No	405 (51%)
- Yes	354 (45%)
- Missing	32 (4%)
Bulky disease at diagnosis:	
- No	504 (64%)
- Yes	241 (30%)
- Missing	46 (6%)
Extranodal involvement:	
- No	286 (36%)
- Yes	464 (59%)
- Missing	41 (5%)
R-IPI at diagnosis:	
- 0	42 (5%)
- 1-2	329 (42%)
- 3-5	346 (44%)
- Missing	74 (9%)
Response after frontline:	
- CR	443 (56%)
- PR	154 (19%)
- SD	45 (6%)
- PD	149 (19%)
Disease status at salvage therapy:	
- Late relapse	314 (40%)
- Early relapse	128 (16%)
- Primary refractory	349 (44%)
Second line therapy:	
- R-ESHAP	442 (56%)
- R-DHAP	48 (6%)
- R-ICE	41 (5%)
- R-GDP	38 (5%)
- Other	195 (25%)
- Missing	27 (3%)
Conditioning regimen:	
- BEAM	628 (79%)
- R-BEAM	75 (9%)
- Z-BEAM	19 (2%)
- TEAM	4 (0.5%)
- Other	49 (6%)
- Missing	16 (2%)
Treatment line at ASCT:	
- Second line	617 (78%)
- Third line	147 (19%)
- Frontline in transformed	27 (3%)
Disease status at ASCT:	
- CR	481 (61%)
- PR	275 (35%)
- SD/PD	21 (3%)
- Not evaluated	14 (2%)

ASCT: Autologous stem cell transplantation. M: Male. F: Female. DLBCL: Diffuse large B cell lymphoma. HGBCL: High grade B cell lymphoma. DH/TH: Double hit/triple hit. PMLBL: Primary mediastinal large B cell lymphoma. CR: Complete response. PR: Partial response. SD: Stable disease. PD: Progression disease. R-ESHAP: Rituximab, etoposide, cytarabine, cisplatin and methylprednisolone. R-DHAP: Rituximab, dexamethasone, cytarabine and cisplatin. R-ICE: Rituximab, ifosfamide, carboplatin and etoposide. R-GDP: Rituximab, gemcitabine, cisplatin and dexamethasone. BEAM: BCNU, etoposide, cytarabine and melphalan. R-BEAM: Rituximab-BEAM. Z-BEAM: Yttrium-90-ibritumomab tiuxetan-BEAM. TEAM: Thiotepa, etoposide, cytarabine and melphalan.

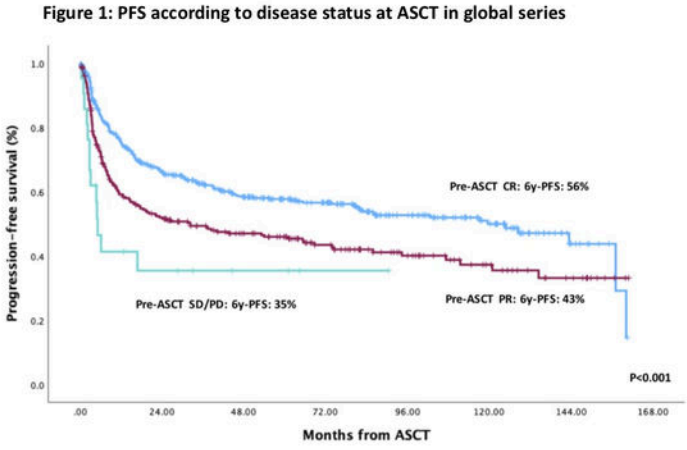

Figure 1

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