BAM induction followed by autologous stem cell transplantation for patients with primary central nervous system lymphoma: a multicenter study from the Spanish group GEL-TAMO

Authors: M. López-Parra[1], A. Martín[1], C. Grande[2], S. Bobillo[3], V. Noriega[4], S. Rojas[1], J.M. Sancho[5], N. Alonso[6], E. González-Barca[7], L. Escoda[8], P. Fernández-Abellán[9], A. Álvarez-Carmona[10], C. Montalbán[11], J.M. Moraleda[12], E. Pardal[13], M. J. Peñarrubia[14], E. Pérez-Ceballos[15], P. González Sierra[16], J. Pérez de Oteyza[17], M.J. Ramírez[18], A. Salar[19], P. Sánchez-Godoy[20], F. Graus[22], M.D. Caballero[1], A. López-Guillermo[21]

Institutions: Departments of Hematology of the following spanish centers: 1. Hospital Universitario de Salamanca and IBSAL, Salamanca; 2. Hospital 12 de Octubre, Madrid; 3. Hospital Valld´Hebron, Barcelona; 4. Complejo hospitalario Universitario A coruña; 5.Hospital Germans Trias i Pujol, Badalona; 6. Hospital Clínico Universitario de Santiago, Santiago; 7.Instituto Catalán de Oncología, L´Hospitalet del Llobregat; 8. Hospital Joan XXIII, Tarragona; 10. Hospital General Universitario de Alicante; 9. Hospital Clínico San Carlos, Madrid; 11. Patología e Investigación Translacional, MD Anderson Cancer Center, Madrid; 12. Vírgen de la Arrixaca, Murcia; 13. Vírgen del Puerto, Plasencia; 14.Hospital Clínico de Valladolid; 15. Hospital Morales Messeguer, Murcia; 16. Hospital General Ciudad de Jaén, Jaén; 17. Hospital Madrid Norte, Sanchinarro, Madrid; 18. Hospital de Jerez de la Frontera, Jerez de la Frontera; 19. Hospital del Mar, Barcelona; 20. Hospital Severo Ochoa, Madrid; 21. Hospital Clinic y Provincial de Barcelona , and departament of Neurology: 22. Departament de Neurology, Hospital Clinic y Provincial de Barcelona, Barcelona

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a rare malignancy with peculiar clinical and biologic features, aggressive course, and unsatisfactory outcome. To date, there is no standardized treatment of PCNSL. Concerns regarding neurocognitive toxicity of whole-brain radiotherapy (WBRT) have motivated development of alternative, dose-intensive chemotherapeutic strategies as consolidation, such as autologous stem-cell transplantation (ASCT). In the present study, we have evaluated the toxicity and efficacy of high-dose consolidation with ASCT after chemotherapy induction in patients with newly diagnosed PCNSL. We present the analysis of 63 patients treated between July 2008 and November 2012

Objectives: Analyze response to treatment, progression-free survival (PFS), overall survival (OS) and toxicity.

METHODS

In 2008, the Spanish group GELTAMO developed a **clinical protocol** for first-line treatment of patients with PCNSL consisting of an induction chemotherapy with 2 cycles of BAM (BCNU 100 mg/m^2 day 1, Ara-C 3000 mg/m^2 days 9, 25 and 41, and methotrexate 2000 mg/m^2 days 8, 24 y 40). Patients who achieved at least partial response (PR) received an intensification with high-dose chemotherapy (BCNU 400 mg/m^2 day -6, and thiotepa 5 mg/Kg days -5 and -4) followed by ASCT (day 0), whereas BAM refractory patients received WBRT (45 Gy), salvage therapy or palliative treatment

Multicenter and **retrospective** study

We present the analysis of 63 patients treated between July 2008 and November 2012

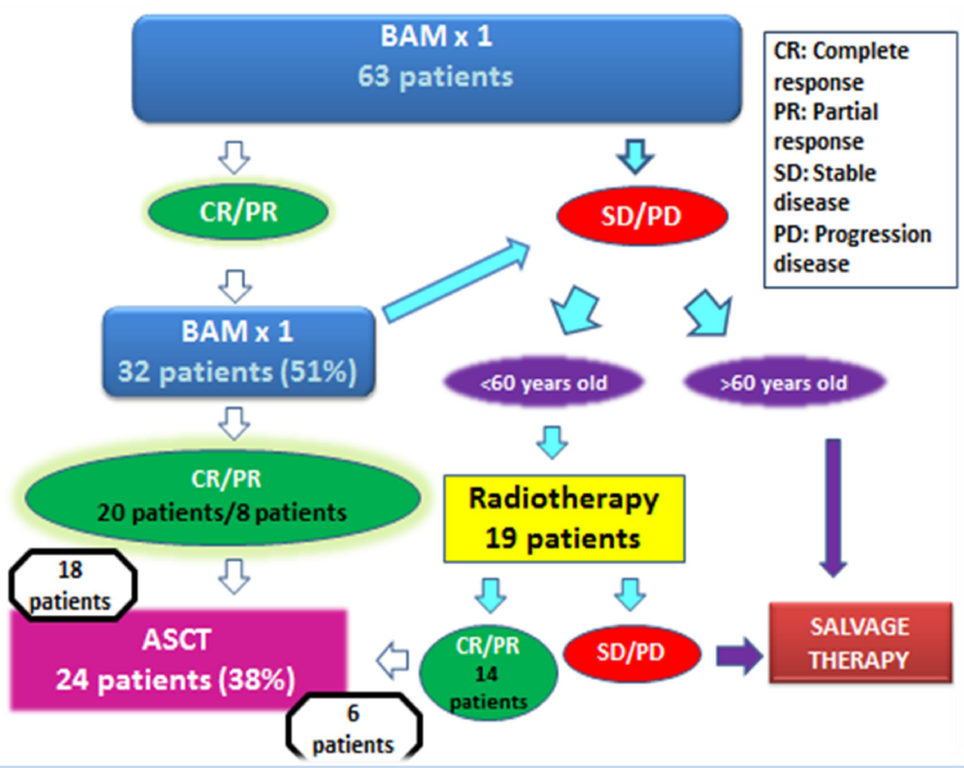
PATIENTS CHARACTERISTICS

Registered in protocol	75
Evaluable patients	63
Median age (range)	59 (29-70)
Less than 60 years old	43%
Male sex	65%
Negative HIV serology	100%
ECOG < 2	54%
Normal LDH	71%
Histology	
-DLBCL	97%
-Follicular lymphoma	1,5%
-Peripheral T-cell lymphoma (NOS)	1,5%

RESULTS

GRADE 3-4 TOXICITIES (WHO)		
	BAM (n=52)	ASCT (n=24)
Leucopenia	43%	96%
Trombocytopenia	21%	83%
Anemia	7%	57%
Hepatic toxicity	5%	0%
Renal toxicity	6%	0%
Pulmonary toxicity	2%	0%
Thrombosis	6%	0%
Infection	22%	26%

RADIOTHERAPY TOXICITY (n=19)	
Mild congnitive impairment	n=1
Severe cognitive impairment	n=2
Leukoencephalopathy	n=3
Cortical atrophy and leukoencephalopathy	n=1
Hidrocephalus	n=2



32 out of 63 patients (51%) completed the 2 planned BAM cycles, achieving CR 20 patients (32%) and 8 (13%) PR. Reasons for not completing the 2 planned BAM courses were: lymphoma progression (n=24) and toxicity (n=3).

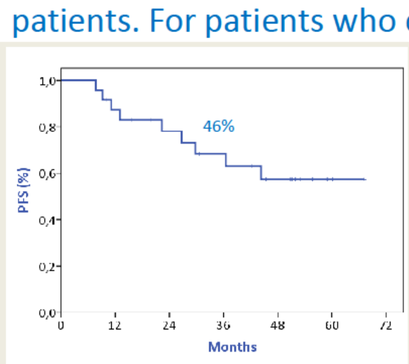
19 patients received WBRT, resulting in 5 and 9 patients achieving CR and PR, respectively. Regarding WBRT toxicity, 1 patient showed mild cognitive impairment, 3 leukoencephalopathy (2 mild, 1 severe), and 2 hydrocephalus.

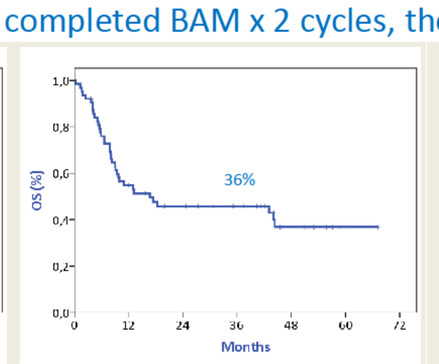
Finally, 24 patients (38%) underwent high-dose therapy and ASCT (18 after BAM and 6 after WBRT). Reasons for not performing the transplant were: progression of lymphoma (n=20), early death (n=6), comorbidities (n=7), mobilization fail (n=2) or physician decision (n=4)

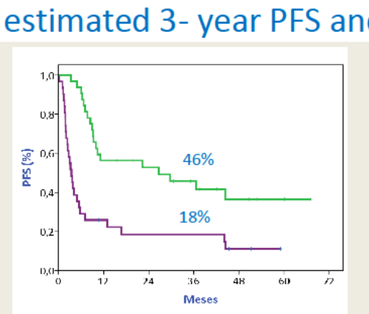
SURVIVAL

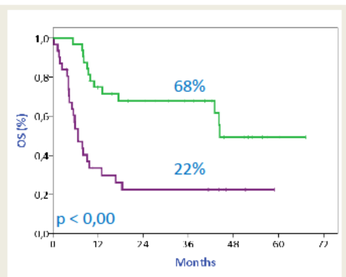
After a median follow up of 42 months (2-67), 27 patients are alive (78% in CR), 36 patients have died (81% due to lymphoma progression, 11% due to infectious complications, and 8% due to other causes) and one patient has developed a secondary myelodisplastic syndrome (RAEB-2).

Estimated 3-year progression-free survival and overall survival were 36% and 46% respectively, for the whole series, and 68% and 85%, respectively for transplanted patients. For patients who completed BAM x 2 cycles, the estimated 3- year PFS and OS were 46% and 88% respectively.

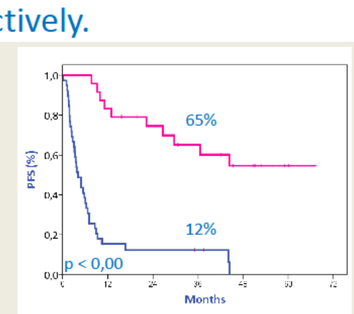


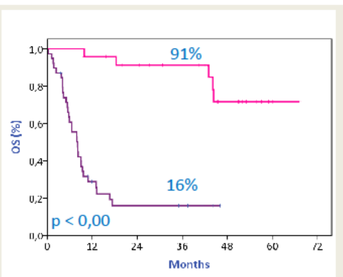






Patients who completed BAMx2
Patients who didn´t complete BAMx2





Patients who underwent ASCT
Patients who didn´t undergo ASCT

CONCLUSIONS

BAM induction regimen followed by high dose therapy and ASCT had an adequate toxicity profile. However, although results after ASCT seem to be good, only 50% of patients completed the 2 planned BAM cycles, mainly due to lymphoma progression. Consequently, more effective induction regimens are needed for these patients.

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Aggressive B-cell lymphoma

MIRIAM LÓPEZ-PARRA

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