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ELEVENTH ANNUAL MEETING

NEW STRATEGY OF FIRST-LINE TREATMENT OF PRIMARY MEDIASTINAL LYMPHOMA (PML):
ONE CENTER EXPERIENCE

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INTRODUCTION

PML is an aggressive lymphoma with a unique biology. Regardless of the first-line therapy, refractory disease can occur in up to 10% of patients and correlates with poor outcomes. The long-term toxicity of radiotherapy and the risk of recurrence with central nervous system (CNS) involvement are subjects of ongoing debate. More intensive regimens are associated with significant toxicity. We developed a hybrid protocol for the first-line treatment of PML. To improve the outcome, we integrated lenalidomide as an inhibitor of the NF-kB pathway.

AIM

To assess the efficacy of two-step pilot prospective protocols PML-16 and PML-19 for untreated PML.

METHOD

From January 2016 to June 2022, 34 previously untreated PML patients were included (median age 32, stage >I - 60%, extramediastinal lesions -14%, bulky disease -73%). PET-CT and ctDNA were performed before CT, after 2 cycles, and after the end of CT.

CONCLUSIONS

Our preliminary results indicate that the new approach had a high cure rate in PML patients. ctDNA is a reliable marker for response assessment in PML.

RESULTS

Our first step (**PML-16 protocol**) was intensifying the induction phase. Eighteen patients received treatment according to this protocol, consisting of 6 cycles: (i) induction (blocks A and B of R-mNHL-BFM-90); (ii) consolidation (4 cycles of R-EPOCH). (Fig.1) The program was interrupted after 2-5 cycles due to prolonged cytopenia in 5/18 patients. After the end of therapy, all 18 patients achieved PET-negative remission.

Given the efficacy of this approach, we developed the next step consisting of only 4 cycles (**PML-19 protocol**): (i) induction (A and B of R-mNHL-BFM-90); (ii) consolidation with 2 courses of R-EPOCH; (iii) lenalidomide 1-10 days of each course. Sixteen patients received treatment according to the PML-19. After the end of therapy, 9 (56%) patients were PET-negative; 7 (44%) were PET-positive (DS 4,5).

ctDNA was performed in 15 patients. Regardless of the PET-CT status, ctDNA was eliminated in all patients after the end of therapy. (Fig.2) No one received radiation therapy, nor auto-SCT after the end of therapy. During follow-up, the PET-CT metabolic activity decreased to physiologic FDG uptake. With a median follow-up of 39 months (11-84 months), all 34 patients are alive in complete remission. (Fig.3)

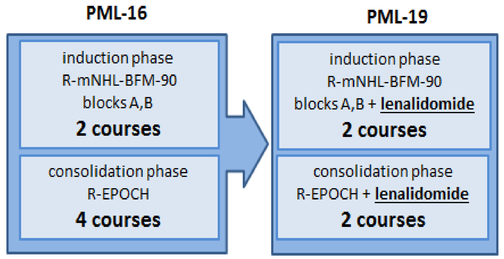


Fig.1 Treatment protocols: PML-16, PML-19

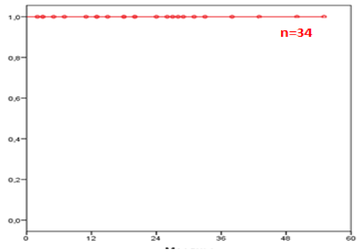


Fig.3 Event-free survival of patients with PML. months

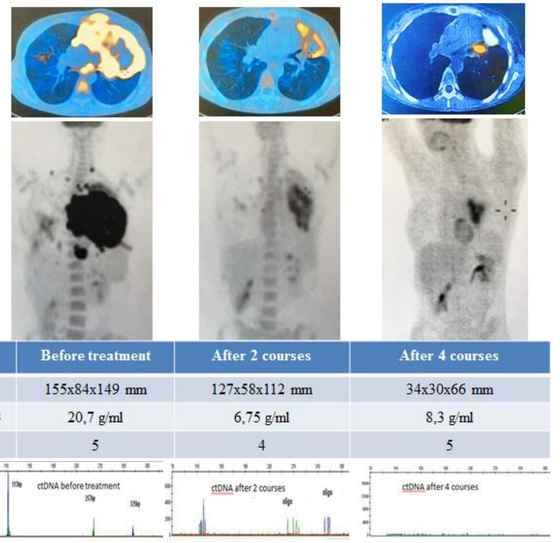


Fig.2 Clinical example: dynamic of tumor size, PET-CT, ctDNA

Characteristics	PML-16 n(%)	PML-19 n(%)
Age, range (years)	19-55	18-50
Median (years)	33	32
Gender (males/females)	5/13	5/11
Stage (Ann Arbor)		
I-II	13 (72%)	12 (75%)
IV	5 (28%)	4 (25%)
Performance status ECOG >2	8 (44%)	8 (50%)
IPI >2	7 (38%)	6 (37%)
«bulky disease»	13 (72%)	12 (75%)
Soft tissue invasion	13 (72%)	12 (75%)
Extramediastinal lesion	2 (11%)	3 (18%)
Spleen	1	1
Kidney	1	1
Stomach	1	0
Pancreas	1	0
Intestines	1	1
B-symptoms	14 (77%)	13 (81%)
Bone marrow involvement	0	0
LDH IU/mL > N	17 (89%)	16 (100%)
MUM1 >30%	11/12 (92%)	16/16(100%)
MYC >40%	2/4 (50%)	1/3 (33%)
Ki67 >=80%	13/16 (81%)	13/15 (87%)
FISH rearrangement		
MYC	0	1/10 (10%)
BCL6	1/5 (20%)	0
BCL2	0	0
trisomy/duplication/amplification		
MYC/BCL6/BCL2	3/5 (60%)	7/10 (70%)
Cytogenetic		
complex karyotype	1/4 (25%)	0
mut*TP53*	0/6 (0%)	1/11 (9%)

CONTACT INFORMATION

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