ELSEVIER

Blood 142 (2023) 6650–6651

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

652.MULTIPLE MYELOMA: CLINICAL AND EPIDEMIOLOGICAL

Mitoxantrone Hydrochloride Liposome, Bortezomib, and Dexamethasone- Based Regimen in Multiple Myeloma Patients with Extramedullary Plasmacytoma: A Pilot Study

Yuan Jian [1], Nian Liu [1], Yan-Ru Zhang [1], Wen Gao, MD PhD [1], Wen-Ming Chen, MD PhD [1], Hong-Hu Zhu, MD [1], Yin Wu, MD PhD [1]

[1] Beijing Chaoyang Hospital, Capital Medical University, Beijing, China

Background
Extramedullary plasmacytoma (EMP) is frequently presented in multiple myeloma (MM), especially in relapsed/refractory MM (RRMM), indicating a high-risk state of disease with inferior survival. Even in novel agent era, most anti-myeloma therapeutics demonstrated limited efficacy in EMP. Since there are no randomized controlled studies specifically addressing this complicated situation, standard treatment recommendations still lacked in this setting. Mitoxantrone hydrochloride liposome (Lipo-MIT) has shown higher concentration in tumor tissues and extended half-life, which exhibited clinical benefits in leukemia and solid tumors. Herein we designed a pilot study to explore the efficacy and safety of Lipo-MIT, bortezomib, and dexamethasone (MVD)- based regimen in MM with EMP.

Methods
MM patients with measurable EMP were enrolled in this study. Patients were planned to receive a maximum of 8 cycles of Lipo-MIT, bortezomib, and dexamethasone (MVD)- based regimen. Other combination agents were chosen based on previous treatments and the tolerance of patients, according to the clinician's decision. For patients who were refractory or intolerant to bortezomib, carfilzomib could be an alternative option. The dose of Lipo-MIT was 12mg/m ^{2} on the first day of every cycle. Both hematological response and EMP response were assessed by the International Myeloma Working Group (IMWG) criteria.

Results
Between Nov 4, 2022 and Jun 25, 2023, fifteen patients were enrolled from Beijing Chaoyang Hospital, with a median age of 65 years (range: 46-77). All patients had at least one kind of EMP, of which 12 (80.0%) patients had paraskeletal plasmacytoma, 7 (46.7%) had soft-tissue plasmacytoma, and 4 (26.7) had plasma cell leukemia. Four (26.7%) patients were newly diagnosed MM (NDMM), three (20.0%) were first relapse, and eight (53.3%) were previously heavily treated (2-12 lines). All of the 11 RRMM patients had been previously treated with proteasome inhibitors and immunomodulatory drugs (IMiDs), seven of them (46.7%) had been treated with CD38 antibodies, five (33.3%) had been treated with anthracyclines, and three (20.0%) had received CAR-T therapy (Table 1).

By the data cut-off date of July 30, 2023, enrolled patients received a median of 2 cycles of Lipo-MIT treatment (range: 1-4). Specific regimens included: Lipo-MIT- bortezomib/carfilzomib- dexamethasone (MVD) triplet regimen (20.0%), MVD plus lenalidomide regimen (M-VRD) (20.0%), MVD plus IMiDs and etoposide regimen (M-VTED) (40.0%), and MVD plus other cytotoxic drugs (cyclophosphamide or cisplatin) (20.0%). The overall response rate (ORR) of EMP was 53.3%. Among the 9 patients who had measurable hematological disease at baseline, the hematological ORR was 77.8% (22.2% ≥VGPR, 33.3% PR, 22.2% MR) (Table 1). The most common adverse effects (AEs) at all grades (incidence >10%) were myelosuppression, including leukocytopenia (80.0%) and thrombocytopenia (53.3%), as well as respiratory infection (46.7%), diarrhea (13.3%), blue skin (13.3%), dizzy (13.3%), and fatigue (13.3%). Common grade ≥3 AEs including leukocytopenia (46.7%), thrombocytopenia (26.7%) and respiratory infection (26.7%) (Table 2). Median follow-up time was 4.5 months. Five patients had died, among which 3 died of disease progression, 1 died of severe respiratory infection, and 1 died of Covid-19 infection. Median PFS and OS have not been reached in this cohort.

Conclusion
This study revealed promising results of early response and efficacy of MVD-based regimen in MM with EMP, which could be further explored in prospective phase 2 studies.

Disclosures No relevant conflicts of interest to declare.

Table 1. Clinical characteristics and responses of enrolled patients

	All patients (n=15)
Clinical features	
Age (years), median (range)	65 (46-77)
Gender (male/female), *n*	6/9
R-ISS stage II/III, *n* (%)	12 (80.0)
High-risk cytogenetics[#], *n* (%)	4 (26.7)
EMP type, *n* (%)	
Paraskeletal	12 (80.0)
Soft-tissue	7 (46.7)
Plasma cell leukemia	4 (26.7)
Previous treatments	
Lines of previous therapy, *n* (%)	
0	4 (26.7)
1	3 (20.0)
≥2	8 (53.3)
Proteasome inhibitors exposure/refractory, *n* (%)	11 (73.3) /5 (33.3)
IMiDs exposure/refractory, *n* (%)	11 (73.3) /7 (46.7)
CD38 antibodies exposure/refractory, *n* (%)	7 (46.7) /5 (33.3)
Anthracyclines exposure/refractory, *n* (%)	5 (33.3) /3 (20.0)
Relapsed after CAR-T therapy, *n* (%)	3 (20.0)
Responses	
EMP responses, *n* (%)	
CR	0 (0.0)
PR	8 (53.3)
SD	5 (33.3)
Missing	2 (13.3)
ORR	8 (53.3)
Hematological responses, *n* (%)	
Unmeasurable at baseline	6
CR/VGPR	2/9 (22.2)
PR	3/9 (33.3)
MR	2/9 (22.2)
SD/PD	2/9 (22.2)
ORR	7/9 (77.8)

EMP, extramedullary plasmacytoma; IMiDs, immunomodulatory drugs; CAR-T, Chimeric antigen receptor T cell; CR, complete response; VGPR, very good partial response; PR, partial response; MR, minimal response; SD, stable disease; PD, progressive disease; ORR, overall response rate.
[#]High-risk cytogenetics: defined as 17p deletion, t(4;14), and/or t(14;16) by fluorescence in situ hybridization (FISH).

Table 2. Safety profile in enrolled patients (n=15).

N (%)	All grades of AEs	Grade ≥3 AEs
Leukocytopenia	12 (80.0)	7 (46.7)
Thrombocytopenia	8 (53.3)	4 (26.7)
Respiratory infection	7 (46.7)	4 (26.7)
Diarrhea	2 (13.3)	0
Blue skin	2 (13.3)	0
Dizzy	2 (13.3)	0
Fatigue	2 (13.3)	0
Covid-19 infection	1 (6.7)	1 (6.7)
Cardiac insufficiency	1 (6.7)	0
Thrush	1 (6.7)	0
Nausea	1 (6.7)	0
Blurred vision	1 (6.7)	0
Peripheral neuritis	1 (6.7)	0

Figure 1

https://doi.org/10.1182/blood-2023-188304