Outcomes of bortezomib combination chemotherapies in autologous stem cell transplantation-ineligible patients with AL amyloidosis

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Background
Treatment protocols for light chain (AL) amyloidosis have been derived from myeloma treatment. Bortezomib is a key drug used for the treatment of myeloma and AL amyloidosis. We retrospectively investigated the efficacy and toxicity of bortezomib-based chemotherapy in patients with newly diagnosed AL amyloidosis.

Methods
We reviewed the outcomes of newly diagnosed autologous stem cell transplantation (auto-SCT)-ineligible AL amyloidosis patients who received bortezomib-based chemotherapy at a referral center between 2011 and 2017.

Results
Of 63 patients who received bortezomib-based chemotherapy, 32 were male, and the median age was 66 years (range, 42–82 yr). The hematologic overall response rate (ORR) was 65.1%, and the chemotherapy regimen with the best hematologic response was VMP (75.7%, 28/37). Sixty patients had significant organ (heart or kidney) involvement; 28.3% of patients (N=17) had major organ responses after chemotherapy. With a median follow-up of 34 months, there was no significant difference in progression-free survival ($P=0.49$) or overall survival ($P=0.67$) according to regimen. Most hematologic and non-hematologic problems were manageable.

Conclusion
Various chemotherapy combinations based on bortezomib are currently employed in the clinical setting, but no difference was found in terms of efficacy or toxicity.

Key Words Bortezomib, Light-chain amyloidosis, Transplant ineligible

INTRODUCTION

Light chain (AL) amyloidosis is a hematologic disorder characterized by major organ dysfunction and deposition in tissues of misfolded amyloid fibrils derived from monoclonal light chains produced by clonal plasma cells [1, 2]. AL amyloidosis is a rare disease occurring at a rate of approx- imately 8–10 cases per million person-years [3, 4]. Clinical manifestations of AL amyloidosis are generally characterized by advanced organ damage of the heart, kidneys, and liver. Moreover, delayed diagnosis worsens the outcomes of AL amyloidosis. The median overall survival of patients with AL amyloidosis from the time of diagnosis is approximately 3 years, but combination of AL with clinically apparent cardiac involvement reduces survival to one year [5, 6]. AL

amyloidosis is a complicated disease which makes early diagnosis and treatment difficult, especially for patients with cardiac involvement [7, 8].

Treatment protocols for amyloidosis are generally derived from multiple myeloma (MM) treatment. Induction chemotherapy with immunomodulatory imide drugs and proteasome inhibitors (PIs) followed by autologous stem cell transplantation (auto-SCT) are the standard frontline therapies for newly diagnosed MM [9]. However, induction chemotherapy before auto-SCT in AL amyloidosis is not standard because of the low tumor burden of AL amyloidosis. However, induction chemotherapy followed by auto-SCT has recently been used, especially in patients with a high tumor burden [6]. Treatment-related mortality of auto-SCT was reported to be as high as 20% in early trials. However, improvement in supportive care and selection of appropriate candidates improved treatment-related mortality by 5% [10]. Due to advanced stage disease and old age, only 20% of AL patients are eligible for auto-SCT. Melphalan with dexamethasone has been the standard treatment for patients who are not eligible for auto-SCT. Bortezomib-based treatment has been reported in phase 2 trials [11-13]. Notably, it has been shown that bortezomib can induce a rapid response in amyloidosis, improving cardiac function and survival [14]. Recent results of a phase three trial with VMD (bortezomib, melphalan, and dexamethasone) versus MD (melphalan and dexamethasone) showed an improvement in overall response rate (ORR), progression-free survival (PFS), and overall survival (OS) [15, 16].

Due to the rarity of AL amyloidosis, there have been few reports of bortezomib-based treatment, especially among Asian patients. Thus, we conducted a retrospective study to examine the role of bortezomib-based regimens, outcomes, and efficacy in patients with AL amyloidosis who were not candidates for auto-SCT as a first-line treatment.

MATERIALS AND METHODS

Patients

We conducted a retrospective study to evaluate the response and survival outcomes of AL amyloidosis patients who received bortezomib combination chemotherapy between 2011 and 2017 at a tertiary referral hospital. The Institutional Review Board of Samsung Medical Center approved this study (approval number: SMC 2012-08-059). Among patients with AL amyloidosis confirmed by histology, we selected patients who were treated with bortezomib-based chemotherapy as a first-line treatment and were ineligible for autoSCT. At our institutions, systemic chemotherapies are primarily used for patients diagnosed with AL amyloidosis with major organ involvement or symptoms related to amyloidosis. Bortezomib-based chemotherapies mainly include five regimens as follows: VMP (bortezomib, 1.3 mg/m^2 D1, 8, 22, 29; melphalan, 9 mg/m^2 D1-4; prednisone, 60 mg/m^2, D1-4; every 6 wk), VD (bortezomib, 1.3 mg/m^2 D1, 8, 15, 22; dexamethasone, 20 mg D1, 2, 8,

9, 15, 16, 22, 23; every 5 wk), VCD (bortezomib, 1.3 mg/m^2 D1, 8, 15, 22; cyclophosphamide, 150 mg/m^2 D1, 8, 15; dexamethasone, 40 mg; every 5 wk), VMD (bortezomib, 1.3 mg/m^2 D1, 8, 22, 29; melphalan, 9 mg/m^2 D1-4; dexamethasone, 20 mg D1, 2, 8, 9, 22, 23, 29, 30; every 6 wk), and VTD (bortezomib, 1.3 mg/m^2 D1, 4, 8, 11; thalidomide, 100 mg D1-28; dexamethasone, 40 mg, D1-4, 8-1; every 4 wk). Chemotherapy was administered for 6–9 cycles.

Clinical information, including sex, age, and Eastern Cooperative Oncology Group (ECOG) performance status, was collected retrospectively by chart review. We also collected crucial laboratory data including complete blood cell counts, serum albumin, serum creatinine, estimated glomerular filtration rate (eGFR), beta-2 microglobulin, electrophoresis (EP) and immunofixation (IFE) of serum and urine, serum-free light chains (FLCs), N-terminal pro-brain natriuretic peptide (NT-pro BNP), troponin T, troponin I, and 24-h urine protein. Systolic blood pressure, electrocardiogram, transthoracic echocardiography (TTE), and New York Heart Association (NYHA) classes were obtained at baseline. At the time of diagnosis, patients were staged according to the MAYO 2012 criteria [17].

Study objectives and statistical analysis

The primary objective was to determine hematologic and organ responses to bortezomib-based chemotherapy. The secondary objectives were PFS, OS, early mortality, and adverse events.

Hematologic and organ responses were assessed according to the most recent criteria from the International Society of Amyloidosis (ISA) [3]. A complete hematologic response (CR) was characterized by normalization of FLC levels and ratio, negative serum, and urine IFE [18, 19]. Responses were categorized as: very good partial response (VGPR, reduction in dFLC to <40 mg/L), partial response (PR, reduction in dFLC of 50%), or no response (NR, less than PR) [18, 19].

Organ involvement was evaluated according to the following international consensus guidelines: kidneys, 24-hr urine protein >0.5 g/day, predominantly albumin; heart, mean wall thickness >12 mm, no other cardiac causes on echo; liver, total liver span >15 cm in the absence of heart failure or alkaline phosphatase >1.5 times the institutional upper limit of normal; peripheral nerves, clinical symmetric lower extremity sensorimotor peripheral neuropathy; autonomic nerves, gastric-emptying disorder, pseudo-obstruction, voiding dysfunction not related to direct organ infiltration; gastrointestinal tract, direct biopsy verification with symptoms; lungs, direct biopsy verification with symptoms, interstitial radiographic pattern; soft tissue, tongue enlargement, arthropathy, claudication, presumed vascular amyloid, skin, myopathy on biopsy or pseudohypertrophy, lymph node (may be localized), and carpal tunnel syndrome.

The organ response was evaluated in the heart, kidney, and liver. First, heart response was defined as a >30% and >300 ng/L decrease in NT-pro BNP in patients with a baseline NT-pro BNP level ≥650 ng/L or a ≥2 class decrease

Table 1. Patient characteristics and clinical presentation factors in primary amyloidosis patients.

Characteristics		N	%
		63	100
Age (yr)	Median (range)	66 (42–82)	
	>65	36	57.1
Sex	Male/female	32/31	50.8/49.2
Presenting symptom	Dyspnea	33	52.4
	Edema	9	14.3
	Proteinuria	5	7.9
	Dizziness or syncope	3	4.8
	Diarrhea	2	3.2
Performance	ECOG PS 2 or more	14	22.2
	NYHA Fc G2 or more	37	58.7
Organ involvement	Cardiac+renal	20	31.7
	Cardiac	41	65.0
	Renal	20	31.7
	Hepatic	4	6.4
	Peripheral neuropathy	23	36.5
	Autonomic neuropathy	46	73.0
	Gastrointestinal	11	17.5
	Pulmonary	2	3.2
	Soft tissue	16	25.4
N of organ involvement	1 site	8	12.7
	2 sites	20	31.7
	3 or more sites	35	55.6
Systolic blood pressure	<100 mmHg	27	42.8
	≥100 mmHg	36	57.1
Heavy chain	IgG	14	22.2
	IgA	6	9.5
	IgD	3	4.8
	Light chain disease	40	63.5
Light chain	Kappa	15	23.8
	Lambda	47	74.6
CRAB	Anemia	32	50.8
	Hypercalcemia	3	4.8
	Renal insufficiency	13	20.6
	Lytic bone lesion	1	1.6
Type (N=50)	MM-CRAB	16	25.3
	MM-PC	26	41.2
	AL	8	12.6
NT-proBNP (N=62)	Median	6,238 (285–35,000)	
	≥332 ng/L	61	98.4
	≥1,800 ng/L	51	82.3
	≥8,500 ng/L	23	37.1
Troponin T (N=54)	Median	0.074 (0.018–0.356)	
	≥0.025 ng/mL	51	94.4
	≥0.035 ng/mL	48	88.8
	≥0.06 ng/mL	38	70.4
Troponin I (N=50)	Median	0.231 (0.010–3.82)	
	≥0.1 ng/mL	38	76.0
dFLC	Median	458 (8–11,633)	
	≥180 mg/L	49	77.8
Beta-2 microglobulin	Median	3.415 (1.06–23.86)	
	>3.5	27	42.8
Serum albumin	Median	3.6 (1.70–4.50)	
	<3.5 g/dL	30	47.7
24-h urine protein	Median	0.698 (0.059–17.104)	
	>5 g	11	17.4
eGFR	Median	64.4 (7.80–308.60)	
	<50 mL/min per 1.73 m^2	21	33.3
Stage 2012 (N=55)	2	2	3.6
	3	18	32.7
	4	35	63.6

Abbreviations: dFLC, difference between involved and uninvolved free light chain; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate; NT-proBNP, NT-proB-type natriuretic peptide; NYHA, New York Heart Association.

in subjects with a baseline NYHA class 3 or 4. Second, renal response was defined as a 50% decrease (at least 0.5 g/day) in 24-h urine protein (pretreatment urine protein must be >0.5 g/day), and creatinine and creatinine clearance that did not worsen by 25% over baseline. Third, liver response was defined as a 50% decrease in abnormal alkaline phosphatase or a decrease in liver size of at least 2 cm determined radiographically.

Descriptive statistics were calculated as proportions and median. Fisher's exact test was used to compare the distribution of the patient characteristics. PFS was defined as the time from initial treatment to significant organ or hematologic progression, next treatment, or death from any cause. OS was determined as the time from the initial diagnosis to death or the last follow-up date. Survival curves were constructed according to the Kaplan–Meier method and compared using the log-rank test using the SPSS software (version 24.0, IBM Corp, Armonk, NY, USA). Other statistical analyses were performed using R version 3.3.2.

RESULTS

Baseline characteristics of patients with AL amyloidosis

Of the 63 patients enrolled in the study, the median age was 66 years (range, 42–82 yr), with 36 (57.1%) patients over 65 years of age. At the time of diagnosis, dyspnea (52.4%) was the most common chief complaint, followed by edema (14.3%). Thirty-seven patients (58.7%) had an estimated NYHA grade of 2 or more, and 14 patients (22.2%) had a performance status of 2 or more. The number of patients with three or more organs involved in AL amyloidosis was 55.6%. Among patients with AL amyloidosis, 25.3% had simultaneous CRAB symptoms, which are part of the multiple myeloma diagnosis criteria. Furthermore, 41.2% of the patients showed more than 10% plasma cells in bone marrow aspiration and biopsy. The majority of patients (65.0%) had cardiac involvement at diagnosis and 31.7% of patients had kidney amyloidosis with over 0.5 g urine albumin per 24 h, of which 17.4% had proteinuria of 5 g/day or more. Twenty patients (31.7%) had both heart and kidney involvement. The median values of different cardiac biomarkers were 6,238

pg/mL (range, 285–35,000) for NT-pro BNP, 0.074 μg/L for troponin T (range, 0.018–0.356), and 0.231 μg/L (range, 0.010–3.820) for troponin I. Of the 55 patients who were assessed using the MAYO 2012 criteria, 63.6% (N=35) were at stage 4 (Table 1).

Treatment outcomes and toxicity effects in patients on bortezomib-based chemotherapies

As first-line chemotherapy, 37 patients (58.7%) received VMP and nine patients (14.2%) received a VD regimen. Eight patients received VCD (12.7%) or VMD (12.7%). VTD chemotherapy was administered to only one patient. Of the 63 patients who received bortezomib-based chemotherapy, 65.1% (N=41) had a hematologic response (21 patients with CR, 12 patients with VGPR, and 8 patients with PR). The chemotherapy regimen with the best hematologic response was VMP (75.7%, 28/37). Sixty patients had significant organ (heart or kidney) involvement; 28.3% of patients (N=17) had major organ responses after chemotherapy (Table 2).

In patients receiving bortezomib combination chemotherapy, most adverse events were of grade 1 or 2 and were manageable. Notably, grade 1 or 2 neuropathy was the most

Table 3. Chemotherapy toxicity.

Variables	Total patients	
	Grade 1/2	≥Grade 3
Anorexia	26 (41.2)	0
Nausea	15 (23.8)	0
Vomiting	8 (12.6)	1 (1.6)
Diarrhea	8 (12.6)	4 (6.3)
Constipation	9 (14.3)	0
Mucositis	6 (9.5)	0
Neuropathy	31 (49.2)	0
Insomnia	5 (7.9)	0
Fatigue	29 (46.0)	1 (1.6)
Rash	8 (12.6)	0
Anemia	5 (11.1)	2 (3.2)
Thrombocytopenia	8 (12.6)	2 (3.2)
Neutropenia	2 (3.2)	2 (3.2)

Table 2. Hematologic and organ response analysis (N=63 patients).

Regimen	N (%)	Hematologic response (%)				Organ response (heart or kidney)
		ORR	CR	VGPR	PR	
Total	63 (100)	41 (65.1)	21 (33.3)	12 (19.0)	8 (12.7)	17/60 (28.3)
VMP	37 (58.7)	28 (75.7)	14 (37.8)	8 (21.6)	6 (16.2)	11/37 (29.7)
VD	9 (14.2)	5 (55.6)	2 (22.2)	2 (22.2)	1 (11.1)	2/9 (22.2)
VCD	8 (12.7)	4 (50.0)	2 (25)	1 (12.5)	1 (12.5)	2/8 (25)
VMD	8 (12.7)	4 (50.0)	3 (37.5)	1 (12.5)	0 (0.0)	2/8 (25)
VTD	1 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)	0/1 (0.0)

Abbreviations: C, cyclophosphamide; CR, complete response; D, dexamethasone; M, melphalan; ORR, overall response rate; P, prednisolone; PR, partial response; T, thalidomide; V, bortezomib; VGPR, very good partial response.

common (49.2%), and grade 3 or higher neuropathy accounted for less than 2% of events (Table 3). Of the 41 patients who died, early death (death before six months after diagnosis) occurred in 33.3% (21/63). The early death rate was highest in VMD chemotherapy (62.5%) and 38.2% of deaths occurred in Mayo stage IV (Supplementary Table 1). On the other hand, among patients who lived longer than six months (N=42), 30.7% and 92.8% of patients achieved a heart and kidney response, respectively, and 85.7% of patients also achieved a hematologic response (19 CR, 10 VGPR, 7 PR, Supplementary Table 2). Median PFS and median OS were 20.1 months (95% CI, 7.8–32.4) and 60.6 months (95% CI, 38.4–82.8) for those who lived longer than six months (Supplementary Fig. 1).

Survival outcomes

Of the 63 patients, the median follow-up duration was 34 months, and the median PFS was 10.5 months (95% CI, 3.6–17.4; Fig. 1A). There was no specific difference in the MAYO 2012 stage (P=0.16, Fig. 1B). Median PFS did not vary with involvement of heart alone (7.7 mo; 95% CI, 0.0–16.4) or kidney alone (15.3 mo; 95% CI, 0.0–30.9) or both organs (6.4 mo; 95% CI, 0.0–49.3) (P=0.58, Fig. 1C). Patients who obtained an organ response in the kidney

and heart had favorable PFS (P=0.00, Fig. 1D). We performed a subgroup analysis of median PFS according to the hematologic response. Median PFS of patients who achieved a complete hematologic response was longer (44.4 mo; 95% CI, 32.6–56.2) compared to the progression hematologic response (0.9 mo; 95% CI, 0.7–1.1; Fig. 1E). Among the five regimens (VCD, VD, VMD, VTD, and VMP), there was no difference in PFS, and hematologic, heart, and kidney responses did not affect survival outcomes (Fig. 1F).

The OS of 63 patients was 38.4 months (95% CR, 2.3–74.5). OS did not significantly differ according to MAYO 2012 stage (P=0.97), organ involvement (P=0.22), hematologic response (P=0.14), or chemotherapy strategy (P=0.67, Fig. 2). However, patients who achieved an organ response after chemotherapy demonstrated better survival outcomes (Fig. 2D).

Additionally, we analyzed the survival outcomes of patients receiving melphalan separately. In subgroup analysis, patients who received melphalan additionally were older than those who did not (68 yr vs. 61 yr, P=0.001). Other than age, there were no differences in baseline characteristics between the two groups (Supplementary Table 3). Melphalan plus bortezomib-based chemotherapy did not lead to better PFS (P=0.69) or OS (P=0.62, Supplementary Fig. 2).
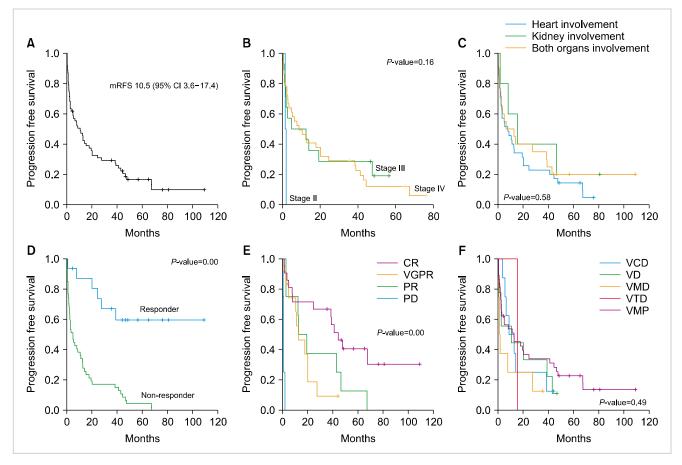

Fig. 1. Progression-free survival (PFS) of all patients (**A**), PFS according to MAYO 2012 stage (**B**), PFS of patients with organ involvement (**C**), PFS of patients who achieved an organ response (**D**), PFS of patients who achieved a hematologic response (**E**), comparison of PFS according to chemotherapy (**F**).

Fig. 2. Overall survival (OS) of all patients **(A)**, OS according to MAYO 2012 stage **(B)**, OS of patients with organ involvement **(C)**, OS of patients who achieved an organ response **(D)**, OS of patients who achieved a hematologic response **(E)**, comparison of OS according to chemotherapy **(F)**.
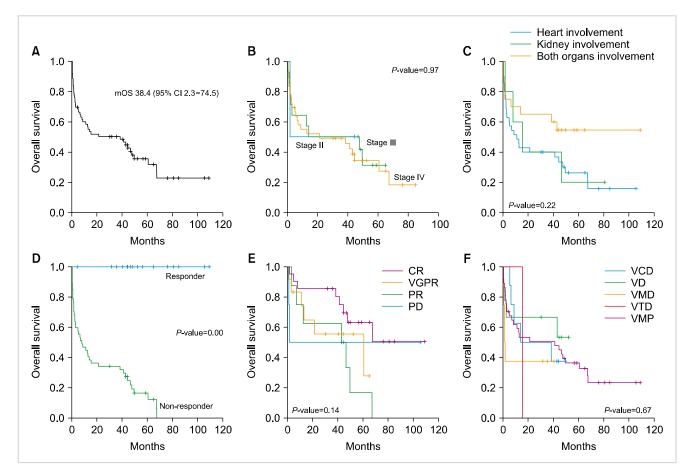
DISCUSSION

We evaluated the efficacy and safety of bortezomib-based chemotherapies used in the initial induction treatment of AL patients ineligible for auto-SCT. It is challenging to compare the efficacy of bortezomib-based chemotherapy in different studies. Nevertheless, the efficacy and safety of previous reports did not vary significantly from those of our study (Table 4). In this study, we reconfirmed that the bortezomib-backbone regimen leads to a considerable response with manageable toxicity in patients with newly diagnosed AL amyloidosis who are not eligible for auto-SCT.

Treatment of AL amyloidosis has been based on anti-myeloma therapy for approximately two decades, and melphalan with dexamethasone was the standard therapy until recently [20]. Among the various drugs used in MM, bortezomib targets plasma cells and induces plasma cell apoptosis, which is the source of amyloid production [21]. According to clinical data for MM or AL amyloidosis, bortezomib has already been proven to be effective as a single agent or when used in combination [22]. Bortezomib-based chemotherapy includes doublet combinations (VP and VD) and triplet combinations (VMP, VCD, VTD, or VRD). In general, triplet combinations are considered the standard induction treatment

for younger transplant-eligible myeloma patients. However, applying the same multi-drug protocols to all AL amyloidosis patients is not appropriate, as most patients are elderly and have age- or disease-related comorbidities. In previous studies comparing induction chemotherapies in elderly MM patients, bortezomib combination chemotherapy (e.g., VP, VCP, or VMP) showed similar efficacy. However, safety issues, discontinuation rate, and early death related to drugs were more frequent in the VMP group, particularly in frail MM patients [23]. Niesvizky *et al.* [24] compared VD, VTD, and VMP among auto-SCT-ineligible patients with MM; VTD and VMP did not appear to offer any advantage over VD. We compared the treatment results of bortezomib-backbone regimens for AL amyloidosis in Table 4. Hematologic and significant organ responses did not vary significantly depending on the combination. Although the patients who received each bortezomib-backbone chemotherapy were not evenly distributed in our study, similar efficacy and safety were found. Thus, doublet bortezomib-based chemotherapy seems to be an appropriate option for elderly patients with AL amyloidosis.

Mayo stage 2012 was a very good prognostic marker for PFS and OS in the literature [17]. However, our data did not support this (Figs. 1B, 2B). The very small number of stage 2 patients might be the reason for this difference.

Table 4. Overview of bortezomib-based chemotherapy studies in untreated AL amyloidosis.

Regimen	Study	Patients	Hematologic response (%)	Cardiac response (%)	Renal response (%)	Grade 3/4 adverse events	Early death	Ref
VMP vs. VD vs. VCD vs. VMD	Retrospective	63 Untreated	65.1%	28.3% (heart or kidney response)		Thrombocytopenia: 3.2% Anemia: 3.2% Diarrhea: 6.3%	35% (21)	
VD	Retrospective	18 Untreated 11/pretreated 7	94%	20%	14%	Thrombocytopenia: 11%	11% (2)	[13]
VCD vs. VD	Retrospective	42 vs. 59 Untreated	78% vs. 68%	21% vs. 29%	41% vs. 43%	Cytopenia <10% in both groups	NA	[25]
VMD vs. MD	Phase III	53 vs. 56 Untreated	73% vs. 52% (after 3 cycles)	38% vs. 28% (after 9 mo)	33% vs. 26% (after 9 mo)	Thrombocytopenia 5% vs. 10% Neutropenia 4% vs. 8% Anemia 2% vs. 4%	4 vs. 2	[16]
VRD	Retrospective	34 Untreated	89%	41%	22%	Thrombocytopenia: 6% Neutropenia: 3% Anemia: 6%	NA	[30]

CR or VGPR are usually the main target hematologic responses that are specified in the clinical guidelines [2]. Although PFS and OS varied according to hematologic response, VGPR did not show superiority in PFS and OS to PR. Further studies are needed to clarify whether the VGPR is sufficient as a primary target. Patients who achieved an organ response showed superior PFS and OS. As organ response is a time-dependent parameter, it is difficult to define the proper timing of organ response. According to our results, the addition of melphalan, cyclophosphamide, or thalidomide did not provide any substantial incremental efficacy to the 'backbone' of bortezomib and steroid. Kastritis *et al.* [25] also reported that the addition of an alkylating agent to bortezomib-backbone regimens did not improve efficacy. Since t(11;14) decreases the efficacy of bortezomib's anti-myeloma activity, we evaluated whether the addition of melphalan improved the efficacy of bortezomib [26]. However, we did not observe any improvement in efficacy with melphalan administration. Because the analysis included a small number (N=5) of patients with t(11;14) in this cohort, these results should be interpreted with caution.

The early mortality rate we reported was 33.3% (21/63), which was higher than the previously reported early death rate for each therapy (Table 4). However, our study included more patients with advanced-stage disease, severe cardiac function, and overlapping symptomatic MM (CRAB or plasma cells in peripheral blood) compared to other studies. However, 42 patients who survived for more than 6 months had better hematologic or organ responses and achieved nearly 5 years of overall survival. Given these results, bortezomib is considered an effective treatment option for some patients, but which patients will benefit most from bortezomib remains controversial.

The survival outcomes of patients with AL amyloidosis have improved over time [27]. We also noted a median OS of 38.4 months (95% CI, 2.3–74.5), similar to other studies. However, we were unable to overcome the early death due to advanced AL amyloidosis. Most patients died from complications associated with cardiac dysfunction. Thus, many researchers are investigating the combination of emerging drugs with a bortezomib backbone, focusing on the rapid suppression of monoclonal protein synthesis and heart stabilization [28]. Recent data on the addition of daratumumab and lenalidomide to bortezomib are promising for newly diagnosed patients with AL amyloidosis who are not eligible for auto-SCT [25, 29, 30].

Consequently, treatment strategies for AL amyloidosis continue to evolve with the development of novel agents. However, bortezomib is an essential drug for AL amyloidosis. Given the small sample size and retrospective methods, the results of this study are limited, but useful because of the lack of amyloidosis research, particularly among Asian patients.

According to this retrospective study and previous studies, the outcomes of each bortezomib therapy (i.e., VCD, VD, VMD, VTD, and VMP) currently employed in real-world clinical settings are similar. Our data show that bortezomib-based chemotherapy is an induction treatment that fully reflects the real world in Asia. We believe that our results will be the basis for further research of AL amyloidosis and provide important insights regarding this disorder in Asia.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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