Outcomes of VDPACE with Immunomodulator Agent as a Salvage Therapy for Relapsed/Refractory Multiple Myeloma

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INTRODUCTION

Multiple myeloma (MM) is a malignant neoplasm of plasma cells that accumulate in bone marrow, leading to bone destruction and marrow failure. Multiple myeloma accounts about 1.8% of all malignancies, and around 15% of hematologic malignancies in the United States. Over the past decade, the median survival of myeloma patients has almost doubled from 4 to 8 years. Despite significant advances in treatment options most patients will ultimately develop resistance to existing therapies. High-risk MM is considered challenging to treat because of the risk of early relapse and increased mortality. The main factors contributing to high risk myeloma are poor prognostic cytogenetic abnormalities that include 17p deletions, 1q21 gains, 1p deletion, t (4;14), t (14;16), and t (14;20). Other features of high risk MM include extramedullary disease (EMD) which is associated with an adverse prognosis in newly diagnosed and in relapsed MM patients with overall survival of less than 6 months.

Aggressive relapsed/refractory multiple myeloma (RRMM) needs rapid cytoreduction for disease control, which may not be possible with standard novel therapies. Main obstacles we face is the refractoriness and limited treatment options in aggressive RRMM.

We report on a highly effective therapy that offers a salvage option for these patients. The aim of this study was to analyze the clinical outcomes of VDPACE with Immunomodulator agent (Imid) in patients with RRMM.

METHODS

We treated 29 patients with relapsed and relapsed/refractory multiple myeloma at the University of Kansas Health System between January 2012 and April 2018, who received salvage therapy VDPACE + Imid Q28 days cycle summarized in Table 1. Descriptive analyses were performed on available data for patient characteristics, disease course, and outcomes. Responses were evaluated using the IMWG criteria.

Table 1: VDPACE+Imids			
Treatment agents	Variable Dosing/day	Route	Schedule
Bortezomib	1.0 mg/m ²	Subcutaneous	Days 1,4,8 and 11
Dexamethasone	*20-40 mg	Oral	Day 1-4
Cisplatin	*7.5-10 mg/m ²	IV Continuous Infusion	Day 1-4
Doxorubicin	*7.5-10 mg/m ²	IV Continuous Infusion	Day 1-4
Cyclophosphamide	*300-400 mg/m ²	IV Continuous Infusion	Day 1-4
Etoposide	*30-40 mg/m ²	IV Continuous Infusion	Day 1-4
**Immunomodulator agents			
Thalidomide	*100-200 mg	Oral	***Day 1-14
Lenalidomide	*15-25 mg	Oral	***Day 1-14
Supportive care agents			
Pegfilgrastim	6 mg	Subcutaneous	Day 7
Fosaprepitant	150 mg	Intravenous	Day 1
Ondansetron	16 mg	Oral	Day 1-5

*Dose adjusted based on performance status, co-morbidities

** Immunomodulator drug were used was either thalidomide or lenalidomide

*** Treatment was discontinued if platelets are less than 25k

RESULTS

Among the 29 patients included in the analysis, the median age at the time of receiving the VDPACE + Imid is was 60 years (range 41-77). Sixteen patients (55%) had IgG isotype, 10 patients (35%) had IgA isotype, 6 patients (21%) had ISS stage III disease at diagnosis, 9 patients (31%) had ISS stage II, 10 patients (35%) had ISS stage I, 15 patients (51%) had high risk cytogenetics, and 17 patients (58%) had extramedullary disease. Patients characterized are summarized in Table 2. Median number of VDPACE + Imid received was 2 (1-3) cycles, median duration of treatment was 3 months (1-4) months. The median number of previous lines of therapy was 2 (1-10). Twenty nine patients (100%) were bortezomib refractory, twenty five patients (86%) were refractory to lenalidomide, 21 patients (72%) received high dose chemotherapy (Melphalan) followed by ASCT prior to VDPACE. Number of patients who received HDCT/ASCT after salvage chemotherapy was 13 patients (45%). See Table 2.

The ORR was 69%, CR 10%, VGPR 28%, PR 38%, with stable disease in 21% of patients. Fourteen patients (48%) proceeded with ASCT and/or allogeneic stem cell transplant (AlloSCT). Eleven patients (38%) received other regimen based therapy. A 1-year PFS was 55%, for those who received ASCT and/or Allo-SCT the 1-year PFS was 71%. The response rates and disease characteristics are summarized in Table 3.

RESULTS CONTINUED

Table 2: Characteristics of patients with RRMM (n=29):	
Gender, male: female	13:16
Age, years, median (range)	60 (41-77)
Race, no of patients (%)	
Caucasian	21 (73%)
African American	6 (21%)
Asian	1 (3%)
Hispanic	1 (3%)
MM paraprotein, no. of patients (%)	
IgG	16 (55%)
IgA	10 (35%)
Light chain	3 (10 %)
Baseline ISS stage, no of patients (%)	
Stage III	6 (21%)
Stage II	9 (31%)
Stage I	10 (35%)
Unknown	4 (13%)
Cytogenetics, no of patients (%)	
High risk	15 (51%)
Standard risk	14 (49%)
Extramedullary disease	17 (58%)
Median no. of previous lines of therapy for relapsed/refractory myeloma (range)	2 (1-10)
Received PI	29 (100%)
Received Imid	25 (86%)
Number of patients who received ASCT prior to VDPACE + Imids	21 (72%)

Table 3: Response rate for VDPACE+Imids	
Response Category	RRMM
Overall response no (%)	20 (69%)
Complete response or better	4 (14%)
Stringent complete response	1 (3%)
Complete response	3 (10%)
Very good partial response or better	8 (28%)
Very good partial response	4 (14%)
Partial response	11 (38%)
Minimal response	1 (3%)
Stable disease	6 (21%)
Progressive disease	3 (10%)

CONCLUSIONS

Our single institution experience shows that patients with high risk MM and EMD can achieve a significant response rate using VDPACE + Imid. This proves VDPACE + Imid can be utilized as salvage therapy in relapsed MM and offers good response rates (ORR 69%) and favorable PFS in RRMM. It is also an excellent salvage regimen with about half of patients undergoing subsequent transplant. Patient selection is required due high treatment related mortality . However, we believe that this treatment followed by high dose chemotherapy with ASCT should be encouraged if the patient is eligible for transplant.

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