Adverse Hematological and Non-Hematological Events in Patients With Relapsed/Refractory Multiple Myeloma That Are Responsive to Daratumumab, Pomalidomide and Dexamethasone

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Abstract

Background: Daratumumab, pomalidomide, and dexamethasone (DPd) is an effective option for treatment of patients with relapsed/refractory multiple myeloma (RRMM). In this study, we sought to analyze the risk of hematological and non-hematological toxicities in patients who responded to DPd treatment.

Methods: We analyzed 97 patients with RRMM who were treated with DPd between January 2015 and June 2022. The patients and disease characteristics, as well as safety and efficacy outcomes were summarized as descriptive analysis.

Results: The overall response rate for the entire group was 74% (n = 72). The most common grade III/IV hematological toxicities in those who responded to treatment were neutropenia (79%), leukopenia (65%), lymphopenia (56%), anemia (18%), and thrombocytopenia (8%). The most common grade III/IV non-hematological toxicities were pneumonia (17%) and peripheral neuropathy (8%). The incidence of dose reduction/interruption was 76% (55/72), which was due to hematological toxicity in 73% of the cases. The most common

reason for discontinuing treatment was disease progression in 61% (44 out of 72 patients).

Conclusions: Our study revealed that patients who respond to DPd are at high risk of dose reduction or treatment interruption because of hematological toxicity, typically due to neutropenia and leukopenia leading to increased risk of hospitalization and pneumonia.

Keywords: Relapsed multiple myeloma; Daratumumab; Pomalidomide; Hematologic toxicity

Introduction

With several new drug approvals and evolving chemoimmunotherapy combinations, the treatment landscape of relapsed/refractory multiple myeloma (RRMM) is becoming increasingly complex. Several classes of drugs are currently considered effective in treating RRMM, including anti-CD38 monoclonal antibodies, proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and have significantly prolonged survival in patients with MM [1]. Despite all these advances in the treatment landscape of RRMM, the disease remains incurable [2].

The pattern of resistance to first-line triplet or quadruplet therapy serves as a guide when considering options for second-line treatment. Several factors must be taken into consideration including prior autologous hematopoietic stem cell transplantation (auto-HSCT), refractoriness to IMiDs and/or PIs, and use of anti-CD38 monoclonal antibodies in their first-line treatment. Pomalidomide is a second-generation IMiD that was initially approved in combination with low-dose dexamethasone by the Food and Drug Administration (FDA) in 2013 [3]. Pomalidomide exhibits several antitumor activities in terms of immunomodulatory response, marrow stroma interaction, activation of proteasomal degradation pathways, and anti-angiogenic activity [4]. These characteristics have made pomalidomide an effective foundation for combined use with other classes of drugs in MM treatment. In several phase II and III trials, pomalidomide has been combined with PIs such

as bortezomib (VPd) [5] and carfilzomib (KPd) [6] as well as with anti-CD38 monoclonal antibodies such as daratumumab (DPd) and isatuximab (Isa-Pd) [7]. These combinations are also listed by the National Comprehensive Cancer Network (NCCN) as being suitable for use in triplet regimens [8].

Several clinical trials have assessed the combination of daratumumab with pomalidomide and dexamethasone (DPd). One phase Ib trial (EQUULEUS; MMY1001) demonstrated safe and rapid responses to an intravenous formulation of daratumumab in combination with pomalidomide and dexamethasone [9]. Another phase III trial (APOLLO) found that intravenous or subcutaneous formulation of daratumumab in combination with pomalidomide and dexamethasone resulted in improved rates of progression-free survival (PFS) compared with pomalidomide and dexamethasone (Pd) alone [10]. Finally, the safety and efficacy of DPd were demonstrated for patients experiencing early relapse after one to two lines of therapy and after lenalidomide failure in the phase II trial MM-14 [11].

High-quality randomized clinical trials follow strict inclusion and exclusion criteria, but these do not fully reflect real-world experience, even when patient's reported outcomes are included. Subjects with poor performance status, organ dysfunction, or marrow failure from advanced RRMM are likely to be excluded from many clinical trials. It is therefore important to study the clinical outcomes of FDA-approved MM regimens in real-world settings. Such studies can assist physicians as they seek to apply the findings of clinical trials when treating MM patients outside of trials and/or in a community setting.

In this study, we carried out retrospective real-world investigation of DPd tolerability and toxicity, including consideration of hematological toxicities and adverse non-hematological events.

Materials and Methods

This retrospective study was conducted at the University of Kansas Medical Center (Westwood, KS, USA) in collaboration with the United States Myeloma Innovations Research Collaborative (USMIRC). The study covered the period between January 2015 and June 2022 and received approval from the University of Kansas Institutional Review Board and conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Subjects with a diagnosis of RRMM who received DPd in the second or subsequent lines of therapy were included. We reviewed electronic health records to extract relevant patient data including age, gender, race, MM type and stage, cytogenetics, and treatment lines including auto-HSCT. In addition, we obtained the hematological laboratory parameters of patients over the course of their DPd treatments, as well as any treatment-related adverse events described in their medical records.

The standard-of-care DPd regimen specified daratumumab administered weekly 16 mg/kg intravenously or 1,800 mg subcutaneously with hyaluronidase for the first 8 weeks, every 2 weeks from weeks 9 to 24, and then monthly until discontinuation of treatment due to disease progression or unacceptable toxicity. Pomalidomide dosage was 4 mg orally every day for 21 days as part of a 28-day cycle. Dexamethasone dosage was 20 mg weekly for patients aged 75 and older and 40 mg weekly for patients younger than 75. Antithrombotic and antiviral prophylaxis was carried out as recommended in clinical trials and practice guidelines. Patients were premedicated with glucocorticoids, acetaminophen, and diphenhydramine to prevent infusion reactions and, if required, with albuterol and montelukast in cases of underlying lung disease. Renal, hepatic, and hematological parameters were monitored during DPd therapy. Pomalidomide dosage was adjusted in line with the package insert if cytopenia occurred. Dose reduction was from 4 mg to 3 mg, then to 2 mg, and then to 1 mg; if the patient could not tolerate the lowest dose, pomalidomide was permanently discontinued. For daratumumab, there is no dose reduction, but delay in treatment until resolution of cytopenia and or infection.

Response to therapy was assessed using the International Myeloma Working Group (IMWG) criteria [12]. Grading of hematological and non-hematological adverse events was determined following the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 [13]. Survival outcomes such as PFS and overall survival (OS) were estimated by means of Kaplan-Meier curves using log-rank testing.

Results

The study included 97 patients with RRMM who had received DPd. Table 1 shows the details of patient and baseline disease characteristics. The overall response rate (ORR) for the entire patient population was 74% (n = 72); 27% of patients exhibited a partial response (PR), 10% had a very good partial response (VGPR), 22% had a complete response (CR) and 15% had a stringent complete response (sCR). The median PFS was 10.3 months (95% confidence interval (CI): 8.7 - 19.6), and median OS was 35.3 months (95% CI: 24.8 - not reached) for all patients who received DPd (n = 97). The median duration of follow-up was 38 months. Previous lines of therapy included bortezomib exposed in 93 patients (96%), bortezomib refractory 51 (53%), lenalidomide exposed 94 (97%), lenalidomide refractory 80 (82%), double refractory (PI/IMiDs) 44 (45%), carfilzomib exposed 34 (35%), carfilzomib refractory 25 (26%), pomalidomide exposure 12 (12%). No previous patient with pomalidomide refractoriness or daratumumab exposure were included in our study. Lastly, 78 patients (80%) had received auto-HSCT.

In patients who responded to DPd (n = 72), the median age was 66 years (range 42 - 81), approximately three-fourths of the patients were Caucasian, majority (60%, n = 43) of the patients had immunoglobulin G (IgG) paraprotein subtype, and two-thirds of patients (64%, n = 46) exhibited high-risk cytogenetics. For the responders, the median duration of response (DOR) was 18 (2 - 62) months, and the median number of treatment cycles was 17 (2 - 58). In the non-responding group, the median age was 66 (range 46 - 84), majority were

Table 1. Characteristics of Patients With RRMM Treated With DPd (N = 97)

Characteristics	Responders (n = 72)	Non-responders (n = 25)
Gender, male/female	43/29	14/11
Age, years, median (range)	66 (42 - 81)	66(46 - 84)
Race, no. of patients (%)		
Caucasian	55 (76%)	19 (76%)
African American	14 (19%)	5 (20%)
Asian	2 (3%)	0
Hispanic	1 (2%)	1 (4%)
MM paraprotein, number of patients (%)		
IgG	43 (60%)	17 (68%)
Non-IgG	22 (30%)	5 (20%)
Light chain	7 (10%)	3 (12%)
Baseline R-ISS stage, number of patients (%)		
Stage I	24 (33%)	6 (24%)
Stage II	27 (38%)	8 (32%)
Stage III	17 (23%)	11 (44%)
Unknown	4 (6%)	0
Cytogenetics, no. of patients (%)		
High risk[a]	46 (64%)	17 (68%)
Standard risk	26 (36%)	8 (32%)
Extramedullary disease	17 (24%)	10 (40%)
Median number of lines of therapy (range)	2 (1 - 6)	2 (1 - 4)
Number of DPd cycles (range)	17 (2 - 58)	4 (1 - 15)
Duration of therapy in months (range)	18 (2 - 62)	4 (1 - 16)
Prior autologous stem cell transplant (%)	61 (84%)	17 (68%)

[a]High risk cytogenetics rearrangements as the following: t(4;14), t(14;16), t(14;20), del 17p, and 1q gain. R-ISS: revised international staging system; RRMM: relapsed/refractory multiple myeloma; DPd: daratumumab, pomalidomide, and dexamethasone; IgG: immunoglobulin G.

Caucasian (76%) and had IgG paraprotein (68%). High-risk cytogenetics were seen in about 68% and median number of treatment cycles was 4.

For these patients who experienced response and no response to DPd, the most common grade 3 and 4 adverse events were leukopenia, neutropenia, and lymphopenia, as shown in Table 2. Around 79% (n = 57) of patients who responded to therapy and 74% (n = 72) of all patients experienced grade III/IV of neutropenia. Similarly, 56% (n = 40) of patients who responded to DPd experienced grade III/IV lymphopenia, and 53% (n = 51) for all patients. The incidence of pneumonia was 14% (n = 14) in the entire cohort and all of them were grade 3 and 4 events. Anemia occurred in 55% (n = 53) in all patients, grades 3 and 4 is 18% (n = 13) in responding group, and 28% (n = 7) in the non-responding group. Thrombocytopenia occurred in 71% (n = 69) in all patients and the grades 3 and 4 were 12% (n = 12). For the responding group, the grades 3 and 4 thrombocytopenia were 8% (n = 6) and in the non-responding group 24% (n = 6). Regarding blood transfusion needs, in the responding group, four patients (6%) received at least one unit of packed red blood cells and one patient (2%) required one unit of platelet transfusion. In the non-responding group, four patients (16%) required blood and five patients (20%) required platelet transfusion. Overall, no major bleeding events were reported. In term of growth factor support, granulocyte colony-stimulating factor (G-CSF) was used in grade 4 neutropenia and utilized in 10 patients (14%) from the responding group and two patients (8%) from the non-responding group.

Additionally, the incidence of dose reduction in the responding group was 76% (n = 55), as shown in Table 3. The most common reason for dose reduction was hematological toxicity in 73% (n = 40) and the incidence of febrile neutropenia was 11% (n = 6), and all of them were reported in the responding group. Hospitalization occurred mostly in the responding group, around 32% (n = 23) and was secondary to pneumonia in 57% (n = 13); four patients had viral pneumonia (influenza and respiratory syncytial virus) and the rest were treated as bacterial pneumonia with no pathogen identified by cultures. Finally, there were no instances of serious infusion reactions, and they were reported as low grade in 25% of all patients. Besides that, no serious gastrointestinal events, including hepatic toxicity, were observed in our study.

Table 2. Most Common DPd Treatment Adverse Events

	All DPd patients (n = 97)		DPd patients who responded to treatment (n = 72)		DPd patients who did not respond to treatment (n = 25)	
	All grades	Grade III/IV	All grades	Grade III/IV	All grades	Grade III/IV
Leukopenia	84 (87%)	57 (59%)	66 (92%)	47 (65%)	18 (72%)	10 (40%)
Neutropenia	84 (87%)	72 (72%)	66 (92%)	57 (79%)	18 (72%)	15 (60%)
Lymphopenia	82 (85%)	51 (53%)	64 (89%)	40 (56%)	18 (72%)	11 (44%)
Anemia	53 (55%)	20 (21%)	40 (56%)	13 (18%)	13 (52%)	7 (28%)
Thrombocytopenia	69 (71%)	12 (12%)	53 (74%)	6 (8%)	16 (64%)	6 (24%)
Elevated LFT	24 (25%)	0 (0)	17 (24%)	0 (0)	7 (28%)	0 (0)
GI symptoms (diarrhea, nausea, vomiting)	7 (7%)	0 (0)	7 (10%)	0 (0)	0 (0)	0 (0)
Pneumonia	14 (14%)	14 (14%)	12 (17%)	12 (17%)	2 (8%)	2 (8%)
Peripheral neuropathy	19 (20%)	10 (10%)	15 (21%)	6 (8%)	4 (16%)	4 (16%)
Infusion-related reaction	23 (24%)	0 (0)	19 (26%)	0 (0)	4 (16%)	0 (0)

DPd: daratumumab, pomalidomide, and dexamethasone; LFT: liver function test; GI: gastrointestinal.

In term of antimicrobial prophylaxis, all patients received acyclovir for herpes simplex and herpes zoster virus prophylaxis. During the period of neutropenia, fluoroquinolone and fluconazole for bacterial and fungal prophylaxis were used until resolution of neutropenia. No routine *Pneumocystis jirovecii* prophylaxis was used as the steroids dose did not exceed 40 mg of dexamethasone weekly. All patients received re-vaccination post auto-HSCT along with yearly flu vaccine per institutional guidelines.

Discussion

More than 30,000 cases of MM are diagnosed in the United States every year. The 5-year survival rate is presently 57% [14]; however, this rate is steadily rising with the rapid development of effective treatments for RRMM. The particular nature of this incurable disease means that a pattern of remission and relapse is expected after first-line treatment. Because of this, healthcare providers consider different treatment goals for elderly, frail patients with comorbidities than for patients who are young and fit. When discussing subsequent lines of therapy, it is essential to consider the likely extent of response to treatment and quality of life during treatment. FDA approval of DPd was based on several trials showing appropriate efficacy and safety profiles for patients with RRMM [15]. In MM, the effects of therapy impact the lymphocytes and natural killer cells that attempt to control proliferation of clonal plasma cells. This process impacts normal plasma cells, leading to secondary hypogammaglobulinemia and increased risk of various infections [16]. Reactivation of herpes simplex and varicella zoster is common during treatment with PIs and after auto-HSCT [17]. Additionally, in heavily pretreated patients, recurrent sinopulmonary infections, especially fungal infections, have a major impact on outcomes and cause high levels of morbidity, leading to the interruption of otherwise effective MM treatments [18].

In the phase III APOLLO trial, 68% of patients who received a combination of DPd developed grade 3 - 4 neutropenia compared with 50% who received pomalidomide and dexamethasone (Pd) only. In addition, 12% of patients in the DPd arm developed grade 3 - 4 lymphopenia compared with 3% in

Table 3. Causes of Dose Reduction in Those Who Responded to DPd[a] vs. Non-Responders[b]

Adverse events	Number of patients required dose reduction in DPd responders (%)	Number of patients required dose reduction in DPd non-responders (%)
Hematological toxicity	40 (73%)	11 (79%)
Fatigue	7 (13%)	1 (7%)
Neuropathy	8 (15%)	3 (21%)
Pneumonia	2 (4%)	0
Rash	2 (4%)	0
Neutropenic fever	1 (2%)	0
Diarrhea	1 (2%)	0

[a]Fifty-five patients underwent dose reduction in the responding group. [b]Fourteen patients required dose reduction in the those who did not respond to DPd. DPd: daratumumab, pomalidomide, and dexamethasone.

the Pd arm; whereas grade 3 - 4 pneumonia was seen in 11% of patients in the DPd arm compared with 6% in the Pd arm [10]. In our study, we found a slightly higher incidence of grade 3 - 4 pneumonia among DPd patients (14%) but similar incidence of grade 3 - 4 neutropenia and lymphopenia, 72% and 53%, respectively. Such levels of cytopenia are clearly indicative of the occurrence of serious infections such as pneumonia. The NCCN guidelines categorize MM as a disease with intermediate infection risk [19]; however, the risk of infection varies over the course of the disease and is affected by the degree of tumor burden, during induction therapy, post-auto-HSCT and during maintenance treatment, and the agents used for MM therapy [20]. Several randomized trials examined the role of antibiotic prophylaxis with ciprofloxacin and trimethoprim-sulfamethoxazole for newly diagnosed MM did not find any benefit with the routine use of antibiotics [21, 22]. However, more recent study examined levofloxacin prophylaxis for 3 months found a substantial reduction in infections and deaths [23]. But on the other hand, there are, as yet, no clear guidelines for antimicrobial prophylaxis therapy in cases of RRMM. Although we did not observe a high incidence of coronavirus disease 2019 (COVID-19) infection in our patient population, daratumumab has been reported to have lower neutralizing antibodies after vaccination and thus higher risk of infection [24]. Immunoglobulin replacement therapy has not improved outcomes and is associated with increased risk of thrombosis and renal injury [25]. There is limited evidence of the efficacy of vaccinations in heavily pretreated RRMM patients due to insufficient T-cell function. The optimal timing of vaccination is essential so that any benefits can be obtained (for example, before starting treatment or after immune reconstitution following auto-HSCT) [26]. The use of growth factors during neutropenia enables patients to remain on a course of treatment for MM, and this might improve outcomes if the patient is responding to therapy. The correction of neutropenia during therapy through the routine use of growth factors rather than by dose adjustment has not yet been studied in randomized trials and cannot therefore be implemented in routine practice. However, in this study, we found higher rates of anemia and thrombocytopenia in the non-responding group, suggesting that these were effects of disease progression, rather than treatment. Overall, our data indicate that non-hematological adverse events are manageable.

The study is limited by the retrospective nature of the analysis and of the small number of patients treated at a single center. Additionally, no precise information about pomalidomide dose reduction was included in our database. However, safety and efficacy profile of the patients treated with DPd at our center were very similar to what has been previously reported. A multicenter study or a registry-based analysis with a larger number of patients will help confirm the findings of our report. This study raises questions about the best strategies for lowering infection risk during treatment of RRMM, whether it being through the use of prophylactic antibiotics, growth factor support, immunoglobulins, and/or identifying the optimal timing for vaccination. While this may be difficult to study in a prospective randomized controlled trial, multicenter collaboration will help inform some of these supportive care strategies.

Conclusions

DPd, although an effective treatment option for RRMM, is associated with high incidence of cytopenia and associated complications. Our study revealed that patients who respond to DPd frequently require dose reduction or treatment interruption because of hematological toxicity, typically due to neutropenia and leukopenia, and an increased risk of hospitalization due to pneumonia. Further research is needed on prophylactic antibiotic treatments, which might reduce the incidence of hospitalizations.

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Financial Disclosure

None to declare.

Conflict of Interest

Omar Alkharabsheh, MD: Advisory board for Agios, Genentech, Incyte, Amgen, NCODA, Inc. - BeiGene, and AstraZeneca. Zahra Mahmoudjafari, PharmD: Advisory board for Omeros and Incyte. Shebli Atrash, MD: Honorarium from Celgene, Jansen, Karyopharm, GSK, Sanofi. Speakers Bureau: Celgene, Jansen, Sanofi. Barry Paul, MD: Advisory board for Genentech, Janssen Pharmaceuticals Inc, AbbVie, and Regeneron. Hamza Hashmi, MD: Advisory board for Janssen, BMS, Sanofi, and speaker bureau of Karyopharm, GSK, Sanofi. Other authors have no conflict of interest to declare.

Informed Consent

This is a retrospective study, approved by IRB and deemed minimal risk so informed consent waiver was obtained.

Author Contributions

OA wrote in the manuscript and reviewed the final venison. AA conceived the study idea, collected the data, performed the statistical analysis, and reviewed the final version. PB, ZM, WC, SA, BP, HH, LS, and NA reviewed the final version of the manuscript and assisted in the critical review of the manuscript and data.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

References

1. Bird SA, Boyd K. Multiple myeloma: an overview of management. Palliat Care Soc Pract. 2019;13:1178224219868235.
2. Durer C, Durer S, Lee S, Chakraborty R, Malik MN, Rafae A, Zar MA, et al. Treatment of relapsed multiple myeloma: Evidence-based recommendations. Blood Rev. 2020;39:100616.
3. Miguel JS, Weisel K, Moreau P, Lacy M, Song K, Delforge M, Karlin L, et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomised, open-label, phase 3 trial. Lancet Oncol. 2013;14(11):1055-1066.
4. Fotiou D, Gavriatopoulou M, Terpos E, Dimopoulos MA. Pomalidomide- and dexamethasone-based regimens in the treatment of refractory/relapsed multiple myeloma. Ther Adv Hematol. 2022;13:20406207221090089.
5. Richardson PG, Oriol A, Beksac M, Liberati AM, Galli M, Schjesvold F, Lindsay J, et al. Pomalidomide, bortezomib, and dexamethasone for patients with relapsed or refractory multiple myeloma previously treated with lenalidomide (OPTIMISMM): a randomised, open-label, phase 3 trial. Lancet Oncol. 2019;20(6):781-794.
6. Shah JJ, Stadtmauer EA, Abonour R, Cohen AD, Bensinger WI, Gasparetto C, Kaufman JL, et al. Carfilzomib, pomalidomide, and dexamethasone for relapsed or refractory myeloma. Blood. 2015;126(20):2284-2290.
7. Attal M, Richardson PG, Rajkumar SV, San-Miguel J, Beksac M, Spicka I, Leleu X, et al. Isatuximab plus pomalidomide and low-dose dexamethasone versus pomalidomide and low-dose dexamethasone in patients with relapsed and refractory multiple myeloma (ICARIA-MM): a randomised, multicentre, open-label, phase 3 study. Lancet. 2019;394(10214):2096-2107.
8. Callander NS, Baljevic M, Adekola K, Anderson LD, Campagnaro E, Castillo JJ, Costello C, et al. NCCN Guidelines(R) insights: multiple myeloma, version 3.2022. J Natl Compr Canc Netw. 2022;20(1):8-19.
9. Chari A, Suvannasankha A, Fay JW, Arnulf B, Kaufman JL, Ifthikharuddin JJ, Weiss BM, et al. Daratumumab plus pomalidomide and dexamethasone in relapsed and/or refractory multiple myeloma. Blood. 2017;130(8):974-981.
10. Dimopoulos MA, Terpos E, Boccadoro M, Delimpasi S, Beksac M, Katodritou E, Moreau P, et al. Daratumumab plus pomalidomide and dexamethasone versus pomalidomide and dexamethasone alone in previously treated multiple myeloma (APOLLO): an open-label, randomised, phase 3 trial. Lancet Oncol. 2021;22(6):801-812.
11. Siegel DS, Schiller GJ, Samaras C, Sebag M, Berdeja J, Ganguly S, Matous J, et al. Pomalidomide, dexamethasone, and daratumumab in relapsed refractory multiple myeloma after lenalidomide treatment. Leukemia. 2020;34(12):3286-3297.
12. Kumar S, Paiva B, Anderson KC, Durie B, Landgren O, Moreau P, Munshi N, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. Lancet Oncol. 2016;17(8):e328-e346.
13. CTEP. Common terminology criteria for adverse events (CTCAE) v5.0. 2018.
14. SEER NCI. Cancer Stat Facts: Myeloma. 2022.
15. FDA. FDA approves daratumumab and hyaluronidase-fihj with pomalidomide and dexamethasone for multiple myeloma. 2021.
16. Gulla A, Anderson KC. Multiple myeloma: the (r)evolution of current therapy and a glance into future. Haematologica. 2020;105(10):2358-2367.
17. Kim SJ, Kim K, Kim BS, Lee HJ, Kim H, Lee NR, Nam SH, et al. Bortezomib and the increased incidence of herpes zoster in patients with multiple myeloma. Clin Lymphoma Myeloma. 2008;8(4):237-240.
18. Lortholary O, Ascioglu S, Moreau P, Herbrecht R, Marinus A, Casassus P, De Pauw B, et al. Invasive aspergillosis as an opportunistic infection in nonallografted patients with multiple myeloma: a European Organization for Research and Treatment of Cancer/ Invasive Fungal Infections Cooperative Group and the Intergroupe Francais du Myelome. Clin Infect Dis. 2000;30(1):41-46.
19. NCCN Guidelines. Prevention and treatment of cancer-related infections. Version 2.2022.
20. Balmaceda N, Aziz M, Chandrasekar VT, McClune B, Kambhampati S, Shune L, Abdallah AO, et al. Infection risks in multiple myeloma: a systematic review and meta-analysis of randomized trials from 2015 to 2019. BMC Cancer. 2021;21(1):730.
21. Oken MM, Pomeroy C, Weisdorf D, Bennett JM. Prophylactic antibiotics for the prevention of early infection in multiple myeloma. Am J Med. 1996;100(6):624-628.
22. Vesole DH, Oken MM, Heckler C, Greipp PR, Katz MS, Jacobus S, Morrow GR, et al. Oral antibiotic prophylaxis of early infection in multiple myeloma: a URCC/ECOG randomized phase III study. Leukemia. 2012;26(12):2517-2520.
23. Drayson MT, Bowcock S, Planche T, Iqbal G, Pratt G, Yong K, Wood J, et al. Levofloxacin prophylaxis in patients with newly diagnosed myeloma (TEAMM): a multicentre, double-blind, placebo-controlled, randomised, phase 3 trial. Lancet Oncol. 2019;20(12):1760-1772.
24. Abdallah AO, Mahmoudjafari Z, Atieh T, Ahmed N, Cui W, Shune L, Mohan M, et al. Neutralizing antibody responses against SARS-CoV-2 in patients with plasma cell disorders who are on active treatment after two doses of mRNA vaccination. Eur J Haematol. 2022;109(5):458-464.
25. Sevinc A, Camci C, Buyukberber S, Akgul B. Intravenous gammaglobulin-induced chronic renal failure in a patient with multiple myeloma. Med Oncol. 2007;24(3):357-359.
26. Alemu A, Richards JO, Oaks MK, Thompson MA. Vaccination in multiple myeloma: review of current literature. Clin Lymphoma Myeloma Leuk. 2016;16(9):495-502.