Revista Médica del
Hospital General de México

PERMANYER

Check for updates

ORIGINAL ARTICLE

Bortezomib, thalidomide, and dexamethasone versus thalidomide and dexamethasone for response rates in multiple myeloma patients: a retrospective study

*Juan M. Cano-Calderón[1], Juan F. Zazueta-Pozos[1], Adán G. Gallardo-Rodríguez[2], Carlos Martínez-Murillo[1], Irma Olarte-Carrillo[3], Adolfo Martínez-Tovar[3], and Christian Ramos-Peñafiel[1]**

[1]Department of Hematology; [2]Department of Hematology Research; [3]Molecular Biology Laboratory, Department of Hematology. Hospital General de México Dr. Eduardo Liceaga, Mexico City, Mexico

Abstract

Introduction: *The most current treatment of multiple myeloma is based on a combination of drugs, including immunomodulators and proteasome inhibitors. The bortezomib, thalidomide, and dexamethasone (VTD) and thalidomide and dexamethasone (TD) regimens are commonly used as a first-line treatment due to limited resources.* **Objective:** *To compare the proportion of favorable responses, survival, and time to the next treatment between two different treatment approaches.* **Materials and methods:** *Retrospective study based on medical records of patients with multiple myeloma, eligible for stem cell transplantation, who received, first-line, the VTD or TD combination.* **Results:** *A total of 83 patients were analyzed. The average age was 57 years. The most common type of MM was immunoglobulin G kappa (79.5%), and 51.8% had an International Staging System score of 3. At diagnosis, 28.9% had renal failure, and 42.2% had albumin levels < 3 g/dL. 37.3% were treated with the TD regimen, whereas 62.7% received the VTD regimen. It was considered that 53% had a favorable response. However, patients treated with ETV showed a higher proportion of responses (54.8% vs. 39.3%, p = 0.011). Regarding survival, no differences were identified between the two treatments (Log Rank 0.076) or between the times until the next treatment (Log Rank 0.288).* **Conclusion:** *The VTD scheme was superior to the TD scheme, presenting response ratios similar to other series worldwide. This makes it a viable option for patients with limited financial resources.*

Keywords: *Multiple myeloma. Bortezomib. Thalidomide. Acute phase response. Survival.*

Introduction

Multiple myeloma is a neoplasm characterized by the presence of plasma cell clones that produce an abnormal immunoglobulin (component M), which leads to osseous destruction, anemia, renal function deterioration, and hypercalcemia[1]. It represents around 10% of the hematological neoplasms and mainly affects individuals over 60 years old[2]. Its treatment has experienced a rapid evolution; chemotherapy has been displaced by drugs that activate the immune system, redirecting it in a specific manner to identify and eliminate malignant plasma cells[3,4]. At present, the most effective treatment consists of a combination of drugs (double, triple, or quadruple), which include immunomodulatory agents (lenalidomide and thalidomide), proteasome inhibitors (bortezomib, carfilzomib, and ixazomib), and monoclonal antibodies (daratumumab and isatuximab), followed by high doses of chemotherapy and hematopoietic stem cell transplantation[5,6].

***Correspondence:**
Christian Ramos-Peñafiel
E-mail: leukemiachop33@gmail.com

Date of reception: 08-01-2024
Date of acceptance: 04-07-2024
DOI: 10.24875/HGMX.24000002

Available online: 05-02-2025
Rev Med Hosp Gen Mex. 2025;88(1):10-17
www.hospitalgeneral.mx

In the Latin American context, and despite the clinical and biological characteristics of the diagnosis which are similar to those in other regions of the world[7], there are great differences, due to, mainly, the limited access to specialized centers and a considerably late diagnosis[8,9]. The Hispanic population faces additional vulnerabilities, such as the low level of participation in clinical trials, and the limited access to new specific therapeutic strategies, such as CAR-T cells, compared to the Anglo population[10].

This has led most of the patients to be treated with drugs which are more readily available at a more affordable cost. Among the drugs used in the region, thalidomide and lenalidomide are used as immunomodulators, bortezomib is used as a proteasome inhibitor, combined as a triplet and, in some cases, as a quadruple, along with the monoclonal antibodies anti-CD38[11].

A rarely discussed aspect that is present in every health-care system is financial toxicity, which affects individuals with a lower educational level mainly, having a significant impact on the quality of life[12].

Finally, a late diagnosis leads to more patients presenting complications, some irreversible, such as kidney failure or the presence of acute extramedullary disease. In addition, more patients are diagnosed at very advanced stages in the region (International Staging System [ISS] 3), which makes the comparison of results of various clinical studies difficult.

In Mexico, multiple myeloma is still considered an uncommon disease with significant underreporting, since very few centers have the necessary tools for the diagnosis, as well as the required drugs to complete first-line treatment[13].

The main purpose of this real-life study was to describe the characteristics of patients with multiple myeloma treated at the reference center in Mexico City, identifying the severity and the rate of favorable responses to both treatments available.

Materials and methods

This retrospective study involves research on the clinical records of patients diagnosed with multiple myeloma treated at Hospital General de México between 2020 and 2023. We included the clinical records of patients who were considered eligible for transplant due to their functional status and who were given some treatment strategy comprising a combination of drugs (double or triple). The excluded criteria included: 1. Incomplete clinical records, 2. Clinical records of patients who abandoned treatment or could not continue with the treatment due to economic or distance issues; 3. Clinical records of patients who presented severe sepsis before the beginning of either treatment (Fig. 1).

Two treatment schemes were analyzed – thalidomide 100 mg-200 mg PO daily alone or in combination with dexamethasone 40 mg PO every 24 h on days 1-4, 8-11 of each cycle, and treatment based on bortezomib 1.3 mg/m^2 SC on days 1, 4, 8, 11 to the thalidomide and dexamethasone (TD) scheme for a total of six treatment cycles[14,15] bortezomib, thalidomide, and dexamethasone (VTD).

The response criteria were established in accordance with the International Multiple Myeloma Working Group criteria. Patients with a greater than partial response (very good partial response and response complete) were considered responders.

The combination of albumin and beta2 microglobulin (ISS score) was used for risk stratification. Renal function deterioration was considered with a creatinine > 2 mg/dL at diagnosis[16]. In cases where cytogenetic results were available, they were described within the general characteristics.

Statistical analysis

The demographic characteristics of the study were presented using median (range) for quantitative variables and cases n, [%] for categorical variables. Non-parametric analysis was used for every variable since they did not follow a normal distribution according to the Shapiro-Wilk test. The difference between the groups was calculated using a Mann-Whitney U test for the quantitative variables and Chi-squared tests for the categorical variables. To determine the relationship between the main variables and the main outcomes (time until the next treatment and overall survival), we calculated the odds ratio. In addition, we used Kaplan–Meier estimates to analyze the time until the next treatment and overall survival. Regardless of the median value, differences between groups were analyzed with a Log-Rank test, and the data were presented in median values. We established a $p < 0.05$ as a statistical difference. We conducted all statistical analyses using the SPSS version 25 (SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp) software and generated figures using GraphPad Prisma version 7.

Ethical considerations

As per the second title of the General Health Law on Health Research, specifically in Chapter I, article 17,

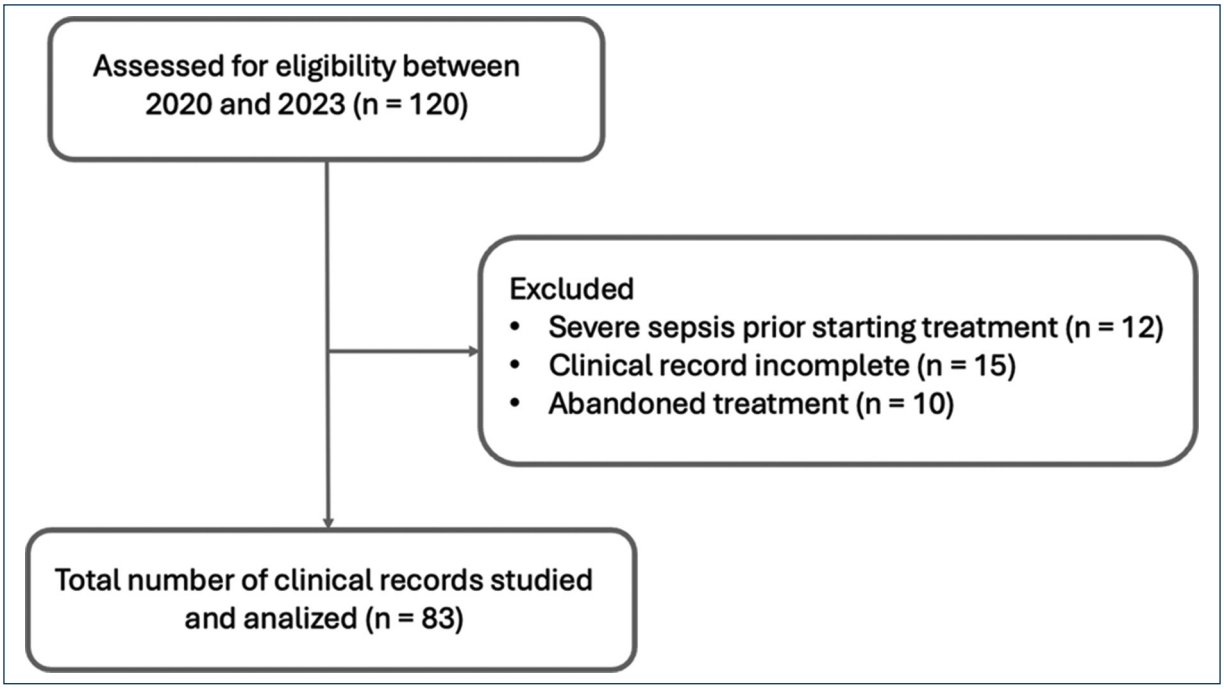

Figure 1. Clinical records selected.

the research study poses no risk to the human patient. The researchers involved in the study confirm that all ethical aspects of privacy and confidentiality have been met while dealing with retrospective information. In addition, the information gathered will be solely used for academic and research purposes. It is also important to note that the researchers involved in this study have no economic, pharmaceutical, political, or social interest in said research.

Results

Patients' general characteristics

A total of 83 patients with a diagnosis of multiple myeloma were studied between January 2020 and June 2023, 54.2% (n = 45) belonged to the male gender and 45.8% (n = 38) to the female gender, and the average age was 57 years (ranging between 34 and 90 years old), not finding a significant difference between genders (p = 0.667, 95% confidence interval [IC]).

The average time for diagnosis was 375 days (with a range from 260 to 490 days, 95% IC), but 24.1% (n = 20) were diagnosed a year after the symptoms began.

Most of the cases were referred by a primary healthcare physician (n = 23, 27.7%), whereas a limited number of cases were referred by a specialist (nephrologist [n = 5, 6%], orthopedist [n = 11, 11.2%], internist [n = 19, 22.9%], oncologist [n = 3, 3.6%] or hematologist [n = 3, 3.6%]). In 16.9% (n = 14) of the cases, the referral happened at the emergency department. In terms of comorbidities, the main ones were diabetes mellitus (n = 11, 12.4%) as well as hypertension (n = 9, 10.8%).

Clinical considerations

The main symptom was pain (n = 72, 86.7%), appearing mainly in the lumbar region, followed by anemia (n = 55, 66.3%), and renal function deterioration (n = 42, 50.6%). Among bone lesions, the majority corresponded to lytic lesions (n = 39, 47%), fractures (n = 24, 28.9%), or the presence of extramedullary disease (n = 14, 16.9%).

In terms of the functional state, 54.2% (n = 45) presented an electrocorticography (ECOG) above 1 (ECOG 2: n = 23, 27.7%, ECOG 3: n = 18, 21.7%, ECOG 4: n = 4, 4.8%). When analyzing the frailty index, 30.1% (n = 25) was considered functional, whereas 37.3% (n = 31) was considered intermediate, and 32.5% (n = 27) was considered frail.

Biological characteristics

When analyzing the different subtypes of clonality, the immunoglobulin G (IgG) type was the most frequent

variant (79.5%) (IgG kappa: n = 33, 39.8% and IgG lambda: n = 26, 31.3%), followed by the IgG variant (n = 7, 8.4%), the IgA variant (unrestricted IgA: 3, 3.6%, IgA kappa: 7, 8.4/, and IgA lambda: 3, 3.6%), and a case of IgE kappa type (1.2%).

In terms of the risk, when combining the ISS risk score (albumin and macroglobulin B2), most cases corresponded to an ISS 3 (n = 43, 51.8%), an ISS 2 (n = 28, 33.7%), and an ISS 1 (n = 12, 14.5%).

Regarding the cytogenetics, the most frequent finding was a normal karyotype (n = 36, 43.4%); in 39 of the cases the karyotype was not assessable (47%), and in 6% (n = 5) it did not present development. In a limited number of samples (n = 3), it was possible to identify some type of abnormality.

Within the abnormalities in the laboratory, 47% (n = 39) presented a level of hemoglobin below 10 g/dL, 28.9% (n = 24) debuted with a level of creatinine above 2 mg/dL, and close to a third of the cases (n = 35, 42.2%) presented a level of albumin below 3g/dL when diagnosed. The main characteristics of the patients are described in table 1.

Types of treatment and responses

Both combinations analyzed were thalidomide–dexamethasone (n = 31, 37.3%), and bortezomib–thalidomide–dexamethasone (n = 52, 62.7%).

In conjunction with the oncological treatment, 16.9% of the cases were combined with radiotherapy, and 45.6% (n = 38) received an addition to the treatment of zoledronic acid or denosumab.

Response to the treatment

When analyzing the overall responses, 45.7% (n = 38) presented a favorable response (full remission or very good partial response), whereas 54.3% (n = 45) presented a non-optimal response (partial response, progression, or stable disease). Of the total cases, 33.7% were considered to have progression criteria. When analyzing the responses to each of the treatments, patients treated through the triplet (VTD) presented a higher rate of favorable responses compared to the patients who received a scheme based exclusively on thalidomide (59.6% vs. 22.5%, p = 0.001, 95% IC). Similarly, the cases treated with the TD scheme presented progression with a higher frequency than the VTD scheme (54.8% vs. 21.1%, p = 0.011, 95% IC). When comparing the effectiveness of both treatments, the time until the next treatment, the patients treated with the TD scheme presented a prolonged time until the following treatment compared to the VTD scheme (536 vs. 479 days, p = 0.38 95% IC) despite the fact that the cases treated with the TD scheme included a higher range of cases with progression. In Fig. 2A and B, the general comparison and detailed range of the responses between both treatments are presented.

Overall survival and associated risk factors

The average survival time was 662 days, with a survival of 3 years in 41% of cases. When comparing the survival according to the type of treatment, no difference between TD or VTD (Log Rank 0.076) was registered, and, despite patients with TD presenting a higher risk of progression, this difference was not reflected in the time until the next treatment (Log Rank 0.288). The overall survival and time until the following treatment are presented in Fig. 3A and B. Fig. 4A and B could include a forest plot on the main variables and the need to initiate the next line of treatment; however, only the triplet (VTD) had an impact on the ratio of favorable responses OR: 0.19 (IC 95% 0.075-0.523; p < 0.001).

Discussion

This real-life study presents the experience of both main combinations used for the treatment of patients with multiple myeloma considered eligible for a transplant. After the introduction of the generic formulation of bortezomib, the inclusion of bortezomib in the TD scheme became more attainable, allowing to treat the majority of patients with triplets (VTD). Other treatments, such as the usage of monoclonal antibodies or stronger drugs such as lenalidomide or carfilzomib, were more limited and destined for patients with social health insurance, used mainly in subsequent lines of treatment[17,18].

Thalidomide is one of the first drugs considered an immunomodulator (IMiD), used at first as a sedative to prevent nausea in pregnant women, it is now one of the most popular drugs for the treatment of MM due to its anti-inflammatory effect in the microenvironment as a stimulant for various lymphocyte subpopulations (CD4+ and CD8+), increasing the levels of IL-2 and interferon γ[19,20]. At present, new and stronger drugs have emerged such as lenalidomide or pomalidomide which, combined with proteasome inhibitors (VRd or KRd) or monoclonal antibodies (elotuzumab-Rd, daratumumab-Rd, isatuximab–pomalidomide–dexamethasone), have become a better option in those patients

Table 1. Demographic characteristics of the study population

Variants	TD (n = 31)	VTD (n = 52)	p
Age (years)	58.00 (49.00-90.00)	52.00 (34.00-80.00)	0.038
Gender (M:F)	18:13	27:25	0.377
Time to diagnosis, n (%) < 6 months > 6 months	 09 (29.0) 22 (71.0)	 30 (57.7) 22 (42.3)	0.010
Type of myeloma, n (%) IgA IgA kappa IgA lambda IgE kappa IgG IgG kappa IgG lambda	 02 (06.5) 02 (06.5) 01 (03.2) 01 (03.2) 04 (12.9) 13 (41.9) 08 (25.8)	 04 (07.6) 05 (09.6) 02 (03.8) 00 (00.0) 03 (05.8) 20 (38.5) 18 (34.6)	
Anemia, n (%) Presence Absence	 19 (61.3) 12 (38.7)	 36 (69.2) 16 (30.8)	0.307
Pain, n (%) Presence Absence	 27 (87.1) 04 (12.9)	 45 (86.5) 07 (13.5)	0.610
Kidney failure, n (%) Presence Absence	 16 (51.6) 15 (48.4)	 26 (50) 26 (50)	0.534
Bone status, n (%) No lesions Lytic lesions Fractures Plasmocytoma	 03 (09.7) 13 (41.9) 11 (35.5) 04 (12.9)	 03 (05.8) 26 (50.0) 13 (25.0) 10 (19.2)	
Frailty score, n (%) Functional Not functional	 21 (67.7) 10 (32.3)	 37 (71.2) 15 (28.8)	0.465
IMPEDE score, n (%) High Low	 21 (67.7) 10 (32.3)	 24 (46.2) 28 (53.8)	0.046
ISS, n (%) 1 2 3	 02 (06.5) 09 (29.0) 20 (64.5)	 10 (19.2) 19 (36.5) 23 (44.2)	
Response to 1st treatment, n (%) Response No response	 09 (29.0) 22 (71.0)	 35 (67.3) 17 (32.7)	0.001
Leukocytes (× 10^3/µL)	5.20 (2.10-15.20)	5.40 (2.37-28.30)	0.980
Hemoglobin (mg/dL)	11.10 (2.80-15.20)	9.60 (4.50-15.20)	0.321
Platelets (× 10^3/µL)	191.00 (9.00-616.00)	221.00 (37.00-493.00)	0.411
Creatinine (mg/dL)	1.00 (0.50-9.40)	1.31 (0.30-12.50)	0.513
Albumin (mg/dL)	2.70 (1.70-4.20)	3.30 (1.96-5.00)	0.029

(Continues)

Table 1. Demographic characteristics of the study population *(continued)*

Variants	TD (n = 31)	VTD (n = 52)	p
LDH (mg/dL)	201.00 (60.00-415.00)	197.50 (5.10-500.00)	0.976
GFR (mL/min/m^2)	74.00 (06.00-109.00)	52.00 (04.00-144.00)	0.479

The Mann-Whitney U test was used for non-parametric variables and is expressed in median (range), and the $\chi 2$ test for qualitative variables and is expressed in absolute values (%). Statistical significance was considered with a $p < 0.05$.
M: male; F: female; IMPEDE: immunomodulatory agent, body mass index, pelvic hip or femur fracture, erythropoietin stimulating agent, dexamethasone/doxorubicin, Asian ethnicity/race; ISS: International staging system; LDH: lactic dehydrogenase; GFR: glomerular filtration rate; IgG: immunoglobulin G.

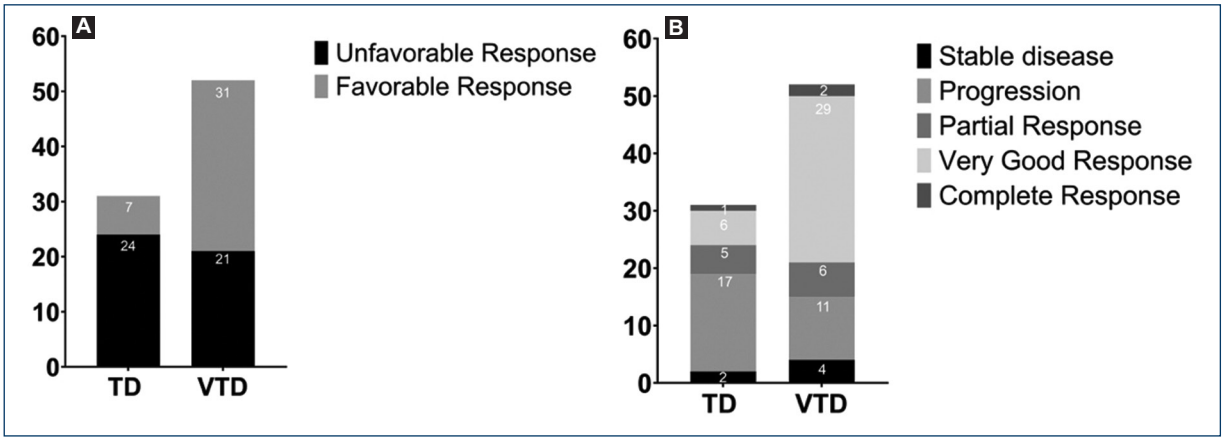

Figure 2. A: the overall ratio of favorable and unfavorable responses and **B:** detailed classified responses between groups.

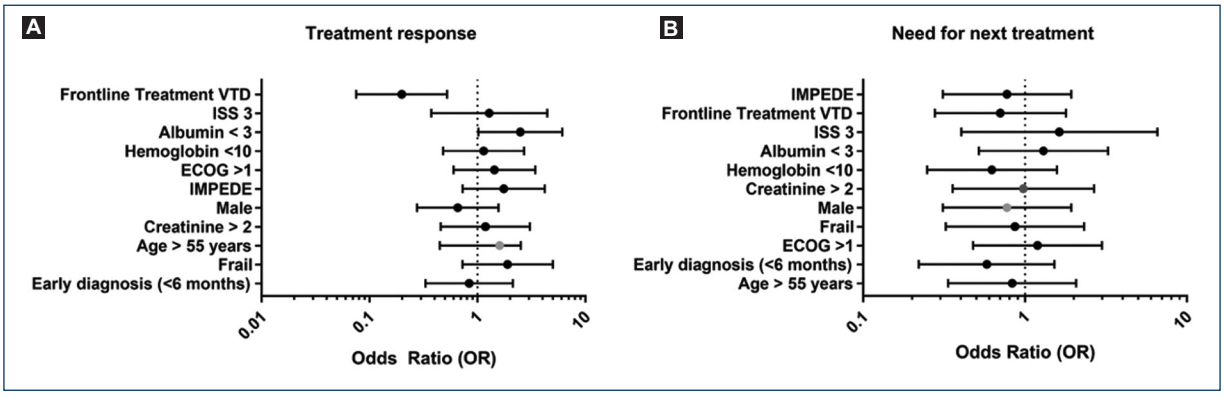

Figure 3. A: overall survival using Kaplan-Meier and **B:** time to next treatment using Kaplan-Meier.

in relapse or resistant to the first treatment or who are not eligible for a transplant[21,22].

Due to the accessibility and cost, both thalidomide and bortezomib are the drugs used with more frequency, be it as a triplet (VTD) or as a double (TD). Despite these combinations having been displaced by more effective combinations, it is important to understand the ratio of favorable responses and their duration, especially since the drugs used are generic. In Turkey, Mersin et al. evaluated the responses to generic bortezomib when compared to the original without finding a difference in the responses or adverse events[23].

In this study, the greater ratio of favorable responses was found in the group treated with bortezomib (67.3%),

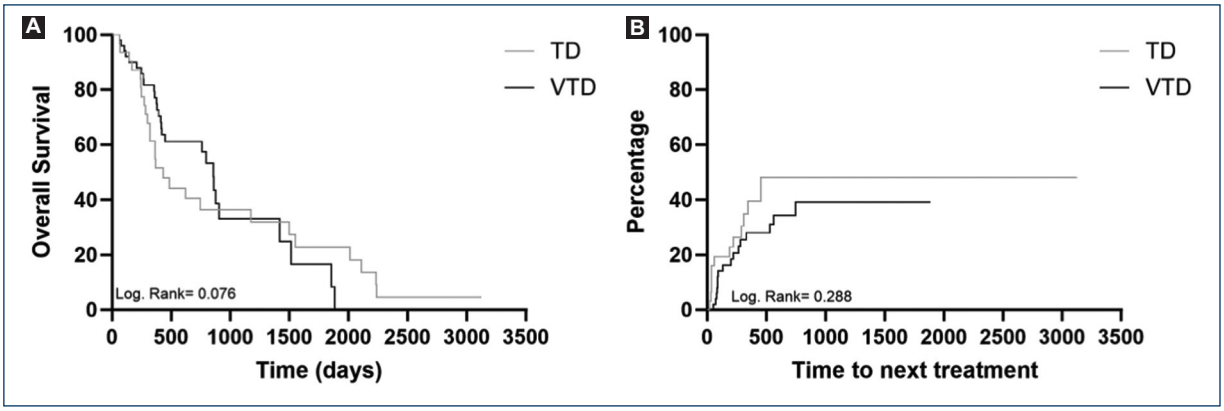

Figure 4. A: forest plot on treatment response and **B:** need for next treatment.

although the percentage of complete responses remained low (3.8%). These data are consistent with the available evidence on combinations based on bortezomib in various clinical trials (APEX, GIMEMA-MM-03-05, and HOVON-65)[24,25].

Since its introduction, bortezomib has presented a synergy with both immunomodulatory agents as well as with chemotherapy (cyclophosphamide and melafan) in various trials, improving the survival and the response to an autologous transplant[26,27]. Another aspect of the combination of an IP with an immunomodulator is its safety profile since the combination of drugs such as anthracyclines (doxorubicin and idarubicin) were more toxic and never better than the double[28].

One of the important aspects of our series is that a significant difference in the overall survival between the treatment regimens (TD vs. VTD) was not found; this had already been described in the first series that compared these combinations before an autologous transplant, where the main benefit was found in the favorable response ratio[29].

When analyzing the group of patients treated with VTD and comparing it to the response ratio in studies where a monoclonal antibody was included (CASSIOPEIA study; VTD vs. daratumumab-VTD), the ratio of favorable responses (RC+VGPR) of the VTD scheme was similar to our series (56.1% vs. 67.3%), but the percentage of full remissions registered for the clinical trial was slightly greater (8.9% vs. 3.8%)[30].

When trying to select the first-line treatment that is more effective without combining it with monoclonal antibodies, Rosiñol et al. analyzed the data from several patient databases treated with VRd (PETHEMA, GEM2012 and IFM2009) or VTD (PETHEMA, GEM2005 and IFM2013-04), who presented a greater benefit with the use of VRd, in particular when reaching a negative measurable residual disease[31]. Similar to the Cassiopeia study (VTD vs. D-VTD), the VRd combination was also challenged with the combination of the monoclonal antibodies anti-CD38. In the GRIFFIN study, Voorhees et al. studied the effect of VRd versus D-VRD; in patients eligible for transplant, they proved an advantage both in the ratio of complete responses (CR/CRs) at the end of the induction (19.2% for D-VRd vs. 13.3% with VRd), with measurable residual disease (21.2% vs. 5.8%), and survival free of progression[32]. When analyzing the results of the different first-line combinations (VTD, VRd, and CyBorD), no significant differences were identified between the ratio of favorable responses (above the partial response), which suggests that VTD remains an effective triplet as a first-line scheme in patients who are eligible for a transplant.

Finally, the greatest benefit at the first line is achieved with the inclusion of the monoclonal antibody anti-CD38 (daratumumab), which allows a greater ratio of complete responses, as well as a greater ratio of negative measurable residual disease as opposed to the schemes based exclusively on IP or immunomodulators[33].

Conclusion

With this real-life data, we conclude that the combination of VTD presents similar evidence in terms of the response to other series around the world, including the results from clinical trials (Cassiopeia study); even when most of the drugs were generic, the responses were superior to the TD combination, without having an influence on survival. When the combination with daratumumab is not available, VTD is a useful first-line option for patients eligible for a transplant.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript.

References

1. Cowan AJ, Green DJ, Kwok M, Lee S, Coffey DG, Holmberg LA, et al. Diagnosis and management of multiple myeloma: a review. JAMA. 2022;327:464-77.
2. Rajkumar SV. Multiple myeloma: every year a new standard? Hematol Oncol. 2019;37 Suppl 1:62-5.
3. Soekojo CY, Chng WJ. Treatment horizon in multiple myeloma. Eur J Haematol. 2022;109:425-40.
4. Nishida H, Yamada T. Monoclonal antibody therapies in multiple myeloma: a challenge to develop novel targets. J Oncol. 2019;2019:6084012.
5. Branagan A, Lei M, Lou U, Raje N. Current treatment strategies for multiple myeloma. JCO Oncol Pract. 2020;16:5-14.
6. Goldschmidt H, Ashcroft J, Szabo Z, Garderet L. Navigating the treatment landscape in multiple myeloma: which combinations to use and when? Ann Hematol. 2019;98:1-18.
7. Curado MP, Oliveira MM, Silva DR, Souza DL. Epidemiology of multiple myeloma in 17 Latin American countries: an update. Cancer Med. 2018;7:2101-8.
8. Mateos MV, Ailawadhi S, Costa LJ, Grant SJ, Kumar L, Mohty M, et al. Global disparities in patients with multiple myeloma: a rapid evidence assessment. Blood Cancer J. 2023;13:109.
9. Mela Osorio MJ, Pavlovsky C, Pavlovsky MA. Inequalities in access to treatment in Argentina: differences in management of CLL and multiple myeloma? Semin Hematol. 2023;60:209-14.
10. Kanapuru B, Fernandes LL, Fashoyin-Aje LA, Baines AC, Bhatnagar V, Ershler R, et al. Analysis of racial and ethnic disparities in multiple myeloma US FDA drug approval trials. Blood Adv. 2022;6:1684-91.
11. Tietsche de Moraes Hungria V, Chiattone C, Pavlovsky M, Abenoza LM, Agreda GP, Armenta J, et al. Epidemiology of hematologic malignancies in real-world settings: findings from the Hemato-Oncology Latin America observational registry study. J Glob Oncol. 2019;5:1-19.
12. Fiala MA, Silberstein AE, Schroeder MA, Stockerl-Goldstein KE, Vij R. The dynamics of financial toxicity in multiple myeloma. Clin Lymphoma Myeloma Leuk. 2023;23:266-72.
13. Ruiz-Argüelles GJ, Gómez-Almaguer D. Lessons learned treating patients with multiple myeloma in resource-constrained settings. Curr Hematol Malig Rep. 2021;16:40-4.
14. Boccadoro M, Blade J, Attal M, Palumbo A. The future role of thalidomide in multiple myeloma. Acta Haematol. 2005;114 Suppl 1:18-22.
15. Kapoor P, Ramakrishnan V, Rajkumar SV. Bortezomib combination therapy in multiple myeloma. Semin Hematol. 2012;49:228-42.
16. Kyrtsonis MC, Maltezas D, Tzenou T, Koulieris E, Bradwell AR. Staging systems and prognostic factors as a guide to therapeutic decisions in multiple myeloma. Semin Hematol. 2009;46:110-7.
17. De la Peña-Celaya JA, Aguilar-Luevano J, Alcivar-Cedeño LM, Álvarez-Vera JL, Anaya-Cuellar I, Añorve-Hernández E, et al. Mexican concensus of multiple myeloma. Gac Med Mex. 2020;156 Suppl 1:S1-45.
18. De Moraes Hungria VT, Martínez-Baños DM, Peñafiel CR, Miguel CE, Vela-Ojeda J, Remaggi G, et al. Multiple myeloma treatment patterns and clinical outcomes in the Latin America Haemato-Oncology (HOLA): observational study, 2008-2016. Br J Haematol. 2020;188:383-93.
19. Zhu YX, Kortuem KM, Stewart AK. Molecular mechanism of action of immune-modulatory drugs thalidomide, lenalidomide and pomalidomide in multiple myeloma. Leuk Lymphoma. 2013;54:683-7.
20. Weber D. Thalidomide and its derivatives: new promise for multiple myeloma. Cancer Control. 2003;10:375-83.
21. Shah UA, Mailankody S. Emerging immunotherapies in multiple myeloma. BMJ. 2020;370:m3176.
22. Sharma NS, Choudhary B. Good cop, bad cop: profiling the immune landscape in multiple myeloma. Biomolecules. 2023;13:1629.
23. Mersin S, Gedük A, Mehtap Ö, Tarkun P, Ünal S, Polat MG, et al. Evaluation of a generic bortezomib molecule in newly diagnosed multiple myeloma patients. Turk J Hematol. 2021;38:211-7.
24. Scott K, Hayden PJ, Will A, Wheatley K, Coyne I. Bortezomib for the treatment of multiple myeloma. Cochrane Database Syst Rev. 2016;4:CD010816.
25. Mateos MV, Richardson PG, Schlag R, Khuageva NK, Dimopoulos MA, Shpilberg O, et al. Bortezomib plus melphalan and prednisone compared with melphalan and prednisone in previously untreated multiple myeloma: updated follow-up and impact of subsequent therapy in the phase III VISTA trial. J Clin Oncol. 2010;28:2259-66.
26. Figueiredo A, Atkins H, Mallick R, Kekre N, Kew A, McCurdy A. Cyclophosphamide-bortezomib-dexamethasone compared with bortezomib-dexamethasone in transplantation-eligible patients with newly diagnosed multiple myeloma. Curr Oncol. 2020;27:e81-5.
27. Schütz NP, Ochoa P, Duarte P, Remaggi G, Yantorno S, Corzo A, et al. Real world outcomes with bortezomib thalidomide dexamethasone and cyclophosphamide bortezomib dexamethasone induction treatment for transplant eligible multiple myeloma patients in a Latin American country. A retrospective cohort study from Grupo Argentino de Mieloma Múltiple. Hematol Oncol. 2020;38:363-71.
28. Sekine L, Ziegelmann PK, Manica D, Da Fonte Pithan C, Sosnoski M, Morais VD, et al. Frontline treatment for transplant-eligible multiple myeloma: a 6474 patients network meta-analysis. Hematol Oncol. 2019;37:62-74.
29. Cavo M, Tacchetti P, Patriarca F, Petrucci MT, Pantani L, Galli M, et al. Bortezomib with thalidomide plus dexamethasone compared with thalidomide plus dexamethasone as induction therapy before, and consolidation therapy after, double autologous stem-cell transplantation in newly diagnosed multiple myeloma: a randomised phase 3 study. Lancet. 2010;376:2075-85.
30. Moreau P, Attal M, Hulin C, Arnulf B, Belhadj K, Benboubker L, et al. Bortezomib, thalidomide, and dexamethasone with or without daratumumab before and after autologous stem-cell transplantation for newly diagnosed multiple myeloma (CASSIOPEIA): a randomised, open-label, phase 3 study. Lancet. 2019;394(10192):29-38.
31. Rosiñol L, Hebraud B, Oriol A, Colin AL, Ríos Tamayo R, Hulin C, et al. Integrated analysis of randomized controlled trials evaluating bortezomib + lenalidomide + dexamethasone or bortezomib + thalidomide + dexamethasone induction in transplant-eligible newly diagnosed multiple myeloma. Front Oncol. 2023;13:1197340.
32. Voorhees PM, Kaufman JL, Laubach J, Sborov DW, Reeves B, Rodriguez C, et al. Daratumumab, lenalidomide, bortezomib, and dexamethasone for transplant-eligible newly diagnosed multiple myeloma: the GRIFFIN trial. Blood 2020;136:936-45.
33. Bazarbachi AH, Al Hamed R, Malard F, Bazarbachi A, Harousseau JL, Mohty M. Induction therapy prior to autologous stem cell transplantation (ASCT) in newly diagnosed multiple myeloma: an update. Blood Cancer J. 2022;12:47.