TURKISH JOURNAL OF INTERNAL MEDICINE

ISSN:2687-4245

Original Article

Mel-200 or Mel-140, Which One is More Advantageous? Retrospectively Analysis of The Multiple Myeloma Patients Treated with Autologous Hematopoetic Stem Cell Transplantation

Fazıl Çağrı HUNUTLU[1], Fahir ÖZKALEMKAŞ[1], Vildan GÜRSOY[2], Vildan ÖZKOCAMAN[1]

[1] Department of Internal Medicine, Division of Hematology, Faculty of Medicine, Bursa Uludag University, Bursa, Turkey.
[2]Department of Hematology, Bursa City Hospital, Bursa, Turkey.

ABSTRACT

Background Autologous hematopoietic stem cell transplantation (AHSCT) is one of the standard treatment modalities for patients with multiple myeloma (MM) under 65 years of age. Renal failure, significant disease comorbidity, significantly affects treatment choices. There are conflicting data in the literature regarding the dose of melphalan to be used for AHSCT in patients with renal failure and comorbid conditions. This study aimed to compare the efficacy and side effect data of different melphalan doses in patients with renal failure.

Material and Methods The study included 107 patients older than 18 years of age with a diagnosis of MM who underwent AHSCT in our centre between January 2010 and January 2019. The data of the patients were analyzed retrospectively. Patients were grouped according to estimated glomerular filtration rate (eGFR: < 60 or ≥ 60 mL/min) and melphalan doses (140-200). In addition to renal failure, patients with low-performance scores (ECOG 3 and above) or severe systemic comorbid disease were included in the Mel-140 group.

Results Comparative analysis of MEL-140 and MEL-200 doses used for AHSCT showed no significant difference between the two groups regarding side effects, disease-free survival, and overall survival. Engraftment times were similar in both groups. When the patients were analyzed according to eGFR level, the incidence and severity of mucositis were higher in the group with low eGFR levels (p = 0.016). The duration of engraftment, complication with a febrile neutropenic attack, and development of septic shock were similar in both groups.

Conclusions In addition to renal failure, MEL-140 emerges as a preferable transplant preparation regimen considering its efficacy and side effect profile in patients with low-performance scores or severe systemic comorbidities.

Turk J Int Med 2023:5(2);92-98
DOI: 10.46310/tjim.1223288

Keywords: *Autologous hematopoietic stem cell transplantation, melphalan, renal failure, multiple myeloma.*

Received: December 23, 2022; Accepted: March 29, 2023; Published Online: April 29, 2023

Address for Correspondence:
Fazıl Çağrı HUNUTLU, Specialist
Division of Hematology, Department of Internal Medicine, Bursa Uludag University, Gorukle Campus Bursa, Turkey
E-mail: fazilhunutlu@gmail.com

INTRODUCTION

Autologous hematopoietic stem cell transplantation (AHSCT) is the standard treatment approach in patients diagnosed with multiple myeloma (MM) aged < 65 years.[1,2] Although different criteria for transplant candidates are used in different centres, AHSCT following induction therapy in young patients with good performance status is the standard treatment. Although the term "young patient" is used for patients who are not older than 65 years of age, patients who are older than 65 years of age without comorbidities and with good performance status can also be considered transplant candidates. Renal function is one of the critical factors, along with age, for AHSCT candidacy in MM patients.1 Renal failure is observed in 20-30% of newly diagnosed MM patients, and hemodialysis may be required in 10% of the patient group.[3] Although a high treatment response rate is obtained with AHSCT with high dose melphalan following remission induction therapies, including the bortezomib-immunomodulatory agent (Imid)-dexamethasone in current studies, there is not enough consensus regarding the use of high-dose melphalan in patient groups with renal failure.[4,5] Studies have shown that AHSCT can be used in all stages of renal failure, including the need for dialysis and does not cause post-transplant engraftment failure.[5] Although studies performed in patients with advanced renal failure are limited and retrospective, studies show that melphalan dose adjustment should be performed mainly in dialysis-dependent patients and transplant-related mortality rates in these patients may be high.[6]

Melphalan used for autologous transplantation in patients with MM is a bifunctional alkylating agent, and the myeloablative dose of 200 mg/m^2 is generally used for transplantation.[7,8] Although spontaneous destruction is the most crucial step in eliminating melphalan from the body, some renal excretion also plays a role in elimination.[9-11] Although the rate of renal excretion is low, it is known that melphalan pharmacokinetics is affected in patients with renal failure.[12] In patient groups with renal failure, some centres aimed to prevent toxicity by reducing the dose of melphalan to 140 mg/m^2.[13] We aimed to contribute to the literature on the effective and safe dose in patient groups with renal failure and vulnerable patients by evaluating the data of patients who were followed up in our centre due to limited and contradictory data in studies on melphalan dose.

MATERIAL AND METHODS

The study included 107 patients older than 18 years of age with a diagnosis of MM who underwent AHSCT in Bursa Uludag University Faculty of Medicine, Department of Hematology, between January 2010 and January 2019. The data of the patients were retrospectively analyzed from their files. The patients were evaluated according to Kidney Disease Improving Global Outcomes (KDIGO) estimated glomerular filtration rate (eGFR: < 60 or ≥ 60 mL/min) levels and melphalan doses (140-200). Patients with low-performance scores (ECOG 3 and above) or severe systemic comorbidities other than renal failure were included in the Mel-140 group. The Mel-140 group included 11 patients, and the Mel-200 group included 96 patients. Age, gender, primary diagnosis, stage, pre-transplant treatment regimens, stem cell collection regimen, transplant preparation regimen, serum creatinine level, need for hemodialysis before transplantation, eGFR level, post-transplant complications, history of febrile neutropenic attack, presence of septic shock, neutrophil and platelet engraftment times, presence of recurrence, presence of mortality in the first 100 days were analyzed. Our study was conducted under the institutional research committee's ethical standards and according to the 1964 Helsinki Declaration.

Statistical Analysis

The compatibility of the variables with normal distribution was analyzed by the Shapiro-Wilk test. Continuous variables were expressed as median (minimum: maximum) and mean ± standard deviation. Categorical variables were expressed as n (%). Mann-Whitney U test was used for comparisons between two groups according to the normality test results. Pearson chi-square, Fisher's exact chi-square, and Fisher-Freeman-Halton tests were used to compare categorical variables between groups. Kaplan-Meier analysis was performed to investigate differences in overall and disease-free survival, and survival curves were compared using the log-rank test. For statistical analyses, SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) programme was used, and $p < 0.05$ was considered statistically significant.

RESULTS

Of 107 patients with MM, 41 (38.3%) were male,

Table 1. Patient characteristics according to estimated glomerular filtration rate (eGFR) level.

	eGFR < 60 mL/min (n: 18)	eGFR ≥ 60 mL/min (n: 89)	*P* value
Age (years)	58 (49:70)	55 (20:71)	0.040[a]
Gender (Male/Female)	5/13	36/53	0.224[b]
ISS phase I	5 (27.8)	28 (31.8)	0.038[b]
ISS phase II	2 (11.1)	32 (36.4)	
ISS phase III	11 (61.1)	28 (31.8)	
Number of treatment received before transplant	2 (1:3)	2 (1:4)	0.700[a]
Lenalidomide based	10 (47.6)	30 (25.6)	0.041[b]
Bortezomib based	18 (85.7)	85 (72.6)	0.205[b]
Stem cell G-CSF	11 (61)	50 (56.8)	0.818[b]
Collection regime chemotherapy+G-CSF	7 (39)	39 (43.2)	
Transplant preparation melphalan 200 mg/m^2	10 (10.4)	86 (89.6)	< 0.001[c]
Regime* melphalan 140 mg/m^2	8 (72.7)	3 (27.3)	
Serum creatinine (mg/dL)	1.60 (1.2:8)	0.70 (0.5:1.2)	< 0.001[a]
eGFR <50 (mL/min)	1 (5.6)	3 (3.38)	0.487[d]
eGFR ≥50 (mL/min)	17 (94.4)	86 (96.62)	

G-CSF: granulocyte colony-stimulating factor. Data were expressed as median (minimum: maximum) or n (%).
*percentages in brackets were calculated according to transplant preparation regime groups.
[a]Mann-Whitney U test, [b] Chi-square test, [c] Fisher Freeman-Halton test, [d] Fisher's exact chi-square test.

and 66 (61.7%) were female. Patient characteristics according to eGFR level were shown in Table 1. 18 patients (16%) were in the group with eGFR < 60 mL/min, while 89 patients (84%) were in the eGFR ≥ 60 mL/min group. The age range was 20-71 years, and the median age was 58 in the low eGFR group and 55 in the normal eGFR group. The subgroup analysis of patients with MM was shown in Table 2.

When melphalan doses used in transplant preparation were compared according to eGFR level, it was found that the melphalan 140 mg/m2 dose was used more in patients with low eGFR. It was statistically significant ($p < 0.001$). Two doses were used in the transplant preparation regime to evaluate the melphalan dose regarding side effects and engraftment time. No significant difference was found between the two groups regarding toxicity or engraftment time. A comparison of the groups according to melphalan dose was shown in Table 3.

In the analysis of the complications that developed during transplantation, the incidence and severity of mucositis were higher in the low eGFR group ($p = 0.040$, $p = 0.012$). No significant difference was found in hepatotoxicity, nephrotoxicity, frequency of febrile neutropenic attacks, septic shock incidence, and diarrhoea development according to eGFR level. No significant difference was found between the two groups in evaluating neutrophil engraftment times according to eGFR level. Median platelet > 20,000/mm3 engraftment time was found to be the 14th day in the eGFR < 60 mL/min group and the 12th day in the eGFR ≥ 60 mL/min groups, but no statistically significant difference was found between the two groups ($p = 0.117$). Median platelet > 50,000/mm^3 time was longer in the group with eGFR < 60 mL/min ($p = 0.006$). Complication evaluation according to eGFR level was summarized in Table 4.

According to the melphalan dose, median disease-free survival (DFS) was 37 months in the Mel-140 mg/m^2 group and 41 months in the Mel-200 mg/m^2 group, and no significant difference was found between the two groups ($p = 0.882$) (Figure 1A). No median value was reached in the overall survival (OS) analysis, and 12, 36, and 60-month OS in the Mel-200

Table 2. Subgroup analysis of patients diagnosed with multiple myeloma.

	eGFR <60 mL/min (n: 18)	eGFR ≥60 mL/min (n: 89)
IgG	9 (50)	43 (48.3)
IgA	2 (11.1)	23 (25.8)
Kappa light chain	6 (33.3)	7 (7.9)
Lambda light chain	0	11 (12.4)
Plasmacytoma	0	4 (4.5)
IgE	1 (5.6)	0
Plasma cell leukemia	0	1 (1.1)

Data were expressed as n (%).

Table 3. Comparison of side effects and engraftment times according to melphalan dose.

Transplant preparation regime	Melphalan 140 mg/m^2 (n: 11)	Melphalan 200 mg/m^2 (n: 96)	*P* value
Transaminase elevation	1 (9.1)	10 (10.4)	> 0.99[a]
Serum bilirubin elevation	2 (18.2)	13 (13.5)	0.651[a]
Mucositis			> 0.99[b]
Grade 1-2	6 (54.5)	51 (53.1)	
Grade 3-4	1 (9.1)	9 (9.4)	
None	4 (36.4)	36 (37.5)	
Diarrhoea			0.337[b]
Grade 1-2	7 (63.6)	38 (39.6)	
Grade 3-4	4 (36.4)	54 (56.3)	
None	0	4 (4.2)	
Neutrophil engraftment (days)	11(10:12)	11 (8:40)	0.322[c]
Platelet 20,000 engraftment (days)	13 (11:28)	12.50 (8:54)	0.297[c]
Platelet 50,000 engraftment (days)	21 (14:35)	17 (10:90)	0.065[c]
Progression free survival (PFS) (months)	39 ± 8.42	54.38 ± 6.76	0.882
Overall survival (OS) (months)	68.47 ± 3.98	124.43 ± 11.27	0.665

Data were expressed as median (minimum: maximum), mean ± standard deviation or n (%).
[a] Fisher's exact chi-square test, [b] Fisher Freeman-Halton test, [c] Mann-Whitney U test.

mg/m^2 group was 97.9%, 88.7%, and 70.5%, respectively. In the Mel-140 mg/m^2 group, 12-36-60 months OS was determined as 100%, 100%, and 53%, respectively. There was no significant difference in OS between the two groups ($p = 0.665$) (Figure 1B).

DISCUSSION

AHSCT performed in combination with high-dose chemotherapy is the standard treatment approach in patients with MM with good performance who

Table 4. Evaluation of complications during transplantation and duration of engraftment according to estimated glomerular filtration rate (eGFR) level.

	eGFR < 60 mL/min (n: 18)	eGFR ≥ 60 mL/min (n: 89)	*P* value
Renal failure in transplantation			0.132[a]
Yes hemodialysis none	7 (38.9)	18 (20.2)	
Yes hemodialysis yes	1 (%5.6)	3 (3.4)	
None	10 (%55.6)	68 (76.4)	
Transaminase elevation	0	11 (12.4)	0.205[b]
Serum bilirubin elevation	2 (11.1)	13 (14.6)	> 0.99[b]
Mucositis			0.016[c]
Grade 1-2	10 (55.6)	47 (52.8)	
Grade 3-4	5 (27.8)	5 (5.6)	
None	3 (16.6)	37 (41.6)	
Diarrhoea			0.297[a]
Grade 1-2	5 (27.8)	40 (44.9)	
Grade 3-4	13 (72.2)	45 (50.6)	
None	0	4 (4.5)	
Febrile neutropenia attack	16 (88.9)	86 (96.6)	0.196[b]
Septic shock	1 (5.60)	3 (3.40)	0.527[b]
Neutrophil engraftment (days)	11 (9:14)	11 (8:40)	0.002[d]
Platelet 20,000 engraftment (days)	14 (10:33)	12 (8:54)	0.117[d]
Platelet 50,000 engraftment (days)	21 (14:39)	17 (10:90)	0.006[d]
Progression free survival (PFS) (months)	42.87 ± 6.33	53.95 ± 6.90	0.331
Overall survival (OS) (months)	81.03 ± 7.49	121.11 ± 11.59	0.387

Data were expressed as median (minimum: maximum), mean±standard deviation or n (%).
[a] Fisher Freeman-Halton test, [b] Fisher's exact chi-square test, [c] Chi-square test, [d] Mann-Whitney U test.

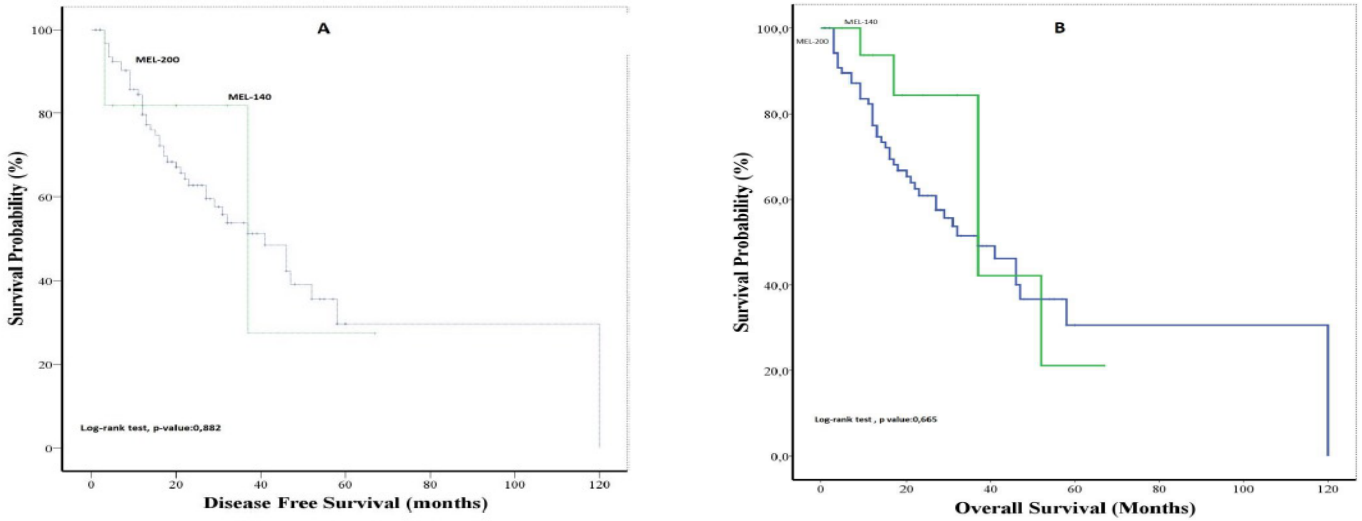

Figure 1. Kaplan-Meier survival analysis according to melphalan doses: (A) disease-free survival; (B) overall survival.

achieve remission with induction therapies.[1,14] However, there is still no consensus about the application of AHSCT in patients with renal failure, especially in patients with MM, and the dose of melphalan to be used as a preparatory regimen. In our survey analysis of the melphalan dose, no significant difference was found between both melphalan doses regarding disease-free survival and overall survival. A study conducted in 2018 on 55 MM patients with renal failure showed that melphalan could be used as an effective treatment option in all stages of renal failure, including patients on dialysis, and that the 140 mg/m^2 dose was safer in terms of side effect management in renal failure. Regarding efficacy, 140 mg/m^2 dose also influenced survival analysis results.[15] Similarly, in a study in which EBMT data were analyzed according to melphalan dose, no significant difference was found between Mel-140 and Mel-200 doses in the survey analysis.[13] In another study in which elderly MM patients were analyzed, it was observed that patients who used Mel-140 mg/m^2 in the transplant preparatory regimen had lower progression-free survival and overall survival rates compared to the Mel-200 mg/m^2 group.[16] In our study, no statistically significant difference was detected between the two groups. The difference between the two studies may be because patients with lower performance scores and lower survey expectations were included in the Mel-140 group and the difference between the number of patients and the induction therapy used before transplantation.

No significant difference was detected between the two groups in the rate of mucositis, development of hepatotoxicity, and engraftment times in the comparison results we performed according to melphalan doses. Similarly, in comparing melphalan doses, side effects and toxicity-related mortality rates were detected between the two groups.[13] As another result of our study, the incidence and severity of mucositis were higher in patients with low GFR levels. Similarly, a study was conducted on 381 newly diagnosed MM patients during AHSCT. Low GFR and high melphalan dose were observed as risk factors for severe mucositis.[17] The two groups had no significant difference regarding non-mucositis side effects and engraftment times compared to melphalan doses. A 1996 study showed that although melphalan was renally excreted, the main route of elimination was spontaneous hydrolysis and melphalan half-life and clearance did not change significantly even in patients with severe renal failure. In the same study, no difference was detected between the groups with and without renal failure in hematopoietic recovery, the frequency of transfusion requirement, and the incidence of severe mucositis (grade 3 and above).[18]

There are few case reports in the literature about lenalidomide-induced hepatotoxicity. One patient presented with a cholestatic injury pattern[19], another patient had lenalidomide-associated hepatitis[20], the third patient had a mixed pattern of liver injury[21], and the fourth patient had asymptomatic transaminase elevation.[22] Most of cases, patients had pre-existing renal failure. Lenalidomide is mainly excreted by kidneys, so patients with renal failure may be more prone to developing hepatotoxicity.[21] In our study results, there were no cases of lenalidomide-induced hepatotoxicity.

Study Limitations

The small number of patients with renal failure, the exclusion of patients with incomplete data due to the study's retrospective design, and the fact that patients with MM constitute a heterogeneous patient population can be considered as the limiting factors of our study. Prospective randomised controlled studies on homogeneous groups of transplant candidates with renal failure will contribute to the literature in the future.

CONCLUSIONS

In conclusion, Mel-140 appears to be an effective and safe transplantation preparatory regimen in frail

patients with renal insufficiency, low-performance scores, or severe systemic comorbid disease. The fact that melphalan undergoes spontaneous hydrolysis along with renal excretion allows it to be used safely in patients with low GFR without a significant increase in side effects.

Conflict of Interest

The authors of this paper have no conflicts of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included.

Funding Sources

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Our study was conducted under the institutional research committee's ethical standards and according to the 1964 Helsinki Declaration. The protocol of the study was approved by the Medical Ethics Committee of Bursa Uludag University (Faculty of Medicine, Bursa, Turkey). (Decision number: 2019-6/39, date: March 2019).

Authors' Contribution

Study Conception, Supervision, Critical Review: FCH, FO, VO; Study Design, Fundings: FCH, FO; Data Collection and/or Processing: FCH, FO, VG; Analysis and/or Interpretation: FCH,FO,VG; Materials: FCH, FO, VG, VO; Literature Review, Writer: FCH.

REFERENCES

1. Turkish Society of Hematology Multiple Myeloma Guidebook Version 1.03. İstanbul: Uniform; 2020.
2. Pettengell R, Morgenstern GR, Woll PJ, Chang J, Rowlands M, Young R, Radford JA, Scarffe JH, Testa NG, Crowther D. Peripheral blood progenitor cell transplantation in lymphoma and leukemia using a single apheresis. Blood. 1993 Dec 15;82(12):3770-7.
3. Dimopoulos MA, Sonneveld P, Leung N, Merlini G, Ludwig H, Kastritis E, Goldschmidt H, Joshua D, Orlowski RZ, Powles R, Vesole DH, Garderet L, Einsele H, Palumbo A, Cavo M, Richardson PG, Moreau P, San Miguel J, Rajkumar SV, Durie BG, Terpos E. International Myeloma Working Group Recommendations for the diagnosis and management of myeloma-related renal impairment. J Clin Oncol. 2016 May 1;34(13):1544-57. doi: 10.1200/JCO.2015.65.0044.
4. Attal M, Lauwers-Cances V, Hulin C, Leleu X, Caillot D, Escoffre M, Arnulf B, Macro M, Belhadj K, Garderet L, Roussel M, Payen C, Mathiot C, Fermand JP, Meuleman N, Rollet S, Maglio ME, Zeytoonjian AA, Weller EA, Munshi N, Anderson KC, Richardson PG, Facon T, Avet-Loiseau H, Harousseau JL, Moreau P; IFM 2009 Study. Lenalidomide, bortezomib, and dexamethasone with transplantation for myeloma. N Engl J Med. 2017 Apr 6;376(14):1311-20. doi: 10.1056/NEJMoa1611750.
5. Badros A, Barlogie B, Siegel E, Roberts J, Langmaid C, Zangari M, Desikan R, Shaver MJ, Fassas A, McConnell S, Muwalla F, Barri Y, Anaissie E, Munshi N, Tricot G. Results of autologous stem cell transplant in multiple myeloma patients with renal failure. Br J Haematol. 2001 Sep;114(4):822-9. doi: 10.1046/j.1365-2141.2001.03033.x.
6. St Bernard R, Chodirker L, Masih-Khan E, Jiang H, Franke N, Kukreti V, Tiedemann R, Trudel S, Reece D, Chen CI. Efficacy, toxicity and mortality of autologous SCT in multiple myeloma patients with dialysis-dependent renal failure. Bone Marrow Transplant. 2015 Jan;50(1):95-9. doi: 10.1038/bmt.2014.226.
7. Selby PJ, McElwain TJ, Nandi AC, Perren TJ, Powles RL, Tillyer CR, Osborne RJ, Slevin ML, Malpas JS. Multiple myeloma treated with high dose intravenous melphalan. Br J Haematol. 1987 May;66(1):55-62. doi: 10.1111/j.1365-2141.1987.tb06890.x.
8. Cunningham D, Paz-Ares L, Milan S, Powles R, Nicolson M, Hickish T, Selby P, Treleavan J, Viner

C, Malpas J, et al. High-dose melphalan and autologous bone marrow transplantation as consolidation in previously untreated myeloma. J Clin Oncol. 1994 Apr;12(4):759-63. doi: 10.1200/JCO.1994.12.4.759.
9. Sarosy G, Leyland-Jones B, Soochan P, Cheson BD. The systemic administration of intravenous melphalan. J Clin Oncol. 1988 Nov;6(11):1768-82. doi: 10.1200/JCO.1988.6.11.1768.
10. Alberts DS, Chang SY, Chen HS, Moon TE, Evans TL, Furner RL, Himmelstein K, Gross JF. Kinetics of intravenous melphalan. Clin Pharmacol Ther. 1979 Jul;26(1):73-80. doi: 10.1002/cpt197926173.
11. Bosanquet AG, Gilby ED. Pharmacokinetics of oral and intravenous melphalan during routine treatment of multiple myeloma. Eur J Cancer Clin Oncol. 1982 Apr;18(4):355-62. doi: 10.1016/0277-5379(82)90006-2.
12. Osterborg A, Ehrsson H, Eksborg S, Wallin I, Mellstedt H. Pharmacokinetics of oral melphalan in relation to renal function in multiple myeloma patients. Eur J Cancer Clin Oncol. 1989 May;25(5):899-903. doi: 10.1016/0277-5379(89)90138-7..
13. Auner HW, Iacobelli S, Sbianchi G, Knol-Bout C, Blaise D, Russell NH, Apperley JF, Pohlreich D, Browne PV, Kobbe G, Isaksson C, Lenhoff S, Scheid C, Touzeau C, Jantunen E, Anagnostopoulos A, Yakoub-Agha I, Tanase A, Schaap N, Wiktor-Jedrzejczak W, Krejci M, Schönland SO, Morris C, Garderet L, Kröger N. Melphalan 140 mg/m2 or 200 mg/m2 for autologous transplantation in myeloma: results from the Collaboration to Collect Autologous Transplant Outcomes in Lymphoma and Myeloma (CALM) study. A report by the EBMT Chronic Malignancies Working Party. Haematologica. 2018 Mar;103(3):514-21. doi: 10.3324/haematol.2017.181339.
14. Zelenetz AD, Abramson JS, Advani RH, Andreadis CB, Byrd JC, Czuczman MS, Fayad L, Forero A, Glenn MJ, Gockerman JP, Gordon LI, Harris NL, Hoppe RT, Horwitz SM, Kaminski MS, Kim YH, Lacasce AS, Mughal TI, Nademanee A, Porcu P, Press O, Prosnitz L, Reddy N, Smith MR, Sokol L, Swinnen L, Vose JM, Wierda WG, Yahalom J, Yunus F. NCCN Clinical Practice Guidelines in Oncology: non-Hodgkin's lymphomas. J Natl Compr Canc Netw. 2010 Mar;8(3):288-334. doi: 10.6004/jnccn.2010.0021.
15. Augeul-Meunier K, Chretien ML, Stoppa AM, Karlin L, Benboubker L, Diaz JMT, Mohty M, Yakoub-Agha I, Bay JO, Perrot A, Bulabois CE, Huynh A, Mercier M, Frenzel L, Avet-Loiseau H, de Latour RP, Cornillon J. Extending autologous transplantation as first line therapy in multiple myeloma patients with severe renal impairment: a retrospective study by the SFGM-TC. Bone Marrow Transplant. 2018 Jun;53(6):749-755. doi: 10.1038/s41409-018-0122-8.
16. Munshi PN, Vesole D, Jurczyszyn A, Zaucha JM, St Martin A, Davila O, Agrawal V, Badawy SM, Battiwalla M, Chhabra S, Copelan E, Kharfan-Dabaja MA, Farhadfar N, Ganguly S, Hashmi S, Krem MM, Lazarus HM, Malek E, Meehan K, Murthy HS, Nishihori T, Olin RL, Olsson RF, Schriber J, Seo S, Shah G, Solh M, Tay J, Kumar S, Qazilbash MH, Shah N, Hari PN, D'Souza A. Age no bar: A CIBMTR analysis of elderly patients undergoing autologous hematopoietic cell transplantation for multiple myeloma. Cancer. 2020 Dec 1;126(23):5077-87. doi: 10.1002/cncr.33171.
17. Grazziutti ML, Dong L, Miceli MH, Krishna SG, Kiwan E, Syed N, Fassas A, van Rhee F, Klaus H, Barlogie B, Anaissie EJ. Oral mucositis in myeloma patients undergoing melphalan-based autologous stem cell transplantation: incidence, risk factors and a severity predictive model. Bone Marrow Transplant. 2006 Oct;38(7):501-6. doi: 10.1038/sj.bmt.1705471.
18. Tricot G, Alberts DS, Johnson C, Roe DJ, Dorr RT, Bracy D, Vesole DH, Jagannath S, Meyers R, Barlogie B. Safety of autotransplants with high-dose melphalan in renal failure: a pharmacokinetic and toxicity study. Clin Cancer Res. 1996 Jun;2(6):947-52.
19. Hussain S, Browne R, Chen J, Parekh S. Lenalidomide-induced severe hepatotoxicity. Blood. 2007 Nov 15;110(10):3814. doi: 10.1182/blood-2007-06-097758.
20. Zanella MC, Rubbia-Brandt L, Giostra E, Chalandon Y, Hadengue A, Spahr L. A case of drug-ınduced hepatitis due to lenalidomide. Case Rep Gastroenterol. 2011 Apr 13;5(1):217-22. doi: 10.1159/000326935.
21. Jain P. Lenalidomide-induced acute liver failure. Blood Transfus. 2009 Oct;7(4):335-6; author reply 337. doi: 10.2450/2009.0086-09.
22. Hussein MA. Lenalidomide: patient management strategies. Semin Hematol. 2005 Oct;42(4 Suppl 4):S22-5. doi: 10.1053/j.seminhematol.2005.10.003.