Turkish Journal of Clinics and Laboratory

To cite this article: Yucel OK. The first 100-day outcomes of autologous hematopoietic stem cell transplantation in multiple myeloma patients: melphalan 200 mg/m² versus 140 mg/m² conditioning regimen . Turk J Clin Lab 2023; 3: 608-615

Research Article

The first 100-day outcomes of autologous hematopoietic stem cell transplantation in multiple myeloma patients: melphalan 200 mg/m² versus 140 mg/m² conditioning regimen

Multiple myelom hastalarında otolog hematopoietik kök hücre naklinin ilk 100 gün sonuçları: melfalan 200 mg/m² 'ye karşı melfalan 140 mg/m² hazırlama rejimi

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Abstract

Aim: Melphalan 200 mg/m² (Mel200) is a standard accepted conditioning regimen during the autologous hematopoietic stem cell transplantation (auto-HSCT) for multiple myeloma (MM) patients. Whereas melphalan 140 mg/m² (Mel140) is generally preferred either in patients with renal disease or elderly patients. We aimed to compare the first 100-day outcomes of the Mel140 and Mel200 conditioning after auto-HSCT in this study.

Material and Methods: We retrospectively analyzed 69 consecutive MM patients who underwent their first auto-HSCT at the Adult Hematopoietic Stem Cell Transplantation Unit at Akdeniz Universi-ty Hospital.

Results: While 41 (59.4%) of patients were male, 28 (40.6%) patients were female. The median age at auto-HSCT was 61 years old (range, 40-75). The ratio of patients with glomerular filtration rate (GFR)<60 ml/min was significantly higher in the Mel140 group than the Mel200 group (P < 0.001). Despite not to reach statistical significance, the median age tended to be higher in the Mel140 group (P = 0.064). There were not any significant difference between the Mel200 and Mel140 groups in terms of hospitalisation time at transplantation (P = 0.691), neutrophil engraftment time (P = 0.907), platelet engraftment time (P = 0.234), febrile neutropenia during the transplantation (P = 1), number of eryth-rocyte transfusion during the hospitalisation (P = 0.661), number of platelet transfusion during the hospitalisation (P = 0.569), patient status at post-transplant day 100 (P = 0.882), and disease status at post-transplant day 100 (P = 0.967), respectively.

Conclusion: Our study shows that the Mel200 and Mel140 conditioning have similar first 100-day outcomes after auto-HSCT in MM. Further comprehensive randomised trials would clarify the impact of melphalan conditioning intensity on early term post-transplant outcomes.

Keywords: multiple myeloma, autologous hematopoietic stem cell transplantation, melphalan, early term post-transplant outcomes

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Doi: 10.18663/tjcl.1346448
Recevied: 19.08.2023 accepted: 08.09.2023

ÖZ

Amaç: Melfalan 200 mg/m² (Mel200), multiple myelom (MM) hastaları için otolog hematopoietik kök hücre nakli (oto-HKHN) sırasında standart olarak kabul edilen bir hazırlama rejimidir. Melfalan 140 mg/m² (Mel140) ise genellikle böbrek hastalığı olan hastalarda veya yaşlı hastalarda tercih edilir. Bu çalışma-da oto-HKHN sonrası Mel140 ve Mel200 hazırlama rejimlerinin ilk 100 günlük sonuçlarını karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Akdeniz Üniversitesi Hastanesi Erişkin Hematopoietik Kök Hücre Nakli Ün-itesinde ilk oto-HKHN uygulanan ardışık 69 MM hastasını retrospektif olarak inceledik.

Bulgular: Hastaların 41'i (%59,4) erkek, 28'i (%40,6) kadındı. Hastaların nakil sırasındaki ortanca yaşı 61 idi (aralık, 40-75). Glomerüler filtrasyon hızı (GFR) <60 ml/dk olan hastaların oranı Mel140 grubunda Mel200 grubuna göre anlamlı olarak daha yüksekti (P < 0.001). İstatistiksel anlamlılığa ulaşmamakla birlikte, medyan yaş Mel140 grubunda daha yüksek olma eğilimindeydi (P = 0.064). Mel200 ve Mel140 grupları arasında sırasıyla transplantasyonda hastanede kalış süresi (P = 0.691), nötrofil engraftman süresi (P = 0.907), trombosit engraftman süresi (P = 0.234), transplantasyon sırasında febril nötropeni gelişimi (P = 1), hastanede yatış sırasında eritrosit transfüzyonu sayısı (P = 0.661), hastanede yatış sırasında trombosit transfüzyonu sayısı (P = 0.569), nakil sonrası 100. gün-deki hasta mortalite oranı (P = 0.882) ve nakil sonrası 100. gündeki hastalık durumu (P = 0.967) açısından anlamlı fark yoktu.

Sonuç: Çalışmamız, oto-HKHN sonrası ilk 100 gün sonuçlarının Mel200 ve Mel140 hazırlama rejim-lerini kullanan MM hastalarında benzer olduğunu göstermektedir. Daha kapsamlı randomize klinik çalışmalar melfalan hazırlama rejimi yoğunluğunun nakil sonrası erken dönem sonuçlarına olan etkisi-ni açıklığa kavuşturacaktır.

Anahtar Kelimeler: multiple myelom, otolog hematopoietik kök hücre nakli, melfalan, nakil sonrası erken dönem sonuçları

Introduction

High-dose chemotherapy and autologous hematopoietic stem cell transplantation (auto-HSCT) is still the standard of care up-front treatment for transplant-eligible multiple myeloma (MM) patients despite new anti-myeloma drug era (1,2). Melphalan 200 mg/m² (Mel200) is a standard accepted conditioning regimen as a high dose chemotherapy during the auto-HSCT for MM patients (3-5). But some studies revealed that using Mel200 in MM patients during the auto-HSCT was associated with increased tox-icity in older patients and in patients with renal failure (6-8). Therefore, melphalan 140 mg/m² (Mel140) has commonly been used in elderly patients and in patients with renal insufficiency in sev-eral studies (9-14). However, there are two studies to show inferior response or survival rates related to Mel140 when compared with Mel200 (13,15). In European Society for Blood and Marrow Trans-plantation (EBMT) study, Mel140 and Mel200 showed similar post-transplant outcomes, except in patients with less than a partial response to pre-transplant induction therapy (16). Similarly, the MD Anderson study revealed Mel140 had comparable efficacy to Mel200, especially in older patients and those with at least a very good partial response at the time of transplant (17).

There are conflicting results related to using reduced dose melphalan in myeloma patients at auto-HSCT in the literature as we mentioned above, and those studies generally focused on long term out-comes of MM patients after auto-HSCT. Therefore, we aimed to compare the first 100-day outcomes of the Mel140 and Mel200 conditioning after auto-HSCT in this study.

Material and Methods

Patient population

We retrospectively analyzed 69 consecutive MM patients >18 years of age who underwent their first auto-HSCT at the Adult Hematopoietic Stem Cell Transplantation Unit at Akdeniz University Hospi-tal between January 2019 and February 2023.

The diagnosis of multiple myeloma was made according to the International Myeloma Working Group (IMWG) criteria (18). The response to the treatment was based on the IMWG criteria as well (19).

Conditioning regimens and Anti-infective prophylaxis

Conditioning regimens that used in patients were Mel200 in 58 (84%) patients and Mel140 in 11 (16%) patients.

All patients received levofloxacin 500 mg/day, fluconazole 200 mg/day, and valacyclovir 500 mg/day until engraftment for anti-infective prophylaxis. After engraftment, trimethoprim-sulfamethoxazole against Pneumocystis jirovecii was started and va-

lacyclovir against herpes viruses continued to use. All patients used both of them for 6 months as an anti-infective prophylaxis.

All patients whose immunoglobulin (Ig) G level were lower than 500 mg/dL, those received 0.4 grams per kilogram intravenous immunoglobulin as a prophylactic dose for the infections.

Granulocyte colony-stimulating factor (G-CSF) 5 microgram/kg/day was started at day +1 or + 5 until the neutrophil engraftment in all patients.

Definitions and Endpoints

The neutrophil engraftment was defined as the first day for three consecutive days where the neutro-phil count was 500 cells/mm^3 or greater. The platelet engraftment was described as the first day for three consecutive days that the platelet count was 20.000/mm^3 or greater without platelet transfusion.

Disease status at transplantation was assessed to the response that obtained from previous therapies according to the IMWG response criteria (19). Comorbidity was defined presence of two or more medical conditions existing simultaneously in a patient.

The primary endpoints were both patients status (alive or death) and disease status (stringent complete response or complete response or very good partial response or partial response or minimal response or stable disease or progressive disease) at post-transplant day 100. The secondary endpoints were the duration of stay at transplant unit, neutrophil and platelet engraftment time, the number of erythro-cyte and platelet transfusions until discharge from the transplant unit and the presence of infection during the stay at transplant unit .

Statistical Analysis

All statistical analyses were performed using SPSS version 23.0 software (Chicago, USA). Descrip-tive statistics are presented as numbers and percentages for categorical variables and mean ± standard deviation, median (minimum value – maximum value) for continuous variables. Normal distribution for continuous variables were assessed with visual (histograms and probability graphics) and analytic methods (Kolmogorov-Smirnov and Shapiro-Wilk's test). Chi-squared tests were used for compari-son of categorical variables in independent groups. Mann-Whitney U test was used to compare the groups according to melphalan conditioning, and the data were presented as median (min-max) values. $p < 0.05$ was considered to be statistically significant.

Results

Patient and disease characteristics are provided in Table 1. While 41 (59.4%) of patients were male, 28 (40.6%) patients were female. The median age at auto-HSCT was 61 years old (range, 40-75), and of 69 patients, 19 (27.5%) were ≥65 years of age. 49 (71%) patients had Eastern Cooperative Oncology Group (ECOG) performance score 0, 18 (26.2%) patients had ECOG 1, 1 (1.4%) patient had ECOG 2, and 1 (1.4%) patient had ECOG 3, respectively. Glomerular filtration rate (GFR) was ≥60 ml/min in 61 (88.4%) patients and <60 ml/min in 8 (11.6%) patients. In addition to the GFR, the creatinine, which is another indicator of kidney function, was <2 mg/dL in 65 (94.2%) patients and ≥2 mg/dL in 4 (5.8%) patients.

A majority of patients (n=37, 53.6%) was in complete response before auto-HSCT, 22 (31.9%) had a very good partial response, and 8 (11.6%) had a partial response. Unfortunately, the disease status before auto-HSCT of 2 (2.9%) patients were not found. Of 69 patients, 61 (88.4%) had received first line therapy, 6 (8.7%) had received second line therapy, and 2 (2.9%) had received third line therapy prior to transplant. The number of chemotherapy cycles received before transplant was 4 in 29 (42%) patients, 5 in 17 (24.6%) patients, 6 in 9 (13%) patients, 7 in 3 (4.3%) patients, 8 in 3 (4.3%) patients, 9 in 1 (1.4%) patient, 12 in 1 (1.4%) patient, respectively. There was no information related to the number of chemotherapy cycles for 5 (7.2%) patients. The median number of chemotherapy cycles received before transplant was 5 (range, 2-12).

Of 69 patients, 64 (92.8%) patients started the G-CSF at the fifth day (+5) of stem cell infusion, and 5 (7.2%) patients started the G-CSF at first day (+1) of stem cell infusion. While 33 (47.8%) patients had no comorbidity, 16 (23.2%) patients had one chronic disease, and 20 (29%) patients had more than one chronic disease. The median hospital stay day at transplantation was 20 (range, 15-34). The median neutrophil engraftment time was 11 (range, 10-14) days. Similarly, the median time of platelet engraftment was 11 (range, 7-14) days as well. The majority of patients developed febrile neutropenia (FEN) (n=64, 92.8%) during the transplantation. The median count of infused CD34+ peripheral stem cells was 4.3x10^6/kg (range, 3.5-5.7x10^6/kg).

While the median number of erythrocyte transfusions during the stay at the stem cell transplantation unit was 1 (range, 0-6) unit, the median number of platelet transfusions was 2 (range, 1-7) units. The majority of patients in our study underwent auto-HSCT with Mel200 (n=58, 84.1%), Mel140 was used in 11 (15.9%) patients. At post-transplant day 100; of 69 patients, 63 (91.3%) patients were alive, 1 (1.4%) patient was dead, and the status of 5 (7.3%) patients were not found because of lost to follow up. The cause of death of the patient, who underwent auto-HSCT with Mel200, was Klebsiella pneumonia infection developed before engraftment occurred. The disease status

of patients at post-transplant day 100 were followed by; 31 (44.9%) patients were in complete response, 21 (30.4%) patients were in very good partial response, 6 (8.7%) patients were in partial response, respectively. Unfortunately, the disease status at post-transplant day 100 was unknown in 11 (15.9%) patients ow-ing to lost to follow up or not evaluated or death.

Comparison of Mel200 versus Mel140 group

The variables such as GFR, serum creatinine level, and the start-ing day of G-CSF were significantly different when compared with Mel200 and Mel140 groups as shown in Table 2. The ratio of patients with GFR<60 ml/min (63.6%) was significantly higher in the Mel140 group than the Mel200 group (1.7%) ($P < 0.001$). Similarly, while patients with serum creatinine≥ 2 mg/dL were 36.4% in the Mel140 group, there was not any patient with se-rum creatinine≥ 2 mg/dL in the Mel200 group ($P < 0.001$). When compared with the Mel200 and Mel140 groups, the ratio of pa-tients with the starting day of G-CSF at 5th day was significantly higher in the Mel200 group (96.6% versus 72.7%, $P = 0.026$).

However, other variables such as age ($P = 0.064$), comorbidity ($P = 0.120$), and infused CD34+ pe-ripheral stem cells ($P = 0.082$) tended to be different between the Mel200 and Mel140 groups, but those variables did not reach statistical significance.

There were not any significant difference between the Mel200 and Mel140 groups in terms of sex ($P = 0.758$), ECOG perfor-mance status ($P = 0.276$), disease status at transplantation ($P = 0.284$), treat-ment line received prior to transplant ($P = 0.424$), number of chemotherapy cycles before transplant ($P = 0.263$), hospitalisation time at transplantation ($P = 0.691$), neutrophil engraftment time ($P = 0.907$), platelet engraftment time ($P = 0.234$), febrile neutropenia during the transplantation ($P = 1$), number of erythrocyte transfusion during the hospitalisation ($P = 0.661$), number of platelet transfusion dur-ing the hospitalisation ($P = 0.569$), patient status at post-transplant day 100 ($P = 0.882$), and disease status at post-transplant day 100 ($P = 0.967$), respectively, (Table 2).

Discussion

The purpose of this single center retrospective study was to investigate the impact of melphalan dose intensity on the early term post-transplant outcomes in MM patients under-went auto-HSCT. There are few studies compared the effects of Mel140 versus Mel200 on post-transplant outcomes, and those studies generally focused on long term outcomes and designed for a specific MM population such as patients with renal impairment or elderly patients. Unlike those studies, our study included all patients who received Mel140 independent of the reason and aimed to evaluate early term outcomes af-ter auto-HSCT. To the best of our knowledge, this is the first study to compare the first 100 days results of the Mel200 and Mel140 group in MM patients after auto-HSCT.

The Mel200 is the standard conditioning regimen for MM patients without comorbidity at auto-HSCT. Reduced-dose melphalan is generally preferred for older patients and those who are fragile or with significant comorbidities. Although there are no randomised clinical trials to compare Mel200 and Mel140, several studies reported that Mel140 was feasible for MM patients, especially patients with renal impairment and older patients (6-8). Our study showed that Mel140 instead of Mel200 was statistically preferred in patients with renal suf-ficiency in our centre in line with the literature. Similar-ly, the percentage of patients ≥65 years was higher in Mel140 group than Mel200 group in the present study, but it did not reach statistical significance. This might be related to small sample size in our study. Consequently, the present study confirms Mel140 is tended to prefer in older patients and pa-tients with renal disease in our transplant center.

While platelet engraftment time was similar between the Mel140 and Mel200 groups, neutrophil en-graftment time was significantly longer in Mel140 group in the study published by Katragadda et al. In addition to, the incidence of febrile neutro-penia increased in patients with Mel140 than Mel200 patients in the same study (9). On the other hand, there were no sig-nificant differences between the Mel140 and Mel200 groups in terms of neutrophil and platelet engraftments in the EBMT and MD Anderson trials (16,17). Despite not to statistically sig-nificant, a higher percentage of patients had febrile neutrope-nia in the Mel200 group in the MD Anderson study, contrary to the study conducted by Katragadda et al. (9,17). We did not find significant differences between the Mel200 and Mel140 groups in terms of neutrophil engraftment, platelet engraft-ment, and the rate of febrile neutropenia, respectively. Our re-sults are compatible with some previous studies. But there are conflicting results related to either neutrophil engraftment time or the incidence of febrile neutropenia in the literature as we mentioned above. This could be related to the sample size of the studies, the difference between the patients included in the studies in terms of disease status at transplantation or comorbidities, and vari-able frequency of non-hematological toxicities such as mucositis.

Table 1. Disease and Patient Characteristics	
Characteristics	Total (n=69)
Sex, n (%) Female Male	 28 (40.6) 41 (59.4)
Age, year Mean±SD Median (min-max)	 59.6±8.5 61 (40-75)
Age, n (%) <65 years ≥ 65 years	 50 (72.5) 19 (27.5)
ECOG Performance Status, n (%) 0 1 2 3	 49 (71) 18 (26.2) 1 (1.4) 1 (1.4)
GFR, n (%) ≥60 ml/min <60 ml/min	 61 (88.4) 8 (11.6)
Serum creatinine, n (%) <2 mg/dL ≥2 mg/dL	 65 (94.2) 4 (5.8)
Disease status at transplantation, n (%) Complete response Very good partial response Partial response Unknown	 37 (53.6) 22 (31.9) 8 (11.6) 2 (2.9)
Treatment line received prior to transplant, n (%) 1 2 3	 61 (88.4) 6 (8.7) 2 (2.9)
The number of chemotherapy cycles received before transplant, n (%) 2 4 5 6 7 8 9 12 Unknown	 1 (1.4) 29 (42) 17 (24.6) 9 (13) 3 (4.3) 3 (4.3) 1 (1.4) 1 (1.4) 5 (7.2)
The number of chemotherapy cycles received before transplant, no Mean±SD Median (min-max)	 5±1.5 5 (2-12)
The starting day of G-CSF during the transplantation, n (%) 1st day 5th day	 5 (7.2) 64 (92.8)
Comorbidity, n (%) No 1 disease >1 disease	 33 (47.8) 16 (23.2) 20 (29)
Hospital stay period at transplantation, days Mean±SD Median (min-max)	 20.5±3.4 20 (15-34)
Neutrophil engraftment time, days Mean±SD Median (min-max)	 11.1±0.8 11 (10-14)
Platelet engraftment time, days Mean±SD Median (min-max)	 11.2±1,6 11 (7-14)
Febrile neutropenia during the transplantation, n (%) No Yes	 5 (7.2) 64 (92.8)
Infused CD34+ peripheral stem cells, 106/ kg Mean±SD Median (min-max)	 4.3±0.5 4.3 (3.5-5.7)
The number of erythrocyte transfusion during the hospitalisation, unit Mean±SD Median (min-max)	 1.2±1.5 1 (0-6)
The number of platelet transfusion during the hospitalisation, unit Mean±SD Median (min-max)	 2.6±1.4 2 (1-7)
Melphalan dose, n (%) 140 mg/m2 200 mg/m2	 11 (15.9) 58 (84.1)
Patient status at post-transplant day 100, n (%) Alive Died Lost to follow-up	 63 (91.3) 1 (1.4) 5 (7.3)
Disease status at post-transplant day 100, n (%) Complete response Very good partial response Partial response Unknown	 31 (44.9) 21 (30.4) 6 (8.7) 11 (15.9)
SD: Standard Deviation, ECOG: Eastern Cooperative Oncology Group, G-CSF: Granulocyte Colony Stimulating Factor	

Table 2. Comparison of Mel200 and Mel140 groups

Variables	Mel200 (n=58)	Mel140 (n=11)	p
Sex, n (%) Female Male	 23 (39.7) 35 (60.3)	 5 (45.5) 6 (54.5)	0.758*
Age, year Median (min-max)	 60.5 (40-73)	 66 (43-75)	0.064**
Age, n (%) <65 years ≥ 65 years	 45 (77.6) 13 (22.4)	 5 (45.5) 6 (54.5)	0.059*
ECOG Performance Status, n (%) 0 ≥1	 43 (74.1) 15 (25.9)	 6 (54.5) 5 (45.5)	0.276*
GFR, n (%) ≥60 ml/min <60 ml/min	 57 (98.3) 1 (1.7)	 4 (36.4) 7 (63.6)	<0.001*
Serum creatinine, n (%) <2 mg/dL ≥2 mg/dL	 58 (100) 0	 7 (63.6) 4 (36.4)	<0.001*
Disease status at transplantation, n (%) Complete response Very good partial response Partial response	n=57 32 (56.2) 17 (29.8) 8 (14)	n=10 5 (50) 5 (50) 0	0.284*
Treatment line received prior to transplant, n (%) 1 2 3	 50 (86.2) 6 (10.3) 2 (3.4)	 11 (100) 0 0	0.424*
The number of chemotherapy cycles received before transplant, no Median (min-max)	 4.5 (4-12)	 5.5 (2-9)	0.263**
The starting day of G-CSF during the transplantation, n (%) 1st day 5th day	 2 (3.4) 56 (96.6)	 3 (27.3) 8 (72.7)	0.026*
Comorbidity, n(%) No 1 disease >1 disease	 30 (51.8) 14 (24.1) 14 (24.1)	 3 (27.3) 2 (18.2) 6 (54.5)	0.120*
Hospital stay period at transplantation, days Median (min-max)	 20 (15-29)	 19 (17-34)	0.691**
Neutrophil engraftment time, days Median (min-max)	 11 (10-14)	 11 (10-13)	0.907**
Platelet engraftment time, days Median (min-max)	 11 (7-14)	 12 (9-14)	0.234**
Febrile neutropenia during the transplantation, n (%) No Yes	 4 (6.9) 54 (93.1)	 1 (9.1) 10 (90.9)	1.000*
Infused CD34+ peripheral stem cells, 106/ kg Median (min-max)	 4.4 (3.5-5.7)	 3.9 (3.6-4.9)	0.082**
The number of erythrocyte transfusions during the hospitalisation, unit Median (min-max)	 0.5 (0-6)	 1 (0-6)	0.661**
The number of platelet transfusions during the hospitalisation, unit Median (min-max)	 2 (1-7)	 2 (1-6)	0.569**
Patient status at post-transplant day 100, n (%) Alive Died Unknown	 53 (91.4) 1 (1.7) 4 (6.9)	 10 (90.9) 0 1 (9.1)	0.882*
Disease status at post-transplant day 100, n (%) Complete response Very good partial response Partial response	n=50 27 (54) 18 (36) 5 (10)	n=8 4 (50) 3 (37.5) 1 (12.5)	0.967*

ECOG: Eastern Cooperative Oncology Group, GFR: Glomerular Filtration Rate, G-CSF: Granulocyte Colony Stimulating Factor, Mel200: Melphalan 200 mg/m2, Mel140: Melphalan 140 mg/m2
SD: Standard Deviation, *:Chi-Square Test **: Mann-Whitney U testi

There are several studies that evaluated the duration of hospital stay at auto-HSCT in MM patients. The Mel140 and Mel200 groups were only compared in the elderly patients (>65 years) in the study of Marini et al. and the median hospital stay at auto-HSCT was similar between the Mel140 and Mel200 groups in the elderly patients (20). Similarly, Katragadda et al. reported that the median inpa-tient days during the auto-HSCT was not significantly different between the Mel140 and Mel200 groups (9). Our results were compatible with previous studies in terms of the hospital stay during the auto-HSCT, and we did not find significant difference between the Mel200 and Mel140 groups like in the literature.

In terms of transfusion support during the hospital stay at auto-HSCT, there is limited knowledge in the literature. Among the elderly patients (>65years), the need for erythrocyte and platelet transfusion was greater in the Mel200 group than the Mel140 group in the study conducted by Marine et al. But it did not reach statistically significance (20). In our study, the need for both erythrocyte and platelet transfusions was not significantly different between the Mel200 and Mel140 groups as well.

Marini et al. reported that five patients died during the first 100 days after the auto-HSCT, resulting in a transplant related mortality (TRM) of 3.8%. The deaths were related to infectious complications (20). In the EBMT study, the non-relapse mortality rate at 3 months after auto-HSCT was 0.8% and 0.5% for the Mel200 and Mel140 groups, respectively, and it was not significantly different (16). Similarly, the mortality ratio at 100 days after the auto-HSCT was 1.4% for the whole population in our study. While one patient died due to infection in the Mel200 group in the first 100 days after the auto-HSCT, nobody died in the Mel140 group. Consequently, the mortality rate at 100 days after au-to-HSCT was statistically similar between the Mel140 and Mel200 groups in our study compatible with the literature.

If we mention early response rate or disease status after the transplant, there have not been enough studies comparing the impact of Mel200 and a reduced dose of melphalan in terms of the disease sta-tus at day-100 after auto-HSCT. The disease status at 3 months after the auto-HSCT was similar be-tween the Mel140 and Mel200 groups in the MD Anderson study (17). Likewise, our study showed that the disease status at day 100 after auto-HSCT was statistically similar between the melphalan groups as well.

In conclusion, our aim was to compare the impact of Mel200 and Mel140 on short term post-transplant outcomes in MM patients who underwent first auto-HSCT. The small number of patients and retrospective nature of the study are limitations of our study. According to the first 100-day re-sults after auto-HSCT, the mortality rate, disease status, need for transfusion, febrile neutropenia ratio, engraftment time, and duration of hospitalisation were not significantly different between the Mel200 and Mel140 groups. Despite the small sample size and retrospective design, our study shows that the Mel200 and Mel140 conditioning have similar first 100-day outcomes after auto-HSCT in MM pa-tients. Further comprehensive randomised trials are needed to clarify the impact of melphalan condi-tioning intensity on early term outcomes after auto-HSCT.

Statement of Ethics

This retrospective and non-interventional study was reviewed and approved by the Institutional Ethics Board of Akdeniz University School of Medicine. The study was conducted in accordance with the Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

Funding Sources

There are no funding sources to declare.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author (O.K.Y.).

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