The Silent Threat of Secondary Malignancies in Multiple Myeloma Patients: A Cohort Study from Turkey in the Era of New Drugs

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Introduction

Advancements in multiple myeloma (MM) treatment have significantly improved survival, as shown in real-world analyses outside of clinical trials. Consequently, some clinical trial endpoints now focus on avoiding high-dose melphalan before autologous stem cell transplantation (ASCT). As patients live longer with MM, the occurrence of second malignancies—whether concurrent, early, or late—remains a critical concern. This study documents our single-center experience with second primary malignancies (SPM) in MM patients.

Methods

This retrospective study accessed data from the institution's automated system for MM-diagnosed patients. The study included patients who were not exposed to the VAD regimen during induction, as new drugs were reimbursed in the country. Typically, first-line treatment consisted of the Cybord regimen, with or without ASCT, and lenalidomide maintenance. For relapse or refractory cases, treatment was adjusted by changing proteasome inhibitors and immunomodulatory drugs and/or adding daratumumab. Demographic characteristics and detailed information regarding SPM were recorded.

Results

A total of 574 MM patients were included in the study, followed between 2018 and 2024. The mean age of the patients was 61.8 years (range: 26–94), with 54.3% male and 45.7% female (Table 1).

SPM was recorded in 34 patients (5.6%). The mean age of the patients with SPM was 66.8 years (SD 12.5, range: 45–94), and no significant age difference was found between the two groups. Six patients (17%) developed synchronous cancers, while 28 patients (83%) developed metachronous cancers (Table 2). Among these, MM was the first diagnosis in 22 patients. The median follow-up period for patients who developed SPM was 59.5 months (range: 2–480 months). The median duration of lenalidomide treatment before the onset of SPM was 15 months (range: 3–74 months), while the median time from MM diagnosis to the development of SPM was 25 months (range: 2–194 months). Myelodysplastic syndromes (MDS) were found to have the most significantly elevated risk as an SPM.

n patients exposed to lenalidomide, there was no significant increase in SPM development (p=0.715). Similarly, ASCT did not show a difference in the risk of SPM between patients who underwent ASCT and those who did not (p=0.455).

Table 1: Demographic and Baseline Characteristics of Patients

	N (574)
Age, y (Mean, SD, İR)	61.8 (11.4) (26-94)
Female, N (%)	257 (45.7%)
Myeloma subtype (%)	
IgG	60.8%
IgA	17.6%
IgD	2.5%
Biclonal	2.2%
Non secratory	.6%
Light chain	15.7%
Kappa	57.5%
Lambda	40.3%
ISS	
I	37.8%
II	28.2%
III	34.0%
Extramedullary disease (%)	55(16.6%)
Prior ASCT, N (%)	221 (44.3%)
Prior any alkylator therapy, N (%)	331 (65.3%)
Lenalidomide maintenance N (%)	265(51.8%)
Any IMiD therapy N (%)	314 (60.4%)
Any secondary malignancy N (%)	34 (5.6%)
Secondary primary malignancy N (%)	22 (3.8%)

Cancer type	First myeloma occured	First other cancer occured
Prostate Cancer	4	2
Breast Cancer	0	4
MDS (Myelodysplastic Syndrome)	4	0
Colon Cancer	2	1
Adenocarcinoma of the lung	1	0
Stomach adenocarcinoma	1	0
Laryngeal Cancer	0	1
Acute Myelogenous Leukemia	1	2
Myelofibrosis	0	1
Chronic Myeloid Leukemia	0	1
Essential Thrombocythemia	1	0
T-cell Lymphoma	1	0
Chronic Lymphocytic Leukemia	0	1
Osteosarcoma	1	0
Other	3	0

Conclusion

In our study, neither lenalidomide maintenance nor ASCT was found to increase the risk of SPM. An increased risk was observed for hematological cancers, particularly

MDS. Overall, both MM patients and physicians must acknowledge the reality of SPMs, and continued monitoring is essential for the early detection and management of SPMs.

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