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OUTCOMES OF SECONDARY ACUTE LYMPHOBLASTIC LEUKEMIA IN MULTIPLE MYELOMA

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INTRODUCTION

Multiple Myeloma outcomes have consistently shown survival improvement almost 2-3-fold over the last decade. Lenalidomide constitutes an important part of effective myeloma therapy, however, it has been associated with a higher incidence of second primary malignancies (SPM), including both hematological and solid malignancies. [1,2]. Cumulative incidence of all secondary malignancies in patients treated with lenalidomide was reported at 6.9% at 5 years compared to 3.8% in patient treated without. Lenalidomide modulates various components of the immune system – targets B-cell transcription factors, segments NK cell cytotoxicity and regulates T-cell co-stimulation. However, the mechanism by which it increases risk of SPM remains unclear. [3]

AIM

To evaluate incidence and outcomes of secondary acute lymphoblastic leukemia (sALL) in myeloma patients

METHODS

We retrospectively analyzed 735 patients who had multiple myeloma between January 2009 and April 2023 and evaluated those who were confirmed with sALL at the University of Kansas Health System in collaboration with the U.S Myeloma Innovations Research Collaborative (USMIRC). Seven patients with confirmed diagnosis of sALL were identified. Descriptive analyses were performed on available data for patient characteristics, disease course, and outcomes.

RESULTS

- 735 patients with MM were reviewed and 7 patients with confirmed diagnosis of sALL were identified. The overall incidence of sALL in our study cohort was 0.95%. The median time from diagnosis of MM until sALL was 62 months (35-146)
- MM was in complete remission at the time of diagnosis of sALL in 6 patients and they were all on lenalidomide maintenance therapy. Four (57%) of patients were on 10 mg daily. Five (71%) patients received high dose chemotherapy with melphalan 200 mg/m2 followed by autologous stem cell transplant (ASCT)
- Cytogenetics at the time of diagnosis of sALL was normal in 3 (42%) of the patients, all patients were t(9;22) negative. Six (85%) patients received treatment for sALL while one patient opted to proceed with comfort measures. Five patients achieved a completed response after therapy, while one patient is on active treatment for ALL. One patient passed away from relapsed myeloma. Four (57%) are currently in remission after treatment for both myeloma and sALL

Characteristics	
Gender (Male:Female)	4:3
Age, years, median (range)	68 (61-81)
Race, number of patients (%)	
Caucasian	6 (86%)
African American	1 (14%)
MM paraprotein, number of patients (%)	
IgG	5 (71%)
Light chain	2 (29%)
Baseline R-ISS stage, number of patients (%)	
Stage III	2 (29%)
Stage II	1 (14%)
Stage I	2 (29%)
Unknown	1 (14%)
Normal cytogenetics (%)	3 (42%)
Patients who received lenalidomide (%)	7 (100%)
Number of patients who received HDCT&ASCT (%)	5 (71%)
Median time from diagnosis of MM until sALL (months)	62 (35-146)

MM: Multiple myeloma, R-ISS: Revised International Staging System, IgG: Immunoglobulin G, HDCT: High-dose chemotherapy, ASCT: Autologous stem cell transplant, sALL: Secondary acute lymphoblastic leukemia

DISCUSSION

Lenalidomide has been shown to have a highly significant improvement in PFS for MM based on studies on the kinetics of MRD.[4] SPM is a very rare complication of its use. Of the hematological malignancies, AML and MDS are more common The IFM-2009 trial, reported incidence of hematologic SPM at 0.9% overall. [2] The Determination Phase III trial, which recruited 772 patients with newly diagnosed myeloma, reported secondary primary hematological malignancies in 0.30% and the incidence of sALL was 0.13% which was lower compared to our study. The difference in incidence of SPM was not statistically significant in the two groups – RVD alone and RVD+ASCT. [6] The myeloma XI trial, which evaluated 1097 patients on lenalidomide, found that patients receiving lenalidomide maintenance for newly diagnosed MM had a higher risk of developing SPM, which was statistically significant compared to the observation arm, with a stronger association in older patients. [7] Our data shows a 1% incidence of sALL in patients with MM, with all but one patient developing sALL while on active lenalidomide treatment. These findings suggest a prominent role of lenalidomide in the etiology of SPM, with a lesser role of autologous transplant.

CONCLUSIONS

Based on these observations, we conclude that –

- The low incidence of sALL in patient with multiple myeloma and the high efficacy of immunomodulatory agents such as lenalidomide should not alter physician's current practice or preclude their use
- Physicians should maintain a high index of suspicion and the risk of SPMs should be discussed with patients prior to initiating therapy

REFERENCES

1. Turesson I, Velez R, Kristinsson SY, *et al.*. *Journal of Clinical Oncology* 2009;28:830–4.
2. Attal M, Lauwers-Cances V, Hulin C, *et al. New England Journal of Medicine* 2017;376:1311–20
3 Lu G, Middleton RE, Sun H, *et al. Science (1979)* 2014;343:305–9.
4. Jackson, Graham H., et al. *The Lancet Oncology* 20.1 (2019): 57-73.
5. Meletios A. Dimopoulos, Paul G. Richardson, Nancy Brandenburg, Zhinuan Yu, Donna M. Weber, Ruben Niesvizky, Gareth J. Morgan. *Blood* 2012; 119 (12): 2764–2767.
6. Richardson PG, Jacobus SJ, Weller EA, *et al. New England Journal of Medicine* 2022;387:132–47.
7. Jackson GH, Davies FE, Pawlyn C, *et al. Lancet Oncol* 2019;20:57–73

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