Acute Lymphoblastic Leukemia Following Multiple Myeloma Therapy: A Single-Center Experience With 9 Patients

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Abstract

Multiple myeloma is heterogenous disease characterized by monoclonal expansion of plasma cell. It is also the second most common hematologic malignancy accounted for **1%** of all cancers. The poor survival of patients with MM is caused not only by often relapsed or refractory outcome due to poor response to treatment but also due to **11-fold** increased risk of second malignancy, especially myeloid neoplasms (t-MDS/AML) when compared to the general population (1,2). Most common reported second malignancies secondary to MM are myeloid malignancies (3). However, little is known about occurrence of lymphoid malignancies, in particular acute lymphoblastic leukemias, where the occurrence of lymphoid malignancies is described mostly as case reports (4). In contrary to reports discussing therapy related B-ALL (t-B-ALL) as rising from the same clone as MM (clonal hematopoiesis, CH), other reports present t-B-ALL as a distinct clonally independent entity associated with poor outcome (5-7), warranting further investigation.

Objective

Patients with multiple myeloma (MM) have an increased risk of developing second malignancies, especially myeloid neoplasms (t-MDS/AML). However, little is known about occurrence of lymphoid malignancies, in particular acute lymphoblastic leukemias.

To characterize and evaluate outcome of patients with B-ALL developed following treatment with Multiple Myeloma.

Main Outcome Measures: Response rates (complete response, CR) and overall survival (OS).

Materials & Methods

We retrospectively analyzed disease characteristics and outcomes of patients diagnosed with ALL, following MM, presenting to the MD Anderson Cancer Center between 2005-2018.

Results

Patient characteristics at the timepoint of MM diagnosis

Category	Number, n=9	(% or range)
Sex		
Female	**8/9**	**88%**
Male	**1/9**	**12%**
Race		
White/Caucasian	**4/9**	**44%**
Latino/Hispanic	**1/9**	**12%**
African/American	**4/9**	**44%**
Age at MM Dx	**67**	**(48-74)**
MM subtype		
IgG	**4/9**	**44%**
IgA	**2/9**	**22%**
Light chain MM	**3/9**	**33%**
MM therapy		
IMiDs as induction	**6/9**	**66%**
Bortezomib	**7/9**	**77%**
Chemotherapy	**3/9**	**33%**
Radiation	**1/9**	**12%**
Auto HCT for MM	**4/9**	**44%**
Maintenance therapy	**8/9**	**88%**
IMiDs for maintenance	**8/9**	**88%**
Cumulative time of IMiDs	**3.91**	**(0.33-6.68)**
Time From MM to ALL	**6.8**	**(0.33-9.86)**
Time from IMiDs to ALL	**5.51**	**(0.33-8.14)**

Patient characteristics at the timepoint of ALL diagnosis

Category	Number, n=9	(% or range)
Age at ALL Dx	**75**	**(54-85)**
MM status at ALL Dx		
CR	**6/9**	**66%**
Active disease	**1/9**	**12%**
% ALL Blast in BM	**83**	**(45-100)**
ALL phenotype		
B-ALL	**9/9**	**100%**
Ph-	**9/9**	**100%**
ALL karyotype		
Normal	**5/9**	**56%**
Complex	**3/9**	**33%**
TP53 del/mut.	**4/9**	**44%**
MLL rearrangement	**1/9**	**12%**
Monosomy 7 or 7q del.	**3/9**	**33%**
Trisomy 8	**1/9**	**12%**
Hyperdiploidy	**3/9**	**33%**
B-ALL Therapy		
mini-CVD+Inotuzumab	**5/9**	**56%**
mini-CVD+Venetoclax	**1/9**	**22%**
R-CVP	**1/9**	**12%**
Hyper-CVAD+Rituximab	**2/9**	**24%**
Number of cycles	**5**	**(4-7)**
POMP Maintenance	**5/9**	**56%**

Outcome

Seven patients (77%) achieved CR (MRD-).

One patient (12%) completed therapy with CR MRD+ and underwent allogeneic SCT.

One patient (12%) relapsed with MM after completing ALL treatment.

Six patients (66%) are alive. Median OS was 2.7 years (0.46-5.21).

Summary

B-ALL can occur in patients with multiple myeloma with a median latency of **6.8** years. All patients were receiving lenalidomide at the time of diagnosis of ALL. All patients in our series had **Ph-neg B-ALL** with **4/9** having a concomitant TP53 mutation.

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The authors declare no competing conflicts of interest

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