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LETTER TO THE EDITOR

Pomalidomide-based maintenance post-autologous hematopoietic cell transplantation in multiple myeloma: a case series

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Dear Editor,

The treatment of multiple myeloma (MM) has undergone tremendous advances in the past two decades and particularly with the advent of two key drug classes: proteasome inhibitors and immunomodulatory drugs (IMiDs). The current dogma in MM treatment relies on continuous plasma cell–directed therapy starting with induction therapy, followed by consolidation (autologous hematopoietic cell transplantation (auto-HCT) in HCT-eligible patients) and maintenance treatment [1]. Lenalidomide (len), an IMiD, is the only FDA-approved agent for maintenance therapy in MM and has demonstrated progression-free (PFS) and overall survival (OS) advantage in newly diagnosed patients [2]. Pomalidomide (pom) is a highly potent third-generation IMiD that has been approved in the relapsed and refractory MM setting but has not been studied in the maintenance setting in a randomized fashion [3, 4].

Herein we report on the clinical characteristics and outcomes of patients treated with pom maintenance post-HCT at our institution.

In this retrospective chart review, 7 patients received pom maintenance after auto-HCT. The median age at diagnosis was 56 years (range, 46–66). Four patients were male (57%). Individual patient characteristics are listed in Table 1. According to the Revised International Staging System (R-ISS), 71% (5 patients) had stage II MM. All patients had normal cytogenetics; one patient had *t*(4;14), three had *t*(11;14), and two had del(13q) on FISH. Anemia and bone involvement were present in most patients (5; 71%).

The median time to auto-HCT was 22 months (range, 17–41). Pom was initiated after a median of 4 prior lines of treatment, including HCT (range, 3–7) and at a median of 3 months (range, 3–5) post-HCT. All seven patients had achieved at least a partial response (PR) before HCT. The main reason for substituting pom for len was prior lack of response to len in five patients (71%). Significant len intolerance prompted using pom in two patients (severe rash in patient 4 and grade 3 colitis in patient 6) (Table 2).

The drug was started at variable doses and was overall well-tolerated. A dose of 2 mg was used in most patients (except patients 4 and 7). Patient 6 was started on 2 mg, which was subsequently reduced to 1 mg due to grade 2 muscle cramps and fatigue. Patient 4 was started on 1 mg, and patient 7 was initially started on 4 mg of pom post-transplant but this had to be reduced to 3 mg due to grade 4 neutropenia and recurrent infections requiring repeated hospitalizations. Neutrophil count recovery was achieved shortly thereafter. Patient 5 had grade 2 thrombocytopenia at the time of pom initiation that worsened while on pom (grade 4); the patient passed away shortly thereafter due to an aggressive relapse. Two patients received 20 mg of dexamethasone weekly in addition to pom.

With regard to efficacy, six patients (86%) maintained their response (≥ PR) with pom-based maintenance therapy. One patient lost his response 1 month after starting pom (patient 5) leading to the addition of doxorubicin. Median PFS was 12 months and median OS was 26 months. Two patients have ongoing response to pom at the time of this report.

To our knowledge, this is the first report shedding light on the role of pomalidomide in the post-HCT maintenance setting in newly diagnosed MM patients. Despite the inherent biases to our study including its retrospective design and the small patient sample, there appears to be an efficacy signal for maintenance with pom after auto-HCT with most patients maintaining their response post-auto-HCT. The drug was initiated at least 3 months after HCT and was well-tolerated overall. A case series from the University of Utah reported

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Table 1 Baseline characteristics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Gender	Male	Female	Female	Male	Male	Male	Female
Age at diagnosis	66	55	68	64	56	46	58
MM subtype	IgG kappa	IgG kappa	IgG lambda	IgG lambda	IgG lambda	IgG kappa	IgG kappa
RISS stage	II	III	II	II	II	I	II
Bone marrow Plasma cells (%)	60	60	50	80	80	40	20
Deletion (13q)	Yes	Yes	No	No	No	No	No
Deletion (17p)	No	No	No	No	No	No	No
t(4;14)	Yes	No	No	No	No	No	No
t(11;14)	No	No	Yes	No	Yes	No	Yes
t(14;16)	No	No	No	No	No	No	No
t(14;20)	No	No	No	No	No	No	No
Bone lesions (Y/N)	Yes (on PET/CT)	No	Yes	Yes	Yes	Yes	No
Hypercalcemia (Y/N)	No	No	No	No	No	No	No

Table 2 Efficacy and survival outcomes

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Time from Dx to AHCT (months)	22	41	30	20	22	21	17
Time to initiation of pom after AHCT (months)	3	8	3	3	4	4	3
No. of lines of therapy prior to pom	4	3	4	4	7	6	4
Most recent line	Carfilzomib	Lenalidomide	Bortezomib	Cyclo, Pom, Dex	Carfilzomib	Dara, Bortezomib, Pom	Len, Dex, Elo
Prior to transplant	Lenalidomide	Cyclo	Dex				
Refractory to lenalidomide (Y/N)	Yes	Yes	Yes	No	Yes	No	Yes
Best response prior to initiation	sCR	CR	VGPR	sCR	CR	PR	VGPR
Best response to pom	sCR	CR	VGPR	sCR	Progression	PR	VGPR
PFS	36	16	60, ongoing	8	Biochemical progression 3 months after HCT before initiation of pom	12, ongoing	8, lost to follow-up
OS	47	60	60	26, deceased	Died a few weeks after pom initiation due to rapid disease relapse and acute kidney injury	12	8, lost to follow-up
Reason for discontinuation	Progression	Initially held for recurrent C. diff and dental procedure, patient then wished to stop	N/A	Progression	Progression	N/A	Unknown/lost to f/u
Adverse events	None	Diarrhea, recurrent *C. difficile* colitis	None	None	None	Grade 1 cramps	Grade 4 neutropenia

on the outcomes of four patients with MM who underwent salvage auto-HCT and received pom subsequently. All patients had a deeper response with pom, and the drug was found to be safe [5]. Pom may be an acceptable substitute for len in patients with prior len intolerance or refractoriness. There is currently an open randomized trial that is comparing auto-HCT with pom maintenance to pom with clarithromycin and dexamethasone in relapsed and refractory MM (NCT01745588) that may clarify the role of pom after HCT (https://clinicaltrials.gov/ct2/show/NCT01745588).

Compliance with ethical standards

All human studies have been approved by the appropriate ethics committee.

Conflict of interest The authors declare that they have no conflict of interest.

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