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Modest Activity of Pomalidomide in Patients with Myelofibrosis and Significant Anemia

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Abstract

We evaluated single agent pomalidomide for myelofibrosis-associated anemia. First, 21 patients received pomalidomide 3.0mg/day on 21-day-on/7-day-off schedule. Due to poor tolerance the study was quickly suspended. Second, 29 patients received pomalidomide 0.5mg/day continuously. Three patients (10%) experienced clinical improvement in hemoglobin per International-Working-Group criteria (median time to response 1.6 months; median response duration 6.7 months). Ten patients were RBC-transfusion-dependent per Delphi criteria; 2 (20%) achieved RBC-transfusion-independence (time to response 0.9 months in both; response duration of 8.3 and 15 months). One grade 3/4 toxicity (neutropenia) occurred. Pomalidomide at low dose is well tolerated but has modest clinical activity in myelofibrosis.

Keywords

pomalidomide; myelofibrosis; anemia

Introduction

Myeloproliferative neoplasms (MPN) are stem cell–derived hemopathies [1, 2]. Bone marrow fibrosis, osteosclerosis and angiogenesis play a central role in the pathogenesis of primary myelofibrosis (PMF) and myelofibrosis evolving from a pre-existing MPN (post

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Authorship and Disclosures
SV was the principal investigator and takes primary responsibility for the paper; SV, TK, AQ, EJ, MK, SO, JC and HK recruited the patients; ND, AS, SP and SV performed the data collection and analysis for this study; SP participated in the statistical analysis; SV and HK coordinated the research; ND, AS, and SV wrote the paper. SV receives research support for conduct of the study from the Celgene Corporation. The remaining authors have no conflict of interest to report.

polycythemia vera- and post essential thrombocythemia-myelofibrosis) [3]. Bone marrow deposition of reticulin fibrils is thought to be mediated by high levels of profibrogenic and proangiogenic cytokines such as transforming growth factor beta (TGF-β), basic fibroblast growth factor (bFGF), tumor necrosis factor alpha (TNF-α) and vascular endothelial growth factor (VEGF) [4, 5]. Anemia and thrombocytopenia are frequently seen in patients with MF and are associated with increased morbidity and mortality [6, 7]. Erythropoietin, androgens, splenectomy and corticosteroids are occasionally effective in addressing the anemia associated with MF [8, 9]. JAK2 inhibitors, unfortunately, have little to no effect in improving the ineffective erythropoiesis and significantly improving hemoglobin in MF [10–12]. Thus, there is a need for novel therapeutic agents that focus on improving erythropoiesis in patients with MF and anemia.

Thalidomide, lenalidomide and pomalidomide are immunomodulatory agents (IMiDs) with clinical activity in a variety of disorders including multiple myeloma, myelodysplastic syndromes and myelofibrosis [13, 14]. These drugs have demonstrated improvements in anemia, thrombocytopenia and splenomegaly in patients with myelofibrosis [15–18]. Single agent thalidomide has an anemia response rate of 10–20% but is poorly tolerated at standard doses, with an adverse dropout rate of greater than 50% at 3 months [16, 19]. Low dose thalidomide in combination with prednisone alleviates anemia in approximately 25% of patients, and is much better tolerated [17]. Lenalidomide is also effective in improving anemia in patients with MF with a response rate of ~30% [20, 21]. However, the use of thalidomide and lenalidomide has been limited secondary to their toxicity profile including neuropathy, fatigue, and constipation with thalidomide, and bone marrow suppression, gastrointestinal toxicity, and rash with lenalidomide [18, 21].

Pomalidomide is a potent second generation IMiD created by modifying thalidomide structure through the addition of an amino group at the 4-position of the phthaloyl ring [22]. All IMiDs display anti-angiogenic, anti-TNF-α, T-cell co-stimulatory activity in addition to inhibition of T-regulatory cell proliferation [22, 23]. Of note, pomalidomide does not possess the limiting toxicities of thalidomide and lenalidomide. The first clinical experience with pomalidomide in MF was a phase II randomized, double-blinded trial that evaluated the efficacy and tolerability of pomalidomide in four different treatment arms [24]. These were pomalidomide 2.0 mg/day plus placebo, pomalidomide 2.0 mg/day plus prednisone, pomalidomide 0.5 mg/day plus prednisone, and prednisone plus placebo. Response was assessed by the International Working Group for Myelofibrosis Research and Treatment (IWG-MRT) criteria [25]. Response rates for clinical improvement (CI) in anemia per IWG-MRT criteria were 23%, 16% 36%, and 19% in the four treatment arms, respectively. The statistical design of the study did not allow for direct comparison of the response rate in the 4 groups, but aimed to identify one group that would be statistically better than the others; however none was statistically superior. Pomalidomide was very well tolerated. Subsequently, a phase 1/2 study of pomalidomide in MF was conducted by Mesa et al. and the maximum tolerated dose (MTD) of pomalidomide was established at 3.0 mg/day at the 21-day on/7-day off schedule [26]. However, no significant clinical efficacy was seen at the MTD and the dose was subsequently decreased in some patients to 0.5 mg/day given continuously. Eight patients received 0.5 mg/day after having initially received three cycles at the MTD dose and schedule, and 7 achieved CI in anemia (all becoming transfusion

independent) as per IWG-MRT criteria [25]. While the phase 1/2 study by Mesa and colleagues was underway, we opened a phase 2 study of single agent pomalidomide for patients with MF and significant anemia. Our experience is described herein.

Patients and Methods

Treatment schedule

Our study was undertaken in 2 parts. The first part of the study involved studying the toxicity and efficacy profile of single agent pomalidomide administered at a dose of 3.0 mg/day at the 21-day on/7-day off schedule. The second part of the study looked at the toxicity and efficacy profile of pomalidomide administered at a lower dose of 0.5 mg/day continuously. The study was performed at MD Anderson Cancer Center (MDACC).

Study group I: Single agent pomalidomide at 3.0 mg/day dose—Pomalidomide was initially administered orally at a dose of 3.0 mg/day in 28-day cycles on a 21-day on/7-day off schedule. The starting dose of 3.0 mg daily was selected based on preliminary experience from the concurrently ongoing phase 1/2 study by Mesa et al [26]. Pomalidomide was to be continued for at least 6 months if tolerated. Subjects were to be taken off-study at 6 months if there was no response, or continued on therapy beyond 6 months if exhibiting clinical benefit, at the discretion of the treating physician, unless disease progression and/or toxicity warranted treatment discontinuation. For patients necessitating dose reduction for adverse events the pomalidomide would be given at a dose of 2.0, 1.0 or 0.5 mg (dose levels -1, -2, and -3, respectively). The dose of pomalidomide could not be escalated. Patients could not receive erythropoietin or corticosteroids (except in the emergency) while on protocol. Filgrastim or pegfilgrastim could be administered for patients that developed neutropenic fever, ≥ grade 3 neutropenia or at the investigators discretion for prolonged neutropenia. Prophylaxis with oral low-dose aspirin was recommended in all patients unless contraindicated or unless the platelet count was $\leq 75 \times 10^9$/L. Patients with prior exposure to thalidomide or lenalidomide were excluded from this study. Study accrual commenced in July 2009.

A total of 21 patients were accrued within 3 months and received pomalidomide at a starting dose of 3.0 mg/day. However, after a median follow up of 3 months, almost all patients had to interrupt the therapy due to side effects and many discontinued it. Due to excessive toxicity that occurred rather rapidly in a majority of the patients, the study accrual was suspended by Principal Investigator and MDACC institutional review board and all participating patients were taken off pomalidomide therapy.

Study group II: Pomalidomide at 0.5 mg/day dose—Concurrently, Mesa et al published the results of their phase 1/2 study, reiterating the data by Tefferi et al, that pomalidomide may be active and better tolerated at a lower dose of 0.5 mg/day [24, 26]. Therein, our study was amended and the starting dose of pomalidomide was reduced to 0.5 mg/day, given continuously in a 28-day cycles. Eligibility criteria for enrollment remained the same. Dose adjustments of pomalidomide were not allowed and patients unable to tolerate the 0.5 mg dose were taken of the study. Study accrual to the 0.5 mg/day pomalidomide commenced in January 2010. Twenty nine patients were included in this

study group, of which 9 were from the prior group of patients that had previously received pomalidomide at a dose of 3.0 mg/day (exposure to high dose was maximum 3 months, and therefore these 9 patients were not considered refractory to pomalidomide).

Patient eligibility

Eligibility criteria were the same for both study groups: patients ≥ 18 years of age with a diagnosis of MF requiring therapy, including primary, post-polycythemia vera or post-essential thrombocythemia MF [27]; a screening total hemoglobin level < 10 g/dL or presence of transfusion dependency (patients that were transfusion dependent were allowed to enter the study with hemoglobin higher than 10 g/dL if it was due to a transfusion); performance status ≤ 2 by the Eastern Cooperative Oncology Group (ECOG) scale; serum creatinine ≤ 2.0 mg/dL; serum bilirubin < 3.0 times the upper limit of the normal range; blood transaminase level ≤ 3 times the upper limit of the normal range; absolute neutrophil count ≥ 1.0×10^9/L and a platelet count ≥ 50×10^9/L; patients were required to have been off growth factors, cytotoxic chemotherapeutic agents (e.g. hydroxyurea and anagrelide), corticosteroids, or experimental therapy for 4 weeks prior to study enrollment and have recovered from the toxic effects of that therapy to grade 1 or better at time of enrollment; negative pregnancy test in women of childbearing age, and practice of effective methods of contraception during study participation for all patients. This was a single center study supported by Celgene Corporation, Summit, NJ, USA. All patients signed an informed consent form approved by the MDACC institutional review board.

Patient evaluation

Patient evaluation schedule was the same for both study groups and included, at minimum: complete physical examination (every 4 weeks), complete blood count (every week for the first 8 weeks, then every 4 weeks), comprehensive biochemistry panel (including liver function tests) every 4 weeks, pregnancy test and counseling (pregnancy test every week for the first 28 days of use and then every 28 days if regular menstrual cycles, or every 14 days if irregular menstrual cycles), and bone marrow aspiration and biopsy with cytogenetics (prior to initiation of therapy and when clinically indicated).

Study design

This study was designed as a two-stage (MiniMax), prospective, single center, phase II trial designed to assess the efficacy of pomalidomide in subjects with primary, post polycythemia vera, or post essential thrombocythemia MF. The primary efficacy endpoint of this trial was best overall response. An evaluable subject was classified as a treatment success for the primary endpoint if the subject's best overall response was complete remission (CR), partial remission (PR) or clinical improvement (CI) as determined by IWG-MRT and/or Delphi consensus criteria over the first 6 cycles of study treatment[28]. The largest success proportion where the proposed treatment regimen would be considered unpromising in this population was 5%, representing the probability of a response by chance. The smallest success proportion that would warrant subsequent studies with the proposed treatment regimen was 20%.

Subjects receiving high dose pomalidomide (3.0 mg/day), and the new study cohort of patients receiving low dose pomalidomide (0.5 mg/day) were evaluated using the same statistical design: a 2 stage design with one interim analysis after the first 20 evaluable subjects had been observed for at least 6 cycles, to permit early reporting of efficacy results and permit early stoppage of the study if there was strong evidence that the study regimen was inactive. If 1 or fewer treatment successes were observed in these 20 subjects, the treatment regimen would have been considered inactive and accrual would be terminated. If 2 or more treatment successes were observed in these 20 subjects, decisions about activity would await the final analysis after the accrual of all 37 patients.

Response was adjudicated in two ways (Table 1). An improvement in red blood cell count was assessed by the IWG-MRT criteria, wherein an increase in hemoglobin of 2 g/dL from baseline, sustained for a duration of at least 8 weeks, is called CI in hemoglobin [25]. Unlike previous clinical studies of pomalidomide in MF the attainment of transfusion independency was NOT assessed by IWG-MRT criteria (Table 1). We used Delphi consensus criteria for assessment of transfusion dependence/independence (Table 1) as these are considered to be more clinically robust than IWG-MRT criteria for transfusion assessment in clinical trials [28]. Toxicity was assessed by the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3.0 [3].

Results

Study group I: pomalidomide at 3.0 mg/day dose

Twenty one patients were enrolled to receive single agent pomalidomide at a dose of 3.0 mg/day (Table 2) at the 21-day on/7-day off schedule. All 21 patients belonged to high or intermediate-2 risk category according to the Dynamic International Prognostic Scoring System [7, 29, 30]. The therapy was poorly tolerated (Table 3) secondary to frequent and early occurrence of grade 3 to 4 hematological toxicity. Grade 3 to 4 non-hematological toxicities were seen as well (Table 3). Multiple dose reductions and interruptions of therapy were performed as per predefined criteria in almost all patients. With a median follow up period of 3 months (range 0.4 to 5.5), 12 of the initial 21 patients discontinued therapy for reasons of: drug-related toxicities in 6 patients (29%), comorbidities in 2 patients (10%), progression to acute myeloid leukemia in 1 patient (5%) and patient preference in 3 patients (14%). Due to poor tolerance and high early drop-out rate further enrolment to protocol therapy was suspended by the Principal Investigator and MDACC investigational review board. Further therapy with pomalidomide was suspended in all patients, pending protocol amendment (9 patients remained on the protocol at the time of study suspension). No responses were documented in the 21 patients that received pomalidomide at a dose of 3.0 mg/day on the 21-day on/7-day off schedule.

Study group II: pomalidomide at 0.5 mg/day dose

The protocol was reopened after amendment and enrolled patients would now receive pomalidomide at a dose of 0.5 mg/day continuously. Twenty nine patients were included (Table 4), including 20 new patients and 9 patients from the previous cohort that remained on therapy at the time study was suspended (the break in therapy for these 9 patients was 3

months at minimum). Pretreatment cytogenetics were available in 28 patients and 7 (25%) had abnormal karytotype including del(13) in three patients, del(7) in two patients, and del(20) in one patient. Mean hemoglobin at the time of study enrolment was 9.0 g/dl and 10 patients were RBC-transfusion-dependent per Delphi criteria [29, 30]. The current median follow up for this group is 23.6 months (range, 1.2 to 28.5).

Three of the 29 patients (10%) experienced an increase in hemoglobin of 2.0 g/dL or more, which was maintained for at least 8 weeks and therefore met response criteria for CI in hemoglobin per IWG-MRT criteria (Table 5). Median time to response was 1.6 months (range, 0.8 to 6.4) and median duration of a response 6.7 months (range, 3.8 to 19.5). These 3 patients were not transfusion dependent at initiation of therapy. One of the patients had no clinical response on the 3.0 mg/day dose of pomalidomide but achieved a response on the 0.5 mg/day dose. Judged to be a response per Delphi criteria, ten enrolled patients were transfusion dependent, and 2 achieved RBC-transfusion-independence (20% response rate) (Table 5). Time to response was 0.9 months in both cases and the duration of response was 8.3 and 15 months, respectively (median 11.7 months). We performed univariate analysis to identify potential factors that may have been associated with clinical response in patients receiving pomalidomide (0.5 mg/day) and noted no significant correlation between response and age, hemoglobin, white blood count, platelets count, circulating blasts, presence of JAK2V617F mutation, presence of constitutional symptoms, prior therapy, transfusion dependence, splenomegaly, prognostic score, cytogenetics, or MF subtype. We noted one patient with a 100% increase in platelet after 2 months of therapy, sustained for 3 months: the patient had a baseline platelet count of 67×10^9/L that peaked at 177×10^9/L. No responses were observed in splenomegaly. There was no significant change in JAK2V617F allelic burden in patients on therapy.

A total of 28 (97%) patients completed at least four cycles of pomalidomide therapy. One patient developed grade 3 rash and generalized edema six days after initiation of therapy and had to be taken off-study. Six patients (21%) remain on study (including 2 responders) with median treatment duration of 19.9 months. Reasons for discontinuation in the remaining 23 patients (79%) included lack of response in 14 patients, loss of response in 2 patients, progression to acute myeloid leukemia in 1 patient, co-morbidities unrelated to protocol therapy in 5 patients and grade 3 toxicity in 1 patient. Among the 5 responders, 2 had to be taken off-protocol due to loss of response after 14.8 and 22.5 months, respectively (median 18.7 months) and one had to be taken off-protocol secondary to other medical reasons after 10.1 months (Table 5). A total of 9 deaths were documented during protocol therapy and were attributed to progressive disease in 2 patients, myocardial infarction in 2 patients, progressive renal failure in 1 patient, diabetes related complications in 1 patient, sepsis with necrotizing fasciitis in 1 patient and unknown causes in 2 patients.

The 0.5 mg/day dose of pomalidomide was well tolerated with only one patient having to discontinue protocol therapy secondary to drug-related adverse event (Table 6). No thrombotic events were noted. No patients developed significant thrombocytosis (platelet count $\geq 1{,}000 \times 10^9$/L) or significant basophilia (more than 100% increase in basophil count) on the 0.5 mg/day dose of pomalidomide. Although the statistical design of the protocol allowed continuation of the study based on the observed response rate, after

departmental review a decision was made to terminate enrollment due to relatively low response rate.

Discussion

Enhanced potency and better tolerability without the dose limiting toxicities of neuropathy and sedation seen with parent compound thalidomide or bone marrow suppression and gastrointestinal toxicity seen with lenalidomide make pomalidomide the favored IMiD for the treatment of myelofibrosis [18, 21]. In accord with initial publications on the activity of pomalidomide in MF by Mesa et al [26] and Tefferi et al[24], we too found that pomalidomide is much better tolerated and has clinical activity at a dose of 0.5 mg/day. A more recent study from Mayo clinic administered single agent pomalidomide at a dose of 0.5 mg per day with an overall response rate of 17% [31]. The cumulative experience with pomalidomide therapy, including patients enrolled in all the aforementioned studies performed at Mayo Clinic (total of 94 patients treated with pomalidomide with or without prednisone) revealed a response rate of 27% [32]. This is in accordance with our results, although it must be mentioned that the Delphi consensus criteria we have used is a more clinically relevant way of assessing the attainment of transfusion independence (Table 1). The response criteria used in our study are the same as those being used in the ongoing Phase 3, placebo controlled, randomized study of pomalidomide which may result in possible approval of pomalidomide for patients with myelofibrosis-associated anemia (results pending).

The exact mechanism by which IMiD's bring about improvement in ineffective erythropoiesis in MF is poorly elucidated. In vitro studies have shown that pomalidomide can slow maturation of erythroid lineage cells, increase erythroid cell proliferation, and induce hemoglobin F potently, resulting in enhanced erythropoiesis [33]. Verhelle et al suggested that IMiDs may exert clone specific proliferative or anti-proliferative activity [34]. In their study, pomalidomide upregulated p21WAF-1 expression in both cancer cell lines and normal CD34+ progenitor cell lines which resulted in downstream antiproliferative effects on cancer cells and pro-proliferative effects on CD34+ cells. Pomalidomide inhibits pro-inflammatory and apoptotic chemokines released by activated monocytes including TNF-α, TGF-β, and IL-6 [22]. It also stimulates lipopolysaccharide induced IL-10 secretion and up regulates IL-2 and interferon-γ secretion from stimulated T-cells [35, 36]. Pomalidomide exhibits a 100-fold increased anti-angiogenic activity over thalidomide [22, 37] and inhibits endothelial cell migration and adhesion by downregulating endothelial cell integrins [37]. The role of cytokine modulation in patients responding to pomalidomide has been suggested by Pardanani and colleagues who documented a direct correlation between the blood levels of selected cytokines in patients and their ability to respond to pomalidomide therapy[38]. However, further studies are warranted to better elucidate the exact mechanisms of improved erythropoiesis with pomalidomide.

Compiled data from the Mayo Clinic and from our current study indicate that low dose pomalidomide (0.5 mg/day) may represent an effective and well tolerated regimen for selected patients with MF and anemia. The overall response rate, however, is low. The initial study by Tefferi and colleagues evaluated the combination of pomalidomide and

prednisone [24]. This combination was selected on the basis of prior experiences whereby addition of prednisone to thalidomide or lenalidomide appeared to improve tolerability and response [18, 20]. However, the role of combining prednisone with low-dose pomalidomide remains poorly defined and needs further exploration. We are currently conducting a phase II study to assess the tolerability and efficacy of low-dose pomalidomide with a short course of prednisone [39]. An ongoing study in Europe is evaluating the activity of pomalidomide at a dose of 2.0 mg/day, with the addition of prednisone after 3 months in patients not responding to pomalidomide alone [40]. An alternative combination approach in patients with MF would be to combine pomalidomide with ruxolitinib, a recently approved JAK1/2 inhibitor that reduces enlarged spleens and controls MF-related constitutional symptoms, but does not improve blood cell count [10–12]. The complementary efficacy profile and non-overlapping toxicities of JAK1/2 inhibitor and pomalidomide suggest that a combination of these drugs may prove to be a viable therapeutic option for patients suffering from MF.

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Table 1

Criteria for assessment of response to therapy

International Working Group (IWG) consensus criteria for treatment response in myelofibrosis

Clinical Improvement (CI) in anemia

1. A minimum 20 g/L increase in hemoglobin level or
2. becoming transfusion independent for at least 8 week duration.*

Transfusion dependency is defined by a history of at least 2 units of red blood cell transfusions in the last month.**

Delphi expert-consensus panel definitions of RBC-transfusion-dependence and – independence

- becoming transfusion independent for at least 3 month duration.*

Transfusion dependency is defined by a history of at least 2 units of red blood cell transfusions every month for last 3 months.**

* applicable only for patients with baseline hemoglobin level of less than 100 g/L

** for a hemoglobin level of less than 85 g/L that was not associated with clinically overt bleeding

Table 2

Baseline Clinical Characteristics of Patients Who Received Pomalidomide 3.0 mg/day (N = 21)

Characteristic	Number (%)/ Median
Age (years)	66 [53–82]
Male	11 (52%)
Diagnosis	
PMF	14 (67%)
Post-ET MF	4 (19%)
Post-PV MF	3 (14%)
Splenomegaly	9 (43%)
Hemoglobin, g/dL	9.5 [7.2–11.4]
White Blood Cell Count × 10^9/L	5.5 [2.0–21.7]
Platelets × 10^9/L	152 [52–858]
JAK 2 V617 F mutated	12 (57%)
Karyotype	
Diploid	14 (67%)
Abnormal	5 (24%)
Indeterminate	2 (9%)
Prior treatment	16 (76%)

Abbreviations: PMF, primary myelofibrosis; Post-ET MF, post essential thrombocythemia myelofibrosis; post-PV MF, post polycythemia vera myelofibrosis.

Table 3

Therapy Related Toxicities in Patients Who Received Pomalidomide 3.0 mg/day (N = 21)

Side Effects	Grade 1	Grade 2	Grade 3	Grade 4
Rash, Itching	5		1	
Hypersensitivity reaction		2		
Fatigue, weakness			1	
Sensory Neuropathy			1	
Neutropenia			4	4
Anemia		1	5	2
Thrombocytopenia			2	

Table 4

Baseline Clinical Characteristics of Patients Who Received Pomalidomide 0.5 mg/day (N = 29)

Characteristic	Number (%)/ Median
Age (years)	68 [39–86]
Male	14 (48%)
Diagnosis	
PMF	20 (69%)
Post-ET MF	8 (28%)
Post-PV MF	1 (3%)
Splenomegaly	11 (38%)
Hemoglobin, g/dL	9.0 [7.1–11.1]
White Blood Cell Count × 10^9/L	6.0 [2.0–21.7]
Platelets × 10^9/L	224.0 [53.0–1478.0]
JAK 2 V617 F mutated	17 (59%)
Karyotype	
Diploid	20 (69%)
Abnormal	8 (28%)
Indeterminate	1 (3%)
Prior treatment	19 (65%)

Abbreviations: PMF, primary myelofibrosis; Post-ET MF, post essential thrombocytosis myelofibrosis; post-PV MF, post polycythemia vera myelofibrosis.

Table 5

Characteristics of patients that responded to Pomalidomide therapy (N = 5)

DX	Age	Spleen	PLT	WBC	Cyto	JAK2V617F	TSF Dependent	Prior RX	Response	Response duration(m)	Off Reason	Status
PMF	67	Out	1478	17.4	Diploid	Pos	Yes	HU+AG	TSF	8.3	Lost Resp	Alive
Post-ET MF	72	2	106	5.2	Abnormal	Pos	Yes	HU	TSF	15.0+		Alive
PMF	77	0	68	5.5	Diploid	Neg	Yes	PRED, JAK inhibitor	TSF&Hgb	19.5	Lost Resp	Alive
PMF	39	0	262	4.6	Diploid	Neg	No	NONE	HGB	6.7+		Alive
Post-ET MF	76	18	220	12.6	Abnormal	Neg	No	AG, Aranesp	HGB	3.8	Comorbidity	Dead

Abbreviations: Dx, diagnosis; PLT, platelets; WBC, white blood cells; Cyto, cytogenetics; TSF, transfusion; RX, treatment; m, months; PMF, primary myelofibrosis; Post ET MF, post essential thrombocytosis myelofibrosis; Pos, positive; Neg, negative; HU, hydroxyurea; AG, anagrelide; PRED, prednisone; Hgb, hemoglobin; Resp, response.

Table 6

Therapy Related Toxicities in Patients Who Received Pomalidomide 0.5 mg/day (N = 29)

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Rash/ Itching	2	1		
Hypersensitivity reaction		1		
Neuropathy	1			
Neutropenia			1	