Original Article

Subcutaneous or Intravenous Administration of Romiplostim in Thrombocytopenic Patients With Lower Risk Myelodysplastic Syndromes

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BACKGROUND: Romiplostim is a peptibody protein that augments thrombopoiesis by activating the thrombopoietin receptor. **METHODS:** In this phase 2, multicenter, open-label study, 28 thrombocytopenic patients with lower risk myelodysplastic syndromes (MDS) were assigned to receive romiplostim 750 μg administered subcutaneously either weekly or biweekly or administered as biweekly intravenous injections for 8 weeks. Patients also could enter a 1-year study extension phase. **RESULTS:** At least 1 adverse event was observed in 93% of patients. The most common adverse events were fatigue and headache (18% for both, and 5 events were grade 3 or 4. There was 1 serious treatment-related adverse event in the biweekly intravenous cohort (hypersensitivity). This hypersensitivity resolved without discontinuation of study treatment. No patients developed neutralizing antibodies or bone marrow fibrosis. Of the patients who completed 8 weeks of treatment, 57% had a complete platelet response, an additional 8% had a major platelet response, and 61% did not require a platelet transfusion during this period. Weekly subcutaneous injections achieved the highest mean trough concentrations. **CONCLUSIONS:** The safety and efficacy profiles of romiplostim in this study suggested that weekly subcutaneous administration of 750 μg romiplostim is an appropriate starting dose for future clinical studies in patients with MDS and thrombocytopenia. ***Cancer*** **2011;117:992–1000.** © *2010 American Cancer Society.*

KEYWORDS: myelodysplastic syndromes, romiplostim, thrombocytopenia, thrombopoietin receptor activation.

Clinically important thrombocytopenia is present in 40% to 65% of patients with myelodysplastic syndromes (MDS),[1,2] and hemorrhage contributes to cause of death in 20%. Among patients with lower risk MDS, approximately 50% have thrombocytopenia, 10% have severe thrombocytopenia, and 35% have ever received a platelet transfusion.[1,2] Thrombocytopenia also is an associated side effect of the US Food and Drug Administration (FDA)-approved agents for the treatment of MDS.[3-7] Currently, platelet transfusions are the only reliably effective treatment option for thrombocytopenia associated with MDS.[8] Romiplostim is an Fc-fusion protein that augments thrombopoiesis by binding to and activating the thrombopoietin receptor.[9] It is approved for the treatment of thrombocytopenia in patients with chronic immune thrombocytopenic purpura who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.[10] Romiplostim is under investigation for thrombocytopenia in patients with International Prognostic Scoring System (IPSS)[11] low-risk or intermediate 1-risk MDS who are not currently receiving disease-modifying treatment

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(considered "lower risk" MDS) and in patients who have MDS with grade 3 or 4 treatment-related thrombocytopenia. At weekly subcutaneous doses of 300 to 1500 μg, romiplostim produced platelet responses in 40% to 50% of patients with lower risk MDS and severe thrombocytopenia who were not receiving other therapy in a phase 1/2 study in which response was defined using modified International Working Group (IWG) criteria.[12,13]

In the current study, we evaluated the safety, efficacy, and pharmacokinetics (PK) of romiplostim (Nplate; Amgen, Thousand Oaks, Calif) in thrombocytopenic patients with lower risk MDS. The study comprised a 4-week dose-finding phase (Part A), an 8-week schedule-finding phase (Part B), and a treatment extension phase. Patients who completed Part A or Part B could continue to receive weekly romiplostim for up to 1 year in the extension phase. Data from the patients treated in Part A (including both the 4-week dose-finding phase and the treatment extension phase) have been reported previously.[12] This article reports for the first time on the 8-week schedule-finding phase and the corresponding treatment extension phase data for the Part B patients only, including duration of platelet responses, long-term safety data, and on the PK profiles of intravenous and subcutaneous dosing routes. This trial is registered with the National Institutes of Health as a National Clinical Trial (NCT00303472; http://www.clinicaltrials.gov; accessed September 28, 2010).

MATERIALS AND METHODS

This phase 2, multicenter, open-label study was conducted at 12 centers in the United States and the European Union from March 2007 to May 2008. In Part B, romiplostim administered at a dose of 750 μg was evaluated in 3 different dosing schedule cohorts: weekly subcutaneous, biweekly subcutaneous, and biweekly intravenous administration. Initially, planned enrolment numbers were 10 patients each for the weekly subcutaneous and biweekly subcutaneous cohorts and 5 patients for the biweekly intravenous cohort. The biweekly intravenous cohort could be expanded to 10 patients after a review of the first 3 cohorts by the Safety Review Panel.

Eligible patients were aged $\geq$18 years, had a diagnosis of MDS (World Health Organization [WHO] classification),[14] had an IPSS low-risk or intermediate 1-risk score, had thrombocytopenia (ie, mean platelet count $\leq 50 \times 10^9$/L with no individual count $>55 \times 10^9$/L), and were receiving only supportive care. During the study, romiplostim administration was suspended if a patient had a platelet count $\geq 600 \times 10^9$/L, and it was resumed after the platelet count returned to $<200 \times 10^9$/L. No randomization scheme was used in the schedule-finding phase of this study. Patients were assigned in the order 1) weekly subcutaneous, 2) biweekly subcutaneous, and 3) weekly intravenous to receive a dose recommended by the Safety Review Panel based on results from Part A of the study.[12]

The protocol was reviewed by an institutional ethics committee or review board at each center and over the course of the study by all primary investigators through scheduled teleconferences. The study was conducted in accordance with applicable regulations and the International Conference on Harmonization for Good Clinical Practice guidelines. All patients provided written informed consent.

The primary endpoint for this 8-week, schedule-finding phase and for the corresponding treatment extension phase for the patients in Part B was cumulative incidence of adverse events, including antibodies to romiplostim and an increase in blast percentage. Patients were considered to have progressed to acute myeloid leukemia (AML) if they met WHO AML criteria[14] or subsequently received treatment for AML. Transient increases in peripheral and bone marrow blast counts $\geq$20% that resolved within 4 weeks were not considered progression to AML but were collected as adverse events. The efficacy endpoint was the proportion of patients achieving a complete platelet response (increased platelet count $>100 \times 10^9$/L) or a major platelet response (increase by $>30 \times 10^9$/L). Rescue medication (including platelet transfusions) was administered when patients were at immediate bleeding risk. Any patient who received platelet transfusions was considered a nonresponder. Platelet counts obtained within 72 hours of platelet transfusion were excluded from the evaluation of response. Serum concentration profiles of romiplostim were measured in Part B.

Statistical Analysis

All patients who received at least 1 administration of romiplostim were included in the safety analysis. The incidence rates for all adverse events that occurred during the study were summarized by system class and preferred term according to the *Medical Dictionary for Regulatory Activities* and severity for each cohort. The efficacy analysis included all enrolled patients who received romiplostim and completed $\geq$8 weeks of treatment. Patients were analyzed according to their assigned treatment schedule. Response rates were estimated using binomial distribution along with 95% exact binomial confidence intervals.

Pharmacokinetics

PK parameters of romiplostim in patients with MDS were measured in Part B of the study and included the estimated initial concentration at time zero (C_0) for the intravenous groups, the maximum observed concentration (C_{max}), the time to reach C_{max} (t_{max}), and the area under the concentration time curve (AUC) from Time 0 to the last time point with quantifiable concentration ($AUC_{0\text{-}t}$). Patients in each of the treatment arms were assigned to have intensive PK measurements as follows: the biweekly subcutaneous cohort, 5 patients in Week 1 and 7 patients during Week 7; the weekly subcutaneous cohort, 5 patients in Week 1 and 6 patients in Week 7; and the biweekly intravenous cohort, 5 patients in Week 1 only. In the weekly subcutaneous cohort, serum samples for PK analysis were taken before administration of the first study dose and at 2 hours, 24 hours, 48 hours, 72 hours, 120 hours, and 168 hours (Week 1) postdose in Weeks 1 and 7. For the biweekly subcutaneous and biweekly intravenous cohorts, samples were taken before the first study dose; at 15 minutes (intravenous cohort only) and 30 minutes (intravenous cohort only); and at 2 hours, 24 hours, 48 hours, 72 hours, 120 hours, 168 hours, 192 hours, 240 hours, and 336 hours (14 days) in Week 1 (both the intravenous and subcutaneous cohorts) and in Week 7 (subcutaneous cohorts only). Variability in PK sampling among the different dosing cohorts was made necessary by the different dosing routes and schedules. Intensive PK analyses were assigned for all arms at Week 1 to establish the romiplostim concentration-time profiles. The weekly cohorts required sampling for 7 days, and the biweekly cohorts required sampling for 14 days to capture PK profiles. To capture the rapid decline, the intravenous cohort needed 2 more early time points than the SC cohorts.

RESULTS

This study included 28 patients: 11, 12, and 5 patients who received romiplostim 750 μg weekly subcutaneously, 750 μg biweekly subcutaneously, and 750 μg biweekly intravenously, respectively. Assignment into the biweekly intravenous arm was not expanded after major hypersensitivity was reported in 1 patient. Twenty-two patients (79%) were men, and the mean age was 71 ± 8 years. Nineteen patients (68%) had received platelet transfusions in the past year and demographic and baseline characteristics among the 3 dosing groups were similar, although slightly more patients (36%) in the 750 μg weekly subcutaneous cohort had an IPSS score ≥1.0 (Table 1). Ten patients had platelet counts that were $<20 \times 10^9$/L at baseline.

Twenty-three patients (82%) were included in the efficacy analysis, because they had received all scheduled doses (8 weeks) during Part B of the study. One patient who was evaluated for efficacy completed 8 doses of romiplostim but died before the end of the study and, thus, was not considered to have completed the study. Six patients discontinued treatment during Part B, including 1 patient who discontinued because of an adverse event (treatment-related papular rash), 1 patient who discontinued because of disease progression to AML, 1 patient withdrew consent, there was 1 death, and 2 patients discontinued because of rising blast counts (Fig. 1).

Six of 11 patients who entered the treatment extension completed the year-long extension. The reasons for study discontinuation during the treatment extension were administrative decision (2 patients), consent withdrawn (1 patient), report of disease progression to AML (1 patient unconfirmed increase in blasts), and other (1 patient who transferred into another romiplostim extension study).

Ninety-three percent of all patients had at least 1 adverse event (Table 2). No patient reported a grade 3 or higher treatment-related adverse event. No neutralizing antibodies to romiplostim or to thrombopoietin were detected. Serious adverse events were reported in 5 patients (18%). These events were cardiac arrest, cerebral infarction, chest pain, coronary artery dissection, febrile neutropenia, Herpes zoster infection, hypersensitivity, mucosal inflammation, pneumonia, rectal hemorrhage, acute renal failure, Staphylococcal infection, and subarachnoid hemorrhage. The cardiac arrest and cerebral infarction occurred in nonresponding patients. One patient in the biweekly intravenous cohort had a treatment-related, serious adverse event of hypersensitivity (allergic reaction) to 2 romiplostim infusions that resolved without discontinuation of study treatment. That patient was switched to subcutaneous injections and experienced no further reactions. One patient died of subarachnoid hemorrhage (not treatment-related).

Five blood and lymphatic system adverse events were recorded, including 3 episodes of neutropenia, 1 episode of leukocytosis, and 1 episode leukopenia; none were treatment-related. The incidence of treatment-related adverse events was 18%, and none occurred during the treatment extension. There were no episodes of thromboembolic events related to romiplostim and no adverse events of reticulin or fibrosis of the bone marrow.

Table 1. Baseline Characteristics

Characteristic	Romiplostim Dose: No. of Patients (%)			
	750 μg SC/QW, n=11	750 μg SC/Q2W, n=12	750 μg IV/Q2W, n=5	Total, N=28
Women	2 (18)	3 (25)	1 (20)	6 (21)
Race				
White or Caucasian	10 (91)	10 (83)	4 (80)	24 (86)
Black or African American	0 (0)	1 (8)	0 (0)	1 (4)
Other	1 (9)	1 (8)	1 (20)	3 (11)
Age: Mean±SD, y	69±6	72±10	72±4	71±8
MDS diagnosis				
RA	2 (18)	4 (33)	1 (20)	7 (25)
RAEB-1	1 (9)	1 (8)	1 (20)	3 (11)
RCMD	5 (46)	5 (42)	3 (60)	13 (46)
RCMD-RS	1 (9)	0 (0)	0 (0)	1 (4)
MDS-U	2 (18)	2 (17)	0 (0)	4 (14)
IPSS score				
Missing	0 (0)	1 (8)	0 (0.0)	1 (4)
0	0 (0)	5 (42)	1 (20)	6 (21)
0.5	7 (64)	4 (33)	4 (80)	15 (54)
1.0	3 (27)	2 (17)	0 (0)	5 (18)
>1.0	1 (9)	0 (0)	0 (0)	1 (4)
Received erythropoietic growth factor for MDS	4 (36)	4 (33)	3 (60)	11 (39)
Received granulocyte growth factor for MDS	2 (18)	3 (25)	1 (20)	6 (21)
Bleeding events in the past year	4 (36)	5 (42)	2 (40)	11 (39)
Received platelet transfusion in the past year	6 (55)	10 (83)	3 (60)	19 (68)
Platelet count $<20\times10^9$/L	4 (36)	4 (33)	2 (40)	10 (36)
Received previous MDS therapies	2 (18)	5 (42)	0 (0)	7 (25)
ECOG performance status				
0	6 (55)	4 (33)	4 (80)	14 (50)
1	4 (36)	6 (50)	1 (20)	11 (39)
2	1 (9)	2 (17)	0 (0)	3 (11)
≥3	0 (0)	0 (0)	0 (0)	0 (0)

SC indicates subcutaneous; QW, weekly administration; Q2W, biweekly administration; IV, intravenous; SD, standard deviation; MDS, myelodysplastic syndrome; RA, refractory anemia, RAEB-1, refractory anemia with excess blasts-1; RCMD, refractory cytopenia with multilineage dysplasia without ringed sideroblasts; RCMD-RS, refractory cytopenia with multilineage dysplasia with ringed sideroblasts; MDS-U, unclassifiable myelodysplastic syndrome; IPSS, International Prognostic Scoring System; ECOG, Eastern Cooperative Oncology Group.

Two patients (7%) experienced an increased blast percentage on study. One patient who progressed to AML during Part B had refractory anemia with excess blasts (baseline IPSS score, 1.5; this score was documented as 0.5 at enrollment and revised at central review). The patient discontinued treatment 1 week after receiving the third weekly subcutaneous romiplostim injection, when a bone marrow blast count of 25% was recorded. No further bone marrow evaluations were available. A second patient who had an unconfirmed increase in blasts during the extension had received 750 μg romiplostim biweekly subcutaneously for 18 weeks. Two weeks after receiving the last dose, the bone marrow blast count was 30%.

Of the 23 patients who completed 8 weeks of treatment, 15 patients (65%) experienced a complete or major platelet response, and higher rates of response were observed in patients who had higher baseline platelet counts (Table 3). Only 39% received platelet transfusions. Overall, 7 patients (30%) achieved a durable platelet response (defined according to IWG criteria). We did not observe any difference in response to romiplostim when patients from different subgroups were compared on IPSS risk scores, French-American-British classification, and baseline platelet counts. There was no evidence that the dose or route of administration had a clinically significant effect on platelet counts (Fig. 2). There was an apparent drop in the median platelet count in the weekly subcutaneous arm from Week 8 to Week 9; however, patient numbers declined, and there was overlap between the interquartile ranges at the 2 time points. The 3 patients

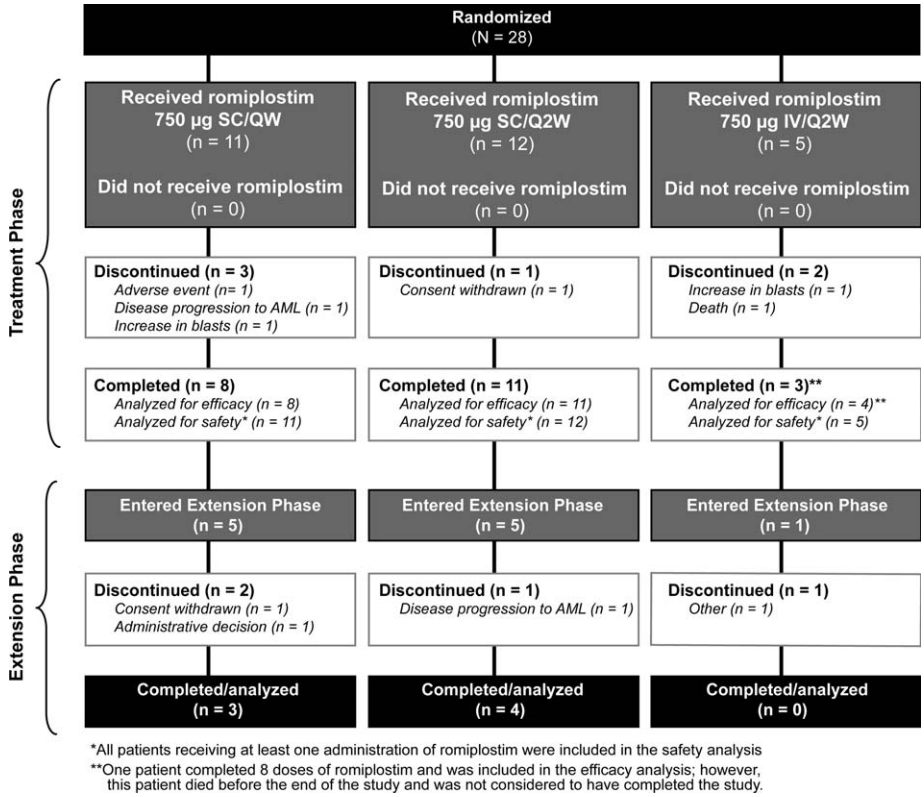

Figure 1. This Consolidated Standards of Reporting Trials (CONSORT) flow diagram illustrates patient disposition for the 8-week schedule-finding treatment phase (Part B) for romiplostim and the corresponding extension phase. SC/QW indicates weekly subcutaneous; SC/Q2W, biweekly subcutaneous; IV/Q2W, biweekly intravenous; AML, acute myeloid leukemia.

Table 2. Incidence of Adverse Events

	Romiplostim Dose: No. of Adverse Events (%)			
Variable	750 µg SC/QW, n=11	750 µg SC/Q2W, n=12	750 µg IV/Q2W, n=5	Total, N=28
Safety[a]				
All adverse events	10 (91)	11 (92)	5 (100)	26 (93)
All serious adverse events	1 (9)	2 (17)	2 (40)	5 (18)
All treatment-related adverse events	2 (18)	2 (17)	1 (20)	5 (18)
All serious treatment-related adverse events	0 (0)	0 (0)	1 (20)	1 (4)
Deaths	0 (0)	0 (0)	1 (20)	1 (4)
Most frequent adverse events by preferred MedDRA term[b]				
Fatigue	4 (36)	1 (8)	0	5 (18)
Headache	4 (36)	1 (8)	0	5 (18)
Back pain	4 (36)	0 (0)	0	4 (14)
Asthenia	2 (18)	1 (8)	1 (20)	4 (14)
Musculoskeletal pain	3 (27)	0 (0)	0 (0)	3 (11)
Cough	2 (18)	1 (8)	0 (0)	3 (11)
Fall	2 (18)	1 (8)	0 (0)	3 (11)
Neutropenia	1 (9)	2 (17)	0 (0)	3 (11)
Adverse events by grade				
Grade 3	1 (9)	5 (42)	1 (20)	7 (25)
Grade 4	1 (9)	0 (0)	1 (20)	2 (7)

SC indicates subcutaneous; QW, weekly administration; Q2W, biweekly administration; IV, intravenous; MeDRA, Medical Dictionary for Regulatory Activities.
[a] Includes all enrolled patients who received at least 1 dose of romiplostim.
[b] MedDRA version 11.0 was used.

Table 3. Platelet Response in Patients Who Completed ≥8 Weeks of Treatment

Treatment Phase: Patients who Completed 8 Weeks of Treatment[a]	Romiplostim Dose: No. of Patients/Total No. (%)			
	750 μg SC/QW, n=8[b]	750 μg SC/Q2W, n=11	750 μg IV/Q2W, n=4[c]	Total, N=23
Achieved a complete or major platelet response	5 (63)	8 (73)	2 (50)	15 (65)
Binomial 95% CI	24-91	39-94	7-93	
Platelet response in patients who had a baseline platelet count $\geq 20\times10^9$/L	1/3 (33)	1/3 (33)	0/2 (0)	2/8 (25)
Platelet response in patients who had a baseline platelet count $>20\times10^9$/L	4/5 (80)	7/8 (88)	2/2 (100)	13/15 (87)
Achieved a complete platelet response	4 (50)	7 (64)	2 (50)	13 (57)
Binomial 95% CI	16-84	31-89	7-93	
Achieved a major platelet response	1 (12.5)	1 (9.1)	0 (0.0)	2 (9)
Binomial 95% CI	0-53	0-41	0-60	
Received platelet transfusions	4 (50)	3 (27)	2 (50)	9 (39)

Extension Phase: Patients who Completed ≥8 Weeks of Treatment[d]	Romiplostim Dose: No. of Patients/Total No. (%)			
	750 μg SC/QW, n=5[b]	750 μg SC/Q2W, n=5	750 μg IV/Q2W, n=1	Total, N=11
Achieved a durable platelet response	2 (25)	4 (36)	1 (25)	7 (30)
Binomial 95% CI	3-65	11-69	0.6-81	
Baseline platelet count $\geq 20\times10^9$/L	1/3 (33)	1/3 (33)	0/2 (0)	2/8 (25)
Baseline platelet count $>20\times10^9$/L	1/5 (20)	3/8 (38)	1/2 (50)	5/15 (33)
Duration of platelet response: Mean±SD, wk	19.5±16.3	9.3±1.5	9.0[e]	—

SC indicates subcutaneous; QW, weekly administration; Q2W, biweekly administration; IV, intravenous; CI, confidence interval; SD, standard deviation.
[a] According to International Working Group (IWG) 2000 response criteria.
[b] One patient in this group had achieved a complete or major platelet response during the 8 week treatment period and then received a prophylactic platelet transfusion 30 days after romiplostim treatment had ended. Therefore, this patient was counted in both the responder group and the transfusion group.
[c] One patient completed 8 doses of romiplostim and was included in the efficacy analysis; however, this patient died before the end of the study and, thus, did not complete the study.
[d] According to IWG 2006 response criteria.
[e] There was no SD for this mean, because the sample size was 1.

who discontinued drug during this time were all responders. These patients had platelet counts $>100 \times 10^9$/L but did not continue into the extension study. The platelet counts for the remaining patients were $>20 \times 10^9$/L.

Blood samples (n = 327) were collected for PK analysis from 28 patients. Mean concentration-time profiles after the first dose were higher than the Week 7 dose (Fig. 3). Patients in the weekly subcutaneous cohort achieved the highest exposure, as indicated by mean profiles (Fig. 3).

DISCUSSION

Thrombocytopenia affects a substantial proportion of patients with lower risk MDS, and >33% receive a platelet transfusion at some point during their disease course.[1] Unfortunately, most agents that have activity in patients with lower risk MDS target hematologic improvements along erythroid lines, leaving these patients without viable options other than platelet transfusions for treating profound or symptomatic thrombocytopenia, with the accompanying risk of alloimmunization and ultimate lack of response over time. Thrombopoietic growth factors, thus, represent promising therapies for this subpopulation of patients.

In the current study, we evaluated the safety, efficacy, and PK profile of romiplostim in thrombocytopenic patients with lower risk MDS. The results verified a previous report on the efficacy of romiplostim in lower risk patients and demonstrated for the first time the efficacy of a variety of routes and schedules of administration. The majority of patients (65%) in our study achieved a complete or major platelet response, and higher response rates were observed in patients who had higher baseline platelet counts, substantiating published MDS prognostic scoring

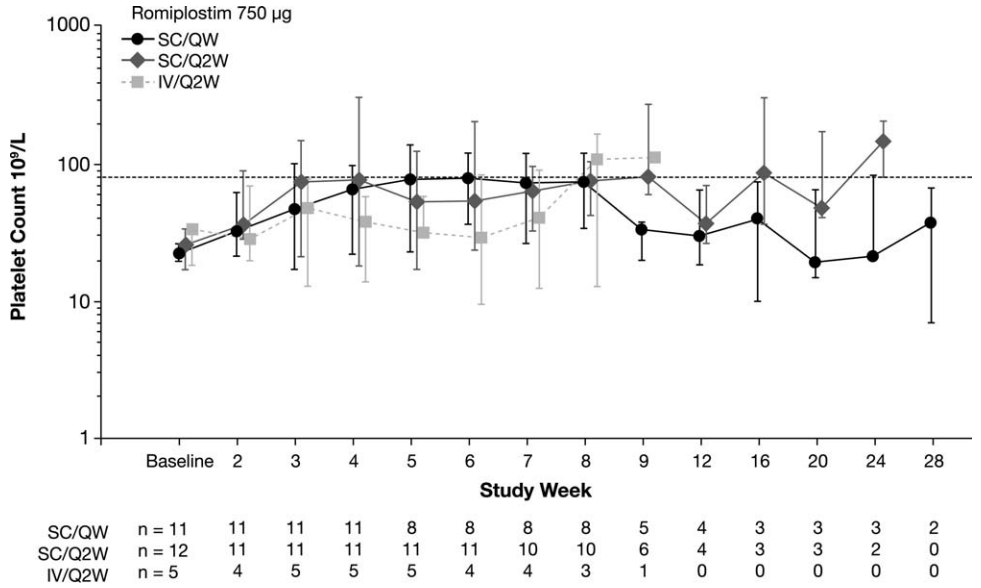

Figure 2. Platelet counts and romiplostim pharmacokinetics are illustrated. The median platelet count is shown after weekly subcutaneous (QW/SC), biweekly subcutaneous (SC/Q2W), and biweekly intravenous (IV/Q2W) dosing of 750 µg romiplostim. The full analysis set was defined as the number of patients who received at least 1 administration of romiplostim. The median values (circles and squares) are illustrated along with the first and third quartiles (vertical lines) at each time point.

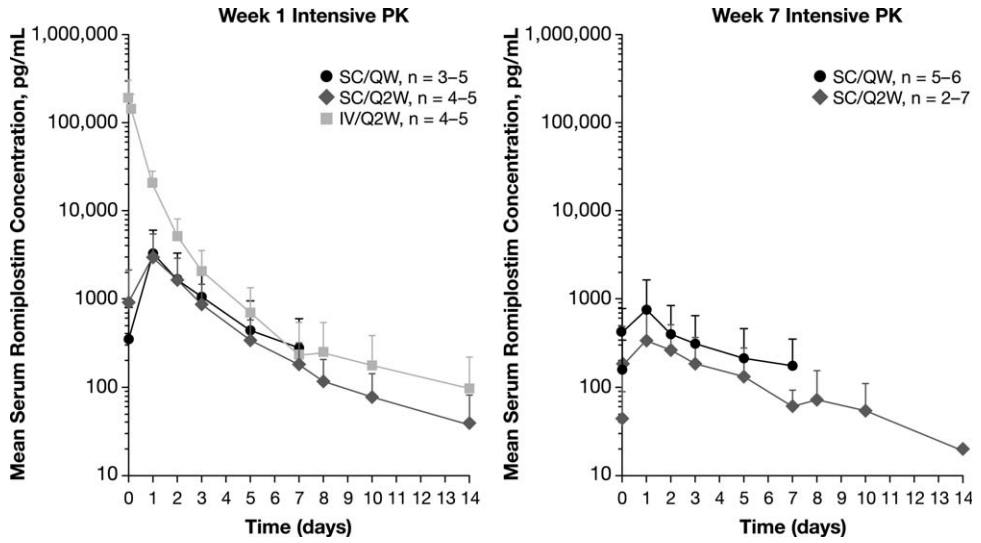

Figure 3. Mean (standard deviation) serum romiplostim concentration-versus-time profiles are illustrated after weekly (QW) subcutaneous (SC) (SC/QW), biweekly (Q2W) subcutaneous (SC/Q2W), and biweekly intravenous (IV/Q2W) dosing of 750 µg romiplostim (*Left*) during Week 1 and (*Right*) during Week 7. Week 7 intensive pharmacokinetics (PK) were not available for the IV/Q2W cohort, because assignment was discontinued into that treatment arm.

systems, which indicate that the degree of thrombocytopenia may indicate a more serious MDS.[2]

We also report on the durability of responses, which hint at more prolonged responses with weekly subcutaneous dosing, with a 2-fold greater duration of response than biweekly dosing, although this finding needs to be substantiated in larger studies. Figure 2 illustrates that platelet counts rose to substantial (although not quite normal) levels for most patients. However, as indicated by IWG response criteria, thrombocytopenic patients do not

need to achieve normal platelet levels to derive clinical and quality-of-life benefit from a therapeutic intervention. They just need to achieve platelet levels that obviate transfusions and lower risks of spontaneous or traumatic bleeding.

In the current study, the majority of patients (61%) did not need to receive platelet transfusions. Reduced platelet transfusions and bleeding events were observed in patients who achieved durable platelet responses.[12] These responses were observed in patients independent of their baseline platelet count. Patients who experienced durable platelet responses had fewer clinically relevant bleeding events and fewer platelet transfusions, as reported in Part A of the study.[12]

Although most patients had at least 1 adverse event; the most common and serious adverse events were consistent with those in a similar populations of patients with MDS who received treatment with romiplostim or other agents.[6,12,15] Serious adverse events included those that are anticipated in an MDS population and that we did not believe were related to study drug. It is noteworthy that there were no episodes of thromboembolic events related to romiplostim, and no adverse events of reticulin or fibrosis of the bone marrow were reported. Two episodes of an increase in blast percentage did occur in study patients in this single arm, schedule-finding phase. Six patients discontinued the study before the extension phase, some because of disease progression. Although this may represent natural disease evolution, particularly in the subset of lower risk patients with thrombocytopenia (who may represent a somewhat higher risk subset of the lower risk population), the safety of long-term romiplostim treatment will be monitored in an ongoing, single-arm, open-label extension study and in an ongoing, placebo-controlled study. The results from our ongoing, placebo-controlled clinical study will help determine the appropriate use of romiplostim in patients with low-risk and intermediate 1-risk MDS patients along with predictors of response.

PK studies indicated that the mean concentration-time profiles after the first dose were higher than the Week 7 dose, which is consistent with target-mediated disposition, because the platelet counts were higher in Week 7, and thrombopoietin receptors on platelets presumably serve as a mechanism for romiplostim clearance.[16] In summary, the safety, efficacy, and PK data described here support further clinical study of romiplostim in patients with MDS. On the basis of the safety and efficacy results reported herein, the starting dose recommendation for this patient population is subcutaneous romiplostim once weekly at a dose of 750 μg.

CONFLICT OF INTEREST DISCLOSURES

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