Use of the Functional Assessment of Cancer Therapy—Anemia in Persons with Myeloproliferative Neoplasm-Associated Myelofibrosis and Anemia

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ABSTRACT

Background: Anemia is common in myeloproliferative neoplasm (MPN)—associated myelofibrosis. The Functional Assessment of Cancer Therapy (FACT) measurement system is a patient-reported outcomes instrument that documents symptoms of the diverse aspects of cancer treatment. One FACT version, FACT-Anemia (FACT-An), documents symptoms of anemia related to cancer. The FACT-An has been validated in diverse cancer populations, but not in MPN-associated myelofibrosis.

Objective: Our aim was to evaluate the relationship between anemia response to therapy with pomalidomide with or without corticosteroids and patient-reported outcomes using the FACT-An instrument.

Methods: Data were obtained from a Phase II, randomized, double-blind Bayesian pick-the-winner trial of prednisone and pomalidomide in patients with MPN-associated myelofibrosis and anemia (red blood cell—transfusion dependence). Details of the study, including definitions of anemia, anemia response, red blood cell—transfusion, red blood cell—transfusion dependence, and red blood cell—transfusion independence, are reported. Change in quality of life from randomization to the last cycle of therapy was evaluated using the FACT-An Physical Well Being, Functional Well Being, Trial Outcome Index, and Anemia domains. Clinically important differences were used to determine the smallest difference in scores that patients perceived as beneficial in the FACT-An domains of interest. Patients were classified as meeting clinically important differences for responsiveness if their change score from baseline was >1 SEM, indicating improvement.

Results: Eighty-five patients were studied. Thirty-one patients (37%) were classified as anemia responders by prospectively defined criteria. Across all FACT-An domains, anemia responders showed greater improvement in Physical Well Being, Functional Well Being, and Trial Outcome Index scores than did nonresponders. This improvement began at the second 28-day cycle of therapy and was sustained.

Conclusions: We show a correlation between anemia response and improved quality of life measured by the FACT-An instrument in patients with MPN-associated myelofibrosis and anemia. (*Clin Ther.* 2014;36:560–566)

Key words: anemia, cancer, clinical trial, FACT-An, fatigue, MPN-associated myelofibrosis, patient-reported outcome, prednisone, quality of life, responsiveness, validation study.

INTRODUCTION

Severe anemia is common in patients with myeloproliferative neoplasm (MPN)—associated myelofibrosis. Red blood cell (RBC)—transfusion dependence is

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common. Anemia and RBC-transfusion dependence are independently correlated with survival in patients with MPN-associated myelofibrosis.[1] Anemia is also inversely correlated with patient-reported quality of life (QOL).[2,3] Patients with MPN-associated myelofibrosis experience substantial loss of vitality or energy compared with norms, as well as numerous other impacts, including sleep problems. In addition, in one qualitative study, patients reported that fatigue related to MPN-associated myelofibrosis affected both their ability to work and their work productivity.[4] Assessment of anemia symptoms, especially fatigue, in patients with MPN-associated myelofibrosis is complex because the disease causes severe fatigue, even in those without anemia. MPN-associated myelofibrosis is also related to constitutional symptoms, including weight loss, night sweats, pruritus, bone pain, mood and sleep disturbances, early satiety, fever, and stress.[5,6] These symptoms can influence a person's subjective experience of anemia.[7] Cancer patients with anemia consistently report a reduced sense of well being and disruptions in their exercise tolerance, ability to work, social interaction, and enjoyment of activities commonly identified as important QOL domains.[7] Although patient-reported outcomes (PROs) for the assessment of cancer-related fatigue, such as the Brief Fatigue Inventory,[8] are available, using them in patients with MPN-associated myelofibrosis might not capture the spectrum of anemia-related symptoms. The Functional Assessment of Cancer Therapy (FACT) measurement system was developed to document patient responses regarding several aspects of cancer treatment[9] and includes an instrument specifically designed to address symptoms of cancer-related anemia (FACT-An). The FACT-An is a 47-item questionnaire consisting of the 27-item Functional Assessment of Cancer Therapy—General, the 13-item Fatigue subscale, and 7 nonfatigue anemia-specific items.[7] Yellen et al[7] stressed that additional studies were needed to validate the FACT-An with different cancers and after different treatments.

The FACT-An has been validated in several cancers, but not in MPN-associated myelofibrosis. The purpose of this study was to test its function in persons with MPN-associated myelofibrosis and anemia participating in a Phase II randomized Bayesian pick-the-winner study of pomalidomide and prednisone.

Current PRO Instruments Used to Assess QOL in Myelofibrosis

As noted earlier, the Brief Fatigue Inventory was developed to address symptoms of fatigue in persons with cancer. It is, however, not specific to fatigue caused by anemia. The Myelofibrosis Symptom Assessment Form[10] is a PRO developed to assess symptoms associated with MPN-associated myelofibrosis. It is not limited to symptoms associated with anemia. The Myelofibrosis Symptom Assessment Form was used recently in a global clinical trial of ruxolitinib in patients with MPN-associated myelofibrosis to measure symptom improvement.[3] This instrument was later expanded to the Myeloproliferative Neoplasm Symptom Assessment Form, a validated QOL PRO available for use in international clinical trials. This more-general instrument assesses symptoms in MPNs, including MPN-associated myelofibrosis.

METHODS

Clinical Trial

Data for this study were obtained from a Phase II, randomized, double-blind trial to determine the tolerability and best numerical regimen of pomalidomide for the treatment of anemia in patients with MPN-associated myelofibrosis. Patients were equally and randomly assigned to the following 4 arms: pomalidomide, 2 mg/d and prednisone; pomalidomide, 2 mg/d and placebo; pomalidomide, 0.5 mg/d and prednisone; and prednisone and placebo. Patients remained in the study for up to twelve 28-day cycles. The primary end point was the best clinical response within the first 6 cycles (168 days), as defined by the International Working Group for Myelofibrosis Research and Treatment criteria.[11] Of the 85 patients in this study, 31 were scored as anemia responders and 54 as nonresponders. A prednisone-only arm was a comparator.

Patients with anemia were defined by the International Working Group for Myelofibrosis Research and Treatment criteria as follows: hemoglobin concentration <85 g/dL or RBC-transfusion dependence, defined as patients receiving ≥ 2 U RBCs ≤ 28 days pre-randomization. Response was defined as hemoglobin concentration increase of ≥ 20 g/dL above baseline for ≥ 56 consecutive days without an RBC transfusion or no RBC transfusions during any consecutive rolling 56-day interval; patients discontinuing without response were scored as nonresponders.