INTRODUCTION

Myelofibrosis (MF) is a chronic disorder of myeloid neoplasms characterized by myelodysplasia and extramedullary hematopoiesis, leading to organomegaly, constitutional symptoms, and progression to acute leukemia.1

A Phase 1/2 Study of NS-018, an Oral JAK2 Inhibitor, in Patients with Primary Myelofibrosis (PMF), Post-Polyhematocytic Veraemia (pPV MF), or Post-Essential Thrombocytemia Myelofibrosis (pET MF)

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METHODS

— Phase 1: Eight patients were enrolled in the 250, 300 and 400 mg BID cohorts, and every 3 cycles thereafter, using the Myelofibrosis Symptom Assessment Form (MF-SAF)11 and ECOG PS data are not available for 1 patient. bOne patient was unable to assess for splenomegaly due to body habitus.

— Phase 2: 12 patients have been treated at 300 mg QD.

— Adverse events (AEs) were graded according to the common toxicity criteria for non-hematologic AEs; Thrombocytopenia

— Safety assessments:

— Efficacy assessments:

— MFI and C-reactive protein (CRP) were measured q4w.

— Bone marrow fibrosis (BMF) was assessed by biopsy and graded (0–6) using the European Consensus Grading Criteria.11

— Changes in MFI grade were recorded as improvement, stabilization, or worsening compared with baseline.

— Circulating cytokines were measured using the ImmunoHUMAIN assay (version 2.0; Myriad RBM, Austin, TX, USA).

— Continuous variables were summarized with descriptive statistics, including mean, standard deviation, median, and range.

— Safety and efficacy results were from the Phase 1 portion of the study, and preliminary safety data from the Phase 2 portion, are presented.

RESULTS

Baseline demographics

— To date 50 patients (Phase 1, n=11; Phase 1/2, n=40) have been treated across 10-dose cohorts (Table 1).

— In the Phase 1 portion of the study (2005–2008), 53 patients (303 mg QD, 16 patients; 300 mg BID, 8 patients; 125 mg QD, 2 patients) have been treated with NS-018 (Table 1).

— In the Phase 1 portion of the study (2008–2011), 8 patients have received previous treatment with a JAK2 inhibitor, whereas all patients in the Phase 1/2 portion had received prior JAK inhibitor therapy.

— In the Phase 1/2 portion of the study (2009–2011), 72 patients have been treated (48 patients in the Phase 1/2 portion; 25 patients in the Phase 2 portion).

— In the Phase 1 portion of the study (2006–2009), X patients have received previous treatment with a JAK2 inhibitor, whereas all patients in the Phase 1/2 portion had received prior JAK inhibitor therapy.

— In the Phase 1/2 portion of the study (2009–2011), 42 patients have been treated (30 patients in the Phase 1/2 portion; 12 patients in the Phase 2 portion).

— Treatment responses were assessed at the first day of Cycles 1, 3, and 4, and every 3 cycles thereafter, according to the International Working Group (IWG) criteria.11

— Splenic size was measured by ultrasound, CT scans, or MRI scans, given in 28-day cycles, in patients with primary MF, post-polyhematocytic veraemia or post-essential thrombocytemia MF (Table 1).

— MF-associated symptoms were measured as adverse events, on the first day of Cycle 2, and 1 cycle thereafter by using the Myelofibrosis Symptom Assessment Form (MF-SAF).11

— Safety assessments:

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