

Study design and objectives for a new cohort of patients with myelofibrosis enrolled in the ongoing Connect[®] Myeloid Disease Registry

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Introduction

- Myelofibrosis (MF) is a life-threatening type of myeloproliferative neoplasm (MPN) with significant morbidity and profound negative effect on quality of life (QoL)^{1,2}
- Current treatments aim to manage symptoms, improve anemia, and delay progress to acute myeloid leukemia (AML)³
 - However, limited real-world data hinder understanding of the safety and effectiveness of emerging therapies, and the association between treatment patterns and patient outcomes
- The Connect[®] Myeloid Disease Registry (NCT01688011), is a large, US, multicenter, prospective, observational, cohort study of patients with newly diagnosed idiopathic cytopenia of undetermined significance, AML, or myelodysplastic syndromes (MDS);^{4,5} the Registry was formerly known as the Connect[®] MDS/AML Registry
 - A new cohort of patients diagnosed with MF began enrollment in February 2021
- The Registry is designed to examine diagnosis patterns, risk assessment, treatment practices, and associated outcomes currently being used in community (CO), government (GOV), and academic (AC) centers when treating patients with MF

Objectives

- To evaluate effectiveness and safety of therapeutic options used in the treatment of MF
- To describe the initiation and sequencing of treatment regimens for cytopenias as well as systemic MF therapy in the real-world setting
- To examine changes in symptom scores/QoL and healthcare resource utilization based on risk group and therapeutic interventions

Registry design

- Approximately 800 patients from 200-250 AC and CO/GOV sites (**Figure 1**) in the US will be enrolled (**Table 1**)
 - The MF cohort allows for enrollment of patients diagnosed with MDS/MPN, excluding juvenile myelomonocytic leukemia (JMML)
- Figure 2** depicts the schema for the Registry design
- Data entry into the electronic data capture system will occur at:
 - Screening
 - Baseline
 - Approximately every 3 months throughout the duration of the patient’s participation in the Registry
- Participation in the Registry is voluntary and patients may withdraw at any time without affecting their ongoing medical care
- The Registry is observational and non-interventional; all medical care, follow-up visits, and laboratory testing are performed solely at the discretion of the treating clinician in accordance with standard clinical practice at each site
- Eligibility criteria are described in **Table 2**
- Patients will be followed for a maximum of 5 years or until early termination, withdrawal, or death
 - Patients with morphologically confirmed diagnosis of MDS/MPN, excluding JMML, in accordance with World Health Organization (WHO) 2016 diagnostic criteria are allowed

Figure 1. Current active Registry sites

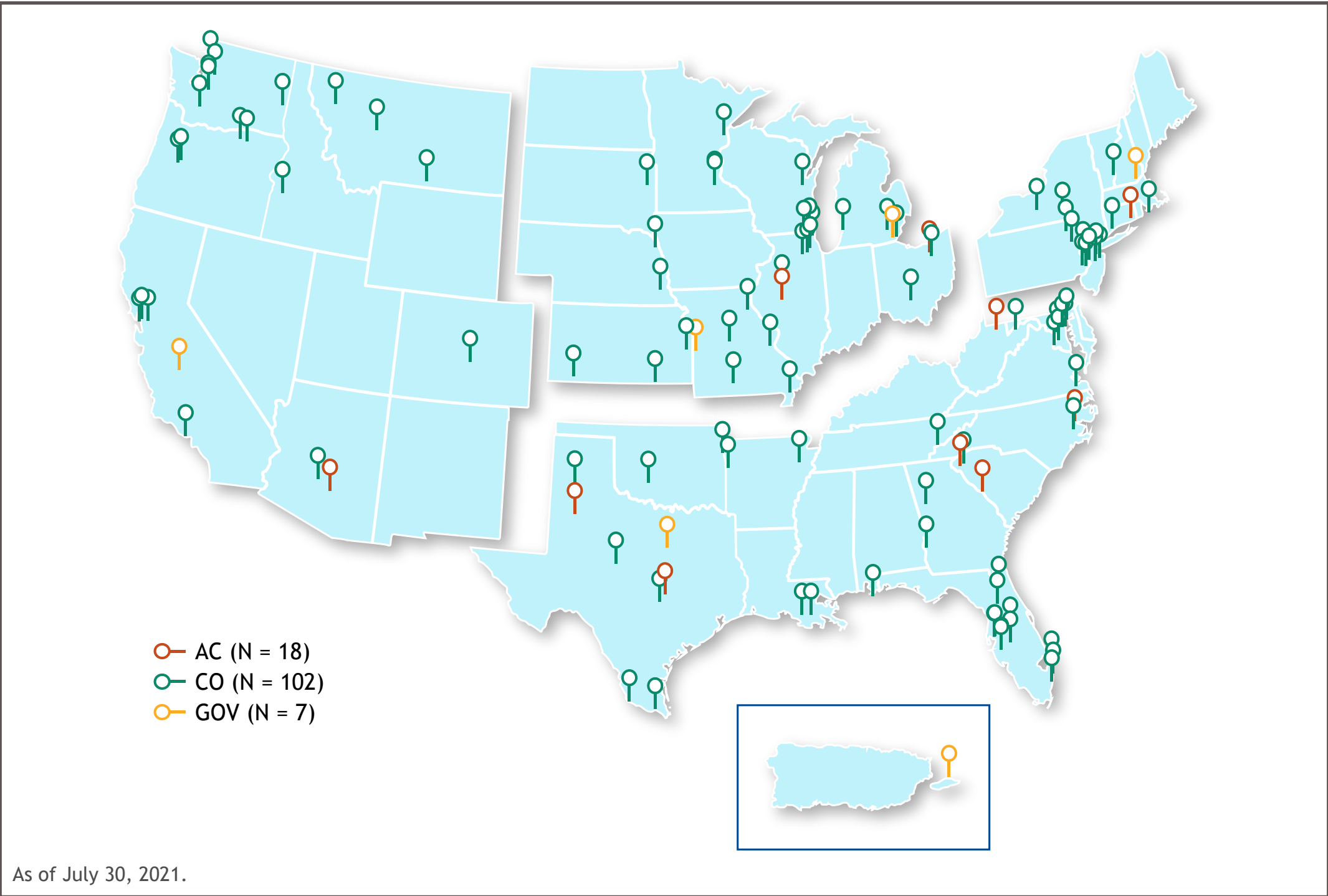
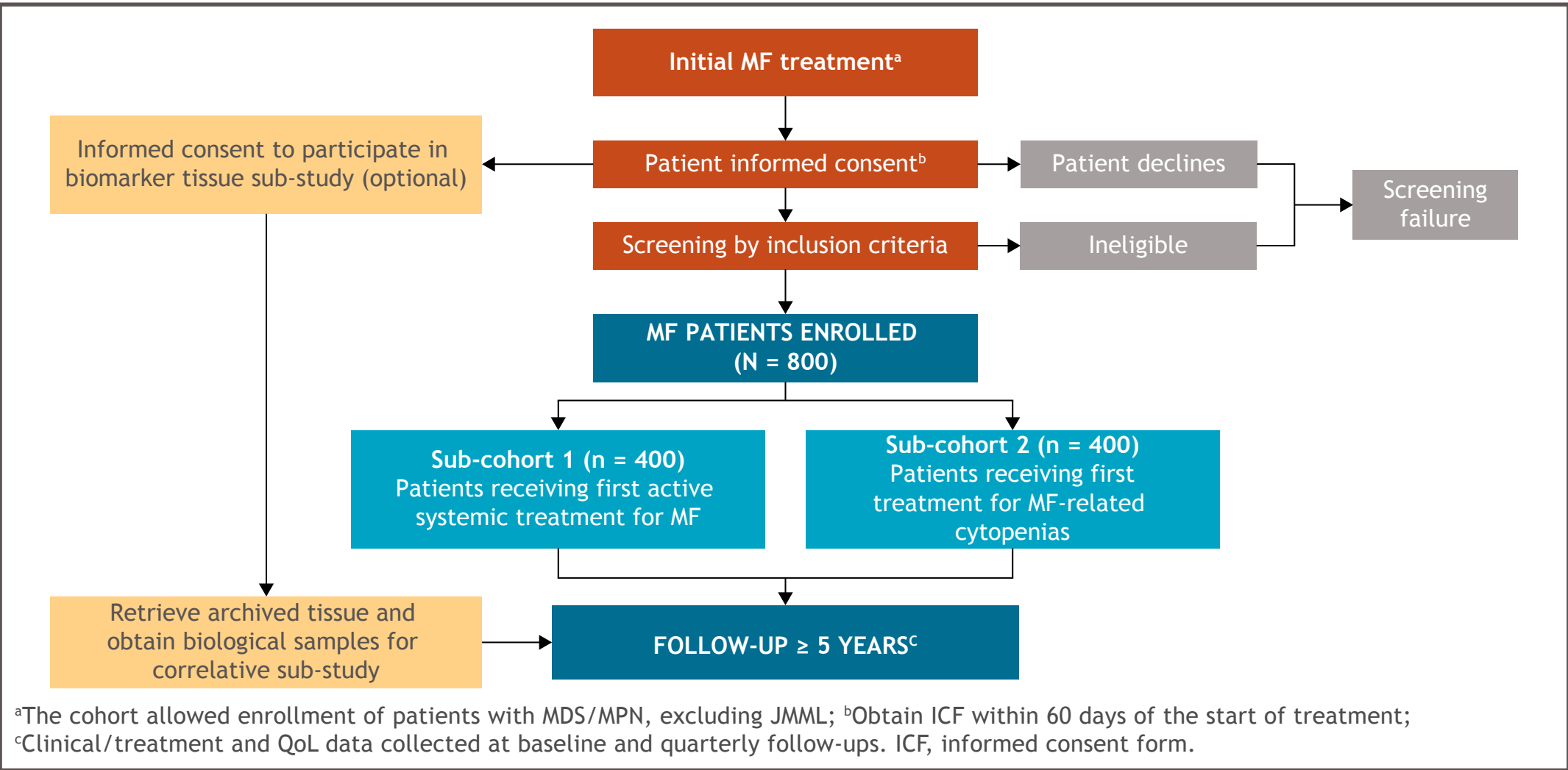


Table 1. Patient cohorts and enrollment

Cohort	Planned enrollment	Enrollment as of July 5, 2021
Total MF cohort^a	800	9
Sub-cohort 1: patients receiving first active systemic treatment for MF	400	7
Sub-cohort 2: patients receiving first treatment for MF-related cytopenias	400	2

^aThis cohort allowed enrollment of patients with a diagnosis of MDS/MPN, excluding JMML.

Figure 2. Study schema for the MF cohort of the Registry



^aThe cohort allowed enrollment of patients with MDS/MPN, excluding JMML; ^bObtain ICF within 60 days of the start of treatment; ^cClinical/treatment and QoL data collected at baseline and quarterly follow-ups. ICF, informed consent form.

Table 2. Patient eligibility criteria

Patient eligibility criteria
Inclusion criteria
≥ 18 years of age at the time of informed consent
MF diagnosis (primary or secondary; MDS/MPN diagnosis allowed)
Initiation of first active systemic treatment for MF and/or MF-related cytopenias within 60 days prior to informed consent ^a
Willing and able to complete baseline and follow-up QoL instruments, for which patients must be proficient in either English or Spanish
Exclusion criteria
Suspected or proven APL (FAB M3 or WHO 2008) based on morphology, immunophenotype, molecular assay, or karyotype
Suspected or proven JMML diagnosis
Current enrollment in any interventional clinical trial where the investigational product cannot be identified

^aActive, systemic treatment for MF may include, but is not limited to, hydroxyurea, JAK inhibitors, hypomethylating agents, interferon agents, and immune-oncology agents. Treatment for MF-related cytopenias may include, but is not limited to, steroids, ESA, danazol, lenalidomide, pomalidomide, thalidomide. Note: patients who have been on an ESA for anemia and then begin first active systemic treatment are eligible. If a patient has initiated and stopped therapy within the 60-day period due to an adverse event, they are eligible if they have not initiated a second line of therapy. APL, acute promyelocytic leukemia; ESA, erythropoiesis stimulating agent; FAB, French-American-British; JAK, Janus kinase.

Data analysis

- Data to be collected include:
 - Health status assessment (Eastern Cooperative Oncology Group performance status and Clinical Frailty Scale)
 - Select laboratory results, if performed as part of routine clinical practice
 - Treatment details
 - Clinical response (by Myelofibrosis Symptom Assessment Form [MFSAF] v4.0, spleen size, cytopenia assessment through laboratory tests or transfusion burden, and bone marrow [BM] biopsy if performed as standard of care)
 - Overall survival
 - Adverse drug reactions
 - Serious adverse events
 - Protocol-defined adverse events of interest
- QoL will be assessed using MFSAF, Functional Assessment of Cancer Therapy-Anemia (FACT-An), and EuroQol 5 dimensions, 3 levels (EQ-5D-3L) questionnaires

Biomarker tissue sub-study (optional)

- Patients may consent to an optional biomarker tissue sub-study designed to profile the molecular landscapes of myeloid cancers to better understand disease biology, response to therapies, and the relationship between karyotypes, molecular/cellular markers, patient risk, and treatment outcomes
- Samples, including BM, peripheral blood, and oral epithelial cells, will be collected at screening and when clinically indicated procedures are performed as part of the routine clinical practice

Conclusions

- Data collected in the MF cohort of the Registry will increase understanding of the clinical effectiveness, safety, and QoL outcomes of current treatment strategies for patients with MF
- Findings may provide new insights into diagnostic patterns, treatment regimens, and treatment sequencing, and how these are associated with clinical outcomes of patients with MF in the US
- Correlative analyses on molecular/cellular data may increase the understanding of and may reveal novel prognostic and predictive biomarkers for MF

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