Myelofibrosis Working Group

Presented at the Eighth Annual PRO Consortium Workshop – Bethesda, MD – April 26-27, 2017

PRO CONSORTIUM
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Background

Rationale for Myelofibrosis (MF) Working Group (WG)

- Based on encouragement by the FDA to pursue qualification of a symptom measure for MF clinical trials, the PRO Consortium attempted to gain sufficient financial support from the pharma industry to begin the project. Unfortunately, the PRO Consortium was unsuccessful in this effort and the FDA was notified accordingly.
- FDA liaisons subsequently requested the PRO Consortium attempt to gain support for an initial step toward qualification. This step would involve gaining stakeholder consensus around a harmonized MF symptom assessment instrument that could be used as a provisional or interim endpoint measure until an FDA-qualified instrument became available.
- The FDA acknowledged that multiple variants of the Myelofibrosis Symptom Assessment Form (MFSAF) are used and believes it would be beneficial to have a single, consensus-defined instrument developed from existing empirical evidence. The instrument could be used by any sponsor with an MF drug development program. No sponsor would be required to use it, but its use would be encouraged by the FDA.

Goals of the Myelofibrosis WG

- Primary Objective: Develop consensus around a harmonized MF symptom assessment instrument that can be used as a provisional or interim endpoint instrument until an FDA-qualified instrument is available.
- Secondary Objective: Assemble evidence that variants of the Modified MFSAF v2 Diary currently being used to assess the core symptoms provide sufficiently equivalent results (even with minor variations in item wording).

Milestones

Milestone	Expected Date	Completed Date
Identify stakeholders for Consensus Development Panel Meeting		OCT 2015
Collect all documentation to be included in review		OCT 2015
Complete review and evaluation of published and unpublished documentation of myelofibrosis symptom-targeted PRO items and instruments and provide a summary of documentation		NOV 2015
Complete final Myelofibrosis WG Information Package		FEB 2016
Convene Consensus Development Panel Meeting		MAR 2016
Complete final report in the form of a manuscript delivered to Myelofibrosis WG		MAR 2016
Conduct preliminary testing of the MFSAF v4.0 using an internet-based survey hosted by Mayo Clinic	Q2 2017	
Develop a concept definition table and preliminary user manual for the MFSAF v4.0	Q2 2017	

Highlights

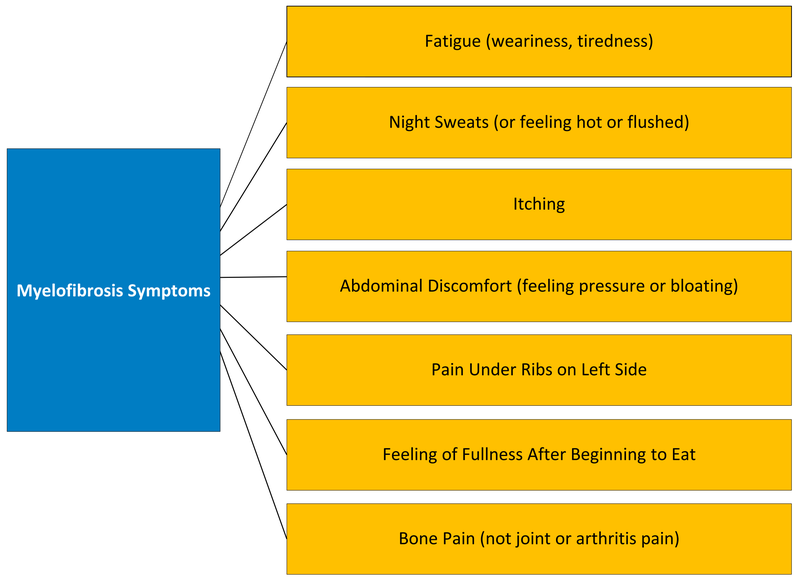
Example Endpoint Model for Treatment of Myelofibrosis

Endpoint Hierarchy	Endpoint Concept(s)	Endpoint Type
Primary	Reduction in spleen volume	Biomarker
Secondary	Reduction in total symptom score on MFSAF v4.0	PRO

Target Population

- Adults aged 18 years and older with a clinical diagnosis of myelofibrosis

Hypothesized Conceptual Framework



Measure – *Myelofibrosis Symptom Assessment Form (MFSAF)* v4.0

Consensus reached on a harmonized MF symptom assessment measure: *Myelofibrosis Symptom Assessment Form* (*MFSAF*) v4.0

Core Items: Seven items covering seven individual symptoms
Recall Period: 24-hour (a 7-day format is also available)
Response Options: 11-point numeric rating scale
Symptom Attribute: Severity

Working Group Updates

Completed Activities

- On March 2, 2016, the MF Working Group convened a face-to-face consensus development meeting
- Meeting participants came to consensus on a seven-item instrument which was identified as the *Myelofibrosis Symptom Assessment Form* (*MFSAF*) v4.0, with 24-hour and 7-day recall period formats. The *MFSAF* v4.0 contains a fatigue item, which was a priority for FDA
- The manuscript titled "Development of a Harmonized Patient-Reported Outcome Questionnaire to Assess Myelofibrosis Symptoms in Clinical Trials" was submitted to *Leukemia Research* on January 26, 2017

Unique Issues for the Working Group

- Copyright/Licensing: Mayo Clinic will retain the copyright to the *MFSAF* v4.0 and will grant C-Path authorization to license and distribute the *MFSAF* v4.0
- Determine what additional data will be necessary to provide sufficient evidence for submission of the *MFSAF* v4.0 for FDA qualification

Next Steps

- Conduct preliminary testing of the *MFSAF* v4.0 will begin in Q2 of 2017 using an internet-based survey hosted via Mayo Clinic's REDCap Survey System
- Develop a concept definition table for use in translating the *MFSAF* v4.0
- Develop preliminary user manual that will include the following:
  - Administration guidelines
  - Scoring function and missing data decision rules
  - Concept definition table
  - Items and response set
  - Recommendations regarding use of 24-hour and 7-day recall period formats
  - Preliminary/default responder definition (e.g., ≥ 50% improvement in total symptom score)

Working Group Participants

Organization	Representatives
CTI BioPharma	Lixia Wang, PhD
Janssen	Jeremiah Trudeau, PhD; Renee Pierson, MBA
Affiliation	**Consultant**
Mayo Clinic	Amylou Dueck, PhD; Ruben Mesa, MD
Quintiles	Jean Paty, PhD
Contract Research Organization	**Research Team**
Gwaltney Consulting, LLC	Chad Gwaltney, PhD
FDA	**Representatives**
	Michelle Campbell, PhD; Wen-Hung Chen, PhD; Virginia Kwitkowski, MS, ACNP-BC; Elektra Papadopoulos, MD, MPH