The Impact of Momelotinib on Patient Reported Quality of Life for Symptomatic and Anemic Patients with Myelofibrosis: Results from the Phase 3 MOMENTUM Study

Poster 4351

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Introduction

- Disease-related inflammation, anemia, and splenomegaly contribute to burdensome symptoms in patients with myelofibrosis (MF), including fatigue, bone, and abdominal pain, which can negatively impact health-related quality of life (HRQOL)[1-4]
- There are no approved treatments for patients with intermediate- and high-risk MF that specifically improve anemia, and approved MF therapies for splenomegaly and symptoms often exacerbate anemia[5]
- Momelotinib, a first-in-class oral Janus kinase (JAK)1/JAK2/activin A receptor type 1 inhibitor, demonstrated clinical activity against anemia, constitutional symptoms, and splenomegaly[6]
- In the phase 3 clinical trial, MOMENTUM, momelotinib significantly improved disease-related symptoms compared with danazol (24.6% vs 9.2%) as measured by achieving at least a 50% reduction in total symptom score (TSS) at week 24 compared with baseline[7]

Objective

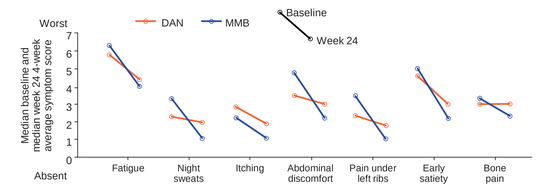
To assess the impact of momelotinib (MMB) on patient-reported health status and HRQOL, including the impact on fatigue and physical function, for patients in the MOMENTUM study

Instruments and Analysis

- Patient-reported outcomes (PRO) analyses were performed for the following assessments in the intention-to-treat population
  - Myelofibrosis Symptom Assessment Form (MFSAF) v4.0 TSS and individual items
  - European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – 30 items v3.0 (EORTC QLQ–C30 v3.0)-derived scales
  - Patient-Reported Outcomes Measurement Information System (PROMIS) short form physical function total score 10b
- Response analyses were performed using corresponding meaningful change thresholds (MCT) for each PRO
- Longitudinal change from baseline scores were analyzed using mixed model for repeated measures (MMRM)
- Longitudinal responder analyses were performed by generalized estimating equation after multiple imputation for missing scores
- Odds ratio (OR) for response, 95% CI, and *P* value were presented as the treatment effect (momelotinib vs danazol)
- Time to first response was analyzed using the Kaplan-Meier method; a stratified log-rank test was performed to compare treatment arms, and hazard ratio (HR) was estimated from a stratified Cox regression model

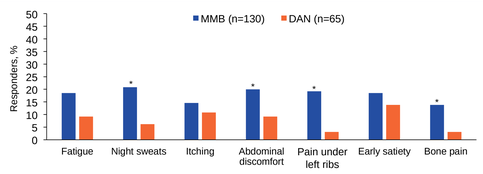
Results

Figure 1. MFSAF Individual Item Scores Demonstrate Lower Symptom Burden at Week 24 in the Momelotinib Compared With the Danazol Group



DAN, danazol; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib.

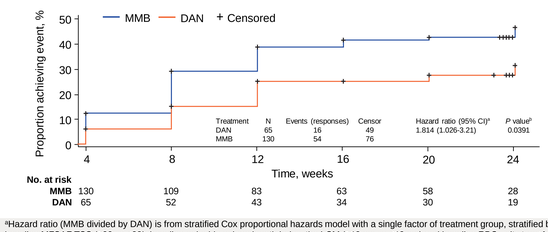
Figure 2. Momelotinib Showed a Higher Proportion of Responders[a] for Each Symptom at Week 24



[a]Response was based on a 3-point threshold. *P<.05.
DAN, danazol; LS, least squares; MMB, momelotinib; MMRM, mixed model for repeated measures.

- In addition to the responder analysis in Figure 2, change from baseline analysis using MMRM showed that the LS mean difference for each individual item ranged from −0.31 (itching) to 1.27 (night sweats) in favor of momelotinib

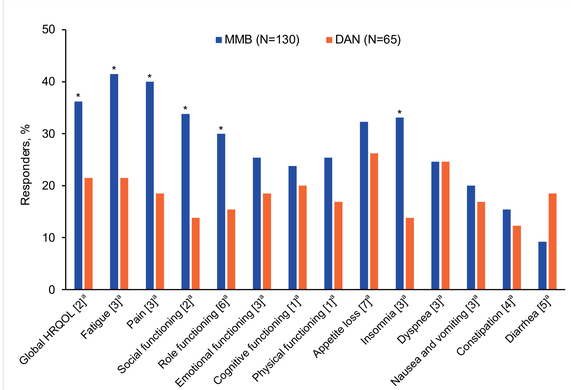
Figure 3. Momelotinib Demonstrated a Higher Proportion of TSS Responders and a Shorter Time to First Response Than Danazol



[a]Hazard ratio (MMB divided by DAN) is from stratified Cox proportional hazards model with a single factor of treatment group, stratified by baseline MFSAF TSS (≥22 vs <22), baseline palpable spleen length below the LCM (≥12 cm vs <12 cm) and baseline RBC units transfused in the 8-week period before randomization (0, 1-4, and 5+). [b]*P* value is from log-rank test stratified by baseline MFSAF TSS (≥22 vs <22), baseline palpable spleen length below the LCM (≥12 cm vs <12 cm), and baseline RBC units transfused in the 8-week period before randomization (0, 1-4, and 5+).
DAN, danazol; MFSAF, Myelofibrosis Symptom Assessment Form; LCM, lower costal margin; MMB, momelotinib; OR, odds ratio; RBC, red blood cell; TSS, total symptom score.

- The OR for achieving a minimum 50% MFSAF TSS response in the overall treatment period was 2.50 (95% CI, 1.24-5.06)
- Treatment responses were seen as early as week 8 for both momelotinib and danazol, although the treatment effect favored momelotinib at every time point from week 8 and thereafter

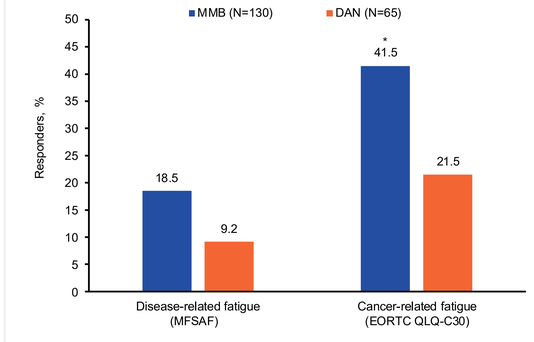
Figure 4. Most EORTC QLQ-C30 Scales Showed Greater Improvement in the Momelotinib Group Compared With Danazol



[a]MCT defined as > [1] 7-, [2] 8-, [3] 9-, [4] 10-, [5] 11-, [6] 12-, [7] 13-point improvement from baseline. †*P*<.05.
DAN, danazol; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – 30 items; HRQOL, health-related quality of life; MCT, meaningful change threshold; MMB, momelotinib.

- The proportion of patients that reported an improvement in pain, fatigue, social functioning, insomnia, and role functioning subscales were significantly higher for MMB compared with DAN (*P*<.05)

Figure 5. Proportion of Responders Were Higher in the Momelotinib Group for Fatigue



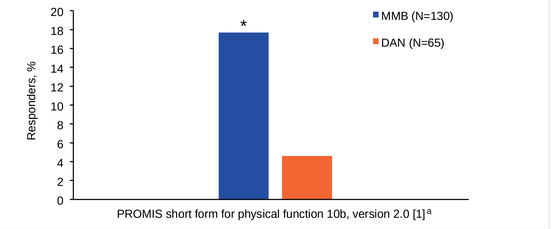
DAN, danazol; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – 30 items;; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib; MMRM, mixed model for repeated measures; RBC, red blood cell; TSS, total symptom score.

Table 1. Momelotinib Patients Showed Greater Improvement in Both Disease-related and Cancer-related Fatigue as Measured by MMRM Change from Baseline

Change from baseline at week 24	MMB (N=130)	DAN (N=65)
Disease-related fatigue by MFSAF		
Least squares mean (SE)[a]	-1.53 (0.20)	-0.82 (0.31)
Least squares mean difference (SE)[a]	-0.71 (0.36)	
95% CI[a]	-1.42, 0.00	
P value[b]	.0513	
Cancer-related fatigue by EORTC QLQ-C30		
Least squares mean (SE)[a]	-14.34 (2.35)	-3.52 (3.65)
Least squares mean difference (SE)[a]	-10.82 (4.21)	
95% CI[a]	-19.15, -2.48	
P value[b]	.0113	

[a]Based on MMRM bed for baseline MFSAF TSS (<22 vs ≥22), baseline palpable spleen length below the LCM (<12 cm vs ≥12 cm), and baseline RBC or whole blood units transfused in the 8-week period before randomization (0, 1-4, ≥5 units). [b]*P* value for the LS mean difference between the 2 groups from the MMRM.
DAN, danazol; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – 30 items; LCM, lower costal margin; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib; MMRM, mixed model for repeated measures; RBC, red blood cell; TSS, total symptom score.

Figure 6. A Greater Proportion of Patients Showed Improvement in Physical Function in the Momelotinib Group at Week 24



[a]MCT defined as > [1] 6-point improvement from baseline. *P<.05.
DAN, danazol; HR, hazard ratio; MCT, meaningful change threshold; MMB, momelotinib; PROMIS, Patient-Reported Outcomes Measurement Information System.

- This trend was supported by shorter times to first response for physical function in more patients in momelotinib compared with danazol (HR, 1.93; 95% CI, 0.95-3.91)

Conclusions

- Patients receiving momelotinib in the MOMENTUM study demonstrated greater and consistent improvement in symptoms compared with danazol, using responder analysis, longitudinal responder analysis, and time to event analyses
- Momelotinib showed significantly greater symptom and quality of life improvement compared with danazol at week 24 for fatigue, abdominal discomfort, night sweats, pain, physical function, social functioning, role functioning, insomnia, and global HRQOL as measured by MFSAF, EORTC QLQ-C30, and PROMIS questionnaires
- Consistent with the primary end point of MOMENTUM, the higher magnitude of response and faster response demonstrate that momelotinib provides progressive and durable symptom benefit (also shown in MOMENTUM week 48 oral presentation 627)

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Further analyses on momelotinib from the MOMENTUM study can be accessed in oral presentation **627** (MOMENTUM week 48 results) and poster presentation **3028** (transfusion independence and overall survival response).

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