

LE CURE PALLIATIVE PRECOCI IN
EMATO-ONCOLOGIA:

la nuova risposta ai bisogni di pazienti e caregivers

19 maggio 2023

Roma, Hotel Donna Camilla Savelli

Novità nella gestione di patologie
oncoematologiche: nuovi approcci e qualità di vita.
Neoplasie mieloproliferative croniche

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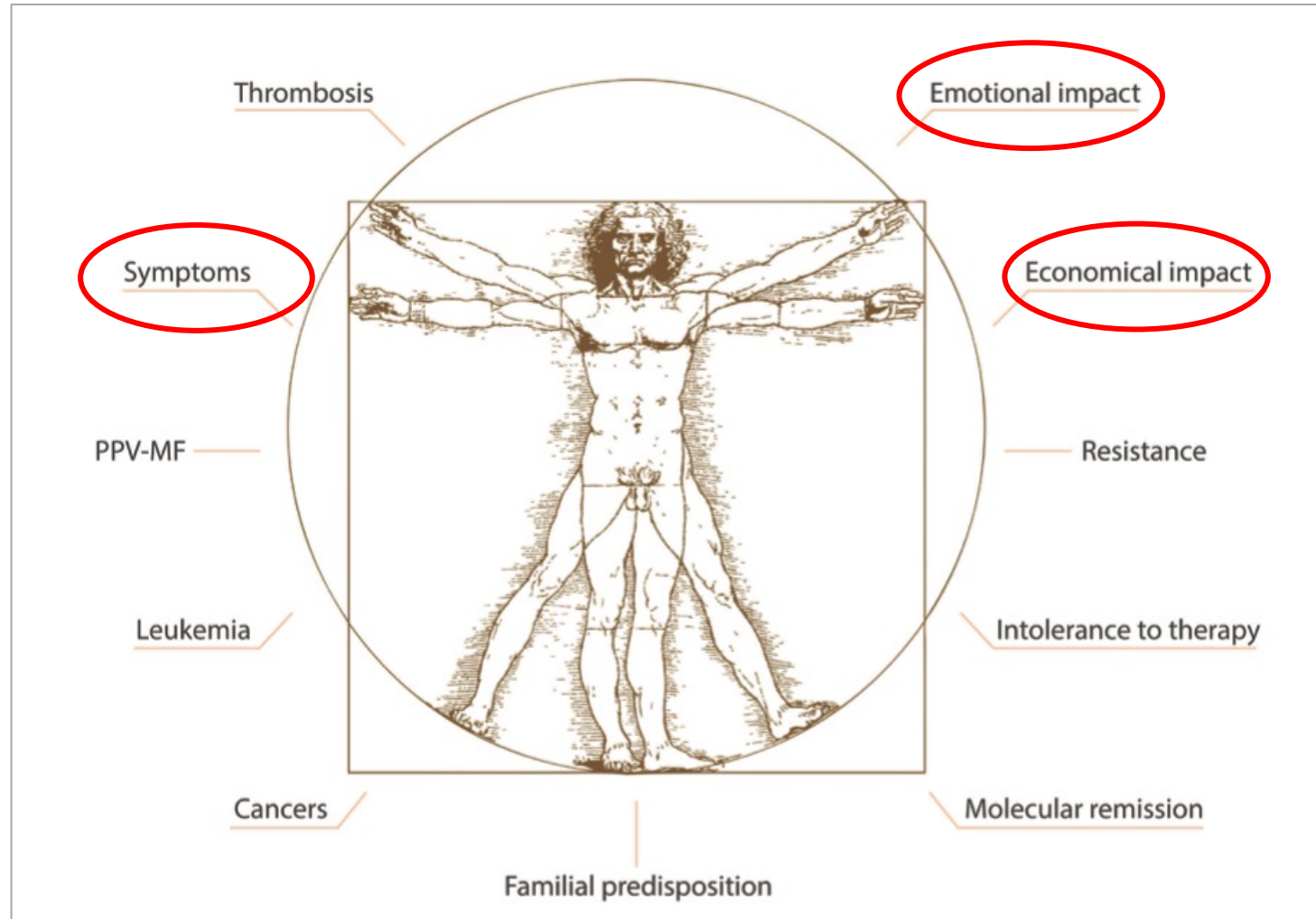


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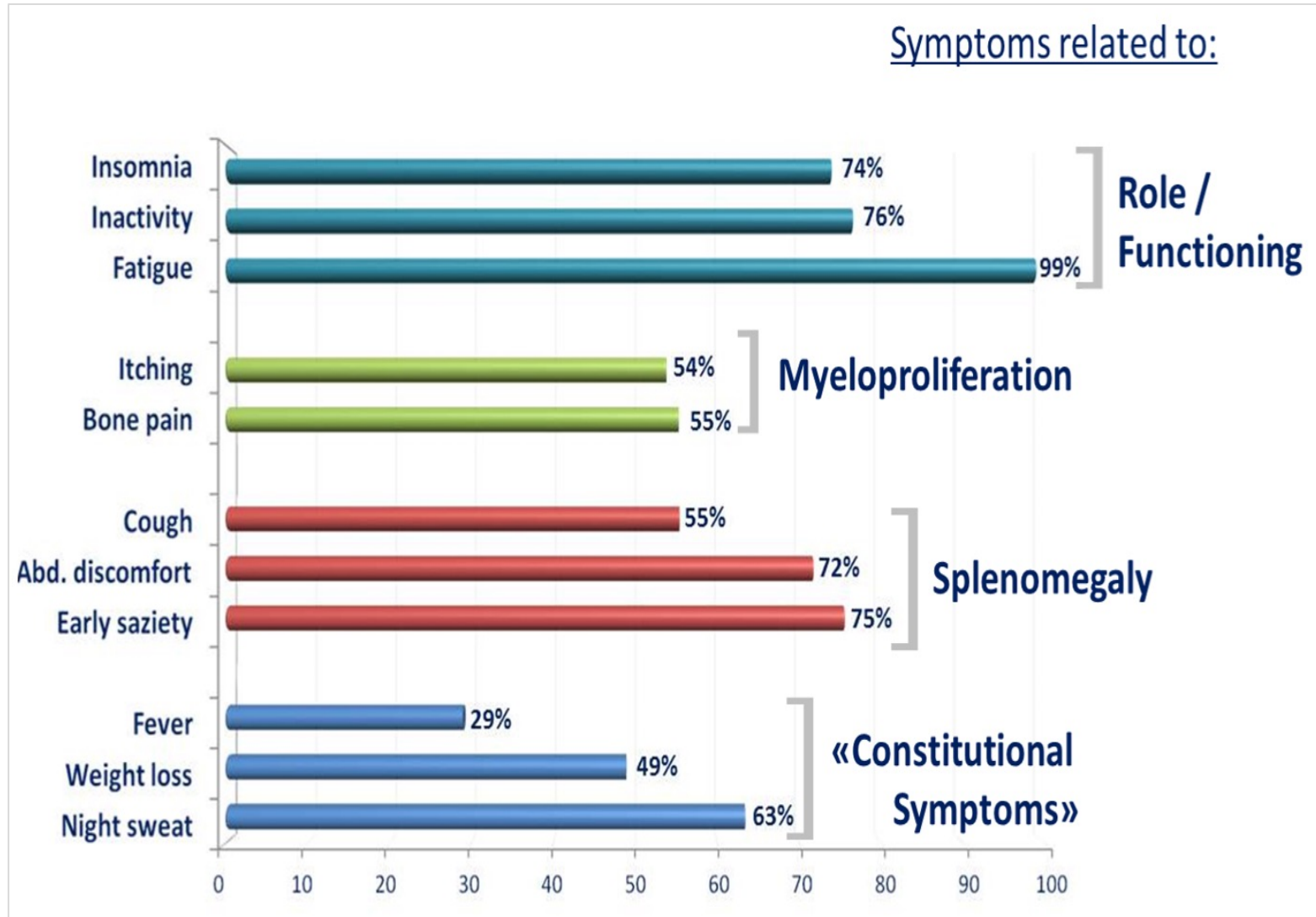
Disclosures - Alessandro M. Vannucchi

- **Novartis:** Advisory board. Speaker bureau.
- **Incyte:** Advisory board. Speaker bureau.
- **AbbVie:** Advisory board.
- **AOP:** Advisory board. Speaker bureau.
- **BMS:** Advisory board. Speaker bureau.
- **CTI:** Speaker bureau.
- **Blueprint:** Advisory board. Speaker bureau.
- **GSK:** Advisory board. Speaker bureau.

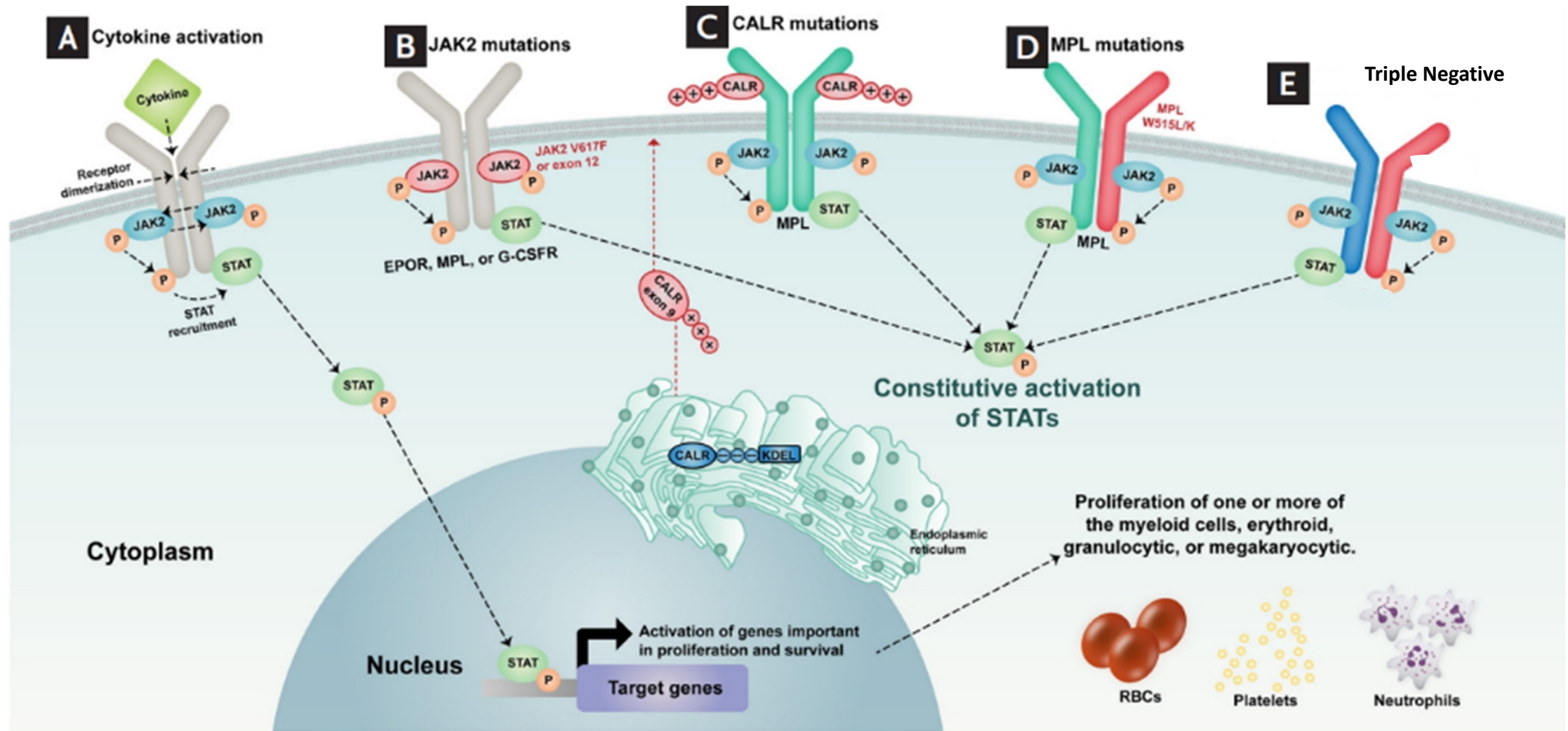
Realizing and Resolving the Intrinsic Complexity of an MPN Patient



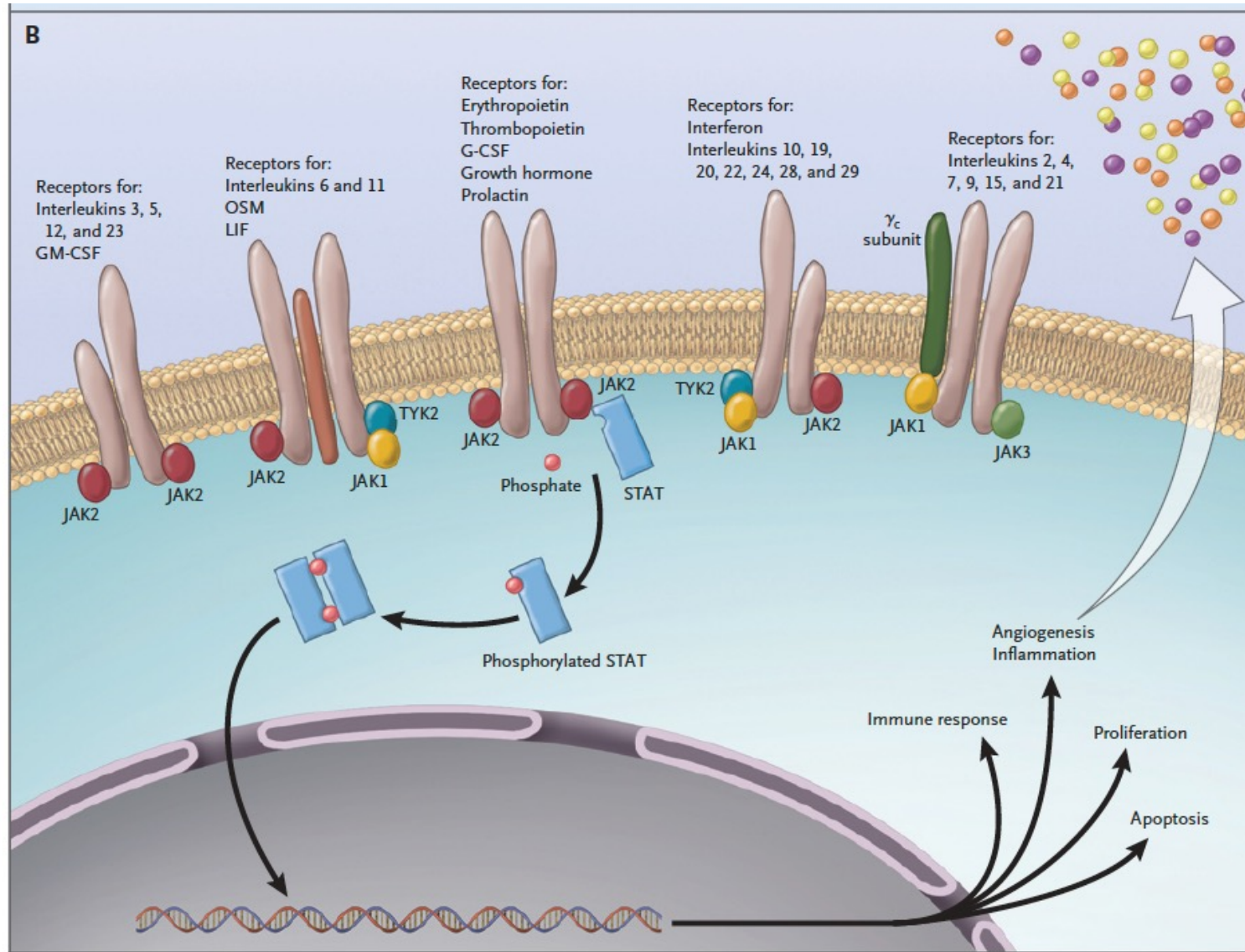
Understanding Symptoms in MPN Patients



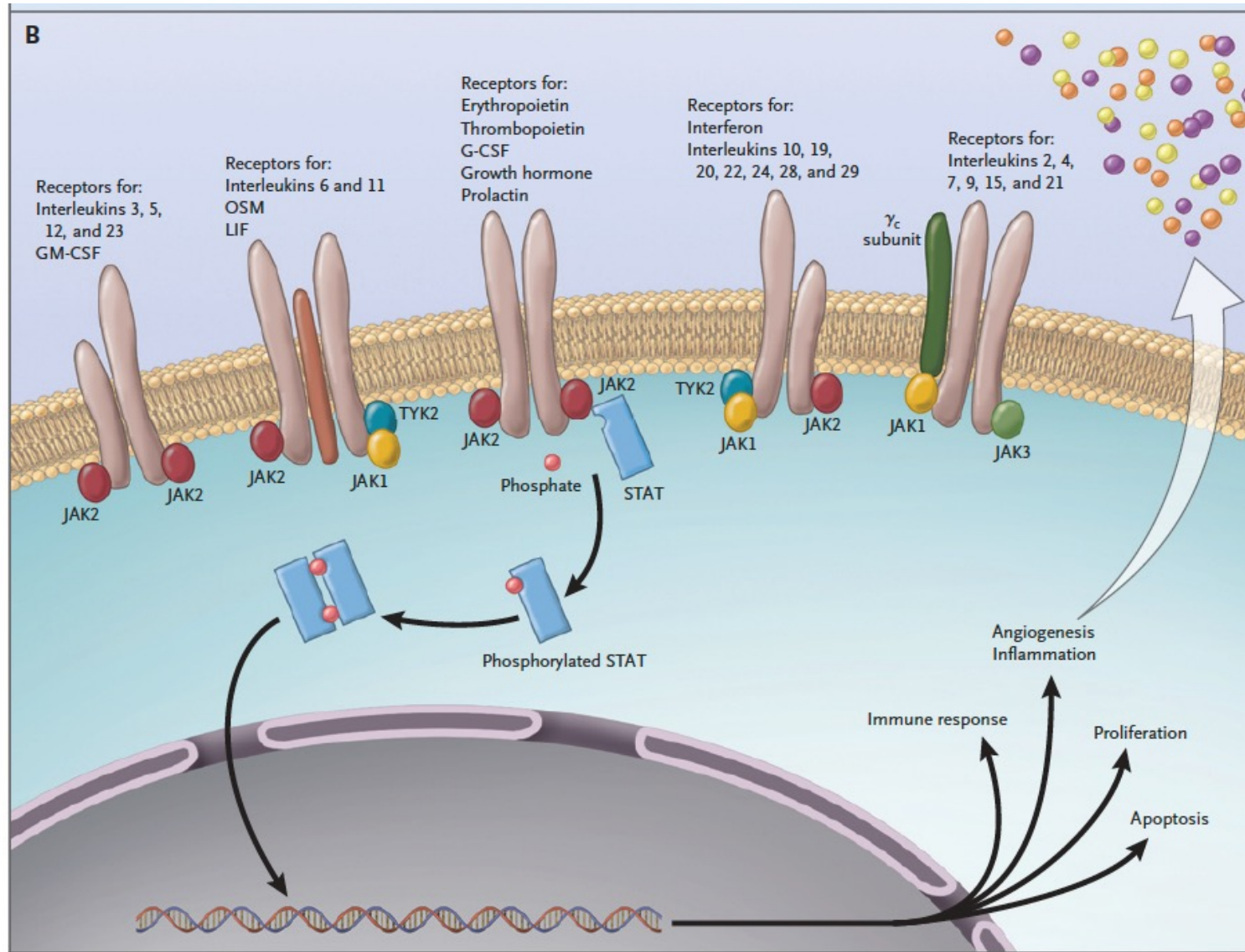
Unifying Molecular Mechanism: JAK/STAT Pathway Activation



JAK/STAT Pathway Activation and Inflammation, Unifying Processes

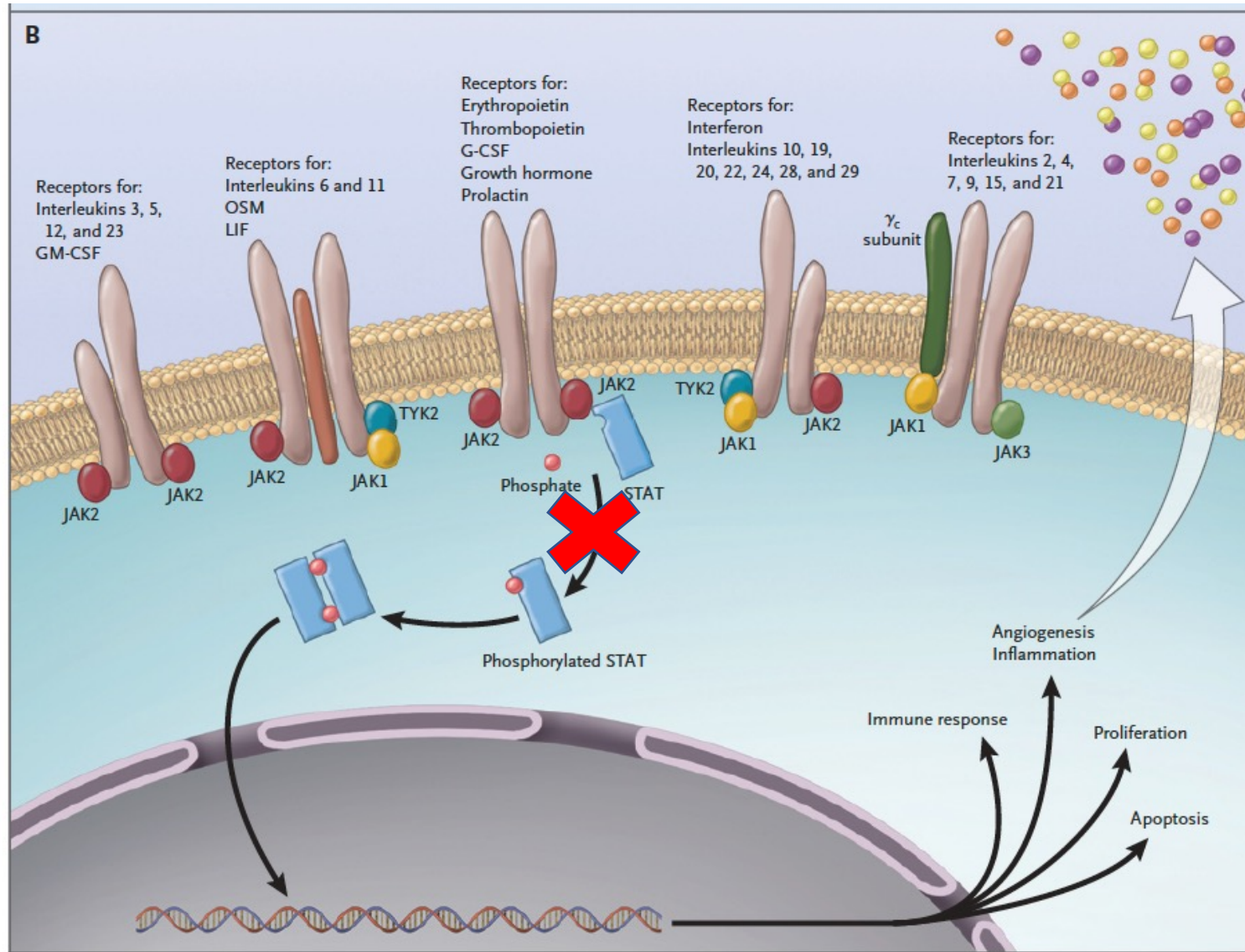


JAK/STAT Pathway Activation and Inflammation, Unifying Processes



- MPN-associated symptoms
- Complications
- Pathogenesis of fibrosis
- Clonal expansion
- Clonal progression
- Response to treatment

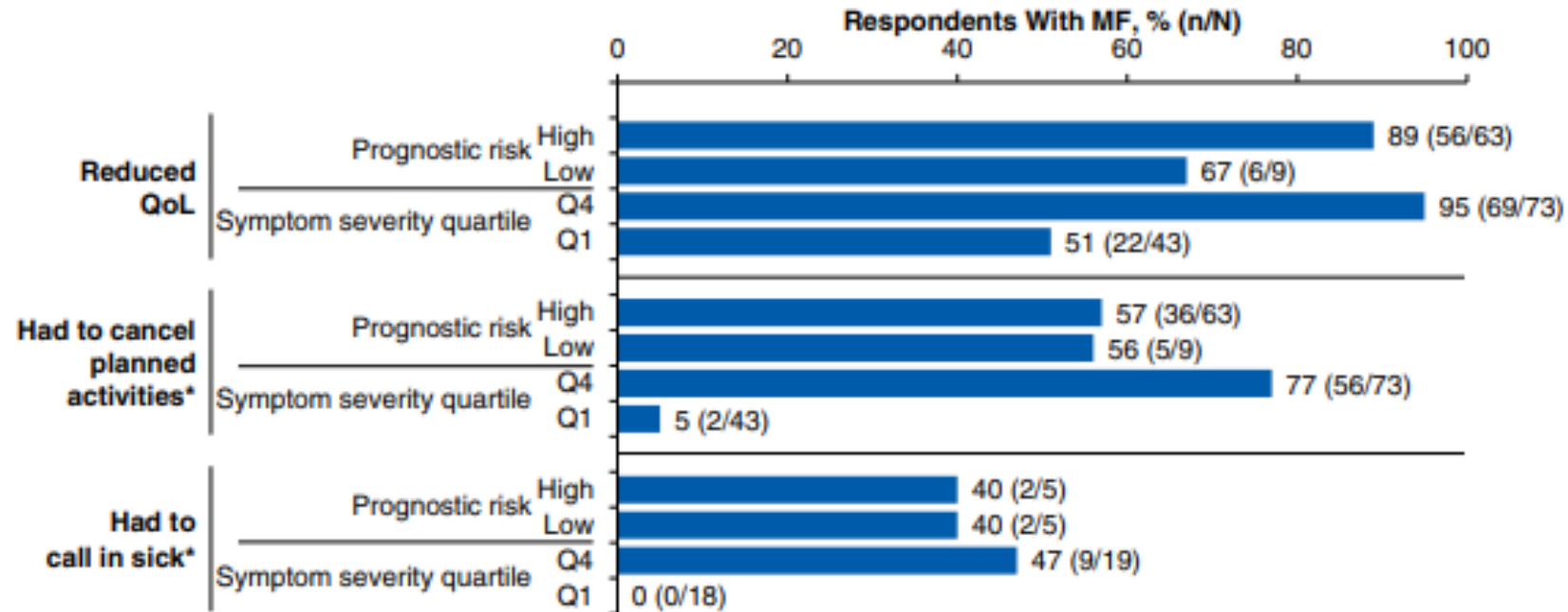
JAK/STAT Pathway Activation and Inflammation, Unifying Processes...



THEN.....

- MPN-associated symptoms
- Complications
- Pathologic fibrosis
- Clonal evolution
- Clonal progression
- Response to treatment

The MPN Landmark survey: MPN symptoms have a significant impact on patients' overall health and productivity

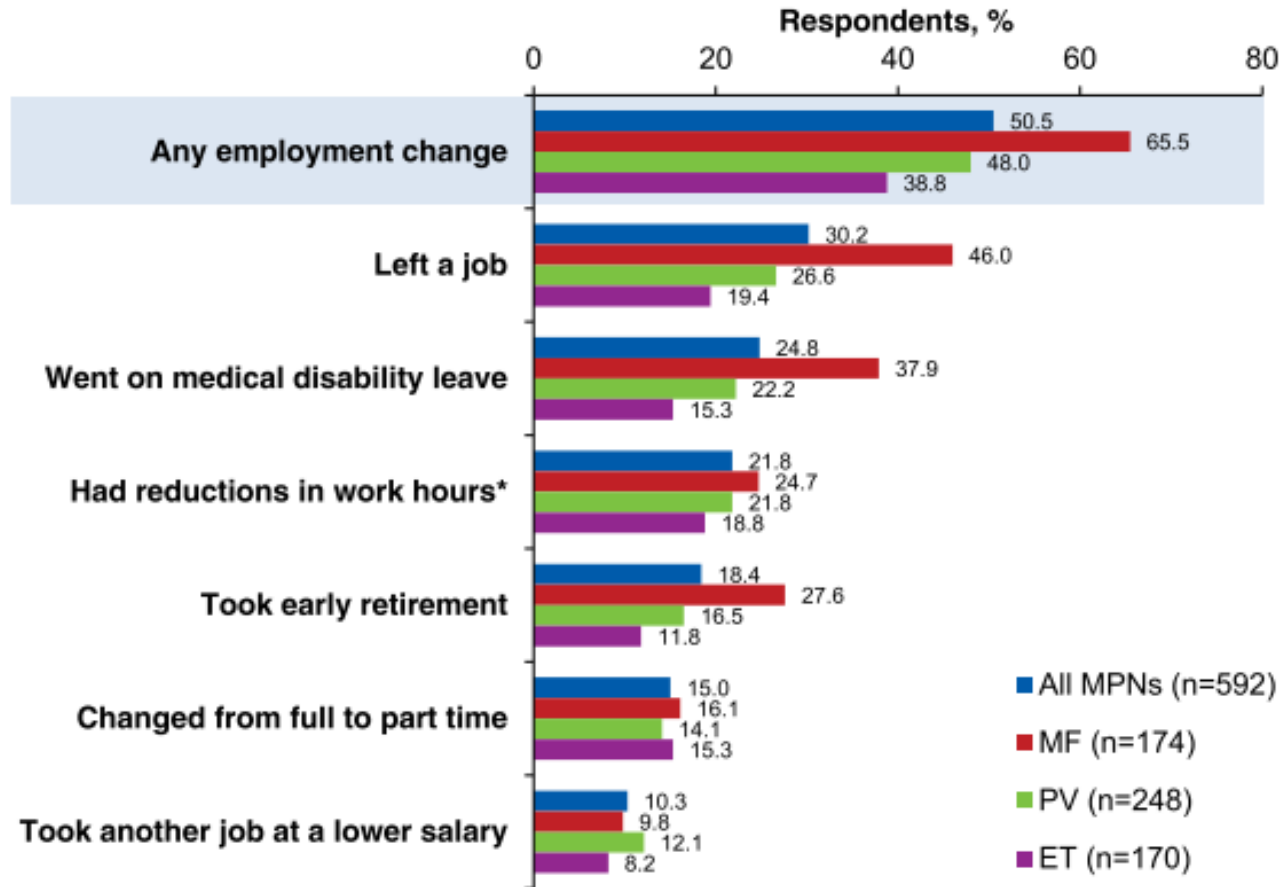


813 MPN patients: ET 226, PV 380, MF 207.

Among MF patients:

- 51% experienced MPN-related symptoms ≥ 1 year before diagnosis .
- 67% had **reduced QoL**.
- Many had to cancel planned activities or call in sick .

The Living with MPNs survey: Impact of MPN on patients' employment status and work productivity



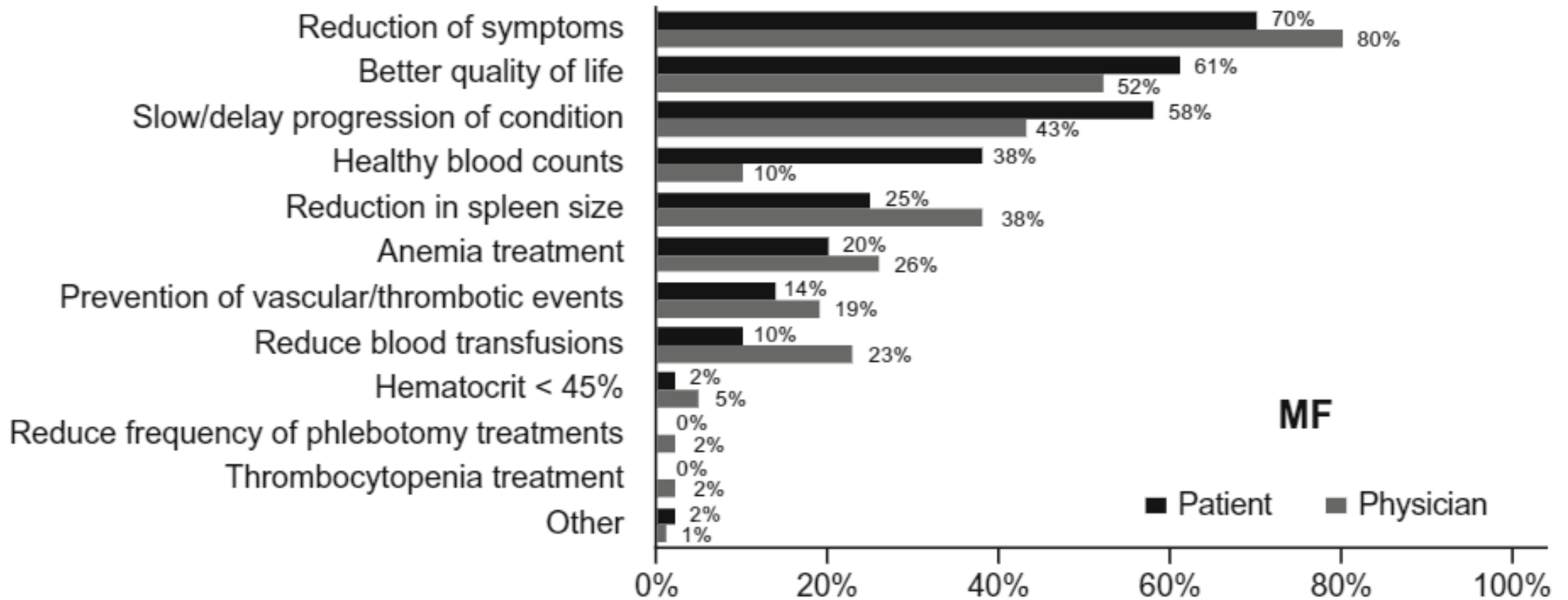
592 employed MPN patients: ET 170, PV 248, MF 174.

Half of the employed experienced an employment status change.

Currently employed reported meaningful impairments in work productivity and activities of daily living that were attributable to their MPNs.

The degree of work impairments correlated with the severity of symptom burden.

Treatment Goals: Patients vs Physicians View



HOW to track symptoms in MF?

Patient-Reported Outcome (PRO) tools

MF-SAF

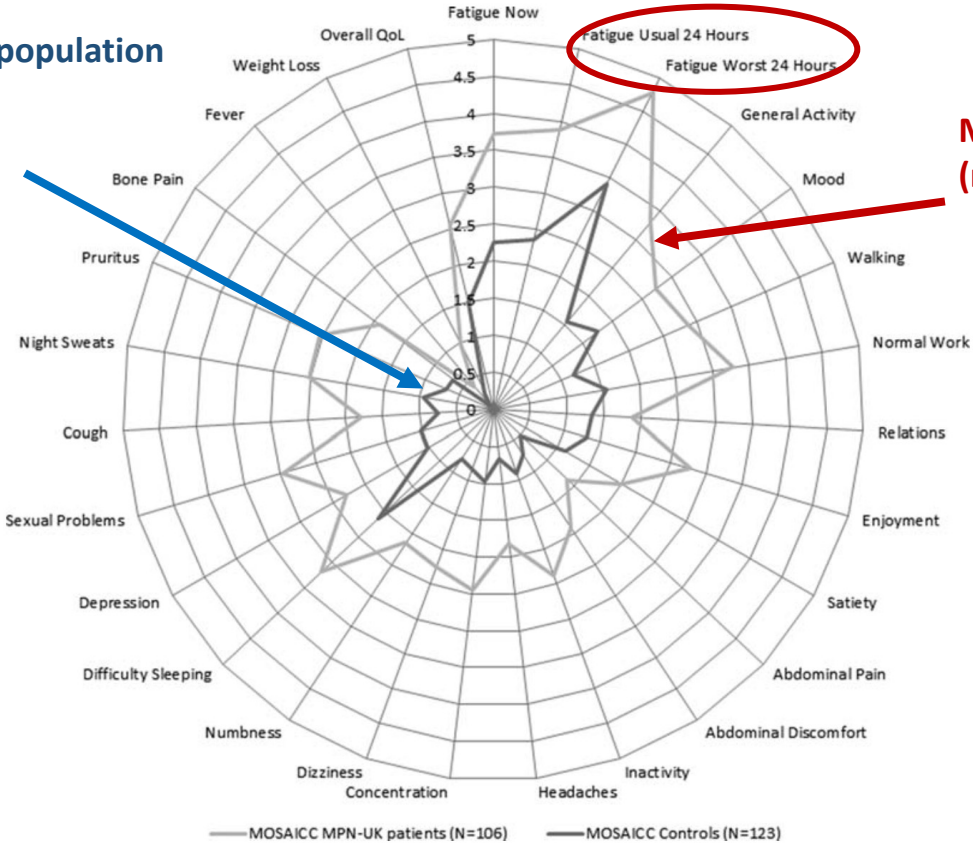
MPN-SAF

MPN-SAF-TSS

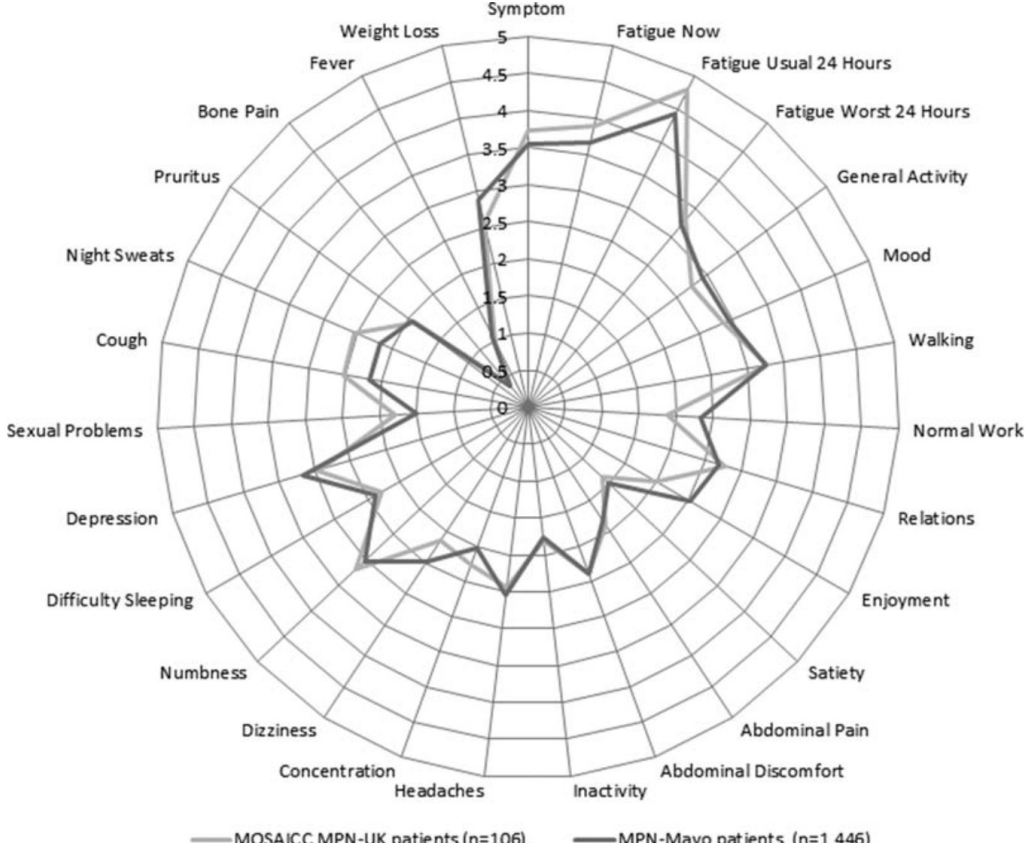
EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core)
BFI (Brief Fatigue Inventory)
FACT-An (Functional Assessment of Cancer Therapy-Anemia)
Godin LAS (Leisure Time Activity Score)

MOSAICC, UK case-control study: the MPN-SAF was administered to MPN patients (n=106) and population controls (n=124) and mean symptom scores were compared adjusting for potential confounders.

General population controls (n=124)



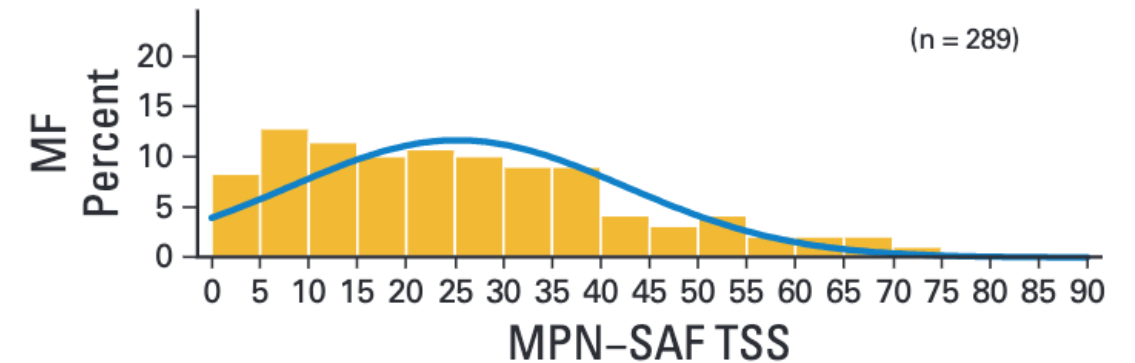
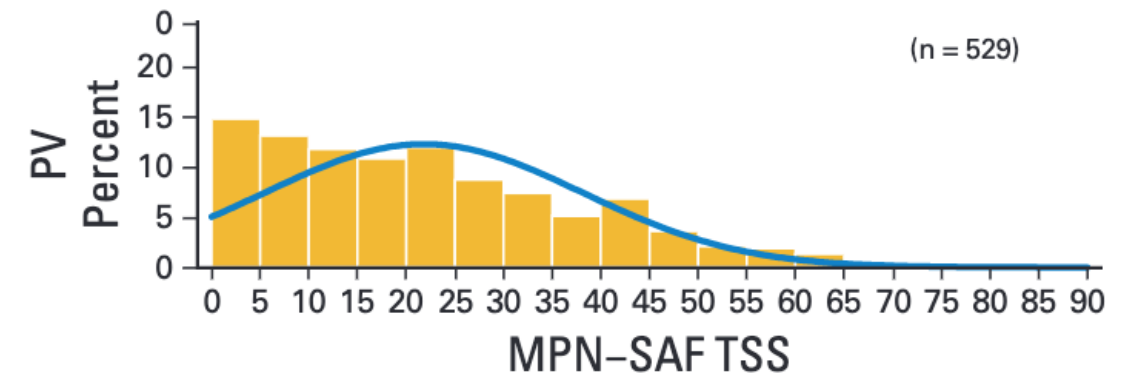
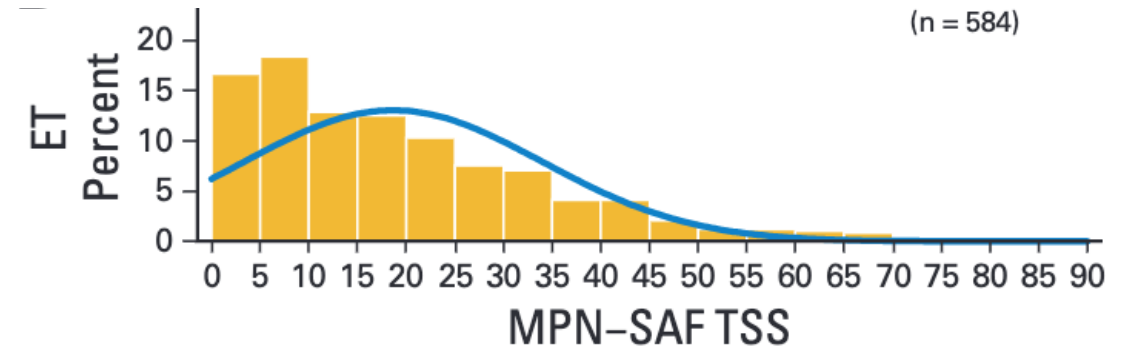
MPN patients (n=106)



MPN-SAF TSS/MPN-10

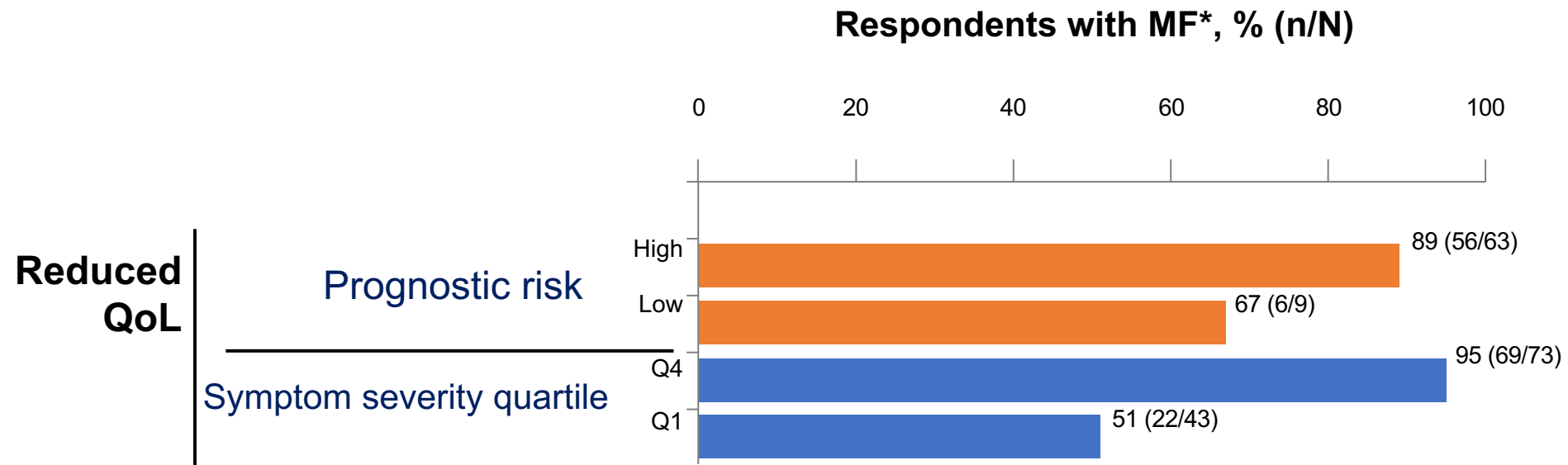
MPN-SAF TSS significantly differed among MPNs:

- Mean TSS 18.7 (SD, 15.3) for ET
- Mean TSS 21.8 (SD, 16.3) for PV
- Mean TSS 25.3 (SD, 17.2) for MF



IPSS low/Int-1-risk Patients May have Symptoms that Impact Their Quality of Life

- 44% of DIPSS lower-risk patients may be symptomatic
- A **single MPN10 symptom score > 5, or total score of >10** have been suggested as predictive for patients who could benefit from treatment



* , respondents to the *MPN Landmark Survey*. MF=207.



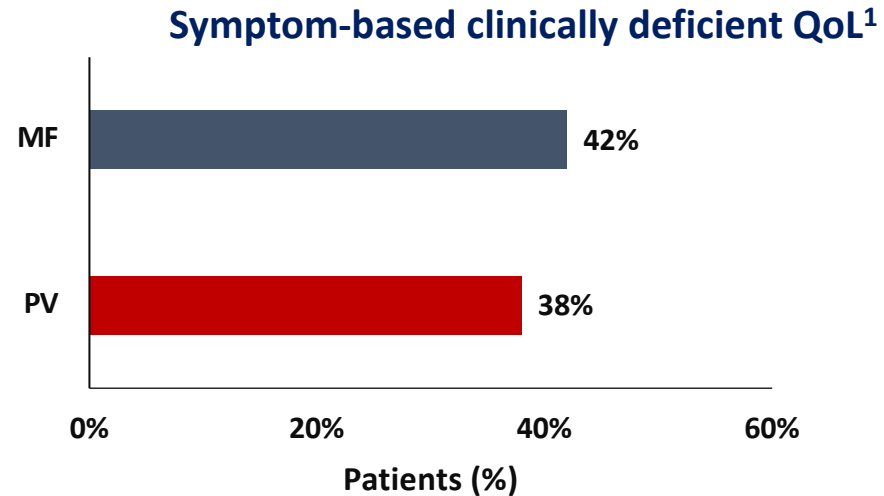
ASSESSMENT OF SYMPTOM BURDEN

- Assessment of symptoms (in provider's office) at baseline and monitoring symptom status (stable, improved, or worsening) during the course of treatment is recommended for all patients.
- **Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS; MPN-10) is recommended for the assessment of symptom burden at baseline and monitoring symptom status during the course of treatment ([See MPN-E, 2 of 2](#)).**
- MPN-SAF TSS is assessed by the patients themselves. Scoring is from 0 (absent/as good as it can be) to 10 (worst imaginable/as bad as it can be) for each item. The MPN-SAF TSS is the summation of all the individual scores (0–100 scale).
- Symptom response requires $\geq 50\%$ reduction in the MPN-SAF TSS. A symptom response $< 50\%$ may be clinically meaningful and justify continued use of ruxolitinib.
- Changes in symptom status could be a sign of disease progression. Therefore, change in symptom status should prompt evaluation of treatment efficacy and/or disease status.

Symptoms in PV May Be Severe

- Not only are symptoms prevalent in PV, but their severity at diagnosis is as high and as deleterious on quality of life as in primary MF^{1,2}

Symptoms result in poor quality of life (QoL) in nearly as many patients with PV as in MF¹

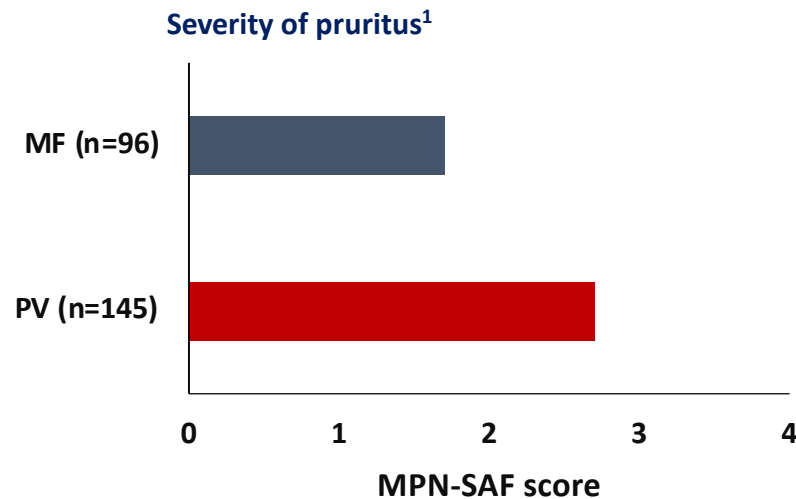


- Symptoms and complications have been associated with declines in physical, functional, and overall health status using a variety of QoL assessment tools (MPN-SAF, EORTC QLQ-C30, BFI, FACT-An, Godin LAS)¹⁻³

MPN-SAF=Myeloproliferative Neoplasm Symptom Assessment Form; EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; BFI=Brief Fatigue Inventory; FACT-An=Functional Assessment of Cancer Therapy-Anemia; Godin LAS=Godin Leisure Time Activity Score.

Pruritus and Fatigue are Among the Most Common and Severe Symptoms of PV

- 65% of patients with PV experience aquagenic pruritus^{1,2}



15% characterize pruritus as 'unbearable' (rating of 6 on a scale of 6)²

94% of pruritus cases are unresolved with traditional PV therapy²

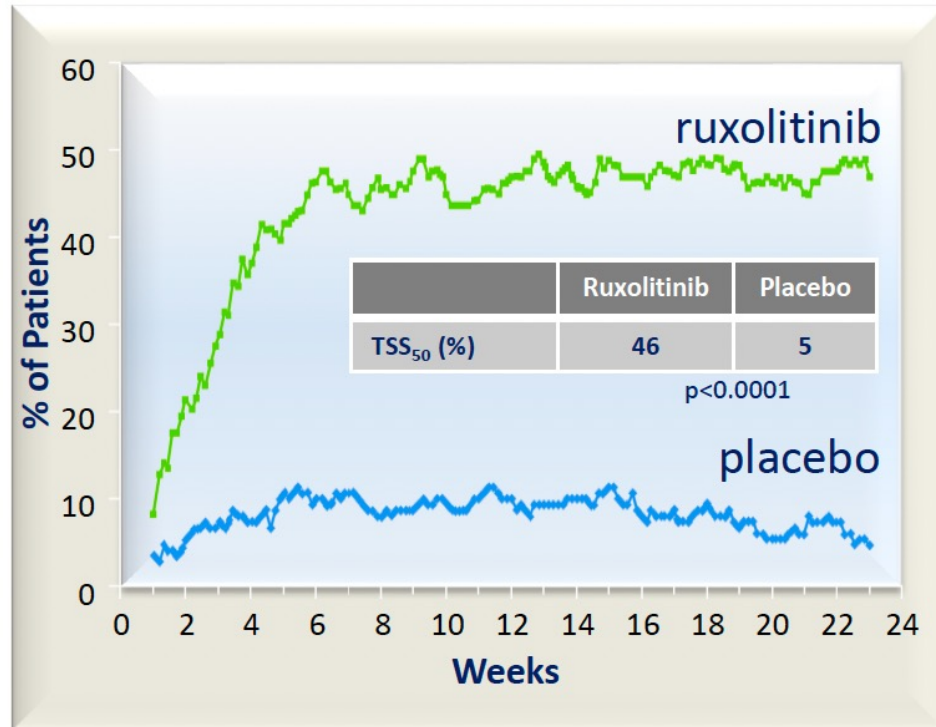
- **Pruritus** interferes with daily activities and has been associated with suicidal ideation³
- **Fatigue** is the most prevalent symptom associated with PV, affecting approximately 85% of patients⁴
- Fatigue was reported regardless of disease severity, occurring in patients who lacked complications of PV, such as thrombosis or splenomegaly⁴

MPN PRO Tools in Clinical Trials

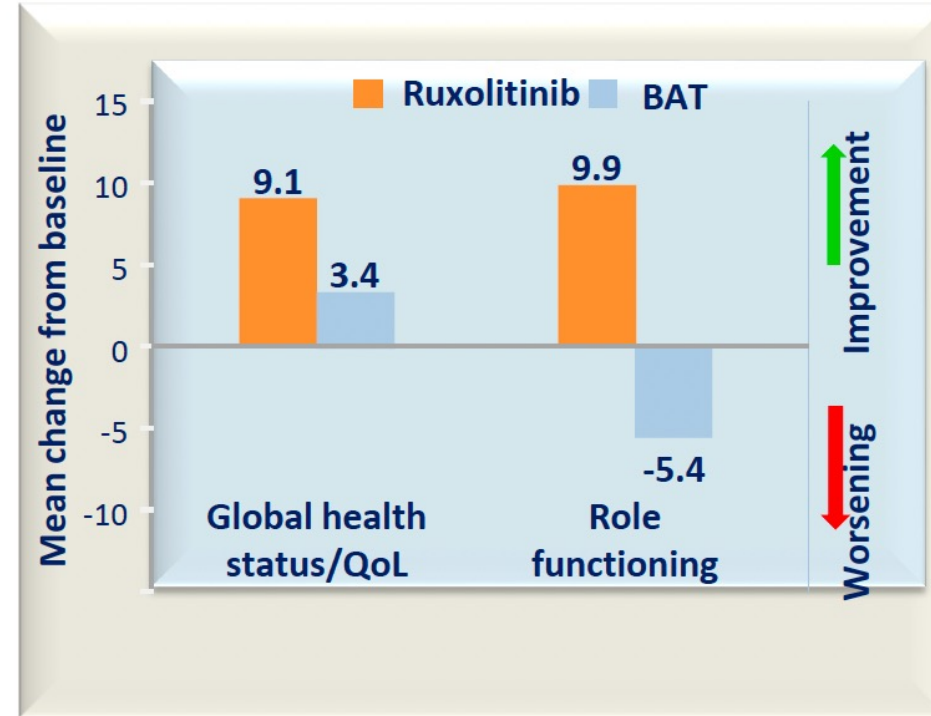
Disease	Drug (Clinical Trial)	MPN PRO Tool
MF	Ruxolitinib (COMFORT-1)	MF-SAF 2.0
MF	Ruxolitinib (COMFORT-2)	FACT-LYM
MF	Fedratinib (JAKARTA)	MF-SAF
MF	Pacritinib (PERSIST1&2)	MPN-SAF
MF	Momelotinib (SIMPLIFY 1&2)	MPN-SAF
MF	Pomalidomide (RESUME)	FACT-An
MF	Ruxolitinib (RETHINK)	MPN-10
PV	Ruxolitinib (RESPONSE)	MPN-SAF
PV	Ruxolitinib (RELIEF)	MPN-SAF
PV	Peg-IFN-a-2° (MPD-RC 112)	MPN-SAF
ET	Ruxolitinib (MAJIC)	MPN-SAF

COMFORT-I and II trials: impact on symptoms and QoL

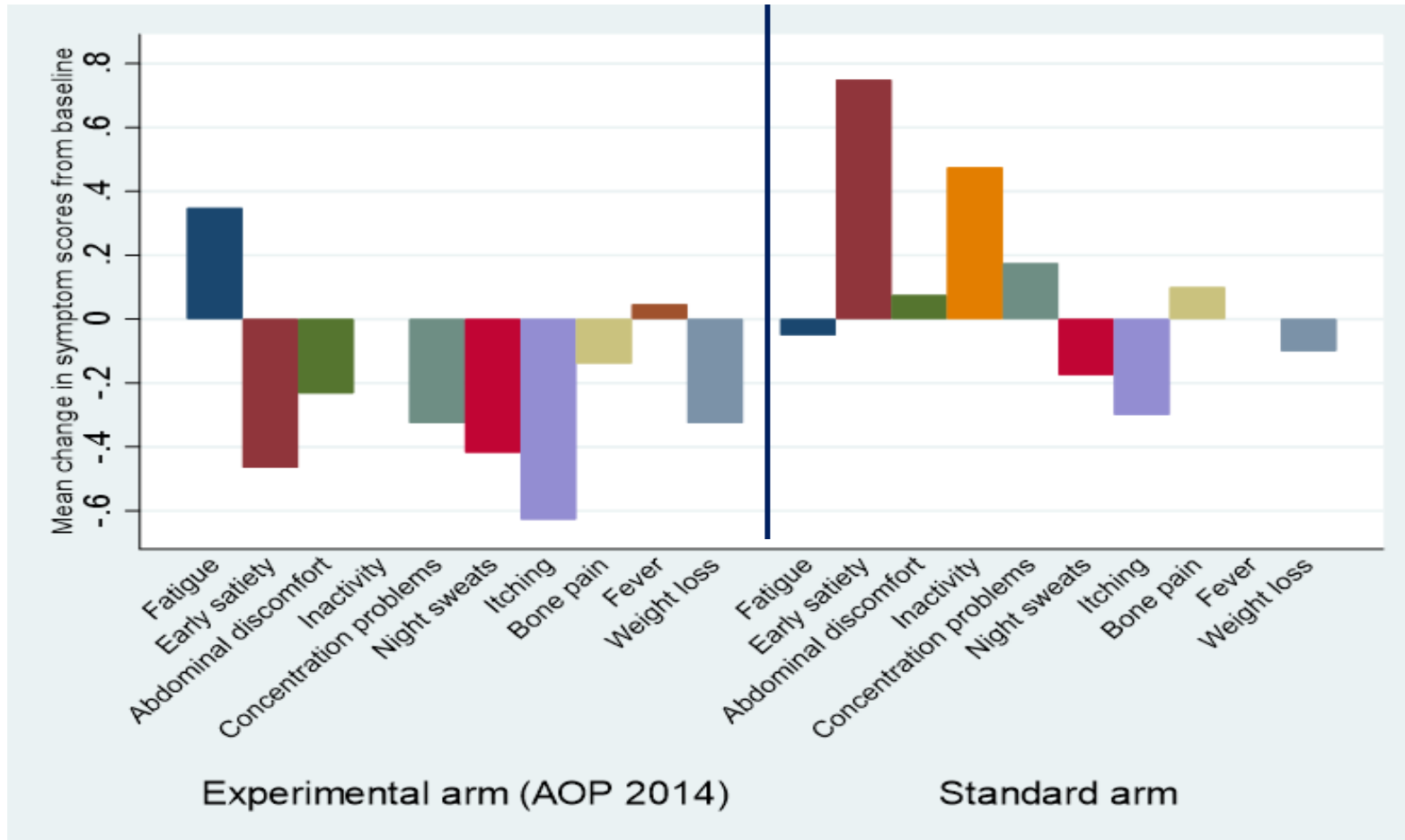
COMFORT-I



COMFORT-II



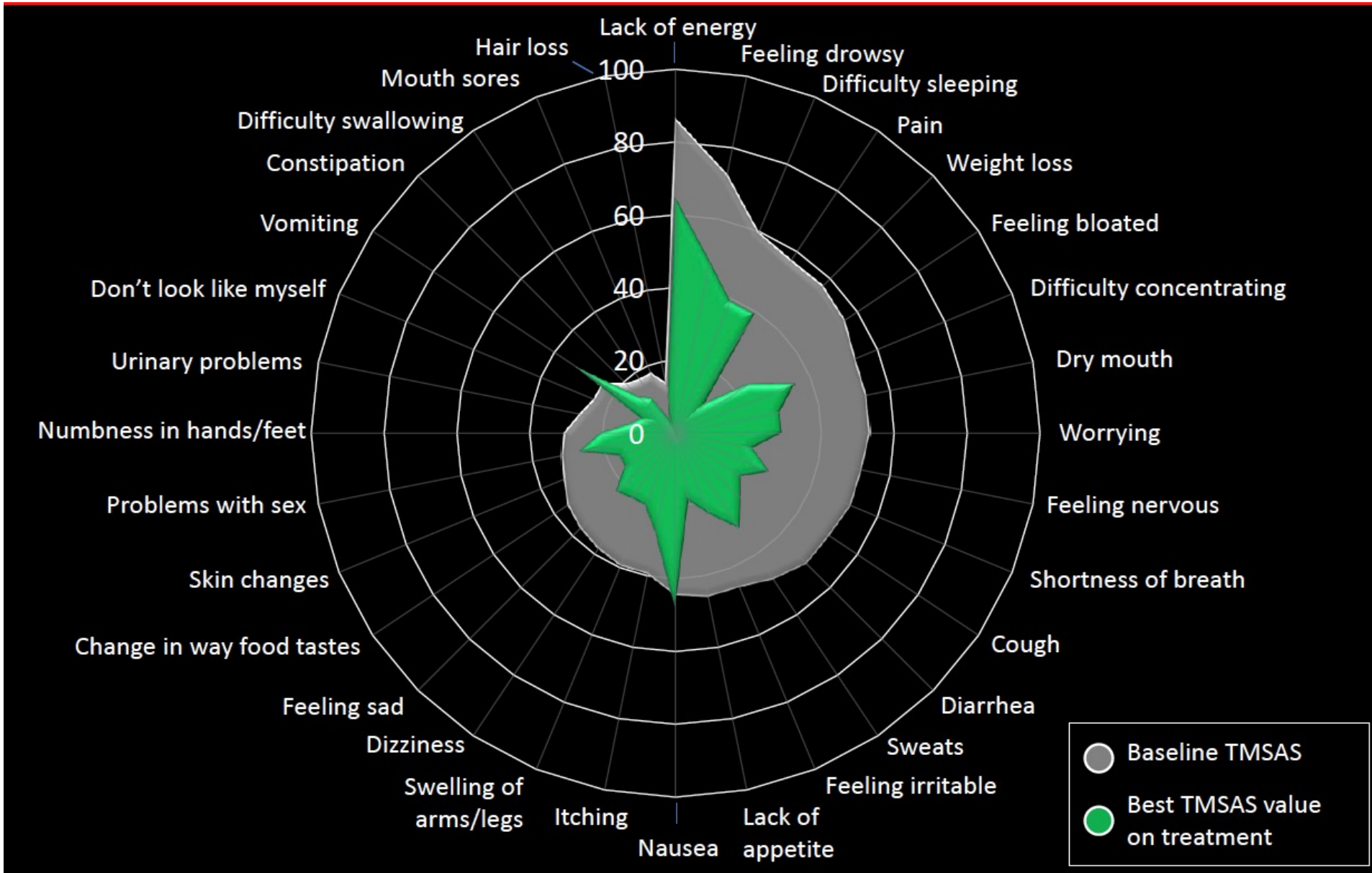
Low-PV Trial – Interim analysis (2)



Mean change
 $p=0.033$
EXP STD
-21% +10%

Negative values indicate a reduction in the severity of symptoms

Effect of Midostaurin on Symptomatic Burden in Systemic Mastocytosis



Conclusions

- MPNs can deeply affect patients' lives **independently of traditional risk** classification.
- Symptoms represent a **strong and common component**.
- Symptoms are **heterogeneous and variable** across MPN subtype.
- MPN-related **symptoms** are multifactorial, closely **linked to the biology** of the disease (inflammation), and they may change with progression.
- **Serial tracking** of symptoms with **validated** and **dedicated tools** is relevant both in clinical trials and in the real-world setting, to appropriately select and manage currently available MPN therapies.
- New drugs have significant impact on symptomatic improvement and overall QoL, that are **endpoint efficacy criteria** included in any novel clinical trial potentially leading to approval
- **Non pharmacological complimentary approaches** are also being evaluated and may have a role, alongside medicines or transplant.