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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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



Leonardo da Vinci (1490). L'uomo Vetruviano. Picture from Vannucchi AM, Haematologica, 2017; 102:18-27

Understanding Symptoms in MPN Patients



Mesa R et al, Cancer 2007; 109:68-71. Scherber R et al, Blood 2011; 118:401-8. Geyer H et al, Blood 2014 123:3803-3810. Verstovsek S, NEJM 2010; 363:1117-27

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

Focusing on MPN-Associated Inflammation





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



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

Reduction of symptoms Better quality of life Slow/delay progression of condition Healthy blood counts Reduction in spleen size Anemia treatment Prevention of vascular/thrombotic events Reduce blood transfusions 2% Hematocrit < 45%0% 2% Reduce frequency of phlebotomy treatments 0% Thrombocytopenia treatment 2% 2% Other 1%



HOW to track symptoms in MF?



JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Myeloproliferative Neoplasm (MPN) Symptom Assessment Form Total Symptom Score: Prospective International Assessment of an Abbreviated Symptom Burden Scoring System Among Patients With MPNs

Robyn M. Emanuel, Amylou C. Dueck, Holly L. Geyer, Jean-Jacques Kiladjian, Stefanie Slot, Sonja Zweegman, Peter A.W. te Boekhorst, Suzan Commandeur, Harry C. Schouten, Federico Sackmann, Ana Kerguelen Fuentes, Dolores Hernández-Maraver, Heike L. Pahl, Martin Griesshammer, Frank Stegelmann, Konstanze Doehner, Thomas Lehmann, Karin Bonatz, Andreas Reiter, Francoise Boyer, Gabriel Etienne, Jean-Christophe Ianotto, Dana Ranta, Lydia Roy, Jean-Yves Cahn, Claire N. Harrison, Deepti Radia, Pablo Muxi, Norman Maldonado, Carlos Besses, Francisco Cervantes, Peter L. Johansson, Tiziano Barbui, Giovanni Barosi, Alessandro M. Vannucchi, Francesco Passamonti, Bjorn Andreasson, Maria L. Ferarri, Alessandro Rambaldi, Jan Samuelsson, Gunnar Birgegard, Ayalew Tefferi, and Ruben A. Mesa

MPN10 Total Symptom Score [MPN-SAF]

• Inflammation

Splenomegaly

Anemia

Fatigue Early satiety Abdominal discomfort Inactivity Problems with concentration Night sweats Itching Bone Pain Fever Unintentional weight loss last 6 months

MPN10 score

 Value	Prog
0	1 to 1 favora
0	(Abse

0

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.



Anderson LA et al. Am J Hematol, 2015

MPN-SAF TSS/MPN-10



- 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 with MF*, % (n/N)

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

Mesa R, et al. BMC Cancer. 2016;16:167.

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021 Myeloproliferative Neoplasms

NCCN Guidelines Index Table of Contents Discussion

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 ≥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 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.

1. Emanuel RM, et al. J Clin Oncol. 2012;30:4098-4103. 2. Scherber R, et al. Blood. 2011;118:401-408. 3. Mesa RA, et al. Cancer. 2007;109:68-76.

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





- 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

1. Scherber R, et al. Blood. 2011;118:401-408. 2. Siegel FP, et al. Am J Hematol. 2013;88:665-669. 3. Mesa RA. Blood. 2009;113:5697-5698. 4. Mesa RA, et al. Cancer. 2007;109:68-76.

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)



Effect of Midostaurin on Symptomatic Burden in Systemic Mastocytosis



Gotlib J et al, NEJM 2016;374:2530-41

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.