VOL 1 | ISSUE 1

Myeloproliferative Neoplasms™

UPDATE

Conversations with Oncology Investigators

Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

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ABIM CME MOC ACCREDITED

CME Certified

Myeloproliferative Neoplasms Update
A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Myeloproliferative neoplasms (MPNs) largely consist of 3 disease entities, all heralding from clonal disorders in which an initial molecular event results in excessive production of blood cells. Importantly, although essential thrombocythemia (ET), polycythemia vera (PV) and myelofibrosis (MF) are clinically distinguishable based on laboratory and molecular parameters, they may represent a disease continuum whereby transformation from ET or PV to the more aggressive MF results in a homogenous pathologic entity with a similarly poor prognosis. In contrast to the rather indolent natural history of untransformed ET and PV, primary MF or post-PV/ET MF is a debilitating disease. Historically no FDA-approved therapy existed, but after the FDA approval of ruxolitinib in 2011 for intermediate- and high-risk MF, including primary MF, post-PV MF and post-ET MF, this agent has rapidly been adopted in clinical practice. Patient selection and dosing of ruxolitinib remain relevant topics of discussion and debate. Not surprisingly, JAK inhibitors have been and continue to be critically evaluated for patients with both PV and ET. Most notably, in December 2014, the US FDA approved ruxolitinib as treatment for patients with PV who have experienced an inadequate response to or are intolerant of hydroxyurea.

To bridge the gap between research and patient care, this issue of *Myeloproliferative Neoplasms Update* features one-on-one discussions with leading hematology-oncology investigators. Upon completion of this CME activity, medical oncologists and hematologists should be able to formulate an up-to-date and more complete approach to the care of patients with MPNs.

LEARNING OBJECTIVES

- Use an understanding of disease biology and natural history to diagnose primary PV, ET and MF and communicate prognosis to patients.
- Consider the evidence-based therapeutic options for patients with PV, ET and MF, and develop clinical algorithms intended to enhance quality and quantity of life for patients with these distinct yet related diseases.
- Appraise the role of ruxolitinib in patients with MF and thrombocytopenia, anemia and compromised renal function.
- Appreciate emerging research data with the use of novel JAK inhibitors in the care of patients with MF, and prepare for their potential availability in clinical practice.
- Recognize the benefits of ongoing clinical trials for patients with MPNs, and inform appropriately selected patients about these options for treatment.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: **Prof Harrison** — Advisory Committee: Celgene Corporation, Gilead Sciences Inc, Novartis, Sanofi Genzyme; Contracted Research: Celgene Corporation, Gilead Sciences Inc, Incyte Corporation, Janssen Biotech Inc, Novartis; Speakers Bureau: Gilead Sciences Inc, Incyte Corporation, Novartis, Sanofi Genzyme. **Dr Verstovsek** — Contracted Research: AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology, Lilly, Pfizer Inc, Roche Laboratories Inc.

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Interview with Professor Claire N Harrison, MD

Tracks 1-17

Interview with Srdan Verstovsek, MD, PhD

Tracks 1-19

Interview with Dr Verstovsek (continued)

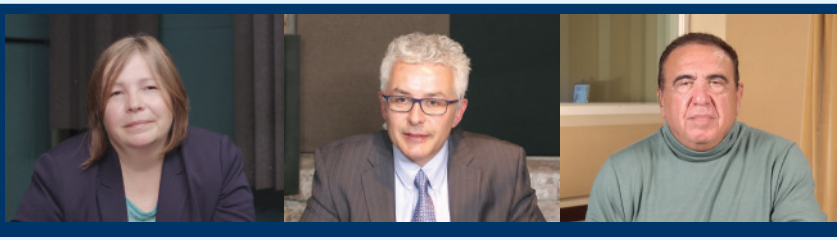
Track 17 Natural disease course of MF and progression to acute myeloid leukemia

Track 18 Novel treatment approaches under investigation for MF

Track 19 Mechanism of action and activity of the telomerase inhibitor imetelstat in patients with MF and ET

Video Program

View highlights from the corresponding video interviews with (from left) Prof Harrison and Dr Verstovsek by Dr Love at www.ResearchToPractice.com/MPNUpdate117/Video.



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Submit them to us via Facebook or Twitter and we will do our best to get them answered for you

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Ruxolitinib is FDA approved for which of the following indications?**
   a. For the treatment of intermediate- and high-risk MF, including primary MF, post-PV MF and post-ET MF
   b. As treatment for patients with PV who have experienced an inadequate response to or are intolerant of hydroxyurea
   c. Both a and b
   d. Neither a nor b

2. **In the treatment of MF, JAK2 inhibition with ruxolitinib has shown to be beneficial for _____.**
   a. Patients with JAK2 mutations
   b. Patients without JAK2 mutations
   c. Both a and b
   d. Neither a nor b

3. **Data reported from the Phase III JAKARTA-1 study evaluating the novel JAK inhibitor fedratinib versus placebo for primary or secondary MF demonstrated fedratinib to be effective in reducing splenomegaly and symptom burden. However, clinical development of the agent was discontinued because of incidences of _____ on the trial.**
   a. Hand-foot syndrome
   b. Encephalopathy
   c. Peripheral neuropathy
   d. All of the above

4. **Results presented at ASCO 2017 of the Phase III SIMPLIFY-1 trial evaluating momelotinib versus ruxolitinib for patients with JAK inhibitor-naïve MF demonstrated momelotinib to be superior to ruxolitinib with regard to _____.**
   a. Reduction in spleen volume
   b. Incidence of anemia
   c. Both a and b
   d. Neither a nor b

5. **Analyses of patients with MF treated with ruxolitinib on the COMFORT studies indicate that unlike disease-related anemia, ruxolitinib-related anemia in patients with MF is manageable and does not appear to adversely affect survival.**
   a. True
   b. False

6. **Which of the following is the mechanism of action of PRM-151?**
   a. Antifibrotic immunomodulatory agent
   b. Hedgehog pathway inhibitor
   c. JAK2 inhibitor

7. **Patients experiencing benefit with ruxolitinib therapy should immediately discontinue treatment once they begin losing response to ruxolitinib.**
   a. True
   b. False

8. **Patients with which of the following disease entities can experience disease progression to acute myeloid leukemia?**
   a. ET
   b. MF
   c. PV
   d. All of the above
   e. Both a and b
   f. Both a and c

9. **The updated revisions to the World Health Organization classification of myeloid neoplasms and acute leukemia published in *Blood* in 2016 introduced which of the following disease entities?**
   a. Prefibrotic myelofibrosis
   b. Post-ET MF
   c. Post-PV MF

10. **What is the mechanism of action of imetelstat?**
    a. Immunomodulatory drug
    b. JAK2 inhibitor
    c. Telomerase inhibitor

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Myeloproliferative Neoplasms Update — Volume 1, Issue 1

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Effect of anemia on overall survival in patients with MF treated with ruxolitinib on the COMFORT studies	4 3 2 1	4 3 2 1
Notable revisions to the World Health Organization diagnostic criteria for MPNs	4 3 2 1	4 3 2 1
Management of MF-associated symptoms, including fatigue, weight loss, night sweats, bone pain and/or itching	4 3 2 1	4 3 2 1
Prognostic and/or clinical significance of common (JAK2, CALR, MPL, TET2) and infrequently observed mutations (ASXL-1, LNK, EZH1 and 2, IDH1 and 2, et cetera) associated with MF	4 3 2 1	4 3 2 1

Practice Setting:

☐ Academic center/medical school ☐ Community cancer center/hospital ☐ Group practice
☐ Solo practice ☐ Government (eg, VA) ☐ Other (please specify).....

Approximately how many new patients with the following do you see per year? MF..... PV..... ET.....

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No If no, please explain:.....

.....

Please identify how you will change your practice as a result of completing this activity (select all that apply).

☐ This activity validated my current practice
☐ Create/revise protocols, policies and/or procedures
☐ Change the management and/or treatment of my patients
☐ Other (please explain):.....

If you intend to implement any changes in your practice, please provide 1 or more examples:

.....

The content of this activity matched my current (or potential) scope of practice.

☐ Yes ☐ No If no, please explain:.....

.....

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Use an understanding of disease biology and natural history to diagnose primary PV, ET and MF and communicate prognosis to patients..... 4 3 2 1 N/M N/A
- Consider the evidence-based therapeutic options for patients with PV, ET and MF, and develop clinical algorithms intended to enhance quality and quantity of life for patients with these distinct yet related diseases..... 4 3 2 1 N/M N/A
- Appraise the role of ruxolitinib in patients with MF and thrombocytopenia, anemia and compromised renal function..... 4 3 2 1 N/M N/A
- Appreciate emerging research data with the use of novel JAK inhibitors in the care of patients with MF, and prepare for their potential availability in clinical practice..... 4 3 2 1 N/M N/A
- Recognize the benefits of ongoing clinical trials for patients with MPNs, and inform appropriately selected patients about these options for treatment..... 4 3 2 1 N/M N/A

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

.....

Would you recommend this activity to a colleague?

☐ Yes ☐ No If no, please explain: .....

Additional comments about this activity:

.....

.....

PART 2 — Please tell us about the faculty and editor for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Professor Claire N Harrison, MD	4 3 2 1	4 3 2 1
Srdan Verstovsek, MD, PhD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty and editor for this activity:

.....

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