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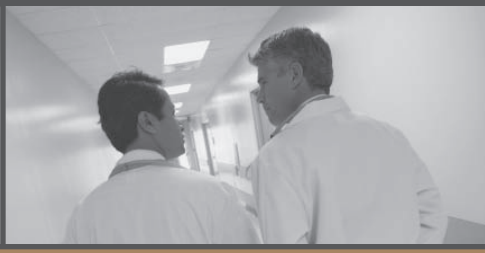

Visiting Professors

A case-based discussion on the management of myeloproliferative neoplasms

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Featuring a clinical investigator's perspective on a day spent visiting patients with myeloproliferative neoplasms in the clinics of general oncologists

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Visiting Professors: A case-based discussion on the management of myeloproliferative neoplasms

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. Equally important, emerging research information on its use for patients with less aggressive MPNs, most notably PV, demonstrates that treatment algorithms for these patients are poised for significant change.

To provide clinicians with therapeutic strategies to address the disparate needs of patients with MPNs, the *Visiting Professors* audio series employs an innovative case-based approach that unites the perspectives of leading investigators and community oncologists. 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

- Utilize an understanding of disease biology and natural history to diagnose and communicate prognosis to patients with primary PV, ET and MF.
- Consider the evidence-based therapeutic options in PV, ET and MF, and develop clinical algorithms intended to enhance quality and quantity of life for patients with these distinct yet related diseases.
- Recognize the recent FDA approval of ruxolitinib for patients with PV, and identify individuals who may be appropriate for therapeutic intervention with this agent.
- Review emerging clinical trial data with and ongoing investigations of novel JAK inhibitors for MPNs.

ACCREDITATION STATEMENT

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Successful completion of this CME activity enables the participant to earn up to 1.5 MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — **Dr Harwin** has no relevant conflicts of interest to disclose. The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Mesa** — ***Consulting Agreement:*** Novartis Pharmaceuticals Corporation; ***Contracted Research:*** Celgene Corporation, Genentech BioOncology. **Dr Reeves** — ***Speakers Bureau and Ownership Interest:*** Celgene Corporation.

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Which of the following is the mechanism of action of PRM-151?**
   a. Antifibrotic immunomodulation
   b. Hedgehog pathway inhibition
   c. JAK2 inhibition

2. **The Phase III RESPONSE trial of ruxolitinib versus best available therapy for patients with PV who are resistant to or intolerant of hydroxyurea resulted in _____ with ruxolitinib.**
   a. Improvements in symptoms
   b. Improvements in splenomegaly
   c. Reduction in the rate of phlebotomy procedures
   d. Both a and b
   e. All of the above

3. **A Phase I/II study evaluating PRM-151 alone or in combination with ruxolitinib for patients with primary MF, post-ET MF or post-PV MF reported improvements in splenomegaly, anemia and thrombocytopenia with _____.**
   a. PRM-151 alone
   b. PRM-151 and ruxolitinib
   c. Both a and b
   d. None of the above

4. **In the treatment of MF, JAK1 and JAK2 inhibition with ruxolitinib has been shown to be beneficial for _____.**
   a. Patients with JAK2 mutations
   b. Patients without JAK2 mutations
   c. Both a and b
   d. None of the above

5. **Patients with MF should discontinue treatment with ruxolitinib if they _____.**
   a. Develop herpes zoster infection
   b. Are to undergo elective surgery
   c. Both a and b
   d. None of the above

6. **Long-term follow-up of patients with MF who received ruxolitinib did not demonstrate a survival advantage with ruxolitinib compared to best available therapy.**
   a. True
   b. False

7. **The recommended starting dose of oral ruxolitinib for patients with PV is _____.**
   a. 10 mg twice daily
   b. 15 mg twice daily
   c. 20 mg twice daily

8. **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 had an inadequate response to or are intolerant of hydroxyurea
   c. Both a and b
   d. None of the above

SELECT PUBLICATIONS

A phase 2, open-label, translational biology study of momelotinib in transfusion-dependent subjects with primary myelofibrosis (PMF) or post-polycythemia vera or post-essential thrombocythemia myelofibrosis (post-PV/ET MF). NCT02515630

A phase 3, randomized, double-blind active-controlled study evaluating momelotinib vs ruxolitinib in subjects with primary myelofibrosis (PMF) or post-polycythemia vera or post-essential thrombocythemia myelofibrosis (post-PV/ET MF). NCT01969838

Gowin KL et al. **Final analysis of a multicenter pilot phase 2 study of ruxolitinib and danazol in patients with myelofibrosis.** *Proc ASH* 2015;**Abstract 1618**.

Guglielmelli P et al. **Impact of mutational status on outcomes in myelofibrosis patients treated with ruxolitinib in the COMFORT-II study.** *Blood* 2014;123(14):2157-60.

Harrison CN et al. **Long-term efficacy and safety in COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for the treatment of myelofibrosis: 5-year final study results.** *Proc ASH* 2015;**Abstract 59**.

Harrison CN et al. **Health-related quality of life and symptoms in patients with myelofibrosis treated with ruxolitinib versus best available therapy.** *Br J Haematol* 2013;162(2):229-39.

Mesa RA et al. **Effects of ruxolitinib treatment on metabolic and nutritional parameters in patients with myelofibrosis from COMFORT-I.** *Clin Lymphoma Myeloma Leuk* 2015;15(4):214-22.

Mesa RA et al. **Effect of ruxolitinib therapy on myelofibrosis-related symptoms and other patient-reported outcomes in COMFORT-I: A randomized, double-blind, placebo-controlled trial.** *J Clin Oncol* 2013;31(10):1285-92.

Passamonti F et al. **Impact of ruxolitinib on the natural history of primary myelofibrosis: A comparison of the DIPSS and the COMFORT-2 cohorts.** *Blood* 2014;123(12):1833-5.

Prick J et al. **Clonal heterogeneity as a driver of disease variability in the evolution of myeloproliferative neoplasms.** *Experimental Hematology* 2014;42(10):841-51.

Vannucchi AM et al. **Ruxolitinib versus standard therapy for the treatment of polycythemia vera.** *N Engl J Med* 2015;372(5):426-35.

Verstovsek S et al. **PRM-151 in myelofibrosis: Durable efficacy and safety at 72 weeks.** *Proc ASH* 2015;**Abstract 56**.

Verstovsek S et al. **Phase 2 trial of PRM-151, an anti-fibrotic agent, in patients with myelofibrosis: Stage 1 results.** *Proc ASH* 2014;**Abstract 713**.

Verstovsek S et al. **The clinical benefit of ruxolitinib across patient subgroups: Analysis of a placebo-controlled, Phase III study in patients with myelofibrosis.** *Br J Haematol* 2013;161(4):508-16.

Verstovsek S et al. **A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis.** *N Engl J Med* 2012;366(9):799-807.

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 JAK2 mutation status on response outcomes with the JAK2 inhibitor ruxolitinib	4 3 2 1	4 3 2 1
Incidence and management of JAK2 inhibitor-associated herpes zoster	4 3 2 1	4 3 2 1
RESPONSE: Efficacy results of a Phase III trial of ruxolitinib versus best available therapy for PV	4 3 2 1	4 3 2 1
Continuation of JAK inhibitor therapy in a patient undergoing surgery	4 3 2 1	4 3 2 1
Activity of the novel antifibrotic immunomodulatory agent PRM-151 alone or in combination with ruxolitinib for patients with primary MF, post-ET MF or post-PV 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?

Myelofibrosis:..... Polycythemia vera:..... Essential thrombocythemia:.....

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:

- Utilize an understanding of disease biology and natural history to diagnose and communicate prognosis to patients with primary PV, ET and MF. .....4 3 2 1 N/M N/A
- Consider the evidence-based therapeutic options in 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
- Recognize the recent FDA approval of ruxolitinib for patients with PV, and identify individuals who may be appropriate for therapeutic intervention with this agent. .....4 3 2 1 N/M N/A
- Review emerging clinical trial data with and ongoing investigations of novel JAK inhibitors for MPNs. .....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
Ruben A Mesa, MD	4 3 2 1	4 3 2 1
William Harwin, MD	4 3 2 1	4 3 2 1
James A Reeves Jr, MD	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

REQUEST FOR CREDIT — Please print clearly

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Signature:..... Date: .....

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