Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS
Steven Coutre, MD
David P Steensma, MD
Philippe Moreau, MD
Peter Martin, MD

EDITOR
Neil Love, MD

CONTENTS
2 Audio CDs
Monograph
OVERVIEW OF ACTIVITY
The treatment of hematologic cancer remains a challenge for many healthcare professionals despite recent gains made in the management of this group of diseases. Determining which treatment approach is most appropriate for a given individual requires careful consideration of patient-specific characteristics, physician expertise and available health system resources. To bridge the gap between research and patient care, this issue of Hematologic Oncology Update features one-on-one discussions with leading hematology-oncology investigators. By providing information on the latest clinical developments and the perspectives of experts, the activity assists medical oncologists, hematologists and hematology-oncology fellows with the formulation of evidence-based and current therapeutic strategies, which in turn facilitates optimal patient care.

LEARNING OBJECTIVES
• Reevaluate your current treatment approach for patients with myeloproliferative disorders and acute and chronic leukemias in light of newly emerging clinical data.
• Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the recent addition of bortezomib, ibrutinib and zanubrutinib as FDA-endorsed options.
• Develop a rational plan to incorporate B-cell receptor signaling inhibitors and novel CD20 monoclonal antibodies into the treatment of chronic lymphocytic leukemia and other B-cell neoplasms.
• Incorporate newly approved agents and strategies in the treatment of newly diagnosed and relapsed or refractory multiple myeloma.
• Develop an understanding of the biologic rationale for and early efficacy data with the use of immunotherapeutic approaches for patients with various hematologic cancers.
• Recognize the benefits of ongoing clinical trials for patients with hematologic cancers, and inform appropriately selected patients about these options for treatment.

ACCREDITATION STATEMENT
Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT
Research To Practice designates this enduring material for a maximum of 3 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY
This CME activity contains both audio and print components. To receive credit, the participant should review the CME information, listen to the CDs, review the monograph, complete the Post-test with a score of 70% or better and fill out the Educational Assessment and Credit Form located in the back of this monograph or on our website at ResearchToPractice.com/HOU315/CME. This monograph contains edited comments, clinical trial schematics, graphics and references that supplement the audio program. ResearchToPractice.com/HOU315 includes an easy-to-use, interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated within the text of the monograph in blue, bold text.

This activity is supported by educational grants from Astellas Pharma Global Development Inc, Celgene Corporation, Genentech BioOncology, Incyte Corporation, Janssen Biotech Inc, Novartis Pharmaceuticals Corporation, Pharmacyclics Inc, Seattle Genetics, Takeda Oncology and Teva Oncology.

Release date: January 2016; Expiration date: January 2017
This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.
CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process: Dr Coutre — Advisory Committee: Celgene Corporation; Consulting Agreement: Janssen Biotech Inc; Contracted Research: AbbVie Inc, Celgene Corporation, Gilead Sciences Inc, Pharmacycics Inc, Takeda Oncology. Dr Steensma — Advisory Committee: Amgen Inc, Celgene Corporation, Genoptix Inc. Dr Moreau — Advisory Committee: Amgen Inc, Bristol-Myers Squibb Company, Celgene Corporation, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Takeda Oncology. Dr Martin — Consulting Agreements: Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology, Idera Pharmaceuticals Inc, Novartis Pharmaceuticals Corporation; Speakers Bureau: Genentech BioOncology.


RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Have Questions or Cases You Would Like Us to Pose to the Faculty?

Submit them to us via Facebook or Twitter

Facebook.com/ResearchToPractice    Twitter @DrNeilLove
Dr Coutre is Professor of Medicine (Hematology) at Stanford University School of Medicine in Stanford, California.

Select Excerpts from the Interview

Tracks 1-2, 4

DR LOVE: Would you discuss the results of the Phase III CLL10 trial of fludarabine/cyclophosphamide/rituximab (FCR) versus bendamustine/rituximab (BR) for patients with untreated advanced chronic lymphocytic leukemia (CLL) (Eichhorst 2014)?

DR COUTRE: FCR has become the major regimen used for initial treatment of CLL in fit patients, but BR is becoming increasingly popular and has a reputation for being a kinder and gentler regimen. The CLL10 trial of FCR versus BR included patients older and younger than age 65. The primary endpoint was progression-free survival (PFS), and FCR was superior. More patients achieved a complete response with FCR, and that translated to a PFS of 55.2 months versus 41.7 months with BR.

The tradeoff was tolerability. FCR led to a higher incidence of neutropenia, thrombocytopenia and infections. By age group, the tolerability issues were observed primarily...
in patients older than age 65. However, there is no cutoff age in place for the use of FCR. The most important aspect is the treatment goal. One has to consider each patient individually, and one size does not fit all.

**DR LOVE:** How have the results of the German Phase III CLL11 trial of chlorambucil with or without the anti-CD20 monoclonal antibodies obinutuzumab or rituximab for patients with untreated CLL and comorbidities influenced your practice?

**DR COUTRE:** The relevant part of the CLL11 trial was the comparison of obinutuzumab/chlorambucil to rituximab/chlorambucil (Goede 2014). In terms of the primary endpoint of PFS, the obinutuzumab/chlorambucil combination was superior at 26.7 months versus 15.2 months for rituximab/chlorambucil. No difference is apparent yet in overall survival (OS). If you’re considering rituximab, you might opt for obinutuzumab instead because patients achieve better and more durable responses. In my practice, I would choose obinutuzumab for an older, symptomatic patient for whom I want to achieve disease control if I didn’t feel that the patient would tolerate BR.

In the trial, obinutuzumab was used in combination with chlorambucil. However, I do not believe that chlorambucil adds any benefit to obinutuzumab, and therefore I always administer obinutuzumab as a single agent rather than in combination with chlorambucil even for older patients.

**DR LOVE:** What is your clinical experience with ibrutinib, and how do you integrate it into the treatment algorithm for patients with CLL with and without adverse cytogenetics?

**DR COUTRE:** Ibrutinib has tremendous activity. Essentially all patients respond to ibrutinib therapy when it is initially administered, including those who often do not respond to the standard agents, such as patients with the 17p deletion or those with fludarabine-refractory disease. It is great to know that you can tell your patients that you are going to recommend a once-a-day pill and they’re going to experience a response.

With ibrutinib, the lymph nodes shrink dramatically in a matter of days and at the same time, you see lymphocytosis. Fortunately, that doesn’t cause any clinical problems, but you need to make your patients aware of this issue. Ibrutinib is generally quite well tolerated. It causes easy bruising and a bit of diarrhea, which eventually goes away. I have patients who’ve been on ibrutinib continuously for up to 5 years. It is not associated with cumulative side effects. As a result, ibrutinib is FDA approved for patients with CLL who have received 1 prior therapy. It is also indicated up front for patients with 17p deletion.

**DR LOVE:** Would you administer ibrutinib up front for patients without 17p deletion?

**DR COUTRE:** Absolutely. We’ve recently reported data from the randomized Phase III RESONATE-2 trial addressing that issue in patients with treatment-naïve disease. Patients aged 65 or older with untreated CLL or small lymphocytic lymphoma (SLL) without 17p deletion received chlorambucil or ibrutinib, and single-agent ibrutinib was superior (Tedeschi 2015; [1.1]).

The RESONATE-2 trial also revealed that ibrutinib can cause atrial fibrillation. However, it was generally brief in duration, occurring only for a matter of days. We
need to understand it better, but for right now, I would say it shouldn’t preclude you from choosing ibrutinib for patients with even chronic atrial fibrillation if you feel it’s the best agent to treat their CLL.

› DR LOVE: How do idelalisib and ibrutinib “match up” in relapsed CLL, and how do you approach sequencing these agents?

› DR COUTRE: Idelalisib is an effective agent. In our early trials of single-agent idelalisib, I couldn’t tell you if its efficacy was any different from that of ibrutinib. The pattern of response is exactly the same, with rapid shrinkage of lymph nodes and lymphocytosis that resolves with time. However, the safety issues are different. Idelalisib does not cause bleeding issues or atrial fibrillation, but many patients may experience asymptomatic transaminitis. When this happens, idelalisib should be discontinued. The transaminitis usually resolves within a couple of weeks, after which idelalisib can be reinitiated. Most often, even without dose reduction, it never reoccurs.

As patients stay on the drug longer, we have also observed a diarrheal illness. The median time to its onset is about 9 months, although it can present up to 2 or 3 years after initiation of treatment. It appears as profuse, watery diarrhea, with all the characteristics of colitis. We’ve learned to treat it with steroids.

Outside of a trial setting, I’ll choose either idelalisib or ibrutinib for patients with previously treated disease. Although I will not administer BR to a patient who received
first-line FCR, I will consider idelalisib or ibrutinib as second-line therapy. I tend to use ibrutinib to avoid idelalisib-associated colitis. We have limited experience with idelalisib after progression on ibrutinib or vice versa, but patients can respond.

**DR LOVE:** What are your thoughts on the investigation of the novel second-generation Bcl-2 inhibitor venetoclax in CLL?

**DR COUTRE:** In a Phase I dose-escalation trial, venetoclax produced extremely high response rates, including among patients with heavily pretreated disease (Seymour 2013). However, it is associated with tumor lysis syndrome, but we have learned that a reduced initial dose followed by slow dose escalation decreases the likelihood of this toxicity. Several trials of venetoclax in CLL are ongoing, including the Phase III CLL14 trial evaluating obinutuzumab in combination with venetoclax or chlorambucil for patients with previously untreated CLL and coexisting comorbidities (1.2). ■

---

**SELECT PUBLICATIONS**

Eichhorst B et al. *Frontline chemoimmunotherapy with fludarabine (F), cyclophosphamide (C), and rituximab (R) (FCR) shows superior efficacy in comparison to bendamustine (B) and rituximab (BR) in previously untreated and physically fit patients (pts) with advanced chronic lymphocytic leukemia (CLL): Final analysis of an international, randomized study of the German CLL Study Group (GCLLSG) (CLL10 study).* *Proc ASH* 2014; Abstract 19.

Fischer K et al. *Results of the safety run-in phase of CLL14 (BO25323): A prospective, open-label, multicenter randomized phase III trial to compare the efficacy and safety of obinutuzumab and venetoclax (GDC-0199/ABT-199) with obinutuzumab and chlorambucil in patients with previously untreated CLL and coexisting medical conditions.* *Proc ASH* 2015; Abstract 496.


Seymour JF et al. *Bcl-2 inhibitor ABT-199 (GDC-0199) monotherapy shows anti-tumor activity including complete remissions in high-risk relapsed/refractory (R/R) chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL).* *Proc ASH* 2013; Abstract 872.

Tedeschi A et al. *Results from the international, randomized phase 3 study of ibrutinib versus chlorambucil in patients 65 years and older with treatment-naive CLL/SLL (RESONATE-2).* *Proc ASH* 2015; Abstract 495.
Tracks 1-9

Track 1  Novel agents under investigation for FLT3-ITD-mutated acute myeloid leukemia (AML)

Track 2  Activity and tolerability of the orally administered inhibitor of FLT3/AXL gilteritinib (ASP2215) in AML

Track 3  Recent developments in myelodysplastic syndromes (MDS)

Track 4  Clinical experience with lenalidomide for patients with MDS with and without del(5q)

Track 5  Management of MDS in patients with disease progression on a hypomethylating agent

Track 6  Case discussion: A 68-year-old man with postpolycythemia vera myelofibrosis whose symptoms begin to recur after 2 years of ruxolitinib therapy

Track 7  Activity and toxicities of novel JAK inhibitors — pacritinib, momelotinib — in myeloproliferative disorders

Track 8  Case discussion: A 65-year-old woman with hydroxyurea-resistant polycythemia vera treated with ruxolitinib

Track 9  Clinical experience with dosing and continuation of ruxolitinib therapy in patients experiencing treatment-associated cytopenias

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you discuss some of the most promising new agents and strategies under investigation for patients with acute myeloid leukemia (AML)?

DR STEENSMA: One area of interest involves investigation of agents targeting FLT3 mutations, which are driver mutations commonly associated with AML. The 2 general classes of FLT3 mutations are internal tandem duplication (ITD) mutations and tyrosine kinase domain (TKD) mutations. Both constitutively activate the FLT3 receptor, but ITD mutations tend to be associated with more proliferative disease and a poorer prognosis, and they’re more common than TKD mutations. Some kinase inhibitors will inhibit both ITD and TKD, and some will inhibit only ITD.

FLT3 inhibitors have typically shown relatively limited efficacy as single agents. They’re often used in the salvage setting after the disease has relapsed. Sorafenib has FLT3-ITD inhibitory activity and has been used in relapsed/refractory FLT3-positive AML, resulting in remission in some patients. Data presented during the plenary session at ASH 2014 from a study in which sorafenib was added to “7 plus 3” chemotherapy indicated that patients receiving that combination fared better in terms of relapse-free survival. A trend toward improved OS regardless of FLT3 status was also apparent (Rollig 2014).
One novel FLT3 inhibitor that is active as a single agent in AML is gilteritinib (ASP2215). Single-agent gilteritinib has demonstrated a high complete response rate (Levis 2015; [2.1]). When you inhibit the FLT3 receptor, the cells upregulate the ligand to try to circumvent the inhibition, and that’s been a challenge that some other FLT3 inhibitors have faced in the past that’s delayed their development.

Another interesting agent in this drug class that is being evaluated in combination with 7 plus 3 is midostaurin. Exciting data from the Phase III CALGB-10603 (RATIFY) trial were presented at ASH 2015 (Stone 2015; [2.2]). These FLT3 inhibitors primarily differ with respect to the narrowness of their kinase inhibitory profiles.

### Results of a Phase I/II Dose-Escalation Study of the Potent FLT3/AXL Inhibitor Gilteritinib (ASP2215) for Patients with Relapsed/Refractory Acute Myeloid Leukemia

<table>
<thead>
<tr>
<th>Clinical response by mutation status</th>
<th>FLT3 mutation-positive</th>
<th>FLT3 wild type</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-450 mg (n = 127) ≥80 mg (n = 106)</td>
<td>20-450 mg (n = 57)</td>
<td></td>
</tr>
<tr>
<td>ORR (CRc + PR)</td>
<td>52%</td>
<td>57.5%</td>
</tr>
<tr>
<td>CRc (CR + CRp + CRi)</td>
<td>40.9%</td>
<td>47.2%</td>
</tr>
<tr>
<td>CR</td>
<td>6.3%</td>
<td>6.6%</td>
</tr>
<tr>
<td>CRp</td>
<td>3.9%</td>
<td>4.7%</td>
</tr>
<tr>
<td>CRi</td>
<td>30.7%</td>
<td>35.8%</td>
</tr>
<tr>
<td>PR</td>
<td>11.0%</td>
<td>10.4%</td>
</tr>
</tbody>
</table>

ORR = overall response rate; CR = complete remission; CRc = composite CR; PR = partial remission; CRp = CR with incomplete platelet recovery; CRi = CR with incomplete hematologic recovery

- Treatment-related adverse events included diarrhea (13.4%), fatigue (12.4%), anemia (7.2%), peripheral edema (7.2%), nausea (6.7%) and dysgeusia (5.2%).
- Serious adverse events included febrile neutropenia (27.3%), sepsis (11.9%), pneumonia (8.8%), hypotension (5.7%) and respiratory failure (5.7%).


### Tracks 8-9

#### CASE DISCUSSION: A 65-year-old woman with hydroxyurea-resistant polycythemia vera receives ruxolitinib

#### DR STEENSMA: Most patients with polycythemia vera fare well with only phlebotomy and aspirin or, if they are considered to be at higher risk, meaning they are older than age 60 or have experienced a prior thrombosis, then phlebotomy in combination with aspirin and hydroxyurea. Some patients don’t fare so well, however, and this 65-year-old woman was one of them. She had received hydroxyurea after presenting with polycythemia vera, and one symptom that the hydroxyurea was unable to control was severe bone pain, especially in her ribs and spine. She also developed constitutional symptoms, such as night sweats, that weren’t as severe.

We discussed other options, including pegylated interferon or ruxolitinib, to control her pain. She opted to try ruxolitinib, which was recently approved by the FDA for patients who are intolerant to or have inadequate response to hydroxyurea. Her bone pain did not completely go away but got much better, and ruxolitinib also improved
her associated symptoms. So I believe a small niche exists in polycythemia vera for JAK inhibitors, but by no means should they be the first-line therapy because hydroxyurea is inexpensive and we have many years of experience with it.

**DR LOVE:** What is your clinical experience with patients in whom ruxolitinib needs to be discontinued?

**DR STEENSMA:** One of the most common questions I hear from community oncologists is whether ruxolitinib can be discontinued for patients who are not faring well. I was involved in the early trials of ruxolitinib, and when patients were hospitalized for an infection, for example, and ruxolitinib was stopped suddenly, their condition became much worse. They experienced something of a “cytokine storm,” and a couple of patients had to be intubated or even died.

An infection or major operation will trigger cytokine release, so a patient who is acutely ill with an infection is not someone for whom you want to suddenly stop a JAK inhibitor, because JAK inhibitors block cytokine signaling. Ruxolitinib is a highly potent inhibitor of cytokines involved in infection and inflammation. That’s probably why patients feel much better and why their symptoms improve after starting therapy with ruxolitinib.

If you suddenly stop the JAK inhibitor, you reverse the benefit received from treatment and patients can become seriously ill. So JAK inhibitors should not be stopped abruptly in those situations. But it is acceptable to stop ruxolitinib “cold turkey” in certain cases — for example, for patients who are chronically ill and have been receiving ruxolitinib for 3 to 4 months without any benefit.

**SELECT PUBLICATIONS**


**Tracks 1-15**

**Track 1**  
*Case discussion:* An 82-year-old man with newly diagnosed Stage III, IgG kappa multiple myeloma (MM) receives lenalidomide/dexamethasone

**Track 2**  
Results of the Phase III FIRST trial of lenalidomide/dexamethasone (Rd) versus melphalan/prednisone/thalidomide (MPT) for transplant-ineligible patients with newly diagnosed MM

**Track 3**  
Continuous versus fixed duration of Rd treatment

**Track 4**  
Dosing of lenalidomide in elderly patients with MM

**Track 5**  
Effect of adverse cytogenetics on outcomes of transplant-ineligible patients with newly diagnosed MM treated with continuous Rd

**Track 6**  
Results of a Phase I/II trial of the newly FDA-approved oral proteasome inhibitor ixazomib in combination with Rd for previously untreated MM

**Track 7**  
Results of the Phase III TOURMALINE-MM1 trial: Improvement in progression-free survival with the addition of ixazomib to Rd for patients with relapsed/refractory MM

**Track 8**  
Perspective on the development and potential role of the oral proteasome inhibitor oprozomib

**Track 9**  
*Case discussion:* A 62-year-old woman whose disease relapses 2 years after autologous stem cell transplant (ASCT) is enrolled on the ASPIRE study and achieves a complete remission with carfilzomib/Rd (CRd)

**Track 10**  
Therapeutic options for induction and maintenance therapy in patients with MM

**Track 11**  
Activity and tolerability of CRd

**Track 12**  
Incidence and management of carfilzomib-associated dyspnea

**Track 13**  
Perspective on the integration of CRd and panobinostat/bortezomib/dexamethasone into the treatment landscape for relapsed/refractory MM

**Track 14**  
Results of ELOQUENT-2: A Phase III trial of lenalidomide/dexamethasone with or without the newly FDA-approved monoclonal antibody elotuzumab for relapsed/refractory MM

**Track 15**  
Activity of the newly FDA-approved anti-CD38 antibody daratumumab for heavily pretreated or double-refractory MM

---

**Philippe Moreau, MD**

Dr. Moreau is Professor of Hematology and Head of the Hematology Department at University Hospital Hotel-Dieu in Nantes, France.

---

**Select Excerpts from the Interview**

**Tracks 2-3, 5**

**DR LOVE:** You were one of the investigators on the Phase III FIRST trial of lenalidomide and dexamethasone for transplant-ineligible patients with multiple myeloma (MM). Would you discuss the results of this study (Benboubker 2014)?

**DR MOREAU:** This trial was primarily for patients age 65 or older. It was a 3-arm study comparing melphalan/prednisone/thalidomide (MPT) for 12 cycles to lenalidomide/
low-dose dexamethasone (Rd) for 18 cycles or continuously until disease progression. A total of 1,623 patients were enrolled and randomly assigned in a 1:1:1 ratio. The primary endpoint was PFS. The study clearly demonstrated that continuous Rd was superior with a median PFS of 25.5 months versus 20.7 months with Rd for 18 cycles and 21.2 months with MPT. Continuous Rd was also associated with a clear OS benefit.

I believe that Rd should be used continuously until disease progression if patients are able to tolerate the combination. Reviewing the data carefully, approximately 35% of patients older than 75 years on the continuous Rd arm had to discontinue treatment because of adverse events such as gastrointestinal (GI) toxicity, fatigue, neutropenia or infections. The message is that continuous Rd should be tried if possible and discontinued when necessary.

\textbf{DR LOVE:} Would you provide some insight into the results of the subanalysis of the “FIRST” trial investigating the effects of cytogenetics on treatment outcomes that were recently presented at the ASH 2015 meeting (Avet-Loiseau 2015; [3.1])?

\textbf{DR MOREAU:} In the relapsed setting, it is known that Rd is less effective for patients with poor cytogenetics. This can also be true in the up-front setting. If a patient presents with disease harboring the t(4;14) translocation, a 3-drug combination such as RVd-lite is probably a good regimen to consider, with the use of once-weekly bortezomib to limit toxicity.

### Effect of Cytogenetics on Treatment Outcomes for Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma (NDMM) Treated with Lenalidomide/Low-Dose Dexamethasone (Rd) in the Phase III FIRST Trial

<table>
<thead>
<tr>
<th>Median PFS</th>
<th>High risk (n = 142)</th>
<th>Nonhigh risk (n = 620)</th>
<th>All patients (n = 762)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd continuous</td>
<td>8.4 mo</td>
<td>31.1 mo</td>
<td>25.3 mo</td>
</tr>
<tr>
<td>Rd18</td>
<td>17.5 mo</td>
<td>21.2 mo</td>
<td>20.4 mo</td>
</tr>
<tr>
<td>MPT</td>
<td>14.6 mo</td>
<td>24.9 mo</td>
<td>23.3 mo</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Three-year OS</th>
<th>n = 142</th>
<th>n = 620</th>
<th>n = 762</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd continuous</td>
<td>40.7%</td>
<td>77.1%</td>
<td>70.7%</td>
</tr>
<tr>
<td>Rd18</td>
<td>39.6%</td>
<td>71.0%</td>
<td>64.9%</td>
</tr>
<tr>
<td>MPT</td>
<td>46.8%</td>
<td>64.8%</td>
<td>61.5%</td>
</tr>
<tr>
<td>ORR</td>
<td>n = 142</td>
<td>n = 620</td>
<td>n = 762</td>
</tr>
<tr>
<td>Rd continuous</td>
<td>76.7%</td>
<td>81.0%</td>
<td>80.2%</td>
</tr>
<tr>
<td>Rd18</td>
<td>67.3%</td>
<td>79.9%</td>
<td>77.4%</td>
</tr>
<tr>
<td>MPT</td>
<td>68.1%</td>
<td>70.9%</td>
<td>70.4%</td>
</tr>
</tbody>
</table>

PFS = progression-free survival; Rd18 = Rd for 18 cycles; MPT = melphalan/prednisone/thalidomide; OS = overall survival; ORR = overall response rate

\textbf{Conclusions:} These data support the use of continuous Rd as a standard treatment option for patients with NDMM who are ineligible for transplant, especially those without high-risk cytogenetics. Additional PFS and OS benefits may be achieved in patients with high-risk cytogenetics when continuous Rd is used as a backbone for combination therapy with a novel agent.

DR LOVE: What are some of the key ongoing trials evaluating oral proteasome inhibitors for patients with MM?

DR MOREAU: Two Phase III TOURMALINE trials of ixazomib in combination with lenalidomide/dexamethasone in MM are ongoing. One is for patients with relapsed/refractory MM (TOURMALINE-MM1). The other is for patients with newly diagnosed MM (NCT01850524). The latter is dedicated to patients who are not eligible for stem cell transplant.

At the ASH 2015 meeting, I will present the results of the pivotal Phase III TOURMALINE-MM1 trial (Moreau 2015; [3.2]). The study will show an improvement in PFS with ixazomib. Based on the results of this study, I believe ixazomib in combination with lenalidomide/dexamethasone will soon be FDA approved as treatment for patients with MM who have received 1 prior therapy. Because this was an international study, the triplet regimen should also be approved in Europe soon.

Oprozomib is another oral proteasome inhibitor. It’s currently under investigation in Phase II trials. Ixazomib was quickly developed based on the simplicity of the dosing schedule. Although ixazomib is associated with no important toxicity, oprozomib is. Oprozomib causes significant GI toxicity, so its formulation is currently under investigation. As yet, the optimal dose of oprozomib is unknown, and a lot of work must be done for its clinical development.

Editor’s note: Subsequent to this interview, on November 20, 2015 the FDA granted approval to ixazomib in combination with lenalidomide/dexamethasone as treatment for patients with MM who have received 1 prior therapy.

3.2 TOURMALINE-MM1: Efficacy and Safety Results of a Phase III Trial of Lenalidomide (R) and Dexamethasone (d) with or without Ixazomib (I) for Patients with Relapsed or Refractory Multiple Myeloma

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>IRd (n = 360)</th>
<th>Rd (n = 362)</th>
<th>Hazard ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median progression-free survival</td>
<td>20.6 mo</td>
<td>14.7 mo</td>
<td>0.742</td>
<td>0.012</td>
</tr>
<tr>
<td>Response</td>
<td>IRd</td>
<td>Rd</td>
<td>Odds ratio</td>
<td>p-value</td>
</tr>
<tr>
<td>Overall response rate</td>
<td>78.3%</td>
<td>71.5%</td>
<td>1.44</td>
<td>0.035</td>
</tr>
<tr>
<td>Median duration of response</td>
<td>20.5 mo</td>
<td>15.0 mo</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Select Grade ≥3 adverse events</td>
<td>IRd</td>
<td>Rd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>19%</td>
<td>16%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>13%</td>
<td>5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6%</td>
<td>8%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6%</td>
<td>2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>4%</td>
<td>1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>2%</td>
<td>3%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Tracks 14-15**

**DR LOVE:** Can you provide an overview of the monoclonal antibodies daratumumab and elotuzumab in the management of MM and where you think these agents are headed?

**DR MOREAU:** These monoclonal antibodies are one of the most important steps forward in the treatment of MM. In my opinion, the most fascinating agent in this class is daratumumab, an anti-CD38 monoclonal antibody. Daratumumab is not toxic, and it has single-agent activity in patients who have received 3 or more lines of prior therapy or have double-refractory MM (Lonial 2015a).

The median duration of response was approximately 8 months. I believe that the future use of daratumumab will likely be in combination with agents such as lenalidomide/dexamethasone or bortezomib/dexamethasone.

We are awaiting the results of the Phase III POLLUX trial of lenalidomide/dexamethasone with or without daratumumab in relapsed/refractory MM (NCT02076009). The trial quickly enrolled about 600 patients. The primary endpoint of the study is PFS. The secondary endpoints include OS, and we are hoping for an improvement in OS with daratumumab. I believe daratumumab will be the first monoclonal antibody to be FDA approved for MM and that it will be the most widely used one in the future.

Elotuzumab targets SLAMF7 but has no single-agent activity. In combination with lenalidomide, synergistic activity is evident. The results of the Phase III ELOQUENT-2 trial for patients with relapsed/refractory MM clearly demonstrated that lenalidomide/dexamethasone in combination with elotuzumab was superior to lenalidomide/dexamethasone alone in terms of PFS (Lonial 2015b). The results of the Phase III ELOQUENT-1 trial of lenalidomide/dexamethasone with or without elotuzumab for patients with newly diagnosed MM should also be presented soon (NCT01335399).

---

**Editor’s note:** Subsequent to this interview, on November 16, 2015 the FDA granted accelerated approval to daratumumab for patients with MM who received at least 3 prior treatments, and on November 30, 2015 the FDA approved elotuzumab for use in combination with lenalidomide and dexamethasone for patients with MM following the failure of 1 to 3 prior therapies.

---

**SELECT PUBLICATIONS**


Lonial S et al. Phase II study of daratumumab (DARA) monotherapy in patients with ≥ 3 lines of prior therapy or double refractory multiple myeloma (MM): 5476414MMY2002 (Sirius). *Proc ASCO 2015a; Abstract LBA8512.*


Moreau P et al. Ixazomib, an investigational oral proteasome inhibitor (PI), in combination with lenalidomide and dexamethasone (IRd), significantly extends progression-free survival (PFS) for patients (pts) with relapsed and/or refractory multiple myeloma (RRMM): The phase 3 Tourmaline-MM1 study (NCT01564537). *Proc ASH 2015; Abstract 727.*
**Tracks 1-14**

**Track 1**  Case discussion: A 35-year-old man with recurrent Hodgkin lymphoma (HL) enters a Phase II trial evaluating brentuximab vedotin as second-line therapy prior to ASCT

**Track 2**  Perspective on the results of the Phase III AETHERA trial: Brentuximab vedotin as consolidation therapy for patients with HL at high risk of disease progression after ASCT

**Track 3**  Activity and ongoing investigations of the immune checkpoint inhibitors pembrolizumab and nivolumab in relapsed/refractory HL

**Track 4**  Sustained remission with lenalidomide/rituximab (R²) as initial therapy for mantle-cell lymphoma (MCL)

**Track 5**  Maintenance therapy options for patients with MCL

**Track 6**  First interim analysis of the Phase III LYMA trial: Rituximab maintenance versus watch and wait after 4 courses of R-DHAP → ASCT in younger patients with previously untreated MCL

**Track 7**  Up-front treatment options for younger patients with MCL

**Track 8**  Perspective on the Phase III LYM-3002 trial results: Bortezomib, rituximab, cyclophosphamide, doxorubicin and prednisone (VR-CAP) versus R-CHOP for newly diagnosed, transplant- ineligible MCL

**Track 9**  Investigation of ixazomib in MCL and follicular lymphoma (FL)

**Track 10**  Sequencing of bortezomib, lenalidomide and ibrutinib for relapsed/refractory MCL

**Track 11**  Activity and tolerability of the CDK4/6 inhibitor palbociclib alone and in combination with bortezomib for MCL

**Track 12**  Integration of idelalisib into the treatment algorithm for FL

**Track 13**  Therapeutic options for patients with relapsed/refractory FL

**Track 14**  Efficacy of the R² regimen for newly diagnosed FL

---

**Select Excerpts from the Interview**

**Track 4**

**DR LOVE:** Would you discuss the Phase II study presented by your group at ASH 2014 evaluating the R² regimen of lenalidomide and rituximab for patients with untreated mantle-cell lymphoma (MCL) (Ruan 2014; [4.1])?

**DR MARTIN:** We’ve known for a long time that lenalidomide has significant activity in MCL. So we wanted to determine if a subset of patients with MCL could benefit from less aggressive therapy with R².

In this study patients with newly diagnosed MCL received R² as induction for 1 year, followed by R² maintenance until disease progression. Overall the regimen was reason-
ably well tolerated. Many patients required a dose reduction of lenalidomide. In some cases, we stopped the rituximab alone if patients developed infections.

To our surprise, the regimen was also remarkably effective. At 2 years, the PFS rate was about 85%. This is significant considering that the average PFS with R-CHOP is in the range of 18 months to 2 years (Ruan 2014; [4.1]).

One could argue that that the R² regimen is continuous therapy, as opposed to R-CHOP, which is intermittent over 18 weeks. Nonetheless, I believe that for patients with MCL who require treatment and have higher MIPI scores, these results are promising. In the future, I believe we’ll see more trials that use continuous therapies with creative regimens in the up-front setting.

### Phase II Trial of Lenalidomide with Rituximab (R²) as Initial Treatment for Mantle-Cell Lymphoma

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>(n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>84.2%</td>
</tr>
<tr>
<td>CR</td>
<td>52.6%</td>
</tr>
<tr>
<td>Median PFS</td>
<td>Not reached</td>
</tr>
<tr>
<td>2-year PFS</td>
<td>83.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Select adverse events</th>
<th>Grade 3 or 4 (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>47%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>13%</td>
</tr>
<tr>
<td>Anemia</td>
<td>8%</td>
</tr>
<tr>
<td>Rash</td>
<td>26%</td>
</tr>
<tr>
<td>Tumor flare</td>
<td>11%</td>
</tr>
</tbody>
</table>

ORR = overall response rate; CR = complete response; PFS = progression-free survival


### Tracks 5-6

**DR LOVE:** How do you approach the issue of maintenance rituximab for patients with MCL?

**DR MARTIN:** Our preference is to enroll patients with MCL who require treatment in the ECOG-E1411 trial. This is a US intergroup study in which patients with untreated MCL receive induction with BR with or without bortezomib. In the maintenance phase patients receive rituximab with or without lenalidomide for 2 years (NCT01415752).

Off study, we generally administer BR, but occasionally, for young patients with aggressive disease, we recommend a cytarabine-containing induction regimen followed by autologous stem cell transplant (ASCT). We do not routinely administer rituximab maintenance in the post-stem cell transplant setting.

Many oncologists do not consider rituximab maintenance after chemotherapy induction to be standard. We know that it’s beneficial after R-CHOP. The European Mantle Cell Lymphoma Network study in older patients with MCL showed compelling data
with an OS benefit in patients who received ongoing rituximab maintenance after that regimen (Kluin-Nelemans 2012). We don’t have data on the efficacy of rituximab maintenance after BR, but we prefer to give patients the benefit of the doubt and often offer them rituximab maintenance.

DR LOVE: Can you talk about the results of the Phase III LYMA study evaluating the efficacy of rituximab maintenance in young patients with previously untreated MCL after R-DHAP followed by ASCT?

DR MARTIN: In the LYMA trial, young patients with newly diagnosed MCL received 4 cycles of R-DHAP induction therapy followed by ASCT and then were randomly assigned to rituximab maintenance versus watch and wait for 3 years. If patients did not achieve at least a partial response after R-DHAP, they could receive R-CHOP. However, most patients fared well with R-DHAP.

A clear benefit in PFS was observed, but no OS benefit has been achieved so far (Le Gouill 2014; [4.2]). The lack of evidence of an OS benefit is the main reason that I do not recommend rituximab maintenance after ASCT. I would like to see the data published and evaluated in a peer review setting. The other reason I don’t offer it is that we don’t do ASCT for many patients at our center.

4.2 First Interim Analysis of the Phase III LYMA Trial of Rituximab Maintenance versus Watch and Wait After R-DHAP and Autologous Stem Cell Transplant in Young Patients with Untreated Mantle-Cell Lymphoma

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Rituximab (n = 119)</th>
<th>Watch and wait (n = 119)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-year EFS</td>
<td>93.2%</td>
<td>81.5%</td>
<td>0.015*</td>
</tr>
<tr>
<td>Two-year OS</td>
<td>93.4%</td>
<td>93.9%</td>
<td>NS</td>
</tr>
</tbody>
</table>

EFS = event-free survival; OS = overall survival; NS = not significant

* Hazard ratio = 2.1

Progression-free survival was statistically significant between the study arms (p = 0.015).

Le Gouill S et al. Proc ASH 2014; Abstract 146.

Tracks 12-14

DR LOVE: Would you discuss the study that led to the approval of idelalisib for follicular lymphoma (FL) and how that agent fits into your practice?

DR MARTIN: Idelalisib was approved by the FDA based on a Phase II trial in which patients with FL that was refractory to both rituximab and an alkylating agent received single-agent idelalisib. In this treatment-resistant group of patients, the median PFS was 11 months and the response rate was 57% (Gopal 2014). So patients without other good options responded well to idelalisib.

Interestingly, that study included a variety of histologies, but the FDA approved idelalisib only for patients with FL who had received at least 2 prior therapies. We generally recommend idelalisib for patients with disease that is refractory to rituximab and an alkylating agent. When patients do not have a lot of other treatment options, idelalisib is an attractive agent.
It is also a good option for older patients and those who have to travel long distances and prefer to have an oral agent. At our academic center at Cornell, we have multiple clinical trials open for these patients. We offer single-agent idelalisib for patients who don’t want to participate in these studies.

DR LOVE: What do you recommend for patients with FL who experience relapse after up-front BR?

DR MARTIN: Most patients with FL in the United States receive BR as front-line therapy, although some patients still undergo treatment with R-CHOP. We have good data for bendamustine-based therapies in the second-line setting as well. We don’t have data on the efficacy of R-CHOP for patients whose disease progresses on bendamustine-based therapy.

FL is a heterogeneous disease. Some patients experience progression quickly and are likely to have chemotherapy-resistant disease. These patients are at high risk and require immediate treatment. One approach is to administer more intensive chemotherapy. If they’ve received an anthracycline, ICE and DHAP would be options. Otherwise, R-CHOP followed by ASCT for patients who are eligible for transplant would be reasonable. Another alternative would be to try an approach without chemotherapy. Idelalisib would be a good option, particularly for older patients who are not candidates for an anthracycline-based regimen or ASCT.

Patients who experience disease progression late after BR or R-CHOP may not need treatment for a long period of time. My preference is to observe these patients. I believe it’s important to remember that we’re not treating FL to cure it but rather to improve longevity and, most importantly, improve quality of life. If patients do need treatment, the same options as in the front-line setting can be considered, namely, single-agent rituximab, immunochemotherapy, idelalisib, lenalidomide or a clinical trial.

DR LOVE: What is your view on the efficacy of the R² regimen for newly diagnosed FL?

DR MARTIN: R² is clearly active in FL. CALGB-50401 was a Phase II clinical trial in which patients with recurrent FL were randomly assigned to the R² regimen or lenalidomide alone. The R² arm was superior to lenalidomide (Leonard 2015). The CALGB-50803 study by our group also showed that this regimen was active as up-front therapy for patients with FL (Martin 2014).

I believe that based on the synergy between lenalidomide and rituximab they should be used in combination. However, lenalidomide is not yet approved by the FDA for the treatment of FL, and that has an effect on insurance coverage.

SELECT PUBLICATIONS


1. The results of the Phase III RESONATE-2 trial of ibrutinib versus chlorambucil for patients age 65 years or older with untreated CLL/SLL without 17p deletion demonstrated that single-agent ibrutinib is superior to chlorambucil in terms of _______________.
   a. PFS
   b. OS
   c. Event-free survival
   d. Overall response rate
   e. All of the above

2. The ongoing Phase III CLL14 trial is evaluating obinutuzumab in combination with ________________ or chlorambucil for patients with previously untreated CLL and coexisting comorbidities.
   a. Venetoclax (ABT-199)
   b. Rituximab
   c. Bendamustine
   d. Ibrutinib

3. Adverse events associated with idelalisib include _________________.
   a. Atrial fibrillation
   b. Hemorrhage
   c. Transaminitis
   d. Both a and b
   e. All of the above
   f. None of the above

4. The Phase III CALGB-10603 (RATIFY) trial evaluating midostaurin in combination with daunorubicin/cytarabine induction therapy and cytarabine consolidation and as maintenance for patients with newly diagnosed AML with FLT3 mutations demonstrated a statistically significant improvement in ________________ on the midostaurin arm.
   a. OS
   b. Grade ≥3 hematologic adverse events
   c. Both a and b
   d. Neither a nor b

5. The results of the Phase III TOURMALINE-MM1 trial of lenalidomide and dexamethasone with or without ixazomib for patients with relapsed or refractory MM failed to demonstrate a statistically significant improvement in PFS with the addition of ixazomib.
   a. True
   b. False

6. ________________ is an anti-CD38 monoclonal antibody with single-agent activity that recently received FDA approval as treatment for patients with MM who have received at least 3 prior lines of therapy.
   a. Elotuzumab
   b. Daratumumab
   c. Ixazomib

7. The results of the Phase III FIRST trial of lenalidomide and low-dose dexamethasone (Rd) versus melphalan/prednisone/thalidomide (MPT) for transplant-ineligible patients with MM demonstrated that ________________ is the superior regimen in terms of PFS and OS.
   a. Rd continuously administered until disease progression
   b. Rd administered for 18 cycles
   c. MPT administered for 12 cycles

8. The first interim analysis of the Phase III LYMA trial of rituximab maintenance therapy versus watch and wait after R-DHAP and ASCT for young patients with untreated MCL demonstrated a statistically significant improvement in ________________ with rituximab maintenance.
   a. Event-free survival rate at 2 years
   b. OS rate at 2 years
   c. PFS
   d. Both a and c
   e. All of the above

9. Side effects observed with the lenalidomide/rituximab combination in the treatment of MCL include _________________.
   a. Neutropenia
   b. Rash
   c. Thrombocytopenia
   d. All of the above

10. Idelalisib has been approved by the FDA for the treatment of FL that is _________________.
    a. Refractory to 1 prior line of therapy
    b. Refractory to 2 prior lines of therapy
    c. Previously untreated
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?**

<table>
<thead>
<tr>
<th>Topic</th>
<th>BEFORE</th>
<th>AFTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activity and incidence of tumor lysis syndrome with the novel second-generation Bcl-2 inhibitor venetoclax (ABT-199) in CLL</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Effect of cytogenetics on outcomes of transplant-ineligible patients with newly diagnosed MM treated with continuous Rd on the Phase III FIRST trial</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Novel agents under investigation for FLT3-ITD-mutated AML (ie, gilteritinib, midostaurin)</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Activity and tolerability of the recently FDA-approved anti-CD38 antibody daratumumab for heavily pretreated or double-refractory MM</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Sustained remission with the lenalidomide/rituximab (R²) regimen as initial therapy for MCL</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Use of single-agent obinutuzumab for previously untreated CLL</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

**Practice Setting:**
- ☐ Academic center/medical school
- ☐ Community cancer center/hospital
- ☐ Group practice
- ☐ Solo practice
- ☐ Government (eg, VA)
- ☐ Other (please specify)

**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:**

<table>
<thead>
<tr>
<th>As a result of this activity, I will be able to:</th>
<th>4 = Yes</th>
<th>3 = Will consider</th>
<th>2 = No</th>
<th>1 = Already doing</th>
<th>N/M = LO not met</th>
<th>N/A = Not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Reevaluate your current treatment approach for patients with myeloproliferative disorders and acute and chronic leukemias in light of newly emerging clinical data.</td>
<td>4 3 2 1</td>
<td>N/M</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Customize the selection of systemic therapy for patients with newly diagnosed and progressive mantle-cell lymphoma, recognizing the recent addition of bortezomib, lenalidomide and ibrutinib as FDA-endorsed options.</td>
<td>4 3 2 1</td>
<td>N/M</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Develop a rational plan to incorporate B-cell receptor signaling inhibitors and novel CD20 monoclonal antibodies into the treatment of chronic lymphocytic leukemia and other B-cell neoplasms.</td>
<td>4 3 2 1</td>
<td>N/M</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Incorporate newly approved agents and strategies in the treatment of newly diagnosed and relapsed or refractory multiple myeloma.</td>
<td>4 3 2 1</td>
<td>N/M</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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

• Develop an understanding of the biologic rationale for and early efficacy data with the use of immunotherapeutic approaches for patients with various hematologic cancers. 4 3 2 1 N/M N/A
• Recognize the benefits of ongoing clinical trials for patients with hematologic cancers, 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

<table>
<thead>
<tr>
<th>Faculty</th>
<th>Knowledge of subject matter</th>
<th>Effectiveness as an educator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steven Coutre, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>David P Steensma, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Philippe Moreau, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
<tr>
<td>Peter Martin, MD</td>
<td>4 3 2 1</td>
<td>4 3 2 1</td>
</tr>
</tbody>
</table>

Please recommend additional faculty for future activities:

Other comments about the faculty and editor for this activity:

REQUEST FOR CREDIT — Please print clearly

Name: ................................................. Specialty: .........................................

Professional Designation: ☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other ..........................

Street Address: ................................................. Box/Suite: ...................................

City, State, Zip: .................................................

Telephone: ................................................. Fax: .................................................

Email: ..........................................................

Research To Practice designates this enduring material for a maximum of 3 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity. I certify my actual time spent to complete this educational activity to be ________ hour(s).

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

The expiration date for this activity is January 2017. To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/HOU315/CME.
Conversations with Oncology Investigators

Hematologic Oncology

UP DATE

Neil Love, MD
Research To Practice
One Biscayne Tower
2 South Biscayne Boulevard, Suite 3600
Miami, FL 33131

Copyright © 2016 Research To Practice.

This activity is supported by educational grants from Astellas Pharma Global Development Inc, Celgene Corporation, Genentech BioOncology, Incyte Corporation, Janssen Biotech Inc, Novartis Pharmaceuticals Corporation, Orph Pharma north, Pfizer, Amgen Inc, Seattle Genetics, Takeda Oncology and Teva Oncology.

Research To Practice®

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Release date: January 2016
Expiration date: January 2017
Estimated time to complete: 3 hours

This program is printed on MacGregor XP paper, which is manufactured in accordance with the world’s leading forest management certification standards.

Conversations with Oncology Investigators

Bringing the Gap Between Research and Patient Care

FAC ULTY I NT E RV IE W S

Steven Coutre, MD
David P Steensma, MD
Philippe Moreau, MD
Peter Martin, MD

CONTENTS

2 Audio CDs
Monograph

2015
Neil Love, MD

Pharmaceuticals
Institute

Neutrophils
Bone Marrow
Infections