5 Minute JournalClub

POST-ASH Issue 6, 2015

Final Efficacy and Safety Results from the 1703 Phase Ib/II Study of Elotuzumab/ Lenalidomide/Dexamethasone in Relapsed/Refractory MM

For more visit ResearchToPractice.com/5MJCASH2015

Research To Practice®

CME INFORMATION

OVERVIEW OF ACTIVITY

Each year, thousands of clinicians, basic scientists and other industry professionals sojourn to major international oncology conferences, like the American Society of Hematology (ASH) annual meeting, to hone their skills, network with colleagues and learn about recent advances altering state-of-the-art management in hematologic oncology. As such, these events have become global stages where exciting science, cutting-edge concepts and practice-changing data emerge on a truly grand scale. This massive outpouring of information has enormous benefits for the hematologic oncology community, but the truth is it also creates a major challenge for practicing oncologists and hematologists.

Although original data are consistently being presented and published, the flood of information unveiled during a major academic conference is unprecedented and leaves in its wake an enormous volume of new knowledge that practicing oncologists must try to sift through, evaluate and consider applying. Unfortunately and quite commonly, time constraints and an inability to access these data sets leave many oncologists struggling to ensure that they're aware of crucial practice-altering findings. This creates an almost insurmountable obstacle for clinicians in community practice because they are not only confronted almost overnight with thousands of new presentations and data sets to consider but they are also severely restricted in their ability to review and interrogate the raw findings.

To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets on novel agents and salvage therapeutic options for the treatment of relapsed or refractory multiple myeloma (MM) and Waldenström macroglobulinemia (WM), high-risk smoldering MM (SMM) and the front-line management of AL amyloidosis from the latest ASH meeting, including expert perspectives on how these new evidence-based concepts may be applied to routine clinical care. This activity will assist medical oncologists, hematologists, hematology-oncology fellows and other healthcare professionals in the formulation of optimal clinical management strategies and the timely application of new research findings to best-practice patient care.

LEARNING OBJECTIVES

- Evaluate the final efficacy and safety results from the Phase I/II 1703 study of elotuzumab in combination with lenalidomide and dexamethasone for patients with relapsed/refractory MM.
- Appraise recent clinical research findings on the effectiveness of the monoclonal anti-CD38 antibodies SAR650984 and daratumumab in combination with lenalidomide and dexamethasone in relapsed/refractory MM.
- Investigate the efficacy and safety of ibrutinib as a single agent or in combination with dexamethasone in relapsed or relapsed/refractory MM.
- Compare and contrast the benefits and risks of lenalidomide and low-dose dexamethasone with or without carfilzomib for patients with high-risk SMM.
- Analyze the role of front-line cyclophosphamide in combination with bortezomib and dexamethasone (CyBorD) in AL amyloidosis.
- Assess the safety and efficacy of the proteasome inhibitor oprozomib as a single agent in the treatment of WM.

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 1.5 *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 slides and edited commentary. To receive credit, the participant should review the slide presentations, read the commentary, complete the Post-test with a score of 75% or better and fill out the Educational Assessment and Credit Form located at ResearchToPractice.com/5MJCASH2015/6/CME.

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 potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent 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 real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

Ola Landgren, MD, PhD
Chief, Myeloma Service
Memorial Sloan Kettering Cancer Center
New York, New York

Contracted Research: Celgene Corporation, Onyx Pharmaceuticals, an Amgen subsidiary.

EDITOR — Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Amgen Inc, Astellas Scientific and Medical Affairs Inc, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, Biodesix Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Corporation, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, Incyte Corporation, Janssen Biotech Inc, Jazz Pharmaceuticals Inc, Lilly, Medivation Inc, Merck, Myriad Genetic Laboratories Inc, NanoString Technologies, Novartis Pharmaceuticals Corporation, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pharmacyclics Inc, Prometheus Laboratories Inc, Regeneron Pharmaceuticals, Sanofi, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Teva Oncology, Tokai Pharmaceuticals Inc and VisionGate Inc.

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

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.

This activity is supported by educational grants from Bristol-Myers Squibb Company, Celgene Corporation, Incyte Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Seattle Genetics and Takeda Oncology.

Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: May 2015
Expiration date: May 2016

5 MinuteJournalClub

POST-ASH Issue 6, 2015

To go directly to slides and commentary for this issue, **click here**.

Sagar Lonial, MD

One of my favorite days of the year occurs every April when the American Society of Clinical Oncology (ASCO) releases their iPlanner for the upcoming annual meeting that provides a first glimpse at the titles of all the oral abstracts that will be presented during the conference. This year my review quickly established that in the world of solid tumors there would be many highlights, including the long-awaited MARIANNE report evaluating pertuzumab and T-DM1 in HER2-positive breast cancer and a ton of impressive checkpoint inhibitor papers in lung cancer (squamous and nonsquamous), melanoma and a number of other diseases.

In terms of hematologic cancers, ASCO is always good for a few headline grabbers, and in reviewing the papers, my attention was immediately drawn to the first abstract in the multiple myeloma (MM) oral session — the Phase III ELOQUENT-2 trial in relapsed/refractory (RR) disease. The study, one of the most anticipated in MM in many years, randomized patients to lenalidomide (len)/dexamethasone (dex) alone or combined with the novel monoclonal antibody elotuzumab (elo).

This was definitely not the first time I became aware ahead of time that an important new data set was about to be presented, and as usual I was desperately curious to find out the results. About a week later I had my chance when the principal investigator, Dr Sagar Lonial, participated in a symposium we were doing as part of our always rewarding annual visit to the Oncology Nursing Society Congress. However, as usual my hopes were crushed by a strict embargo, and Sagar was a complete stone-wall Buddha sphinx, rebuffing all my attempts to squeeze the information out of him and leaving me totally clueless whether the study proved what earlier smaller trials suggested, namely that a special synergy exists between this antibody, which has no single-agent activity, and len.

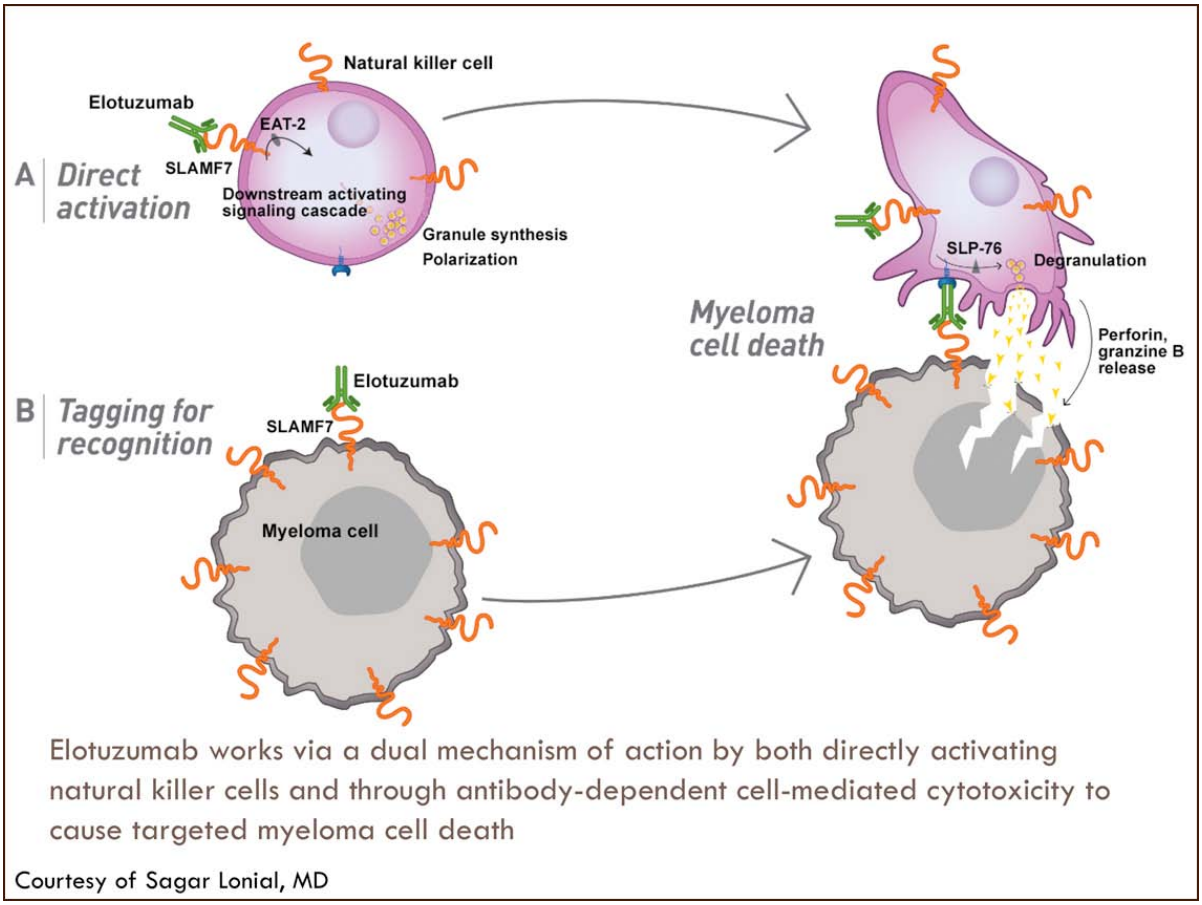
Fast forward to a week ago, when ASCO released online all but the late-breaking abstracts. My first click was to ELOQUENT-2, and to my delight, elo/len/dex resulted in a 30% reduction in the risk of disease progression and also a mortality benefit. While we most definitely need to see the data and hear Sagar and the rest of the myeloma community's take, if first impressions are any indication it could be that finally a cancer of cells that produce antibodies is soon going to have one as part of its treatment.

However, until the fun begins in Chicago, there is still much work to be done, and this issue of our American Society of Hematology (ASH) review series highlights a number of new directions in the treatment of MM, including antibodies, and several other related (at least in terms of who manages them) diseases, including Waldenström macroglobulinemia and AL amyloidosis.

Monoclonal antibodies in MM

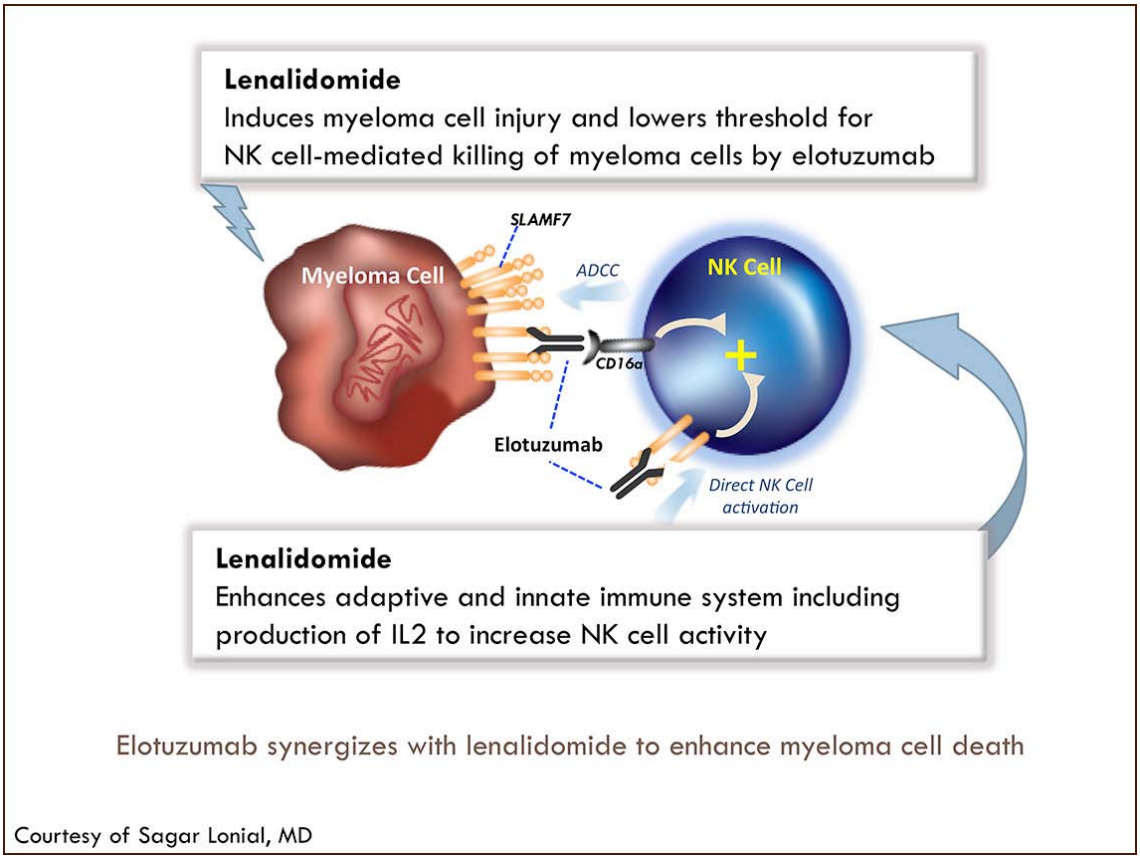
• Elo/len/dex

After years of asking investigators to explain how immunomodulating drugs work (and still not completely understanding the answer), I suspect that elo may be even more of a challenge. Signaling lymphocytic activation molecule F7 (SLAMF7) is a glycoprotein that is highly expressed on MM and natural killer (NK) cells but not on normal tissue. As a monoclonal antibody targeted against SLAMF7, elo is thought to directly activate and engage NK cells and selectively target SLAMF7-expressing MM cells for destruction.



Elotuzumab works via a dual mechanism of action by both directly activating natural killer cells and through antibody-dependent cell-mediated cytotoxicity to cause targeted myeloma cell death

Courtesy of Sagar Lonial, MD



Elotuzumab synergizes with lenalidomide to enhance myeloma cell death

Courtesy of Sagar Lonial, MD

As we learn more about the biologic basis of the apparently important synergy of len and elo, ongoing trials are evaluating this approach clinically. At ASH we saw Paul Richardson's **report of 73 patients** with RR MM who were treated with this regimen in the Phase II portion of the 1703 study, revealing similar encouraging outcomes as a prior single-arm study (response rate: 84%) with good tolerability. The bottom line now is that on Tuesday, June 2nd at 9:45 AM in the McCormick Place Convention Center, we will find out just how much it helps patients.

- **Anti-CD38 antibodies with len/dex**

While elo may be first with Phase III data, among MM investigators there is perhaps even more excitement about anti-CD38 agents, particularly daratumumab (dara) and the as yet nameless SAR650984 (sar). For quite some time now on our CME programs we have been hearing about the single-agent activity of these compounds, and I can recall a number of cases with impressive responses after disease progression on multiple therapies. However, the future of MM treatment seems to be combinations, which are firmly entrenched in the induction setting and gaining traction in RR disease. Thus it is no surprise to see strategies like **the 2 featured here** of combining these antibodies with len/dex and producing very good outcomes (77% very good partial response or greater with dara/len/dex; 64.5% overall response rate with sar/len/dex).

Many investigators, including Dr Lonial, believe that depth of response is critical in MM, and the hope has been that bringing in new classes of effective agents might push the disease into a more prolonged remission, also raising the possibility of cure as a treatment goal. Much more to come.

Ibrutinib in MM

Ibrutinib has been a revelation in terms of efficacy and activity across many variants of non-Hodgkin lymphoma, and when laboratory evidence emerged regarding the activation of Bruton tyrosine kinase in MM cells, there was optimism that this drug might play an important role in the management of this disease. Unfortunately, at ASH we saw data from **a Phase II trial** evaluating ibrutinib as a single agent or in combination with dex for patients with RR MM that demonstrated modest, somewhat underwhelming activity (clinical benefit rate of 8% with single-agent ibrutinib and 25% with the combination of ibrutinib/dex). Although further research is ongoing, few are optimistic that ibrutinib in MM will be anything close to what it is in chronic lymphocytic leukemia and mantle-cell lymphoma.

High-risk smoldering MM (SMM)

Although the standard therapy for these patients continues to be observation, a variety of predictive factors identify a subgroup with at least a 75% risk of disease progression at 5 years. As such, there continues to be significant interest in whether early intervention could help improve outcomes for these patients. In this regard, in San Francisco we saw more follow-up from the **landmark Spanish Phase III QUIREDEX trial** that had previously demonstrated an important benefit with the use of len/low-dose dex. With a median follow-up of 64 months, these findings continue to be positive, revealing that progression to symptomatic disease occurred in 25% of patients who received treatment versus 85% in the control group (overall survival rate at 7 years: 94% versus 64% with a hazard ratio of 4.6 and $p = 0.001$).

The NCI group formerly led by Ola Landgren, MD, PhD decided to take things even further and evaluate a triplet regimen, in this case carfilzomib/len/dex, followed by len maintenance in patients with high-risk SMM. Among the 12 patients who received treatment in this manner, 10 became MRD-negative after 8 cycles as determined by next-generation sequencing, which, by way of indirect comparison, appears to be an even greater benefit than the approach taken by the Spanish.

Importantly, a number of ongoing studies are pursuing these encouraging leads, including a major ECOG trial chaired by Dr Lonial in an attempt to confirm the Spanish len/dex data, and it could very well be that one day soon treating high-risk SMM will become part of practice.

Cyclophosphamide/bortezomib/dex (CyBorD) in AL amyloidosis (ALA)

Based on the results from a number of smaller trials, CyBorD has become one of the most commonly used up-front regimens for the treatment of this disease. To further confirm the benefits of this approach, 2 major ALA centers in London, England and Pavia, Italy prospectively collected findings from 230 cases of patients with newly diagnosed disease who received this regimen. The result is the **largest data set ever reported** with up-front CyBorD in the disease, from which a number of important observations can be made. Notably, of 30 patients with Stage I ALA (no cardiac

involvement), 80% responded (56% complete response/very good partial response) and there were no deaths with a median of 25 months of follow-up. Median survival of all patients was 72 months.

However, it appears that cardiac stage was the main determinant of survival, and patients with advanced heart disease (defined as those with N-terminal pronatriuretic peptide type B >8,500 ng/L) had poor outcomes, although 37% did achieve a response and seemed to fare better overall. The key takeaway from this data set is that due to the high clonal response and excellent outcome in early-stage ALA, CyBorD remains a preferred induction option and further research is needed to determine whether autologous stem cell transplant should be initiated as part of up-front treatment.

Novel agents in Waldenström macroglobulinemia (WM)

On January 29, 2015, ibrutinib became the first ever agent approved by the FDA for the management of WM. This significant milestone, along with emerging data indicating the activity of a number of other established and novel therapeutics, has breathed new life and interest into the treatment of this rare disease. At ASH we saw several examples of work attempting to move the field forward, including a Phase I/II trial evaluating **single-agent len** in 17 patients with RR WM. Thirty-six percent of these individuals responded to therapy, and with a median follow-up of 36 months, 35% of patients had a progression-free survival greater than 24 months.

Similarly, we also saw data from a Phase Ib/II trial evaluating the oral proteasome inhibitor oprozomib, which, like its intravenous cousin carfilzomib, appears to have significant efficacy in this disease. Notably, responses were observed in 5 of 7 patients refractory to bortezomib, and treatment was reasonably well tolerated, although some of the gastrointestinal toxicity that has plagued this agent was observed. To potentially eliminate this troubling side effect there is great interest in evaluating an extended-release formulation of the agent in both MM and WM.

Next, on the final issue of our ASH series, we check out papers on non-Hodgkin lymphoma, including the evaluation of anti-CD20 maintenance treatment in mantle-cell lymphoma.

Neil Love, MD
Research To Practice
Miami, Florida

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

Research To Practice designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

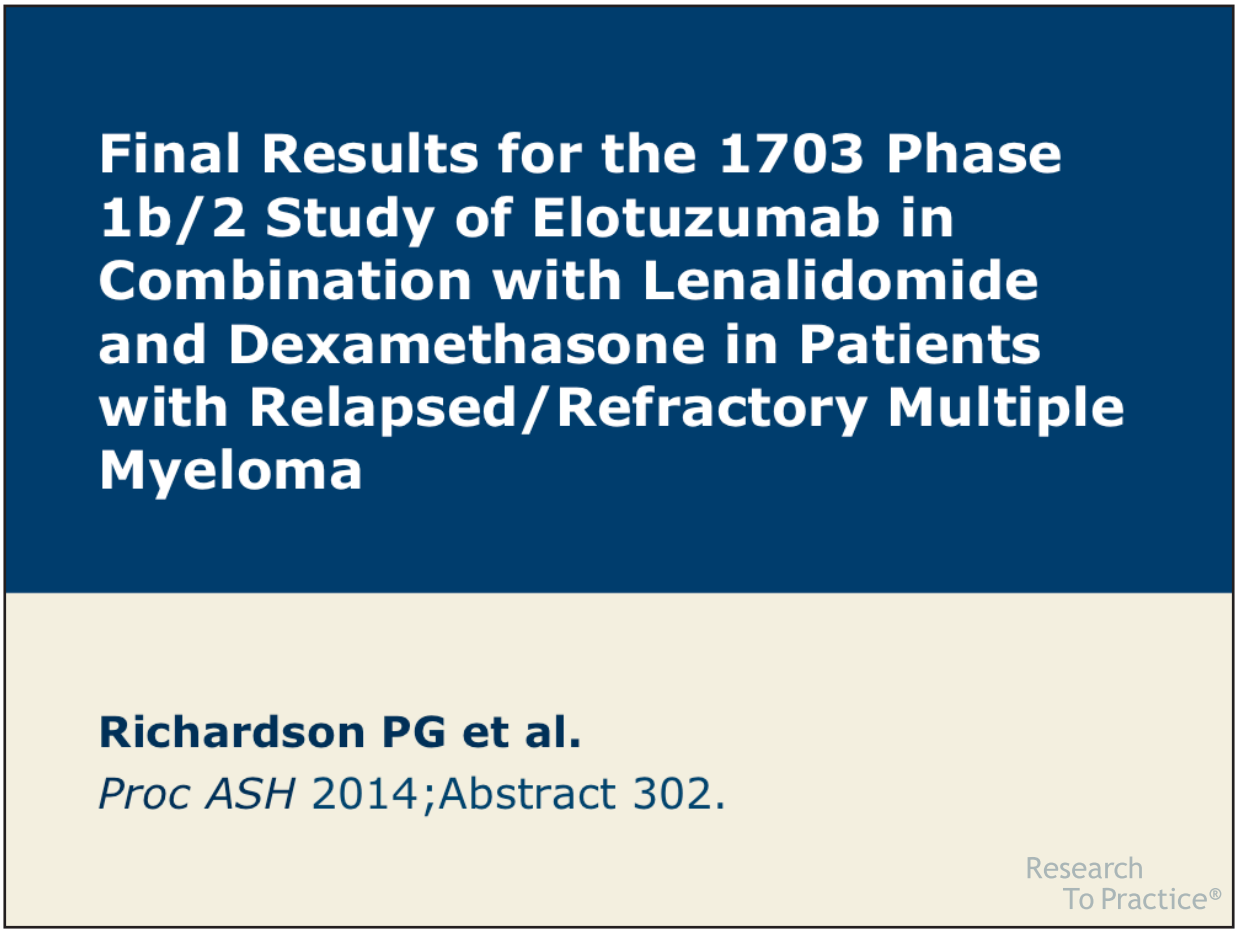
This activity is supported by educational grants from Bristol-Myers Squibb Company, Celgene Corporation, Incyte Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Seattle Genetics and Takeda Oncology.

Final Efficacy and Safety Results from the 1703 Phase Ib/II Study of Elotuzumab/Lenalidomide/Dexamethasone in Relapsed/Refractory MM

Presentation discussed in this issue

Richardson PG et al. **Final results for the 1703 phase 1b/2 study of elotuzumab in combination with lenalidomide and dexamethasone in patients with relapsed/refractory multiple myeloma.** *Proc ASH* 2014;**Abstract 302**.

Slides from a presentation at ASH 2014 and transcribed comments from a recent interview with Ola Landgren, MD, PhD (2/9/15)



Background

- Elotuzumab (Elo) is a humanized IgG1 monoclonal antibody targeted against the signaling lymphocytic activation molecule F7 (SLAMF7, also known as CS1).
  - SLAMF7 is a glycoprotein that is highly expressed on multiple myeloma (MM) and natural killer (NK) cells but not on normal tissues (*Clin Cancer Res* 2008;14:2775).
  - Through direct activation and engagement of NK cells, Elo selectively targets and kills SLAMF7-expressing MM cells.
- In the Phase I part of the 1703 study, Elo in combination with lenalidomide (Len) and low-dose dexamethasone (dex) resulted in an objective response rate (ORR) of 82% among patients with relapsed/refractory MM (RRMM) (*JCO* 2012;30:1953).
- **Study objective:** To report the final Phase I and II efficacy and safety results from the 1703 study for patients with RRMM.

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

Phase Ib/II 1703 Trial Design (NCT00742560)

Eligibility

Patients with RRMM
1-3 prior therapies
No prior Len therapy
No peripheral stem cell transplant
≤12 weeks before first dose of Elo
No Grade ≥3 neuropathy

Phase Ib (dose escalation)
Elo at 5, 10, 20 mg/kg
+ Len/dex
(n = 28*)

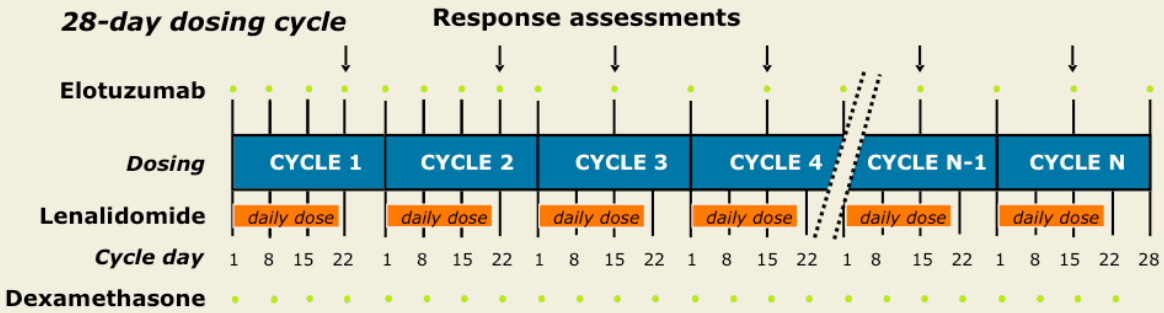
Phase II
Elo at 10 or 20 mg/kg
+ Len/dex
(n = 73)

* The first 5 patients were limited to 6 cycles of tx; the remaining 23 patients received tx until progression or unacceptable toxicity.

- Len dose: 25 mg; dex dose: 40 mg
- **Primary endpoints:**
  - Phase Ib: The maximum tolerated dose (MTD) of Elo
  - Phase II: ORR
- **Secondary endpoints** include progression-free survival (PFS) and safety

Richardson PG et al. *Proc ASH* 2014;Abstract 302; Lonial S et al. *J Clin Oncol* 2012;30(16):1953-9.

Phase II Dosing Schedule



- Patients were randomly assigned to receive Elo at 10 or 20 mg/kg and Len/dex.
- Premedication regimens were administered to reduce the risk of infusion reactions.

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Summary of Results from the Phase Ib Portion of Study 1703

- No dose-limiting toxicities were observed.
- The MTD was not reached.
- As of data cutoff date August 20, 2010
  - The ORR: 23/28 (82%)
  - After a median follow-up of 16.4 months, the median time to progression (TTP) was not reached in the 20-mg/kg cohort
- As of data cutoff date January 16, 2014
  - Median TTP: 33 months for all treatment groups (n = 28)
- These results compare favorably to results in 2 randomized studies of Len/dex with similar patient populations (*NEJM* 2007;357:2133; *NEJM* 2007;357:2123).

Richardson PG et al. *Proc ASH* 2014;Abstract 302; Lonial S et al. *J Clin Oncol* 2012;30(16):1953-9.

Phase II: Response

Response rate	Elo (10 mg/kg) (n = 36)	Elo (20 mg/kg) (n = 37)	Total (n = 73)
ORR	33 (92%)	28 (76%)	61 (84%)
sCR	2 (6%)	1 (3%)	3 (4%)
CR	4 (11%)	3 (8%)	7 (10%)
VGPR	17 (47%)	14 (38%)	31 (43%)
PR	10 (28%)	10 (27%)	20 (27%)
Stable disease	3 (8%)	7 (19%)	10 (14%)

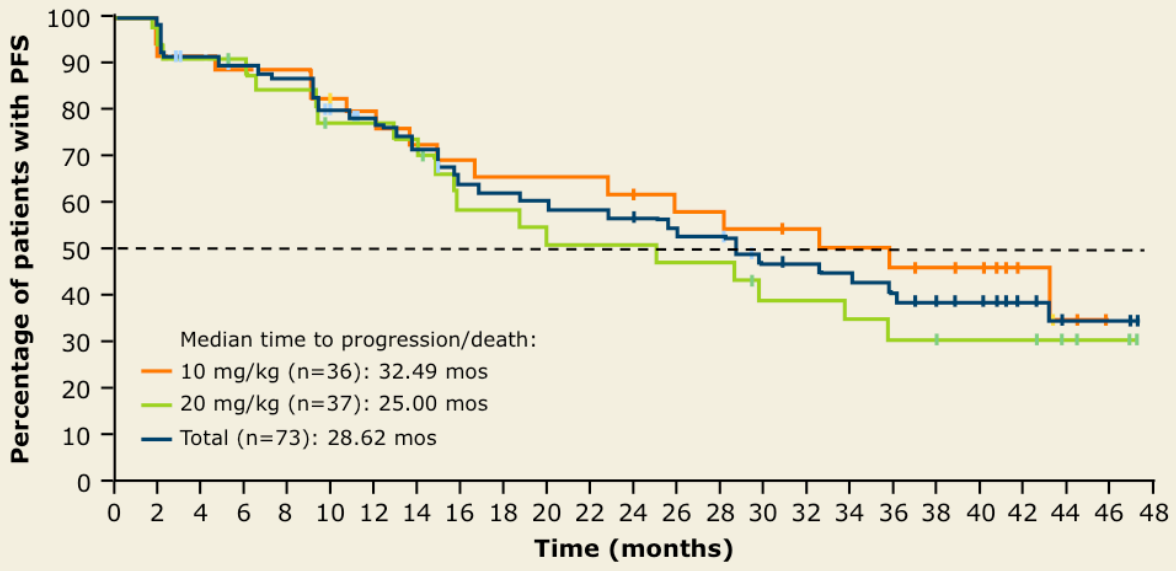
CR = complete response; sCR = stringent CR; PR = partial response; VGPR = very good PR

- Missing data: 10 mg/kg (none); 20 mg/kg (n = 2)
- Median time to first response: 1 mo (10 mg/kg); 1.7 mo (20 mg/kg), 1 mo (all)
- Median duration of response: 23 mo (10 mg/kg); 18 mo (20 mg/kg), 20.8 mo (all)

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

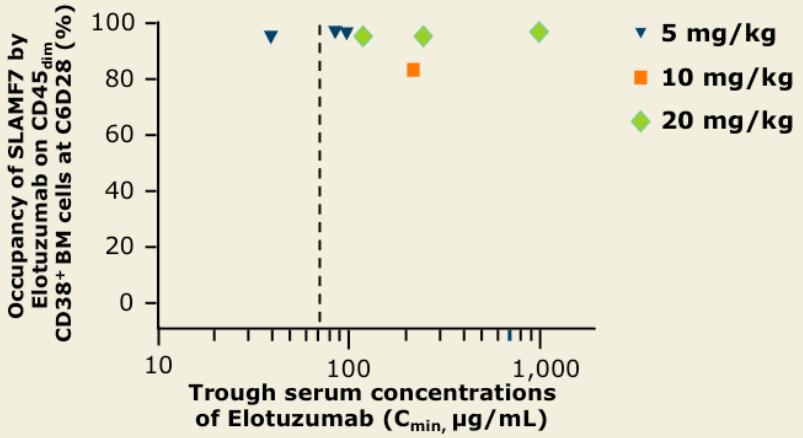
PFS



With permission from Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

Pharmacokinetics (PK)/ Pharmacodynamics (PD)



- Steady state Elo serum concentrations >70 µg/mL maintained at both 10- and 20-mg/kg doses, consistent with optimal antitumor concentration observed in a preclinical model (*JCO* 2012;30:1953; *Blood* 2008;112:1329).
- Saturation of SLAMF7 sites on bone marrow MM cells >80% observed at both 10- and 20-mg/kg doses (*JCO* 2012;30:1953).
- Equivalent tolerability, efficacy and PD between 10- and 20-mg/kg doses observed during the 2 phases of Study 1703.

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

Phase II: Select Adverse Events (AEs)

Event	Elo at 10 mg/kg (n = 36)		Elo at 20 mg/kg (n = 37)	
	All grades	Grade 3/4	All grades	Grade 3/4
Diarrhea	67%	14%	65%	5%
Fatigue	67%	8%	46%	5%
Anemia	47%	17%	32%	14%
Back pain	47%	8%	35%	3%
Pyrexia	39%	3%	46%	3%
Lymphopenia	36%	28%	22%	14%
Thrombocytopenia	36%	19%	19%	16%
Neutropenia	31%	19%	22%	19%
Hyperglycemia	25%	6%	32%	14%

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

Phase II: Select Infusion-Related Reactions (IRRs)

Event (n)	Rate ≤2 mL/min		Rate >2 mL/min	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Pyrexia	3	0	0	0
Rash	2	1	0	0
Nausea	1	0	1	0
Abdominal pain	1	0	0	0
Chest discomfort	1	0	0	0
Chills	1	0	0	0

- Other Grade 1 or 2 IRRs at ≤2 mL/min: 1 each of flushing, hot flush, pain.
- For patients who tolerated infusion at 2 mL/min, the flow rate was progressively increased to a maximum of 5 mL/min (infusion time <1 h).
- The overall rate of IRRs was 11%.
- 7 patients had an IRR at <2 mL/min; 1 patient had an IRR at ≥2 mL/min.
- Of the 3,412 infusions given, 1,127 (33%) were at a rate of 5 mL/min.

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Author Conclusions

- In the Phase II portion of the study, Elo in combination with Len/dex demonstrated encouraging efficacy:
  - ORR: 92% in the 10-mg/kg treatment group (84% overall)
  - Median PFS: 32.49 mo in the 10-mg/kg group (29 mo overall)
- The most common treatment-emergent AEs included diarrhea (66%), fatigue (56%), muscle spasms (52%) and constipation (51%).
- The use of premedication regimens successfully mitigated IRRs.
- A faster infusion rate at 5 mL/min with infusion time <1 h was well tolerated.
- Efficacy and safety outcomes observed in the Phase II portion of the study concur with previous Phase Ib study results (*JCO* 2012;30:1953).

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Future Directions

- Phase III controlled trials with 10 mg/kg of Elo in combination with Len/dex in newly diagnosed MM and RRMM are ongoing (ELOQUENT-1 and ELOQUENT-2).
- A Phase II trial to evaluate the safety and tolerability of Elo at 10 mg/kg infused at 5 mL/min and administered in combination with Len/dex to patients with RRMM is under way (NCT02159365).
- An ongoing Phase II trial to evaluate the efficacy of Elo monotherapy for patients with high-risk smoldering MM has completed enrollment (NCT01441973).
- A Phase II trial to evaluate the efficacy of Elo in combination with Len/dex for patients with high-risk smoldering MM is under way (NCT02279394).

Richardson PG et al. *Proc ASH* 2014;Abstract 302.

Research To Practice®

Investigator Commentary: Final Efficacy and Safety Results from the Phase Ib/II Trial of Elo/Len/Dex in RRMM

In this small study Elo was administered in combination with Len/dex to patients with RRMM. Consistent with what has been shown before in other smaller studies, the combination is meaningful and translates into ORR and PFS outcomes better than those with Len/dex alone. This is another good option for patients who do not achieve results with Len/dex, and I'm happy to see these results. The combination will be tested in a Phase III study, and we are awaiting those results.

The interactions between Len and Elo are not fully understood. Elo targets an antigen, CS1, or SLAMF7, that is expressed on the surface of MM cells, and it also directly activates NK cells. Why it works when combined with Len but not alone is not clear. Initially Elo was tested as a single agent, but it was not effective. Len has immunostimulatory properties, and it seems to stimulate NK cells. One of the reasons why the combination works may be the ability to activate an increased number of NK cells that are targeted against SLAMF7-expressing MM cells, and this has been the proposed mode of action. I don't believe we have preclinical data to prove these proposed models.

Interview with Ola Landgren, MD, PhD, February 9, 2015

Research To Practice®