5 Minute JournalClub

Key ASCO Presentations
Issue 3, 2010

Lenalidomide as Initial Treatment for Elderly Patients with Chronic Lymphocytic Leukemia (CLL)

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CME INFORMATION

OVERVIEW OF ACTIVITY

Each year, thousands of clinicians and basic scientists sojourn to the American Society of Clinical Oncology (ASCO) Annual Meeting to learn about recent clinical advances that yield alterations in state-of-the-art management for all tumor types. Attracting tens of thousands of attendees from every corner of the globe to both unveil and digest the latest research, ASCO is unmatched in attendance and clinical relevance. Results presented from ongoing trials lead to the emergence of new therapeutic agents and changes in the indications for existing treatments across all cancer medicine. Despite the importance of the conference, the demands of routine practice often limit the amount of time oncology clinicians can realistically dedicate to travel and learning. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the key presentations from the ASCO Annual Meeting and expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists and other cancer clinicians in the formulation of optimal clinical management strategies for patients with diverse forms of cancer.

LEARNING OBJECTIVE

- Cite the most common adverse events and objective response rates with lenalidomide in the initial treatment of elderly patients with CLL.

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Stephanie A Gregory, MD
The Elodia Kehm Chair of Hematology
Professor of Medicine
Director, Section of Hematology
Rush University Medical Center/Rush University
Chicago, Illinois

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To go directly to the slides, **click here**.

Oncologists who were reared on the "shock and awe — MTD" approach to systemic anticancer therapy now understand that the chronic disease model is where the field has been headed for years, and about a decade ago, when imatinib was first being administered indefinitely in CML, Paul Goss proved that in breast cancer, fewer relapses occurred when endocrine therapy was extended beyond five years. This important development led Paul and others to compare breast cancer to follicular lymphoma (FL), with its relapsing and remitting nature and long-term requirement for treatment.

In the past six months, the breast cancer/FL analogy has become even more evident, beginning at ASH with the emergence of bendamustine/rituximab (BR), or as I see it, the "TC" of indolent lymphoma, and then at ASCO, where for the first time, we saw conclusive evidence that the duration of rituximab for FL, as in endocrine therapy for breast cancer, really matters.

A slew of imperfect answers for the question of R maintenance in FL have been reported in the past few years, but investigators were skeptical that more R after R-chemo made a difference. Oncologists in practice weren't as doubtful, and our Patterns of Care data have demonstrated that many have used this strategy for some time. The issue was somewhat laid to rest at ASCO with the **PRIMA presentation**, and Dr Richard Fisher, the paper's discussant, didn't mince words when he stated that R maintenance should now be used in patients with FL requiring treatment. However, after speaking with a number of investigators in the field, I don't see a consensus yet on the clinical and research implications of this data set, in spite of the reduction in two-year risk of disease progression from 34 percent without R maintenance to 18 percent with it. Meanwhile, the Germans, who already created BR and were kicking butt in the World Cup until they encountered Spain, continue to be ahead of the game and 14 months ago launched a randomized trial evaluating BR followed by either two or four years of R maintenance.

Also in this issue:

1. **Pretransplant R purging and post-transplant maintenance** extends progression-free survival in patients with FL.

2. **A Phase II study of the IMiD®** lenalidomide combined with rituximab for indolent lymphoma results in complete tumor responses in more than two thirds of patients.

3. In another **Phase II study for patients older than age 65 with CLL**, treatment with lenalidomide results in responses in 62 percent of patients, without Grade III/IV tumor lysis syndrome or flare.

Next up on 5-Minute Journal Club: The chronic disease model comes to multiple myeloma as two major randomized trials demonstrate benefit for lenalidomide maintenance after transplant.

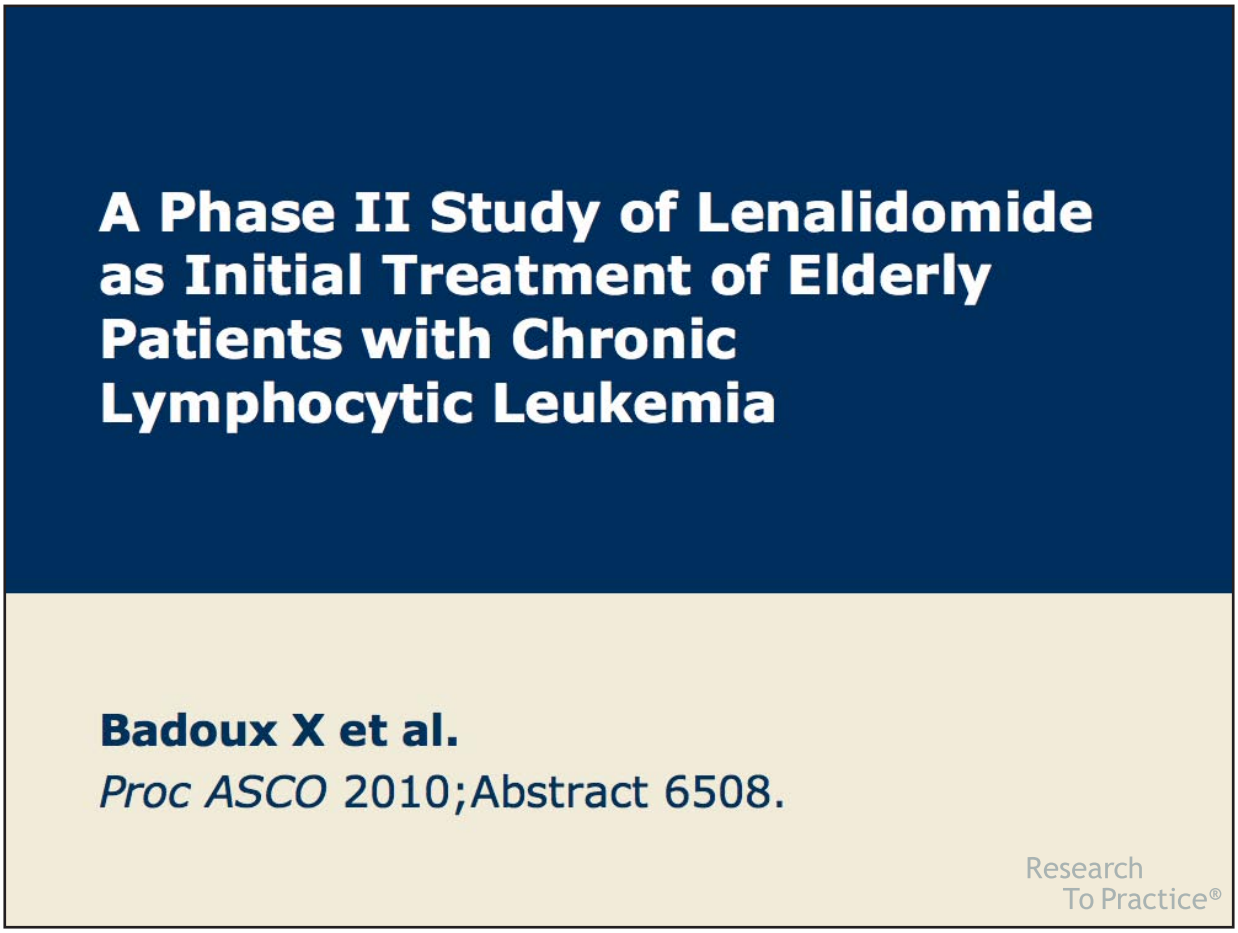
Neil Love, MD
Research To Practice
Miami, Florida

Lenalidomide as Initial Treatment for Elderly Patients with Chronic Lymphocytic Leukemia (CLL)

Presentation discussed in this issue

Badoux X et al. **A Phase II study of lenalidomide as initial treatment of elderly patients with chronic lymphocytic leukemia.** *Proc ASCO* 2010;**Abstract 6508**.

Slides from a presentation at ASCO 2010 and transcribed comments from a recent interview with Stephanie A Gregory, MD (6/18/10)



Introduction

- Median age of diagnosis of patients with chronic lymphocytic leukemia (CLL) is 72 years.
- Elderly patients with CLL are under-represented in clinical trials and have increased toxicity with immunochemotherapy.
- Lenalidomide is an oral immunomodulatory drug that has activity in relapsed CLL (*J Clin Oncol* 2006;24:5343, *Blood* 2008;111:5291).
- **Current study objective:**
  - To evaluate the activity of lenalidomide as initial treatment in elderly patients with CLL.

Badoux X et al. *Proc ASCO* 2010;Abstract 6508.

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Phase II Study of Lenalidomide in Elderly Patients with CLL

Eligibility (N = 60)

Untreated and symptomatic CLL
Age ≥ 65 years
PS 0-2

↓

Lenalidomide 5 mg/day x 2 cycles (56 days)
Increase by 5 mg/cycle (28 days) to maximum 25 mg/day
Treatment continued until progression

Allopurinol 300 mg PO QD days 1-14 cycle 1

No mandated antibiotic, antiviral, DVT or tumor flare prophylaxis

Response assessed at the end of cycle 3 and then every 6 cycles

Badoux X et al. *Proc ASCO* 2010;Abstract 6508.

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Efficacy Results

Clinical Parameter	NCI Response* (N = 60)	
	Patients, n	%
Complete response (CR)	6	10
CRi	3	5
Nodular partial response	3	5
Partial response	25	42
Overall response rate (ORR)	**37**	**62**

Clinical Parameter	Response at Assessment Times			
	3 cycles	9 cycles	15 cycles	21 cycles
ORR, n (%)	24 (40)	34 (57)	36 (61)	30 (57)

* 2008 NCI-WG criteria used; CRi = CR with incomplete blood count recovery.

Badoux X et al. *Proc ASCO* 2010;Abstract 6508.

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Efficacy by Patient Pre-Treatment Characteristics

Patient Characteristic		n	ORR
Age, years	65-74	43	72%
	≥75	**17**	**35%***
IGHV genes	mutated	22	50%
	unmutated	33	73%
FISH hierarchy	del13q	15	73%
	negative	12	50%
	trisomy 12	13	92%
	del 11q	14	57%
	del 17p	**6**	**0%***

* $p < 0.05$

Badoux X et al. *Proc ASCO* 2010;Abstract 6508.

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Adverse Events (N = 60)

Adverse Event	Grade ≥3
Neutropenia	38%
Thrombocytopenia	<14%
Neutropenic fever	5%
Pneumonia/bronchitis	3%
Fatigue	3%
Sepsis	2%
Tumor flare*	0%

* 50% of patients had Grade 1/2 tumor flare.

Badoux X et al. *Proc ASCO* 2010;Abstract 6508.

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Conclusions

- Lenalidomide as a single agent induces clinical responses in the front-line treatment of elderly patients with CLL.
  - ORR: 62%
  - 2-year overall survival: 90% (data not shown)
  - 2-year progression-free survival: 60% (data not shown)
- Quality of responses improve over time.
- Myelosuppression is the most common toxicity.
- No severe tumor flare or tumor lysis syndrome was observed.
- A Phase II trial of lenalidomide in combination with rituximab as up-front treatment in CLL is ongoing.

Badoux X et al. *Proc ASCO* 2010;Abstract 6508; Rai K. ASCO 2010;Discussion.

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Investigator comment on lenalidomide as initial treatment for CLL in the elderly

With lenalidomide in CLL, we don't use the doses used in myeloma or MDS because patients with CLL get tumor lysis syndrome and tumor flare, in which the lymph nodes become large, swollen, red and painful.

In this MD Anderson study of patients with CLL over 65 and requiring treatment, investigators started gingerly with a 5-mg daily dose of lenalidomide for two 28-day cycles, and then if patients tolerated that, they escalated by another five mg every cycle, up to a 25-mg dose.

There was a 62 percent response rate and it was relatively nontoxic. There was no Grade III or IV tumor lysis or tumor flare. The presenter also noted that the drug continues to work over time, so you can't be impatient and stop after the first couple of cycles because best response occurred after nine cycles.

A new trial concept in CLL is maintenance lenalidomide — after patients have had a response from FCR, for example. A few years ago we investigated alemtuzumab maintenance but there was too much toxicity from immunosuppression. We need something in CLL for maintenance, similar to the rituximab maintenance in the low-grade lymphomas.

Interview with Stephanie A Gregory, MD, June 18, 2010

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