5 Minute JournalClub

Key ASCO Presentations
Issue 3, 2010

In Vivo Purging with Rituximab Before Stem Cell Collection and Maintenance Rituximab After Transplant for Patients with Relapsed Follicular Lymphoma (FL)

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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

- Describe the clinical impact of in vivo purging and/or maintenance rituximab in patients with relapsed FL who have experienced a response to reinduction and proceeded to transplant.

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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:

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Consultant: Amgen Inc, Genentech BioOncology, Novartis Pharmaceuticals Corporation, Spectrum Pharmaceuticals Inc; Research Support: Celgene Corporation, Curatech Co, Genentech BioOncology, GlaxoSmithKline, Immunomedics Inc, Onyx Pharmaceuticals Inc; Speakers Bureau: Cephalon Inc, Genentech BioOncology, GlaxoSmithKline, Millennium Pharmaceuticals Inc, Spectrum Pharmaceuticals Inc.

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Consulting Agreements: Biogen Idec, Biotest Pharmaceuticals Corporation, Calistoga Pharmaceuticals Inc, Celgene Corporation, Cephalon Inc, CT International, Eisai Inc, EMD Serono Inc, Genentech BioOncology, GlaxoSmithKline, Gloucester Pharmaceuticals, Immunomedics Inc, Intellikine, Johnson & Johnson Pharmaceuticals, Millennium Pharmaceuticals Inc, Novartis Pharmaceuticals Corporation, Pfizer Inc, Sanofi-Aventis, Wyeth.

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: Abraxis BioScience, Allos Therapeutics, Amgen Inc, AstraZeneca Pharmaceuticals LP, Aureon Laboratories Inc, Bayer HealthCare Pharmaceuticals/Onyx Pharmaceuticals Inc, Biogen Idec, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Cephalon Inc, Eisai Inc, EMD Serono Inc, Genentech BioOncology, Genomic Health Inc, Genzyme Corporation, Lilly USA LLC, Millennium Pharmaceuticals Inc, Monogram BioSciences Inc, Novartis Pharmaceuticals Corporation, OSI Oncology, Sanofi-Aventis and Spectrum Pharmaceuticals Inc.

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This program is supported by educational grants from Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology and Millennium Pharmaceuticals Inc.

Last review date: July 2010
Expiration date: July 2011

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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
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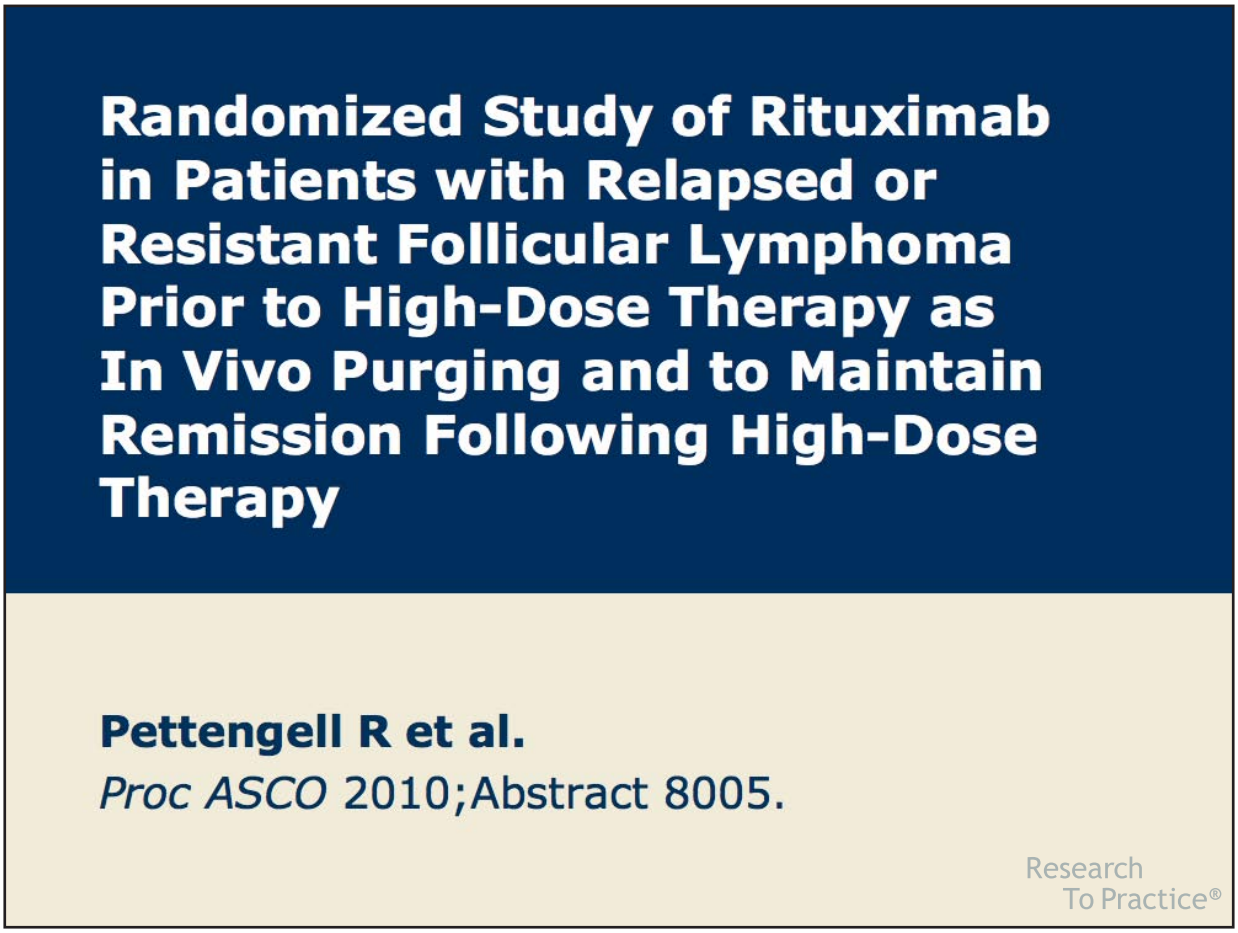
In Vivo Purging with Rituximab Before Stem Cell Collection and Maintenance Rituximab After Transplant for Patients with Relapsed Follicular Lymphoma (FL)

Presentation discussed in this issue

Pettengell R et al. **Randomized study of rituximab in patients with relapsed or resistant follicular lymphoma prior to high-dose therapy as in vivo purging and to maintain remission following high-dose therapy.** *Proc ASCO* 2010;**Abstract 8005**.

Slides from a presentation at ASCO 2010 and transcribed comments from recent interviews with Stephanie A Gregory, MD (6/18/10) and John P Leonard, MD (6/28/10)



Introduction

- Retrospective series have shown improved progression-free survival (PFS) with in vivo rituximab purging with or without rituximab maintenance in patients with follicular lymphoma (FL) undergoing transplantation (*Bone Marrow Transplant* 2008;43:701, *JCO* 2008;26:3614).

- **Current study objective:**
  - To evaluate the effects of in vivo rituximab purging and maintenance rituximab on PFS in patients with relapsed FL undergoing high-dose therapy with BEAM conditioning.

Pettengell R et al. *Proc ASCO* 2010;Abstract 8005.

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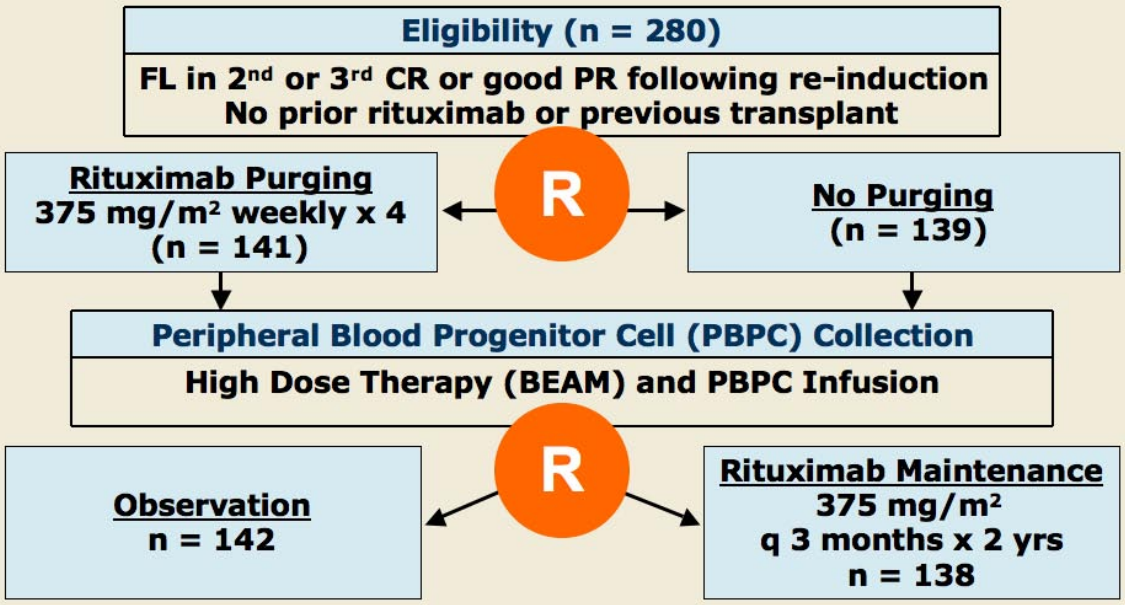
Study Design



Pettengell R et al. *Proc ASCO* 2010;Abstract 8005.

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Survival Analysis

	5-Year PFS*	5-Year OS†
Purging and maintenance (n = 69)	62.9%	79.5%
Purging only (n = 72)	46.0%	84.8%
Maintenance only (n = 69)	56.0%	80.5%
No purging or maintenance (n = 70)	37.6%	78.4%

* *p*-value = 0.004 (trend test), hazard ratio = 0.76
† *p*-value > 0.1 (trend test); OS = overall survival

Pettengell R et al. *Proc ASCO* 2010;Abstract 8005.

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Effect of Rituximab Purging and Maintenance on Survival

	Purging	No Purging
5-year PFS	54.1%	48.0%
Hazard ratio (*p*-value)	0.81 (*p*>0.2)	
	Maintenance	**No Maintenance**
5-year OS	80.0%	81.5%
Hazard ratio (*p*-value)	0.88 (*p*>0.6)	

Pettengell R et al. *Proc ASCO* 2010;Abstract 8005.

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Conclusions

- Rituximab maintenance after transplant improves PFS (p = 0.01).
- A combination of in vivo purging with rituximab before stem cell collection and rituximab maintenance after transplant results in superior PFS compared to no rituximab.
- No improvement in overall survival with either in vivo rituximab purging or rituximab maintenance was seen in this patient population.

Pettengell R et al. *Proc ASCO* 2010;Abstract 8005; Fisher RI. ASCO 2010;Discussion.

Investigator comments on rituximab purging and maintenance after transplant for FL

In this study, the European Bone Marrow Transplant Group evaluated patients with relapsed follicular lymphoma who were going to go through autologous stem cell transplant. The question was, can you obtain better results if you purge prior to the transplant preparative regimen? Purging consisted of administering four weeks of rituximab prior to transplant. After transplant, a second randomization took place to maintenance rituximab or observation. Progression-free survival was much better in the group that received both purging and maintenance therapy.

Most of these patients were being transplanted after first relapse. You want to ensure that if you're going to perform a transplant, you perform it sooner rather than later — usually at first or second relapse. That's what this study demonstrated.

Neutropenia had previously been reported with rituximab after transplant, but Dr Pettengell stated that they did not observe neutropenia in their patients who received maintenance rituximab.

I think purging with rituximab and administering maintenance rituximab is probably going to be a new standard.

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

Investigator comments on rituximab purging and maintenance after transplant for FL

One of the kickers in this study is that although autologous stem cell transplant has a role in recurrent indolent lymphoma and certainly can be associated with long-term positive outcomes for some patients, it is not something that we're doing frequently lately, particularly because so many new drugs have come along. However, the use of rituximab in conjunction with autotransplant has become more common, particularly in follicular lymphoma, and this trial provides support for it.

One major caveat of this study is that it dates back. Many of these patients had not received rituximab prior to entering this protocol. So these patients had largely rituximab-naïve disease prior to receiving an autologous stem cell transplant. Obviously, someone undergoing an autologous stem cell transplant today will have received rituximab at various points in time, and it is not clear whether these data apply to patients who have received prior rituximab on multiple occasions prior to autotransplant for follicular lymphoma. This is the main criticism of these data.

Interview with John P Leonard, MD, June 28, 2010

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