



Key ASCO Presentations
Issue 5, 2010

**Effect of Targeted Intraoperative
Radiation Therapy on Local Recurrence
Rate in Early Breast Cancer**

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

- Demonstrate knowledge of the efficacy and safety of targeted intraoperative radiation therapy (TARGIT) in the treatment of early breast cancer.

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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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Consulting Agreement and Paid Travel: Carl Zeiss.

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No real or apparent conflicts of interest to disclose.

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The oral sessions on breast cancer in Chicago this year reflected a huge volume of ongoing research, and as usual there were lots of important messages for oncologists in practice, including the following:

1. Axillary node dissection is on the way out, while intraoperative breast irradiation may be on the way in

[Several related trial reports](#) were the highlight of one major oral session. The NSABP confirmed what most have believed for years: There is no value in axillary dissection for a patient with a clinically negative axilla and a well-performed negative sentinel node biopsy. Two American College of Surgeons trials demonstrated no prognostic value in IHC staining of H&E-negative sentinel nodes and showed that axillary dissection may not be necessary in all patients with positive sentinel nodes. Finally, the legendary trial champion Mike Baum [proved that](#) 30 minutes of intraoperative radiation therapy with a \$300,000 device may yield comparable results to six weeks of conventional radiation therapy in patients after lumpectomy.

2. Anti-HER2 therapy continues to gallop along

[Kathy Miller's early data](#) evaluating the fascinating combination of the chemo/trastuzumab conjugate T-DM1 plus the novel anti-HER2 dimerization inhibitor pertuzumab demonstrated safety, and a related study revealed some possible tissue correlates with efficacy. It's challenging to think of a more creative systemic strategy presented at ASCO.

3. More of the same and something new for advanced disease

[Two presentations on bevacizumab/chemotherapy](#) reinforced much of what we already knew. The first, Joyce O'Shaughnessy's presentation of a mini-meta-analysis of first-line bev/chemo trials confirmed the benefit of this agent on progression-free but not overall survival. This seems to be an emerging theme in cancers with long natural histories, as first-line trials often fail to show a survival benefit, whereas studies with patients who have received multiple prior treatments may show a survival advantage, perhaps because of the complexities of post-first-line therapy, including the potential for crossover. Chris Twelves' ASCO data set

demonstrating a survival advantage with the [new antitubulin agent eribulin](#) is a clear example of this increasingly discussed phenomenon.

In a second presentation addressing anti-angiogenic therapy for advanced breast cancer, Adam Brufsky's reanalysis of the second-line RIBBON 2 trial demonstrated what most believed already: The impact of bev seems relatively independent of its chemo partner.

Next up on 5-Minute Journal Club: The once-mighty imatinib gets another shove out the door with new data on dasatinib, nilotinib and bosutinib in CML.

Neil Love, MD

[Research To Practice](#)

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Effect of Targeted Intraoperative Radiation Therapy on Local Recurrence Rate in Early Breast Cancer

Presentations discussed in this issue

Vaidya JS et al. **Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): An international, prospective, randomised, non-inferiority phase 3 trial.** *Lancet* 2010;[Epub ahead of print].

Abstract

Baum M et al. **Safety and efficacy of targeted intraoperative radiotherapy (TARGIT) for early breast cancer: First report of a randomized controlled trial at 10-years maximum follow-up.** *Proc ASCO* 2010;**Abstract LBA517.**

Slides from a presentation at ASCO 2010 and transcribed comments from recent interviews with Michael Baum, MD, ChM (6/6/10) and Eric P Winer, MD (7/6/10)

Targeted Intraoperative Radiotherapy versus Whole Breast Radiotherapy for Breast Cancer (TARGIT-A Trial): An International, Prospective, Randomised, Non-Inferiority Phase 3 Trial

Baum M et al.

Proc ASCO 2010;Abstract LBA517.

Vaidya JS et al.

Lancet 2010;[Epub ahead of print].

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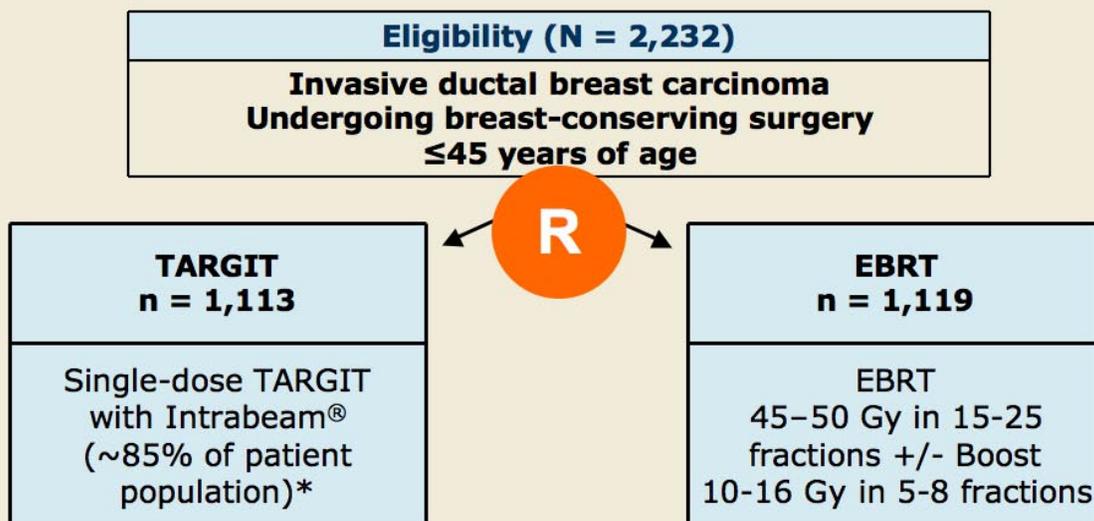
Introduction

- Local recurrence after breast-conserving surgery is located in the index quadrant 90% of the time.
- Restriction of radiation therapy to immediate area surrounding the tumor bed following removal of primary tumor may be adequate (*Br J Cancer* 1996;74:820).
- External beam radiation therapy (EBRT) is a safe and effective treatment.
 - Side effect risk is low but schedule can be inconvenient and is often untenable for elderly women.
- **Current study objective:**
 - Evaluate the approach of substituting targeted intraoperative radiotherapy (TARGIT) for the conventional policy of whole breast EBRT in selected patients with early breast cancer.

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Targeted Intraoperative Radiotherapy (TARGIT-A) Study Design



* Plus EBRT (45-50 Gy, no boost) in patients at high risk (~15%); Pre-specified criteria (unsuspected lobular carcinoma, lymphovascular invasion, etc)

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Local Recurrence Rates in the Conserved Breast

	TARGET n = 1,113	EBRT n = 1,119	p-value
Local recurrence rate	1.2%	0.95%	0.41
95% confidence interval	0.53–2.71	0.39–2.31	—

* Restricted to 4 years as less than 420 patients (<20%) have follow-up beyond this point. All patients (with maximum follow-up of 10 years) are included in the analysis.

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Complications

	TARGET n = 1,113	EBRT n = 1,119	p-value
Any	196 (17.6%)	174 (15.4%)	0.19

Clinically important wound complications	TARGET	EBRT	p-value
Hematoma requiring surgical evacuation	11 (1.0%)	7 (0.6%)	0.338
Seroma requiring more than 3 aspirations	23 (2.1%)	9 (0.8%)	0.012
Infection requiring intravenous antibiotics or surgery	20 (1.8%)	14 (1.3%)	0.292

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Complications

Major toxicity	TARGIT n = 1,113	EBRT n = 1,119	p-value
Skin breakdown or delayed wound healing	31 (2.8%)	21 (1.9%)	0.155
RTOG toxicity Grade 3-4	6 (0.5%)	23 (2.1%)	0.002
Major toxicity	37 (3.3%)	44 (3.9%)	0.443

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Conclusions

- For selected patients with early breast cancer, a single dose of radiotherapy delivered at the time of surgery by use of TARGIT should be considered as an alternative to EBRT delivered over several weeks.
- Rate of local recurrence is not statistically different among TARGIT and EBRT groups at 4 years (1.2% vs 0.95%, $p = 0.41$)
 - Non-inferiority established for TARGIT
- Frequency of any complications and major toxicity overall were similar in TARGIT group versus EBRT group.
 - Major toxicity (3.3% vs 3.9%, $p = 0.44$)
 - RTOG toxicity Grade 3 to 4 (0.5% vs 2.1%, $p = 0.002$)

Baum M et al. *Proc ASCO* 2010;Abstract LBA517; Vaidya JS et al. *Lancet* 2010;[Epub ahead of print].

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Investigator comment on the results of the TARGIT trial of intraoperative radiation therapy

The real challenge of this study was that 90 percent of local recurrences after surgery with or without radiation therapy are in the index quadrant, even though 70 percent of cases have other foci outside the index quadrant. So we now believe that the out-of-the-index-quadrant foci are latent disease. We challenged conventional thinking in two ways: Using partial breast irradiation and completing treatment within 25 to 45 minutes during surgery.

Local recurrence rates were low and equivalent to external beam radiation therapy (EBRT). At a median of four years, the Kaplan-Meier curves are superimposable, with a difference of 0.25 percent in a good-prognosis group of patients.

There were no overall differences in toxicity, but in terms of RTOG radiation toxicity, there was significantly more Grade 3/4 toxicity, particularly skin complications, with EBRT. There was a specific wound complication of seroma with the intraoperative approach. Interestingly, the cosmesis is better with intraoperative radiation therapy due to the seroma, which acts as a "biological implant." We also believe there are other long-term cosmesis advantages, particularly following oncoplastic surgery, because the intraoperative approach provides perfect conformal treatment at the time of surgery.

Interview with Michael Baum, MD, ChM, June 6, 2010

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Investigator comment on the results of the TARGIT trial of intraoperative radiation therapy

The TARGIT study randomly assigned patients to intraoperative or external beam radiation therapy. They did not observe any significant difference in outcome between the two groups, which, at least on the surface, would suggest that a targeted, more limited, less time-consuming therapy might be as effective as administering external beam radiation therapy. The problem is that the two-year follow-up is short.

This is not a treatment that we should all be embracing at the moment, but it is a treatment that we should pay attention to and it's a study result that we should follow. It's quite likely that in the years ahead these more targeted, localized therapies will be the way to go for some patients with breast cancer.

Interview with Eric P Winer, MD, July 6, 2010

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