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To interview Ian Kunkler, please contact Julia Gunther at julia.gunther@aacr.org or 770-403-7690. For a photo of Kunkler, click [here](#).

Omitting Radiation Therapy After Breast-Conserving Surgery May Not Impact 10-year Survival Rates for Older Patients With HR-positive Breast Cancer

SAN ANTONIO – Older patients with hormone receptor-positive breast cancer who did not receive radiation therapy after breast-conserving surgery had higher rates of local recurrence but similar 10-year survival rates when compared to patients who received postoperative radiation therapy, according to updated 10-year data from the [PRIME II study](#), presented at the [2020 San Antonio Breast Cancer Symposium](#), held Dec. 8-11.

“Over half the patients diagnosed with breast cancer in developed countries are over the age of 65 years,” said [Ian Kunkler, FRCPE](#), professor of clinical oncology at the Western General Hospital, University of Edinburgh. Despite the less aggressive breast cancers typically diagnosed in this population, most patients who undergo breast-conserving surgery continue to be treated with whole breast radiation therapy after surgery, he explained. “We were interested in determining whether older patients with low-risk breast cancer could be spared radiation therapy.”

The PRIME II study enrolled 1,326 patients with non-metastatic hormone receptor (HR)-positive breast cancer. All patients were at least 65 years of age, had undergone breast-conserving surgery, and were receiving adjuvant hormone therapy. Patients were randomly assigned to either receive or not receive radiation therapy after surgery. Kunkler and colleagues previously [reported](#) greater rates of local recurrence (defined as recurrence in the same breast as the primary tumor) in patients who did not receive radiation therapy, but no significant differences in overall survival, distant metastases, or new breast cancers between the two arms after five years.

The latest data presented at the symposium report results from a 10-year follow-up. Kunkler reported that the rate of local recurrence after 10 years was significantly greater in patients who did not receive radiation therapy compared with patients who did (9.8 percent vs. 0.9 percent).

While postoperative radiation therapy affected the risk of local recurrence, it did not significantly impact certain other clinical outcomes. After 10 years, patients who did not receive radiation therapy had similar rates of distant metastasis (1.4 percent vs. 3.6 percent), recurrence in the opposite breast (1.0 percent vs. 2.2 percent), and overall survival (80.4 percent vs. 81.0 percent) as patients who did receive radiation therapy. Most deaths were due to reasons other than breast cancer.

“We found that omitting postoperative radiation therapy did not compromise survival or increase the risk of distant metastasis,” said Kunkler. “Based on these results, we believe that omission of radiation therapy after breast-conserving surgery should be an option for older patients with localized, HR-positive breast cancer who are receiving adjuvant hormone therapy and meet certain clinico-pathological criteria.”

A limitation of the study is that only a few patients with grade 3 tumors were recruited, so the results of the study may not be applicable to patients with high-grade tumors or with tumors larger than 3

centimeters. An additional limitation is that data on comorbidities or adherence to adjuvant hormone therapy were not collected.

The study was supported by the Chief Scientist Office for Scotland and the Edinburgh Breast Cancer Institute NHS Endowment Fund. Kunkler declares no conflicts of interest.

Abstract

GS2-03

Prime 2 randomised trial (postoperative radiotherapy in minimum-risk elderly): Wide local excision and adjuvant hormonal therapy +/- whole breast irradiation in women \geq 65 years with early invasive breast cancer: 10 year results

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Background: There is limited level 1 evidence on the long term outcomes after loco-regional radiotherapy after breast conserving surgery (BCS) in older patients when they are also receiving appropriate systemic therapy. Practice and guidelines vary. PRIME 2 is an international phase 3 RCT designed to address this specific question.

Methods: From April 2003 to December 2009, 1326 patients were randomised to receive (n=658) or not receive (n=668) whole breast radiotherapy (RT). Eligible patients were aged \geq 65 years, T1-2 (up to 3cm) NO, MO, hormone receptor positive, clear excision margins (minimum 1mm), axillary node negative (pNO) receiving adjuvant hormonal therapy. Patients were eligible if they had grade 3 tumours or lymphovascular invasion but not both. The target accrual was 1300 patients based on detecting a difference in local recurrence rates between 5% in the no RT arm and 2% in the RT arm at 5 years, with 80% power and 5% significance. Ipsilateral breast tumour recurrence (IBTR) was the primary endpoint. Secondary endpoints were regional recurrence, contralateral breast cancer, distant metastases and overall survival.

Results: Median follow up is 7.3 years. At 10 years IBTR was 9.8% (95% CI 6.5, 13.2%) in the no RT arm and 0.9% (95% CI 0.1, 1.6%) in the RT arm. The hazard ratio for IBTR for those receiving RT was 0.12 (95% CI 0.05, 0.31)($p < 0.0001$). Significant differences were found in regional recurrence (2.3% no RT vs 0.5% RT ($p = 0.014$), but not in contralateral breast cancer (1.0% no RT, 2.2% RT, $p = 0.20$) or distant metastases (1.4% no RT, 3.6% RT, $p = 0.07$). Breast cancer free survival was 12.7% (95% CI 9.1, 16.2%) for the no RT arm and 6.6% (95% CI 4.1, 9.1%) for the RT arm. Breast specific survival: no RT 98.2% (95% CI 96.9, 99.4%); RT 97.8% (95% CI 96.0, 99.5%) $p = 0.91$. Overall survival at 10 years was 80.4% (95% CI 76.4, 84.5%) without RT and 81.0% (95% CI 76.7, 85.3%) with RT ($p = 0.68$), with most deaths (80/88 no RT vs 76/79 RT) not linked to breast cancer recurrence with no influence of RT ($p = 0.17$).

Causes of death are shown in Table.

Cause of death	No RT	RT	Total
Cancer	25 (28%)	29 (37%)	54
<i>Of which breast cancer</i>	8 (9%)	3 (4%)	11
Cardio-vascular	9 (10%)	14 (18%)	23
Other/unknown	54 (61%)	36 (45%)	90
Total	88	79	167

Conclusions: 10 year follow data from the PRIME 2 trial shows that the omission of RT after BCS in women aged \geq 65 years with T1-2, pN0 hormone receptor positive breast cancer results in only 9.8% IBTR. While this rate is significantly reduced by RT (to 0.9%), the absolute reduction is modest, and there were no differences in the secondary endpoints of distant metastases, contralateral breast cancer or

overall survival and a small but significant difference in regional recurrence. These data suggest that postoperative radiotherapy in this patient group who are receiving adjuvant hormonal therapy does not impact on overall survival in the context of modern approaches to local and systemic adjuvant therapy, with most patients in both arms dying of causes unrelated to breast cancer or its treatment.

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