Prof. Lorenzo Livi
Università di Firenze

Studies from:

- *Journal of Clinical Oncology*

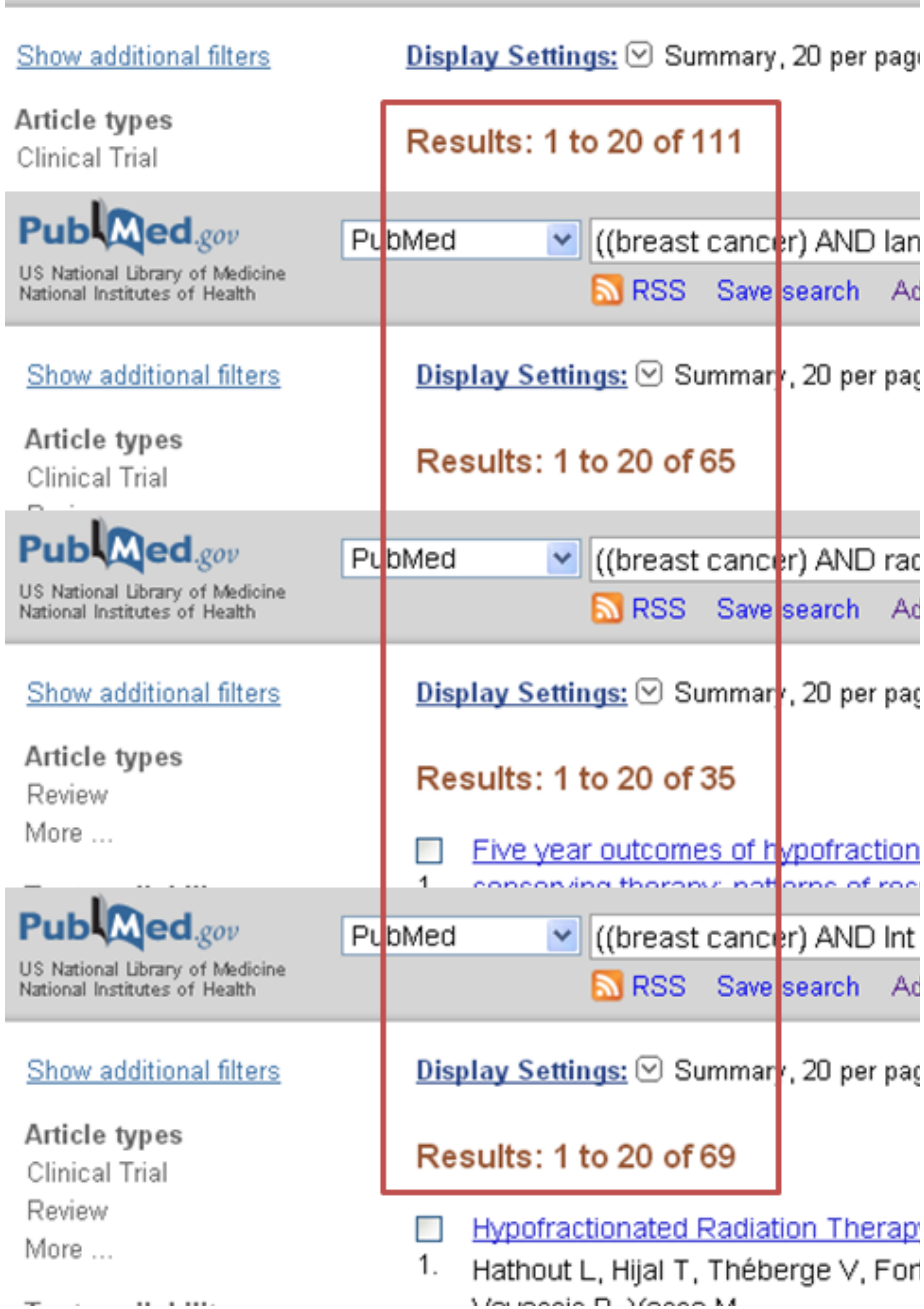
- *Lancet Oncology*

- *International Journal of Radiation Oncology * Biology * Physics*

- *Radiotherapy and Oncology*

- *ASCO Congress 2013*

- *S. Antonio Breast Cancer Simposium 2012*



ASCO Congress 2013

ACOSOG Z1041 (Alliance): Definitive analysis of randomized neoadjuvant trial comparing FEC followed by paclitaxel plus trastuzumab (FEC → P+T) with paclitaxel plus trastuzumab followed by FEC plus trastuzumab (P+T → FEC+T) in HER2+ operable breast cancer

Buzdar A, et al

L'incidenza di pCR è elevata indipendentemente dall'introduzione iniziale del trastuzumab; la somministrazione concomitante di antracicline e trastuzumab comunque non comporta un aumento delle pCR e gli eventi cardiaci non hanno incidenza diversa a seconda del braccio di trattamento.

Pathological response rates in the breast

	Arm 1 N = 138	Arm 2 N = 142	p-value
pCR in breast	56.5%	54.2%	0.72
95% CI	47.8% – 64.9%	45.7% – 62.6%	

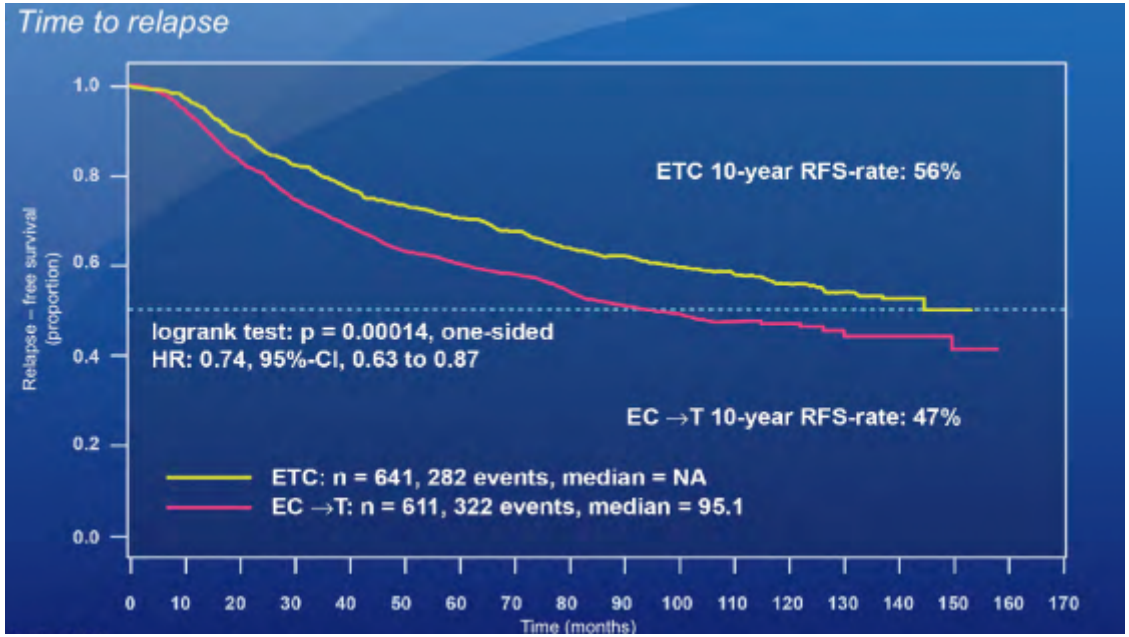
Pathological response rate in the breast and axilla among cN1-3 patients

	Arm 1 N = 89	Arm 2 N = 90	p-value
pCR in axilla	48.3%	46.7%	0.88
95% CI	37.6% – 59.2%	36.4% – 56.9%	

S. Antonio Breast Cancer Simposium 2012

Ten year follow-up analysis of intense dose-dense adjuvant ETC (epirubicin (E), paclitaxel (T) and cyclophosphamide (C)) confirms superior DFS and OS benefit in comparison to conventional dosed chemotherapy in high-risk breast cancer patients with ≥ 4 positive lymph nodes

Moebus V, et al.



Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Definitive Results of a Phase III Adjuvant Trial Comparing Three Chemotherapy Regimens in Women With Operable, Node-Positive Breast Cancer: The NSABP B-38 Trial

Sandra M. Swain, Gong Tang, Charles E. Geyer Jr, Priya Rastogi, James N. Atkins, Paul P. Donnellan, Louis Fehrenbacher, Catherine A. Azar, André Robidoux, Jonathan A. Polikoff, Adam M. Brufsky, David D. Biggs, Edward A. Levine, John L. Zapas, Louise Provencher, Donald W. Northfelt, Soonmyung Paik.

Patients and Methods

We randomly assigned 4,894 women with node-positive early-stage breast cancer to six cycles of docetaxel, doxorubicin, and cyclophosphamide (TAC), four cycles of dose-dense (DD) doxorubicin and cyclophosphamide followed by four cycles of DD paclitaxel (P; DD AC→P), or DD AC→P with four cycles of gemcitabine (G) added to the DD paclitaxel (DD AC→PG). Primary granulocyte colony-stimulating factor support was required; erythropoiesis-stimulating agents (ESAs) were used at the investigator's discretion.

Results

There were no significant differences in 5-year disease-free survival (DFS) between DD AC→PG and DD AC→P (80.6% *v* 82.2%; HR, 1.07; $P = .41$), between DD AC→PG and TAC (80.6% *v* 80.1%; HR, 0.93; $P = .39$), in 5-year overall survival (OS) between DD AC→PG and DD AC→P (90.8% *v* 89.1%; HR, 0.85; $P = .13$), between DD AC→PG and TAC (90.8% *v* 89.6%; HR, 0.86; $P = .17$), or between DD AC→P versus TAC for DFS (HR, 0.87; $P = .07$) and OS (HR, 1.01; $P = .96$). Grade 3 to 4 toxicities for TAC, DD AC→P, and DD AC→PG, respectively, were febrile neutropenia (9%, 3%, 3%; $P < .001$), sensory neuropathy (< 1%, 7%, 6%; $P < .001$), and diarrhea (7%, 2%, 2%; $P < .001$). Exploratory analyses for ESAs showed no association with DFS events (HR, 1.02; $P = .95$).

Conclusion

Adding G to DD AC→P did not improve outcomes. No significant differences in efficacy were identified between DD AC→P and TAC, although toxicity profiles differed.

Lancet Oncology

Adjuvant docetaxel, doxorubicin, and cyclophosphamide in node-positive breast cancer: 10-year follow-up of the phase 3 randomised BCIRG 001 trial

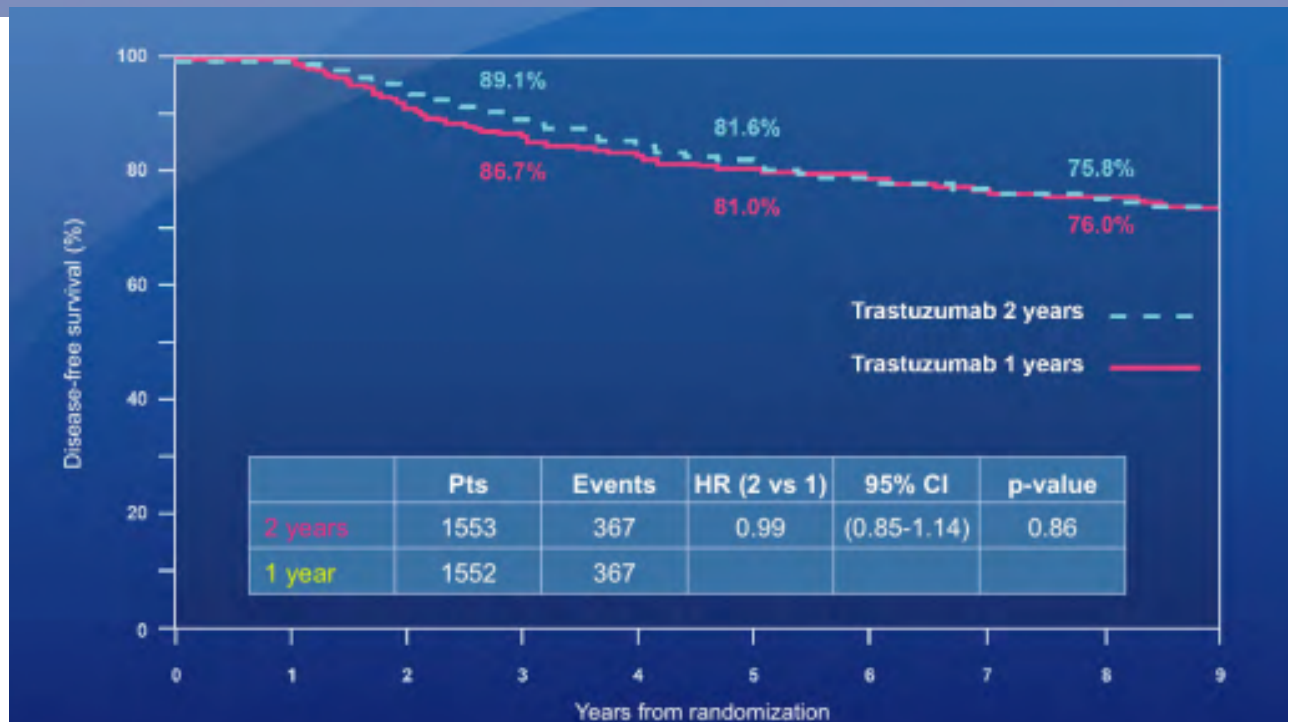
*John R Mackey, Miguel Martin, Tadeusz Pienkowski, Janusz Rolski, Jean-Paul Guastalla, Amer Sami, John Glaspy, Eva Juhos, Andrew Wardley, Tommy Fornander, John Hainsworth, Robert Coleman, Manuel R Modiano, Jeferson Vinholes, Tamas Pinter, Álvaro Rodríguez-Lescure, Bruce Colwell, Pierre Whitlock, Louise Provencher, Kara Laing, David Walde, Chris Price, Judith C Hugh, Barrett H Childs, Kimberly Bassi, Mary-Ann Lindsay, Véronique Wilson, Matthieu Rupin, Vincent Houé, Charles Vogel, for the TRIO/BCIRG 001 investigators**

Interpretation Our results provide evidence that the initial therapeutic outcomes seen at the 5-year follow-up with a docetaxel-containing adjuvant regimen are maintained at 10 years. However, a substantial percentage of patients had a decrease in left ventricular ejection fraction, probably caused by anthracycline therapy, which warrants further investigation.

S. Antonio Breast Cancer Simposium 2012

HERA TRIAL: 2 years versus 1 year of trastuzumab after adjuvant chemotherapy in women with HER2-positive early breast cancer at 8 years of median follow up

Goldhirsch A, et al.



	Pts	Events	HR (2 vs 1)	95% CI	p-value
2 years	1553	367	0.99	(0.85-1.14)	0.86
1 year	1552	367			

Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Trastuzumab-Related Cardiotoxicity Among Older Patients With Breast Cancer

Mariana Chavez-MacGregor, Ning Zhang, Thomas A. Buchholz, Yufeng Zhang, Jiangong Niu, Linda Elting,

Purpose
The use of trastuzumab in the adjuvant setting improves outcomes but is associated with cardiotoxicity manifested as congestive heart failure (CHF). The rates and risk factors associated with trastuzumab-related CHF among older patients are unknown.

Patients and Methods
Breast cancer patients at least 66 years old with full Medicare coverage, diagnosed with stage I-III breast cancer between 2005 and 2009, and treated with chemotherapy were identified in the SEER-Medicare and in the Texas Cancer Registry–Medicare databases. The rates and risk factors associated with CHF were evaluated. Chemotherapy, trastuzumab use, comorbidities, and CHF were identified using International Classification of Diseases, version 9, and Healthcare Common Procedure Coding System codes. Analyses included descriptive statistics and Cox proportional hazards models.

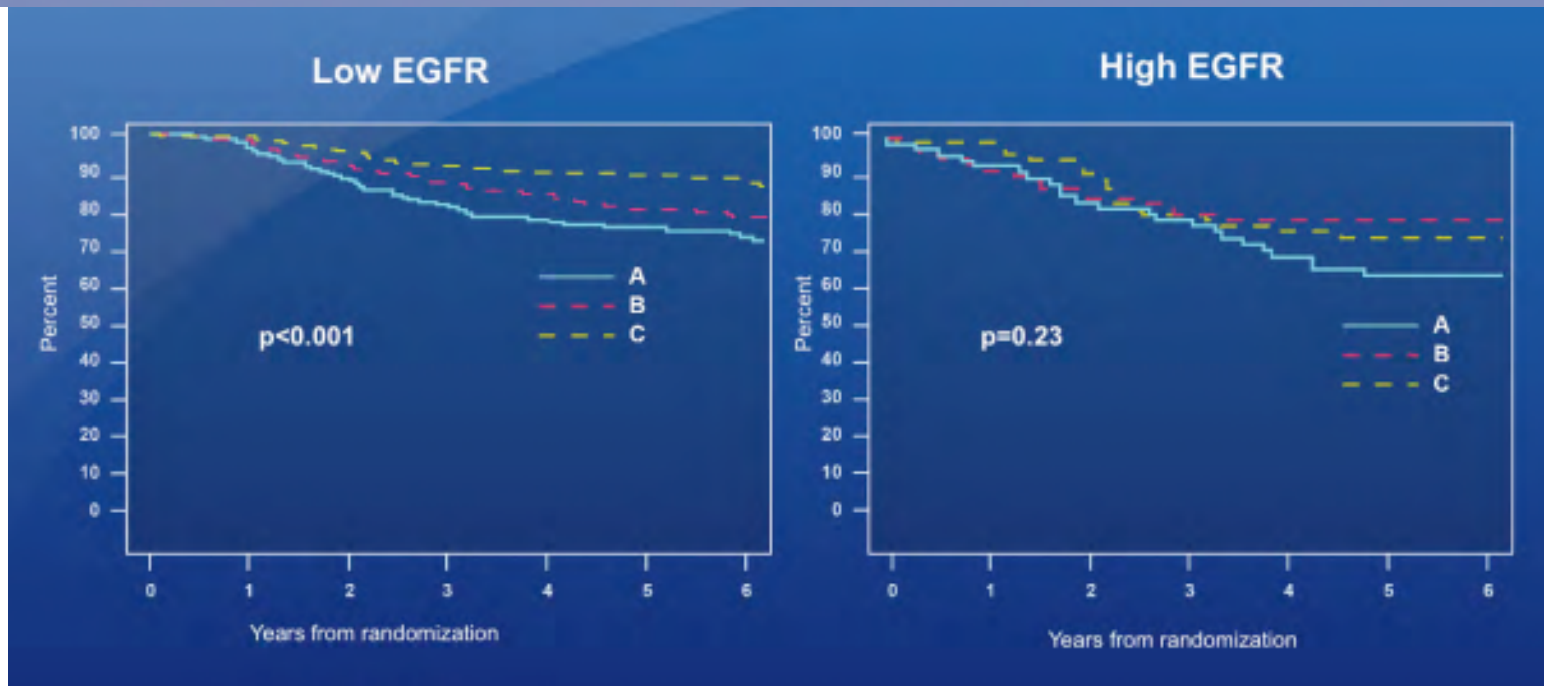
Results
In total, 9,535 patients were included, of whom 2,203 (23.1%) received trastuzumab. Median age of the entire cohort was 71 years old. Among trastuzumab users, the rate of CHF was 29.4% compared with 18.9% in nontrastuzumab users ($P < .001$). Trastuzumab users were more likely to develop CHF than nontrastuzumab users (hazard ratio [HR], 1.95; 95% CI, 1.75 to 2.17). Among trastuzumab-treated patients, older age (age > 80 years; HR, 1.53; 95% CI, 1.16 to 2.10), coronary artery disease (HR, 1.82; 95% CI, 1.34 to 2.48), hypertension (HR, 1.24; 95% CI, 1.02 to 1.50), and weekly trastuzumab administration (HR, 1.33; 95% CI, 1.05 to 1.68) increased the risk of CHF.

Conclusion
In this large cohort of older breast cancer patients, the rates of trastuzumb-related CHF are higher than those reported in clinical trials. Among patients treated with trastuzumab, those with cardiac comorbidities and older age may be at higher risk. Further studies need to confirm the role that the frequency of administration plays in the development of trastuzumab-related CHF.

S. Antonio Breast Cancer Simposium 2012

EGFR expression measured by quantitative immunofluorescence is associated with decreased benefit from trastuzumab in the adjuvant setting in the NCCTG N9831 trial

Rimm DL, et al.



Lancet Oncology

Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study

Sandra M Swain, Sung-Bae Kim, Javier Cortés, Jungsil Ro, Vladimir Semiglazov, Mario Campone, Eva Ciruelos, Jean-Marc Ferrero, Andreas Schneeweiss, Adam Knott, Emma Clark, Graham Ross, Mark C Benyunes, José Baselga

Findings In the intention-to-treat population, 267 patients died by data cutoff (May 14, 2012), 154 (38%) of 406 in the placebo group and 113 (28%) of 402 in the pertuzumab group. Median overall survival was 37·6 months (95% CI 34·3–NE [not estimable]) in the placebo group but had not been reached (95% CI 42·4–NE) in the pertuzumab group (hazard ratio 0·66, 95% CI 0·52–0·84; p=0·0008). Investigator-assessed median progression-free survival was 12·4 months (95% CI 10·4–13·5) in the placebo group and 18·7 months (16·6–21·6) in the pertuzumab group (hazard ratio 0·69, 95% CI 0·58–0·81). Serious adverse events were reported in 115 (29%) of 396 patients who received placebo, trastuzumab, and docetaxel and 148 (36%) of 408 who received pertuzumab, trastuzumab, and docetaxel, and included febrile neutropenia, neutropenia, diarrhoea, pneumonia, and cellulitis. Overall, adverse events were similar to those reported at the primary analysis with respect to frequency, severity, and specificity.

Interpretation Our analysis shows a significant improvement in overall survival with pertuzumab, trastuzumab, and docetaxel in patients with HER2-positive metastatic breast cancer, compared with placebo, trastuzumab, and docetaxel. Since this effect was not achieved at the expense of adverse events, this regimen represents a substantial improvement on the standard of care for this population of patients.

Lancet Oncology

Adjuvant bevacizumab-containing therapy in triple-negative breast cancer (BEATRICE): primary results of a randomised, phase 3 trial

David Cameron, Julia Brown, Rebecca Dent, Christian Jackisch, John Mackey, Xavier Pivot, Guenther G Steger, Thomas M Suter, Masakazu Toi, Mahesh Parmar, Rita Laeufle, Young-Hyuck Im, Gilles Romieu, Vernon Harvey, Oleg Lipatov, Tadeusz Pienkowski, Paul Cottu, Arlene Chan, Seock-Ah Im, Peter S Hall, Lida Bubuteishvili-Pacaud, Volkmar Henschel, Regula J Deurloo, Celine Pallaud, Richard Bell

Findings Between Dec 3, 2007, and March 8, 2010, we randomly assigned 1290 patients to receive chemotherapy alone and 1301 to receive bevacizumab plus chemotherapy. Most patients received anthracycline-containing therapy; 1638 (63%) of the 2591 patients had node-negative disease. At the time of analysis of IDFS, median follow-up was 31·5 months (IQR 25·6–36·8) in the chemotherapy-alone group and 32·0 months (27·5–36·9) in the bevacizumab group. At the time of the primary analysis, IDFS events had been reported in 205 patients (16%) in the chemotherapy-alone group and in 188 patients (14%) in the bevacizumab group (hazard ratio [HR] in stratified log-rank analysis 0·87, 95% CI 0·72–1·07; p=0·18). 3-year IDFS was 82·7% (95% CI 80·5–85·0) with chemotherapy alone and 83·7% (81·4–86·0) with bevacizumab and chemotherapy. After 200 deaths, no difference in overall survival was noted between the groups (HR 0·84, 95% CI 0·64–1·12; p=0·23). Exploratory biomarker assessment suggests that patients with high pre-treatment plasma VEGFR-2 might benefit from the addition of bevacizumab (Cox interaction test p=0·029). Use of bevacizumab versus chemotherapy alone was associated with increased incidences of grade 3 or worse hypertension (154 patients [12%] *vs* eight patients [1%]), severe cardiac events occurring at any point during the 18-month safety reporting period (19 [1%] *vs* two [<0·5%]), and treatment discontinuation (bevacizumab, chemotherapy, or both; 256 [20%] *vs* 30 [2%]); we recorded no increase in fatal adverse events with bevacizumab (four [<0·5%] *vs* three [<0·5%]).

Interpretation Bevacizumab cannot be recommended as adjuvant treatment in unselected patients with triple-negative breast cancer. Further follow-up is needed to assess the potential effect of bevacizumab on overall survival.

Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Osteonecrosis of the Jaw and Oral Health–Related Quality of Life After Adjuvant Zoledronic Acid: An Adjuvant Zoledronic Acid to Reduce Recurrence Trial Subprotocol (BIG01/04)

Emma J. Rathbone, Janet E. Brown, Helen C. Marshall, Michelle Collinson, Victoria Liversedge, Geraldine A. Murden, David Cameron, Richard Bell, Saiqa Spensley, Rajiv Agrawal, Rema Jyothirmayi, Prabir Chakraborti, Frances Yuille, and Robert E. Coleman

Results

With a median follow-up time of 73.9 months (interquartile range, 60.7 to 84.2 months), 33 possible cases of ONJ were reported, all in the zoledronate-treated patients. Twenty-six cases were confirmed as being consistent with a diagnosis of ONJ, representing a cumulative incidence of 2.1% (95% CI, 0.9% to 3.3%) in the zoledronate arm. Three hundred sixty-two patients (74%) returned the OHIP-14 questionnaire. Neither the prevalence nor severity of impacts on Oral-QoL differed significantly between zoledronate patients and control patients.

Conclusion

Adjuvant zoledronate used in the intensive schedule studied in the AZURE trial is associated with a low incidence of ONJ but does not seem to adversely affect Oral-QoL.

S. Antonio Breast Cancer Simposium 2012

ATLAS – Adjuvant Tamoxifen: Longer Against Shorter

10 vs 5 years of adjuvant tamoxifen (TAM) in ER+ disease: Effect in the first & second decade after diagnosis

On Behalf of ATLAS Collaborators Worldwide

Davies C, et al.

	5 years TAM. vs 0 Meta-analysis (n=10645)	10 years TAM. vs 5 ATLAS trial (n=6846)	10 years TAM. vs 0 (estimated as product of RRs)
YEARS 0–4	0.71❖ (0.62–0.80)	(1.0)	0.71❖ (0.62–0.81)
YEARS 5–9	0.66❖ (0.62–0.80)	0.97 (0.79–1.18)	0.64★ (0.62–0.80)
YEARS 10+	0.73★ (0.62–0.80)	0.71◆ (0.58–0.88)	0.52❖ (0.40–0.68)

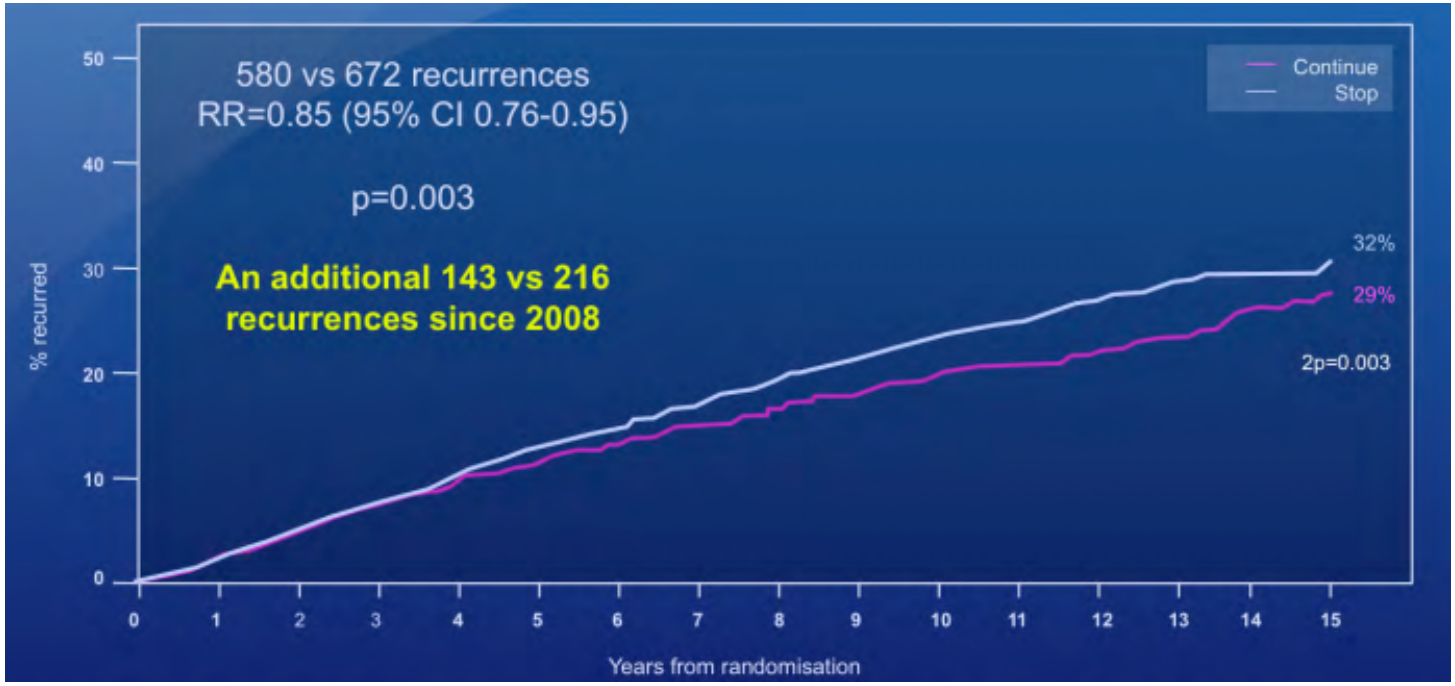
★p=0.0001
❖p=0.00001
◆p=0.0016

10 years TAM. reduces breast cancer mortality by a third in first decade & half in second decade

ASCO Congress 2013

aTTom: Long term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6,953 women with early breast cancer

Gray R



Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Lumpectomy Plus Tamoxifen With or Without Irradiation in Women Age 70 Years or Older With Early Breast Cancer: Long-Term Follow-Up of CALGB 9343

Kevin S. Hughes, Lauren A. Schnaper, Jennifer R. Bellon, Constance T. Cirrincione, Donald A. Berry, Beryl McCormick, Hyman B. Muss, Barbara L. Smith, Clifford A. Hudis, Eric P. Winer, and William C. Wood

Results

Median follow-up for treated patients is now 12.6 years. At 10 years, 98% of patients receiving TamRT (95% CI, 96% to 99%) compared with 90% of those receiving Tam (95% CI, 85% to 93%) were free from local and regional recurrences. There were no significant differences in time to mastectomy, time to distant metastasis, breast cancer–specific survival, or OS between the two groups. Ten-year OS was 67% (95% CI, 62% to 72%) and 66% (95% CI, 61% to 71%) in the TamRT and Tam groups, respectively.

Conclusion

With long-term follow-up, the previously observed small improvement in locoregional recurrence with the addition of radiation therapy remains. However, this does not translate into an advantage in OS, distant disease-free survival, or breast preservation. Depending on the value placed on local recurrence, Tam remains a reasonable option for women age ≥ 70 years with ER-positive early-stage breast cancer.

Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Breast-Conserving Treatment With or Without Radiotherapy in Ductal Carcinoma In Situ: 15-Year Recurrence Rates and Outcome After a Recurrence, From the EORTC 10853 Randomized Phase III Trial

Mila Donker, Saskia Litière, Gustavo Werutsky, Jean-Pierre Julien, Ian S. Fentiman, Roberto Agresti, Philippe Rouanet, Christine Tunon de Lara, Harry Bartelink, Nicole Duez, Emiel J.T. Rutgers, and Nina Bijker

Conclusion
At 15 years, almost one in three nonirradiated women developed an LR after LE for DCIS. RT reduced this risk by a factor of 2. Although women who developed an invasive recurrence had worse survival, the long-term prognosis was good and independent of the given treatment.

Lancet Oncology

Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23–01): a phase 3 randomised controlled trial

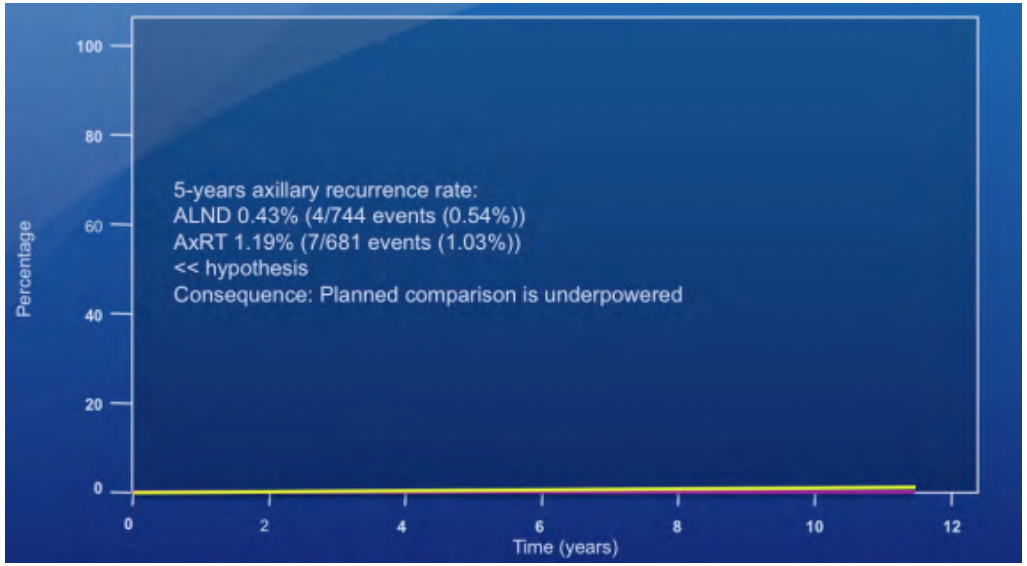
Viviana Galimberti, Bernard F Cole, Stefano Zurrida, Giuseppe Viale, Alberto Luini, Paolo Veronesi, Paola Baratella, Camelia Chifu, Manuela Sargenti, Mattia Intra, Oreste Gentilini, Mauro G Mastropasqua, Giovanni Mazzarol, Samuele Massarut, Jean-Rémi Garbay, Janez Zgajnar, Hanne Galatius, Angelo Recalcati, David Littlejohn, Monika Bamert, Marco Colleoni, Karen N Price, Meredith M Regan, Aron Goldhirsch, Alan S Coates, Richard D Gelber, Umberto Veronesi, for the International Breast Cancer Study Group Trial 23–01 investigators

Interpretation Axillary dissection could be avoided in patients with early breast cancer and limited sentinel-node involvement, thus eliminating complications of axillary surgery with no adverse effect on survival.

ASCO Congress 2013

Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer patients: Final analysis of the EORTC AMAROS trial

Rutgers EJ



Per quanto riguarda l'obiettivo primario, il numero di recidive ascellari osservato è stato particolarmente basso in entrambi i bracci: 4/744 vs 7/681. ***Il confronto pianificato è così risultato sottopotenziato a causa di questa rarità degli eventi.***

International Journal of Radiation Oncology, Biology and Physics

International Journal of Radiation Oncology biology • physics

Early-Stage Breast Cancer Treated With 3-Week Accelerated Whole-Breast Radiation Therapy and Concomitant Boost

Manjeet Chadha, MD,* Rudolph Woode, MS,* Jussi Sillanpaa, PhD,* David Lucido, PhD,† Susan K. Boolbol, MD,‡ Laurie Kirstein, MD,‡ Michael P. Osborne, MD,‡ Sheldon Feldman, MD,‡ and Louis B. Harrison, MD*

*Department of Radiation Oncology, †Department of Biostatistics, and ‡Division of Breast Surgery, Beth Israel Medical Center, New York, New York

Clinical Investigation

Hypofractionated Radiation Therapy for Breast Ductal Carcinoma In Situ

Lara Hathout, MD,* Tarek Hijal, MD,† Valérie Théberge, MD,‡,§ Bernard Fortin, MD,* Horia Vulpe, MD,† Jean-Charles Hogue, MD,§,‖ Christine Lambert, MD,† Houda Bahig, MD,* Louise Provencher, MD,§,‖ Peter Vavassis, MD,* and Michael Yassa, MD*

*Department of Radiation Oncology, Hôpital Maisonneuve-Rosemont, Centre affilié à l'Université de Montréal; †Department of Radiation Oncology, McGill University Health Centre, Montreal; ‡Department of Radiation Oncology, Centre hospitalier universitaire de Québec, L'Hôtel-Dieu de Québec; §Centre des maladies du sein Deschênes-Fabia; and ‖Centre hospitalier universitaire de Québec, Hôpital St-Sacrement, Quebec, Canada

Radiotherapy and Oncology

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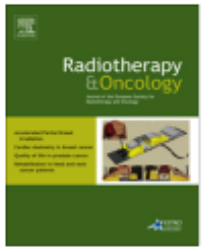

Accelerated partial breast irradiation

Accelerated partial breast irradiation with interstitial brachytherapy as second conservative treatment for ipsilateral breast tumour recurrence: Multicentric study of the GEC-ESTRO Breast Cancer Working Group

Jean-Michel Hannoun-Levi [a,*], Alexandra Resch [b], Jocelyn Gal [c], Daniela Kauer-Dorner [b], Vratislav Strnad [d], Peter Niehoff [e], Kristina Loessl [f], Gyoergy Kovács [g], Erick Van Limbergen [h], Csaba Polgár [i], On behalf of the GEC-ESTRO Breast Cancer Working Group

[a] *Department of Radiation Oncology, Antoine Lacassagne Cancer Center, University of Nice-Sophia, France;* [b] *Department of Radiotherapy and Radiobiology, University of Vienna,*

Review

Accelerated fractionation with a concurrent boost for early stage breast cancer

Gary M. Freedman [a,*], Julia R. White [b], Douglas W. Arthur [c], X. Allen Li [d], Frank A. Vicini [e]

[a] *University of Pennsylvania, Philadelphia;* [b] *Ohio State University, Columbus;* [c] *Virginia Commonwealth University, Richmond;* [d] *Medical College of Wisconsin, Milwaukee; and* [e] *Michigan Healthcare Professionals/21st Century Oncology, Royal Oak, United States*

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Phase III randomised trial

Hypofractionated whole breast irradiation for patients with large breasts: A randomized trial comparing prone and supine positions

Thomas Mulliez [a,*], Liv Veldeman [a], Annick van Greveling [a], Bruno Speleers [a], Simin Sadeghi [a], Dieter Berwouts [a], Frederik Decoster [a], Tom Vercauteren [a], Werner De Gersem [a], Rudy Van den Broecke [b], Wilfried De Neve [a]

[a] *Department of Radiotherapy;* [b] *Department of Gynaecology, Ghent University Hospital, Belgium*

Five year outcomes of hypofractionated simultaneous integrated boost irradiation in breast conserving therapy; patterns of recurrence

Enja J. Bantema-Joppe [a], Eline J. Vredeveld [a], Geertruida H. de Bock [b], Dianne M. Busz [a], Marleen Woltman-van Iersel [a], Wil V. Dolsma [a], Hans Paul van der Laan [a], Johannes A. Langendijk [a], John H. Maduro [a,*]

[a] *Department of Radiation Oncology; and* [b] *Department of Epidemiology, University of Groningen, University Medical Center Groningen, The Netherlands*

Lancet Oncology

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dobbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss*, John R Yarnold*, on behalf of the START Trialists' Group†

Interpretation Long-term follow-up confirms that appropriately dosed hypofractionated radiotherapy is safe and effective for patients with early breast cancer. The results support the continued use of 40 Gy in 15 fractions, which has already been adopted by most UK centres as the standard of care for women requiring adjuvant radiotherapy for invasive early breast cancer.

International Journal of Radiation Oncology, Biology and Physics

International Journal of Radiation Oncology biology • physics

Long-term Cardiac Mortality After Hypofractionated Radiation Therapy in Breast Cancer

Kristin Holm Tjessem, MD,* Safora Johansen, PhD,† Eirik Malinen, PhD,‡ Kristin V. Reinertsen, MD, PhD,* Turi Danielsen, PhD,‡ Sophie D. Fosså, MD, PhD,* and Alexander Fosså, MD, PhD*

**Department of Oncology, Oslo University Hospital, National Resource Centre for Late Effects after Cancer Treatment; †Department of Oncology, Oslo University Hospital-Radium Hospital, and Division of Radiotherapy/Radiography, College of Oslo and Akershus, Faculty of Health; and ‡Department of Medical Physics, Oslo University Hospital, Oslo, Norway*

Results: Patients given 4.3 Gy × 10 had an increased risk of dying of IHD compared with both the 2.5 Gy group (hazard ratio [HR] = 2.37; 95% confidence interval [CI]: 1.06-5.32; $P = .036$) and the control group (HR = 1.59; 95% CI: 1.13-2.23; $P = .008$). Photon beams for parasternal fields gave an increased risk of dying of IHD compared with electron beams (HR = 2.56; 95% CI: 1.12-5.84; $P = .025$). Multivariate analysis gave an increased risk for the 4.3-Gy versus 2.5-Gy regimen with borderline significance (HR = 2.90; 95% CI: 0.97-8.79; $P = .057$) but not for parasternal irradiation.

Conclusions: The degree of hypofractionation and parasternal photon beams contributed to increased cardiac mortality in this patient cohort. Differences emerged after 12 to 15 years, indicating the need of more studies with observation time of 2 decades.

Journal of Clinical Oncology

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Interim Cosmetic and Toxicity Results From RAPID: A Randomized Trial of Accelerated Partial Breast Irradiation Using Three-Dimensional Conformal External Beam Radiation Therapy

Ivo A. Olivotto, Timothy J. Whelan, Sameer Parpia, Do-Hoon Kim, Tanya Berrang, Pauline T. Truong, Iwa Kong, Brandy Cochrane, Alan Nichol, Isabelle Roy, Isabelle Germain, Mohamed Akra, Melanie Reed, Anthony Fyles, Theresa Trotter, Francisco Perera, Wayne Beckham, Mark N. Levine, and Jim A. Julian

Results

Between 2006 and 2011, 2,135 women were randomly assigned to 3D-CRT APBI or WBI. Median follow-up was 36 months. Adverse cosmesis at 3 years was increased among those treated with APBI compared with WBI as assessed by trained nurses (29% *v* 17%; $P < .001$), by patients (26% *v* 18%; $P = .0022$), and by physicians reviewing digital photographs (35% *v* 17%; $P < .001$). Grade 3 toxicities were rare in both treatment arms (1.4% *v* 0%), but grade 1 and 2 toxicities were increased among those who received APBI compared with WBI ($P < .001$).

Conclusion

3D-CRT APBI increased rates of adverse cosmesis and late radiation toxicity compared with standard WBI. Clinicians and patients are cautioned against the use of 3D-CRT APBI outside the context of a controlled trial.

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Breast cancer radiotherapy

Radiotherapy boost dose-escalation for invasive breast cancer after breast-conserving surgery: 2093 Patients treated with a prospective margin-directed policy

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Conclusions: Our experience showed that a margin-directed policy of RT boost dose-escalation seems to reduce the negative impact of FMS on LR, but it is not able to overcome the unfavorable effect of higher nuclear grade, higher T stage and triple negative subtype.

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Impact of Boost Radiation in the Treatment of Ductal Carcinoma In Situ: A Population-Based Analysis

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Methods and Materials: All women diagnosed with DCIS and treated with breast-conserving surgery and radiation therapy in Ontario from 1994 to 2003 were identified. Treatments and outcomes were identified through administrative databases and validated by chart review. The impact of boost radiation on the development of local recurrence was determined using survival analyses. **Results:** We identified 1895 cases of DCIS that were treated by breast-conserving surgery and radiation therapy; 561 patients received boost radiation. The cumulative 10-year rate of local recurrence was 13% for women who received boost radiation and 12% for those who did not ($P = .3$). The 10-year local recurrence-free survival (LRFS) rate among women who did and who did not receive boost radiation was 88% and 87%, respectively ($P = .27$), 94% and 93% for invasive LRFS ($P = .58$), and was 95% and 93% for DCIS LRFS ($P = .31$). On multivariable

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Risk of Local Failure in Breast Cancer Patients With Lobular Carcinoma In Situ at the Final Surgical Margins: Is Re-excision Necessary?

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Conclusion: Our results suggest that the presence of LCIS at the surgical margin after lumpectomy does not increase the risk of LRR or the final outcome. These findings suggest that re-excision or mastectomy in patients with LCIS-positive/close final surgical margins is unnecessary.

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Ten-Year Survival Results of a Randomized Trial of Irradiation of Internal Mammary Nodes After Mastectomy

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Results: T total of 1334 patients were analyzed after a median follow-up of 11.3 years among the survivors. No benefit of IMN irradiation on the overall survival could be demonstrated: the 10-year overall survival was 59.3% in the IMN-nonirradiated group versus 62.6% in the IMN-irradiated group ($P = .8$). According to stratification factors, we defined 6 subgroups (medial/central or lateral tumor, pN0 [only for medial/central] or pN+, and chemotherapy or not). In all these subgroups, IMN irradiation did not significantly improve overall survival.

Conclusions: In patients treated with 2-dimensional techniques, we failed to demonstrate a survival benefit for IMN irradiation. This study cannot rule out a moderate benefit, especially with more modern, conformal techniques applied to a higher risk population.

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ORIGINAL REPORT

Randomized Trial of Decongestive Lymphatic Therapy for the Treatment of Lymphedema in Women With Breast Cancer

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Purpose
Because of its morbidity and chronicity, arm lymphedema remains a concerning complication of breast cancer treatment. Although massage-based decongestive therapy is often recommended, randomized trials have not consistently demonstrated benefit over more conservative measures.

Patients and Methods
Women previously treated for breast cancer with lymphedema were enrolled from six institutions. Volumes were calculated from circumference measurements. Patients with a minimum of 10% volume difference between their arms were randomly assigned to either compression garments (control) or daily manual lymphatic drainage and bandaging followed by compression garments (experimental). The primary outcome was percent reduction in excess arm volume from baseline to 6 weeks.

Results
A total of 103 women were randomly assigned, and 95 were evaluable. Mean reduction of excess arm volume was 29.0% in the experimental group and 22.6% in the control group (difference, 6.4%; 95% CI, −6.8% to 20.5%; $P = .34$). Absolute volume loss was 250 mL and 143 mL in the experimental and control groups, respectively (difference, 107 mL; 95% CI, 13 to 203 mL; $P = .03$). There was no difference between groups in the proportion of patients losing 50% or greater excess arm volume. Quality of life (Short Form-36 Health Survey) and arm function were not different between groups.

Conclusion
This trial was unable to demonstrate a significant improvement in lymphedema with decongestive therapy compared with a more conservative approach. The failure to detect a difference may have been a result of the relatively small size of our trial.