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ORIGINAL REPORT

Adjuvant Capecitabine, Docetaxel, Cyclophosphamide, and Epirubicin for Early Breast Cancer: Final Analysis of the Randomized FinXX Trial

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A B S T R A C T

Purpose

Capecitabine is an active agent in the treatment of breast cancer. It is not known whether integration of capecitabine into an adjuvant regimen that contains a taxane, an anthracycline, and cyclophosphamide improves outcome in early breast cancer.

Patients and Methods

Women with axillary node–positive or high-risk node-negative breast cancer were randomly assigned to receive either three cycles of docetaxel and capecitabine (TX) followed by three cycles of cyclophosphamide, epirubicin, and capecitabine (CEX; n = 753) or three cycles of docetaxel (T) followed by three cycles of cyclophosphamide, epirubicin, and fluorouracil (CEF; n = 747). The primary end point was recurrence-free survival (RFS).

Results

During a median follow-up time of 59 months, 214 RFS events occurred (local or distant recurrences or deaths; TX/CEX, n = 96; T/CEF, n = 118). RFS was not significantly different between the groups (hazard ratio [HR], 0.79; 95% CI, 0.60 to 1.04; $P = .087$; 5-year RFS, 86.6% for TX/CEX *v* 84.1% for T/CEF). Fifty-six patients assigned to TX/CEX died during the follow-up compared with 75 of patients assigned to T/CEF (HR, 0.73; 95% CI, 0.52 to 1.04; $P = .080$). In exploratory analyses, TX/CEX improved breast cancer–specific survival (HR, 0.64; 95% CI, 0.44 to 0.95; $P = .027$) and RFS in women with triple-negative disease and in women who had more than three metastatic axillary lymph nodes at the time of diagnosis. We detected little severe late toxicity.

Conclusion

Integration of capecitabine into a regimen that contains docetaxel, epirubicin, and cyclophosphamide did not improve RFS significantly compared with a similar regimen without capecitabine.

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INTRODUCTION

Capecitabine (Xeloda; Roche, Basel, Switzerland) is an active agent for advanced breast cancer, and it is frequently selected for therapy either as a single agent or as a partner in a combination regimen.[1,2] Yet little is known about the efficacy of capecitabine as adjuvant treatment of early breast cancer. Single-agent capecitabine was less effective than cyclophosphamide, methotrexate, and fluorouracil or doxorubicin and cyclophosphamide as adjuvant treatment for elderly women with early breast cancer,[3] but an important question to address is whether capecitabine adds efficacy when it is integrated into an adjuvant regimen containing commonly used agents, such as an anthracycline, cyclophosphamide, and a taxane.

Capecitabine is a prodrug of fluorouracil. After ingestion, it is absorbed almost completely from the intestine and metabolized in the liver and malignant tumors to fluorouracil. The final step of conversion to fluorouracil is catalyzed by thymidine phosphorylase (TP), which is present at high concentrations in many cancers, leading to high intratumoral concentrations of fluorouracil.[4] In xenograft models, cyclophosphamide, paclitaxel, and docetaxel administration increases tumor tissue TP concentration.[5-7]

Treatment of women with docetaxel or with cyclophosphamide combined with either doxorubicin or epirubicin increased tumor TP expression, supporting the integration of capecitabine into regimens that contain these agents.[8] In accordance with these data, women with anthracycline-treated advanced breast cancer had improved survival when treated with docetaxel plus capecitabine compared with docetaxel alone.[1] Adding capecitabine to a neoadjuvant anthracycline/taxane regimen improved the pathologic complete response (pCR) rate in a randomized study.[9]

Here, we report the final results of the Finland Capecitabine Trial (FinXX). The planned interim analysis of the study, based on a median follow-up time of approximately 3 years, suggested that integration of capecitabine into an adjuvant regimen that contains docetaxel, epirubicin, and cyclophosphamide improves recurrence-free survival (RFS).[10] In this trial, capecitabine was administered up front concomitantly with docetaxel, followed by concomitant administration with cyclophosphamide plus epirubicin in an attempt to fully exploit the putative synergism between capecitabine and other chemotherapy agents.

PATIENTS AND METHODS

Patients

Women eligible for this randomized, prospective, phase III, open-label, multicenter study had histologically confirmed invasive breast cancer with regional lymph nodes containing cancer (isolated tumor cells < 0.2 mm in diameter were not considered metastases) or node-negative cancer with primary tumor diameter greater than 20 mm and negative progesterone receptor (PgR) expression in immunohistochemistry (usually defined as staining of $< 10\%$ of cancer cells).[11,12] Eligibility criteria were as follows: age 18 to 65 years; WHO performance status less than 2; time interval between surgery and random assignment of ≤ 12 weeks; and normal hepatic, renal, and cardiac function (serum ALT $\leq 1.5\times$ upper limit of normal [ULN], alkaline phosphatase $\leq 2.5\times$ ULN, and bilirubin $\leq 1.0\times$ ULN). Patients who had distant metastases or node-negative mucinous, papillary, medullary, or tubular cancer were excluded, as were patients who had received neoadjuvant chemotherapy. The study protocol (ClinicalTrials.gov identifier NCT00114816) was approved by the institutional review boards. The patients provided written informed consent, and patient safety was monitored by an independent data safety monitoring committee.

Study Procedures

The primary end point was RFS, which was defined as the time interval between random assignment and date of diagnosis of invasive breast cancer recurrence (local or distant) or death if the patient died before recurrence. Contralateral breast cancers and second cancers were not counted as RFS events. Secondary end points were treatment safety and overall survival, which was defined as the time from random assignment to death.

Patients were randomly assigned in a 1:1 ratio to capecitabine-containing chemotherapy or to the control group. Random assignment was central and computer assisted and was performed using permutated blocks with a randomly varying block size.[10] Patients were stratified at random assignment by the number of axillary lymph nodes containing cancer ($\leq v >$ three nodes), tumor human epidermal growth factor receptor 2 (HER2) status (negative *v* positive; determined either by immunohistochemistry or in situ hybridization), and center.

Study participants assigned to the investigational group received three cycles of docetaxel (Taxotere; sanofi-aventis, Paris, France) plus capecitabine (TX) followed by three cycles of cyclophosphamide, epirubicin, and capecitabine (CEX). TX comprised capecitabine 900 mg/m^2 given orally twice per day on days 1 to 15 and docetaxel 60 mg/m^2 administered as a 1-hour intravenous infusion on day 1 of every 3-week cycle. CEX consisted of intravenous cyclophosphamide 600 mg/m^2 and epirubicin 75 mg/m^2 administered on day 1 and oral capecitabine 900 mg/m^2 given twice per day on days 1 to 15 every 3 weeks. The first capecitabine dose of each cycle was administered in the evening of day 1 and the last dose was administered in the morning of day 15, followed by a 7-day rest period. Patients allocated to the control group received three cycles of docetaxel (T; 80 mg/m^2 as a 1-hour intravenous infusion on day 1 of every 3-week cycle) followed by three cycles of cyclophosphamide (600 mg/m^2), epirubicin (75 mg/m^2), and fluorouracil (600 mg/m^2; CEF), all administered on day 1 of each 3-week cycle.

Table 1. Baseline Patient Demographics and Clinical Characteristics

Demographic or Clinical Characteristic	TX/CEX (n = 753) No. of Patients	%	T/CEF (n = 747) No. of Patients	%
Age, years				
Median	52		53	
Range	26-65		27-65	
Menstrual status*				
Premenopausal	331	44	321	43
Postmenopausal	422	56	426	57
WHO performance status				
0	663	88	664	89
1	90	12	83	11
Tumor classification†				
pT1	314	42	340	46
pT2	389	52	351	47
pT3	40	5	41	5
pT4	8	1	14	2
Not available	2	< 1	1	< 1
No. of positive axillary nodes				
0	86	11	71	10
1-3	461	61	466	62
> 3	206	27	210	28
Histologic type				
Ductal	569	76	566	76
Lobular	138	18	118	16
Other	46	6	63	8
Histologic grade				
1	86	11	80	11
2	362	48	351	47
3	300	40	312	42
Not available	5	1	4	1
ER status				
Positive	581	77	565	76
Negative	172	23	182	24
PgR status				
Positive	478	63	456	61
Negative	275	37	291	39
HER2 status				
Positive	146	19	139	19
Negative	607	81	608	81
Type of breast surgery				
Breast sparing	302	40	277	37
Mastectomy	451	60	469	63
Biopsy	0	< 1	1	< 1
Type of axillary surgery				
Sentinel node	42	6	44	6
Dissection	710	94	702	94
Other	1	< 1	1	< 1

Abbreviations: CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; PgR, progesterone receptor; T, docetaxel; TX, docetaxel and capecitabine.

*Menstrual periods within 6 months before starting chemotherapy.

†Defined as per the International Union Against Cancer TNM Classification of Malignant Tumors (sixth edition).

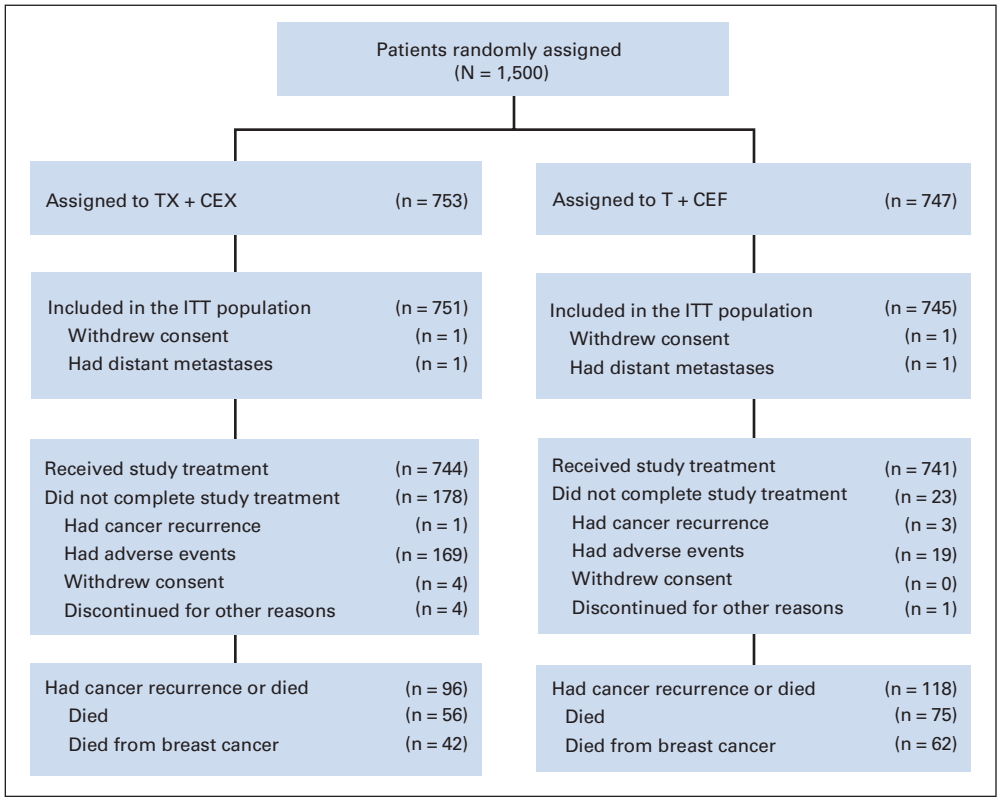

Fig 1. Enrollment, random assignment, and follow-up of study participants. CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; ITT, intent-to-treat; T, docetaxel; TX, docetaxel and capecitabine.

Chemotherapy was given for six cycles unless intolerable toxicity occurred or disease recurrence was detected. Corticosteroids were given orally at the time of docetaxel infusions. Administration of prophylactic hematopoietic growth factor support was not scheduled. Radiation therapy was given after completion of chemotherapy according to the institution's practice. Patients with estrogen receptor (ER) –positive or PgR-positive cancer received adjuvant endocrine therapy for 5 years; patients considered premenopausal before starting chemotherapy received tamoxifen 20 mg/d, and postmenopausal women received anastrozole 1 mg/d. Endocrine therapy was initiated within 2 months after completion of chemotherapy.

Toxicity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0, and chemotherapy doses were modified based on toxicity observed.[10] When scheduled treatment was discontinued for toxicity, TX was replaced by CEX or CEF, single-agent docetaxel by CEF, and CEX by CEF or cyclophosphamide and epirubicin. Adverse events that occurred during study treatment or within 28 days of the last dose of chemotherapy were recorded.

Staging examinations (computed tomography of the chest or chest x-ray; bone scan; and abdominal computed tomography, magnetic resonance imaging, or ultrasound) were mandatory at screening for patients with more than

Table 2. Breast Cancer Recurrence, Second Cancer, and Survival Events

Event	TX/CEX (n = 751)*		T/CEF (n = 745)*		Hazard Ratio	95% CI	P†
	No. of Patients	%	No. of Patients	%			
Any recurrence or death	96	12.8	118	15.8	0.79	0.60 to 1.04	.087
Local recurrence	8	1.1	20	2.7	0.39	0.17 to 0.88	.024
Distant recurrence	90	12.0	112	15.0	0.78	0.59 to 1.03	.080
Death from any cause	56	7.5	75	10.1	0.73	0.52 to 1.04	.080
Death from breast cancer	42	5.6	64	8.6	0.64	0.44 to 0.95	.027
Death from other cause	14	1.9	11	1.5	1.25	0.57 to 2.76	.575
Any second cancer‡	24	3.2	25	3.4	0.94	0.54 to 1.65	.833
Contralateral breast cancer	11	1.5	8	1.1	1.35	0.54 to 3.35	.519
Other cancer	13	1.7	17	2.3	0.75	0.36 to 1.55	.437

Abbreviations: CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; T, docetaxel; TX, docetaxel and capecitabine.

*A total of four patients were excluded from the analysis because of presence of distant metastases at the time of study entry (n = 2) or withdrawal of consent (n = 2).

†Unadjusted Cox proportional hazards model.

‡Second cancers were not included in the primary end point (recurrence-free survival).

three positive axillary nodes[13,14]; staging of other patients was performed according to the institutional practice. Blood cell counts and chemistries were performed ≤ 3 days preceding the planned start of each chemotherapy cycle. Study participants were scheduled to be observed for ≥ 5 years after random assignment.

Statistical Analysis

We assumed that RFS would improve from 83.0% to 88.5% (hazard ratio [HR], 0.65) after median follow-up of 5 years. On the basis of this assumption, 1,500 patients and 210 events were required to achieve 80% power assuming a 3% annual dropout rate, when $\alpha = .028$ (two-sided). Study recruitment time was estimated to be 3.5 years. The significance level in the interim and final analyses was set at $\alpha = .028$ to maintain it at 5% in the entire study.[15] The sample size was calculated using nQuery Advisor version 6.0 (Statistical Solutions Ltd, Cork, Ireland).

Efficacy analyses were based on the intent-to-treat (ITT) principle. Exploratory subgroup analyses (for center, number of axillary nodes [≤ or > three nodes], ER status [positive or negative], and HER2 status) were defined in the statistical plan for the interim analysis (approved on November 6, 2008). The safety population included all patients who received ≥ one dose of a study drug. Frequency tables were analyzed using the χ^2 test. Survival between groups was compared using the Kaplan-Meier life-table method and an unadjusted Cox proportional hazards model; the log-rank test was used to confirm the robustness of the analysis. The subgroup analyses were performed by including the treatment group, the subgroup variable, and their interaction in the Cox model. All *P* values are two-sided and not adjusted for multiple testing. Statistical analyses were performed with SAS version 8.2 for Windows (SAS Institute, Cary, NC).

RESULTS

Patients and Treatments

A total of 1,500 participants were entered onto the study from 15 Finnish centers (n = 1,199) and five Swedish centers (n = 301) between January 27, 2004, and May 29, 2007. Of these, 753 patients were assigned to TX/CEX, and 747 patients were assigned to T/CEF. The study participant demographics and breast cancer characteristics were balanced between the groups (Table 1). Most patients were treated with mastectomy (n = 920, 61%) followed by axillary dissection (n = 1,412, 94%). The majority of patients (90%) had node-positive cancer, 28% had more than three positive axillary lymph nodes, and 19% had HER2-positive disease.

The study protocol was amended to allow administration of adjuvant trastuzumab for HER2-positive cancer in May 2005. Subsequently, 96 patients (13%) and 83 patients (11%) assigned to TX/CEX and T/CEF, respectively, received trastuzumab; in each group, 75% of these patients received adjuvant trastuzumab for up to 12 months.[10] After completion of chemotherapy, 592 patients (79%) and 575 patients (77%) received adjuvant endocrine therapy in the capecitabine and control groups, respectively. Tamoxifen, anastrozole, or other endocrine therapy was administered to 325 (43%), 316 (42%), and 29 patients (4%) in the TX/CEX group, respectively, and to 287 (38%), 328 (44%), and 27 patients (4%) in the T/CEF group, respectively.

Efficacy

The median follow-up time was 59 months (range, 1 to 80 months) at the time of data lock (September 15, 2010). Four patients were excluded from the intent-to-treat population (two patients withdrew informed consent, and two patients had overt distant metastases at the time of study entry; Fig 1). Of the 214 RFS events (distant or local relapses or deaths) that triggered the final analysis, 96 (12.8%) occurred in the TX/CEX group and 118 (15.8%) occurred in the T/CEF group (Table 2). RFS was not significantly different between the groups (HR, 0.79; 95% CI, 0.60 to 1.04; $P = .087$; Fig 2). After excluding patients who received adjuvant trastuzumab (n = 179), the HR for RFS was 0.80 (95% CI, 0.61 to 1.06; $P = .129$).

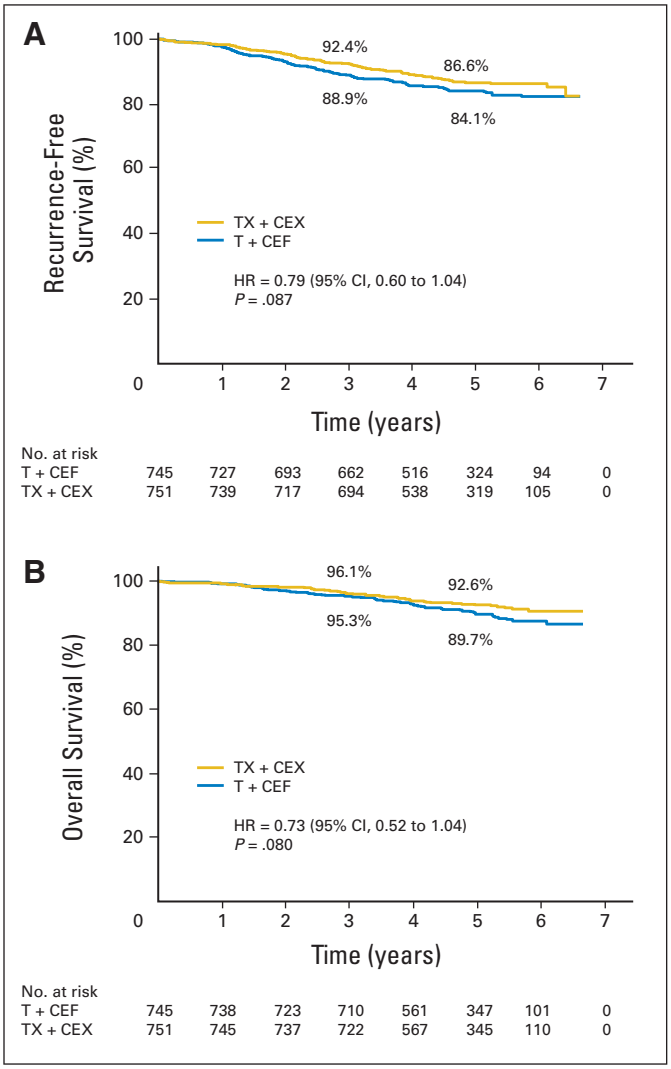

Fig 2. (A) Recurrence-free survival. (B) Overall survival. Three- and 5-year survival rates are shown. CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; HR, hazard ratio; T, docetaxel; TX, docetaxel and capecitabine.

Fifty-six patients assigned to capecitabine-containing chemotherapy died during the follow-up compared with 75 patients treated with T/CEF. Analysis of overall survival yielded an HR of 0.73 (95% CI, 0.52 to 1.04; $P = .080$; Fig 2). There were significantly fewer local relapses of breast cancer in the TX/CEX group compared with the T/CEF group (eight *v* 20 relapses, respectively; HR, 0.39; 95% CI, 0.17 to 0.88; $P = .024$).

Deaths specifically from breast cancer occurred less often in the TX/CEX arm compared with the T/CEF arm (42 *v* 64 deaths, respectively), and women assigned to TX/CEX had better breast cancer–specific survival than women assigned to T/CEF (HR, 0.64; 95% CI, 0.44 to 0.95; $P = .027$). The HR for disease-free survival (which

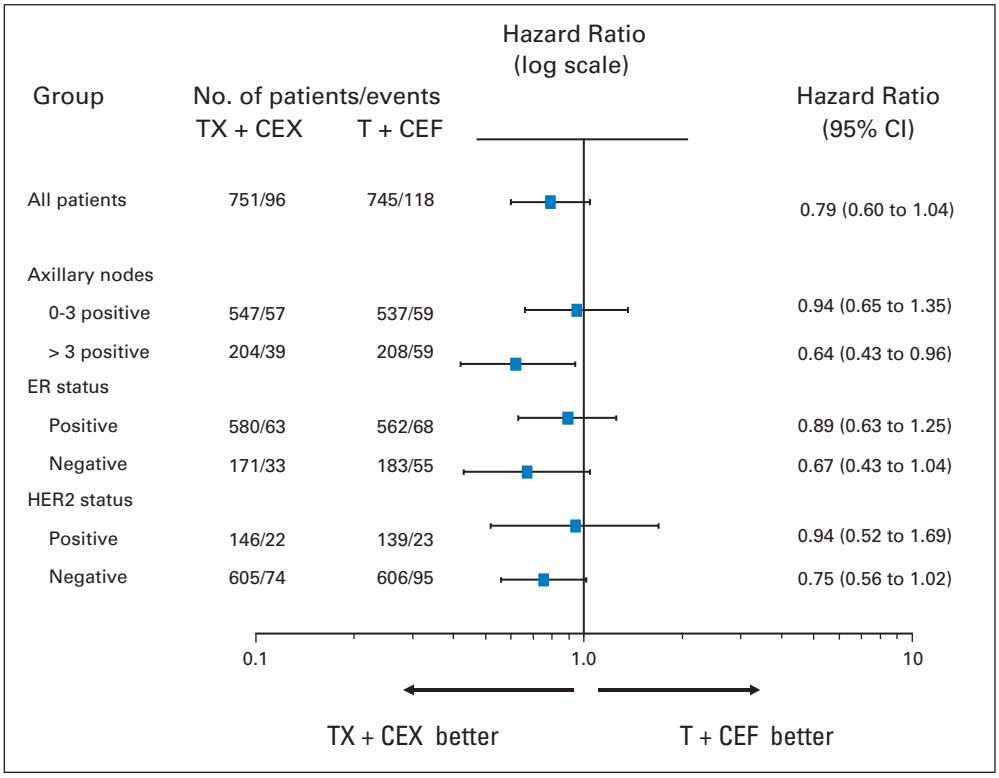

Fig 3. Results of exploratory subgroup analyses for recurrence-free survival. A forest plot shows the hazard ratios and 95% CIs (horizontal lines) according to the number of positive axillary nodes and tumor estrogen receptor (ER) and human epidermal growth factor receptor 2 (HER2) expression. CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; T, docetaxel; TX, docetaxel and capecitabine.

includes invasive contralateral breast cancers and second cancers) was 0.78 (95% CI, 0.59 to 1.03; $P = .080$).

In the exploratory subgroup analyses predefined in the study statistical plan, patients treated with TX/CEX had significantly longer RFS than patients treated with T/CEF in the subgroup of patients who had more than three metastatic axillary lymph nodes at diagnosis, whereas no significant differences were present in the subgroups defined by tumor ER or HER2 status (Fig 3). The interactions between treatment and nodal status, tumor ER status, or HER2 status were not statistically significant. Finally, we compared efficacy of TX/CEX and T/CEF in a post hoc exploratory analysis, where the tumors were stratified into four subgroups based on ER, PgR, and HER2 status. In this analysis, TX/CEX was more effective than T/CEF in the triple-negative subgroup (HR, 0.48; 95% CI, 0.26 to 0.88; $P = .018$), whereas no significant differences in RFS were found between the treatment groups in the remaining subgroups (Fig 4; $P = 0.29$ for the interaction between treatment and the subgroups).

Safety

The safety profiles of the two regimens differed as described in a detail elsewhere.[10] TX/CEX was associated with more capecitabine-related toxicity including stomatitis, hand-foot syndrome, nail changes, and diarrhea, whereas T/CEF was associated with more frequent neutropenia, febrile neutropenia, infection with neutropenia, myalgia, and amenorrhea, probably as a result of the higher docetaxel dose. Six patients died during chemotherapy possibly from a treatment-related cause (TX/CEX, n = 4; T/CEF, n = 2).

Patients assigned to TX/CEX discontinued the scheduled treatment more often than patients assigned to T/CEF (178 [24%] *v* 23 [3%] patients, respectively; $P < .001$),[10] most commonly as a result of adverse events. Ninety-eight patients (13%) discontinued the scheduled treatment during TX cycles, and a further 80 patients (11%) discontinued treatment during CEX cycles. In the T/CEF group, 16 patients (2%) discontinued treatment during docetaxel therapy, and seven patients (1%) discontinued treatment during CEF. Most patients (n = 1,461, 97%) received a total of six cycles of chemotherapy because planned cycles not administered were replaced. Docetaxel dose was reduced as a result of toxicity in 8% (n = 58) and 19% (n = 139) of women assigned to TX/CEX and T/CEF, respectively, and epirubicin dose was reduced in 8% and 7%, respectively. Three hundred nineteen patients (47%) took less than the planned starting dose of capecitabine on one or more occasion during the treatment course as a result of toxicity or other reasons.

We detected little late toxicity. Second malignancy other than breast cancer was diagnosed in 30 patients (2%). Of these, 13 malignancies occurred among women assigned to TX/CEX, and 17 occurred among women who received T/CEF ($P = .447$). Two patients died from a cardiac cause after completion of chemotherapy; both had received TX/CEX.

DISCUSSION

The final results of the FinXX trial show that the addition of capecitabine to a chemotherapy regimen containing docetaxel, epirubicin, and cyclophosphamide did not significantly improve RFS or overall survival compared with docetaxel followed by CEF. In exploratory analyses, adding capecitabine seemed to improve breast cancer–specific survival and benefit some women with early breast cancer, such as those with triple-negative disease and those

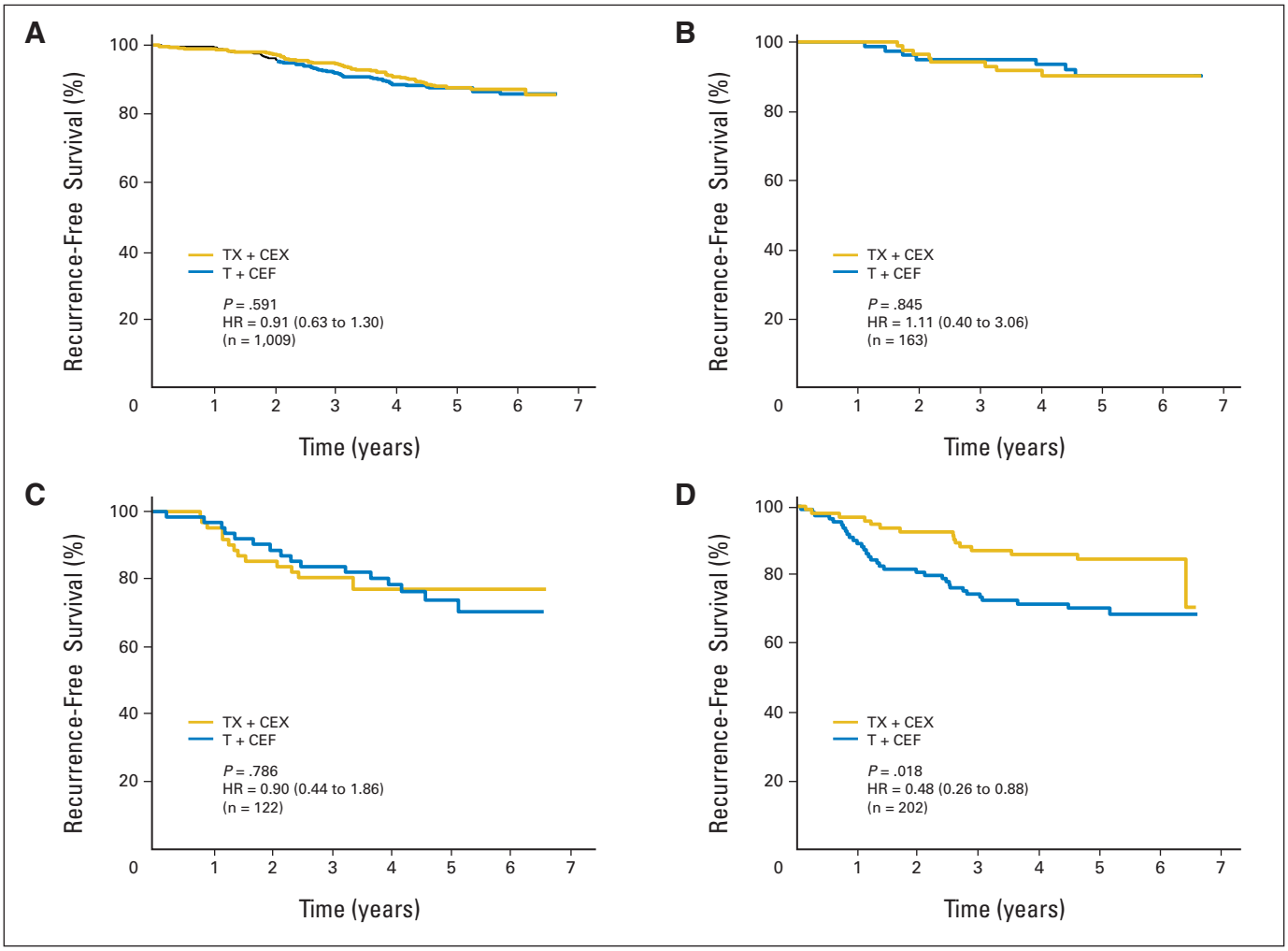

Fig 4. Exploratory analyses of recurrence-free survival based on breast cancer estrogen receptor (ER), progesterone receptor (PgR), and human epidermal growth factor receptor 2 (HER2) status: (A) ER and/or PgR positive, HER2 negative; (B) ER and/or PgR positive, HER2 positive; (C) ER and PgR negative, HER2 positive; and (D) ER, PgR, and HER2 negative. CEF, cyclophosphamide, epirubicin, and fluorouracil; CEX, cyclophosphamide, epirubicin, and capecitabine; HR, hazard ratio; T, docetaxel; TX, docetaxel and capecitabine.

with more than three metastatic axillary lymph nodes at the time of diagnosis. Confirmation of these observations would require prospective study.

Besides FinXX, integration of capecitabine into a regimen containing an anthracycline and a taxane has been evaluated in one other randomized study in the adjuvant setting[16] and in two randomized studies in the neoadjuvant setting.[9,17] In a trial carried out by the US Oncology Group (USON01062), 2,611 women with either node-positive cancer or moderate- to high-risk node-negative cancer were assigned to receive four cycles of doxorubicin and cyclophosphamide in both arms, followed by either four cycles of T or four cycles of TX.[16] During a median follow-up of 5 years, there was no significant difference in the primary end point (disease-free survival) between the groups, but patients assigned to TX may have had better overall survival. In the Austrian Breast Cancer Study Group neoadjuvant trial 24 (ABCSG-24), where 536 patients with breast cancer were assigned to receive six cycles of epirubicin plus docetaxel (ED) with or without capecitabine, the addition of capecitabine to ED increased the pCR rate significantly from 16.0% to 24.3%.[9] However, in the three-arm neoadjuvant German GeparQuattro trial with 1,509 participants, four cycles of TX did not result in a superior pCR rate compared with four cycles of docetaxel or four cycles of docetaxel followed by four cycles of capecitabine when each regimen was administered after completion of four cycles of epirubicin plus cyclophosphamide.[17]

The current results suggest that the efficacy benefit of capecitabine may be limited to some subtypes of early breast cancer, such as triple-negative cancer and cancers with extensive axillary involvement, which are associated with a high risk of cancer recurrence. These findings are in line with an exploratory analysis carried out in the USON01062 trial, where patients with a high cell proliferation rate (Ki-67 $>$ 10%) seemed to benefit from integration of capecitabine into the chemotherapy regimen,[16] and with the analysis of the ABCSG-24 trial data, which suggested that the addition of capecitabine to ED is associated with a greater chance of achieving pCR when the cancer is hormone receptor negative or has grade 3 differentiation.[9] The reasons for these findings remain speculative, but interactions of capecitabine with other chemotherapy agents or its prolonged mode of administration may play a role.

TX/CEX improved RFS significantly compared with T/CEF in the planned interim analysis of the FinXX trial, which was based on a smaller number of events and shorter follow-up (HR, 0.66; 95% CI, 0.47 to 0.94; $P = .020$).[10] The 3-year RFS rates are virtually identical in the interim and final analyses of the trial (TX/CEX, 92.5% and 92.4%, respectively; T/CEF, 88.9% and 88.9%, respectively), and when the follow-up time of the final analysis is truncated to the first 3 years, the HR is also almost identical to the HR reported in the interim analysis (0.67). These findings support the hypothesis that the addition of capecitabine to standard chemotherapy works best for cancers that recur early during the first few years of follow-up and may have a rapid cell proliferation rate. Triple-negative breast cancers generally recur early compared with most other breast cancer subtypes,[18] and TX/CEX might improve outcome in triple-negative cancer (Fig 4).

We initiated chemotherapy with a taxane instead of an anthracycline-containing combination. This might be advantageous,[19-22] but the optimal sequence and the best way to integrate capecitabine into chemotherapy regimens remain inadequately studied.

Administration of TX/CEX with the current dosages was feasible, and the associated toxicity was generally manageable, although the study participants discontinued TX/CEX more frequently than T/CEF (24% *v* 3%, respectively). The doses of docetaxel and capecitabine selected to be administered were close to the median doses actually delivered in a study that evaluated TX in advanced breast cancer,[23] and considering the number of patients who discontinued treatment, selection of these doses may not have been overcautious. In an analysis of the FinHer trial data, efficacy of docetaxel doses of 80 mg/m^2 and 100 mg/m^2 was similar in the adjuvant treatment of breast cancer,[24] but this retrospective analysis needs to be interpreted with caution. The FinXX trial was carried out in only 20 centers, and thus, the number of patients treated at each center was often high, which also suggests that toxicity associated with the current doses is acceptable.

We conclude that the integration of capecitabine into a chemotherapy regimen containing docetaxel, epirubicin, and cyclophosphamide did not significantly improve RFS compared with a similar regimen without capecitabine. Yet, the results are compatible with a hypothesis that the integration of capecitabine into a regimen of standard agents improves breast cancer–specific survival and may improve outcome in some biologic subgroups of early breast cancer. In particular, further research is warranted in triple-negative breast cancer.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

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