International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Which is More Effective; Docetaxel, Doxorubicin and Cyclophosphamide or 5-Fluorouracil, Doxorubicin and Cyclophosphamide in Adjuvant Treatment of Early Stage Node Positive Breast Cancer?

Rehab F Mohamed[1], Abeer F Amin[2], Mohamed Alaa Elden Hassan Mohamed[3], Rania A Abdelhamid[4]

Department of Clinical Oncology and Nuclear Medicine, Faculty of Medicine, Assiut University, Assiut, Egypt

Abstract: ***Background: The aim of this study is to compare the efficacy and the safety of docetaxel, doxorubicin and cyclophosphamide (TAC) with 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) as adjuvant treatment for early stage node positive breast cancer patients. Methods: Sixty patients with pathologically confirmed early stage node-positive breast cancer were randomly assigned to receive six cycles of eitherdocetaxel (75mg/m²),doxorubicin (50mg/m²) and cyclophosphamide (500mg/m²) every three weeks or 5-fluorouracil (500mg/m²), doxorubicin (50mg/m²) and cyclophosphamide (500mg/m²) every three weeks as adjuvant treatment. The two chemotherapy regimens were compared in term of disease free survival (DFS) and overall survival (OS). Results: At a median follow-up of 30 month, the median estimated rate of DFS for patients in the TAC group was 24 month compared to 20 month for patients in the FAC group which was statistically significant (95% confidence interval [CI], 0.49 to 7.17; P <0.04).In terms of OS, no significant difference between the two treatment groups, the median estimated rate of OS in the TAC arm was 25 month compared to 24 month in the FAC arm (CI, 2.84 to 5.27; P= 0.522).No significant difference in DFS as regarding the prognostic factors as number of involved axillary lymph nodes (p=0.485), menopausal status (P=0.684), hormone-receptor status (P=0.795) and HER2/neustatus (P=0.509). The incidence of grade 2-3 anemia was higher in the TAC group than in the FAC group (23.3% versus 13.3%, P<0.04). As regarding neutropenia, it occurred more frequently in the TAC group (13.3% versus 6.7%, P<0.04). The incidence of grade 3 febrile neutropenia in the TAC group was 10% versus 3.3% in the FAC group (P=0.372). Conclusion: Incorporation of docetaxel in the adjuvant treatment of early node-positive breast cancer patients improves the DFS with tolerable toxicity compared to FAC regimen. However, further follow-up is needed to demonstrate its effect on the OS.***

Keywords: TAC/FAC, adjuvant, node-positive, breast cancer, survival

1. Introduction

The most frequently diagnosed cancer and the leading cause of death in women is breast cancer [1].In the United States breast cancer is the most common malignancy in women and is second to lung cancer as a cause of cancer death. The American Cancer Society estimates that 255,180 Americans will be diagnosed with breast cancer and 41,070 will die of the disease in the United States in 2017[2]. At presentation the majority of patients are diagnosed at early stages, about 61%, with a 5-year survival about 90%, regionally advanced in 32 %, and metastatic in 7 %of cases [3].Adjuvant systemic therapy should be considered after surgical treatment based on individual risk of relapse and predicted sensitivity to a particular treatment. The results of Early Breast Cancer Trialists' Collaborative Group (EBCTCG) overview analysis show convincing reductions in the recurrence and death for adjuvant chemotherapy in all age group [4].

In the mid-1990s the introduction of taxanes in the treatment of metastatic breast cancer (MBC) marked a significant advance [5, 6].In 1960s paclitaxel was isolated from extracts from pacific yew trees (Taxusbrevifolia). Docetaxel was discovered in 1980s, a more potent semisynthetic derivative of paclitaxel, derived from extracts of the yew trees (Taxusbaccata) [7-9].

In 1996 docetaxel received FDA approval for locally advanced and MBC after failure of prior chemotherapy marking a second milestone in the treatment of MBC [10, 11].

Docetaxel has been investigated for early breast cancer as an adjuvant treatment in combination with anthracyclin-containing regimens. After a median follow-up of 124 month of patients with operable node-positive breast cancer, the multicentre phase III randomized Breast Cancer International Research Group (BCIRG) 001 trial showed that six cycles of docetaxel, doxorubicin and cyclophosphamide (TAC)was significantly more effective than six cycles of 5-fluorouracil, doxorubicin and cyclophosphamide (FAC) for the adjuvant treatment reducing the risk of recurrence by 28% and the risk of death by 30%.The benefit in DFS was irrespective of nodal, hormone receptor, and HER2 status but TAC was associated with considerably more toxicity, including febrile neutropenia [12,13]. The present study compares the efficacy of TAC with FAC as adjuvant chemotherapy in women with early, axillary lymph node-positive, breast cancer.

2. Patients and Methods

Study Population

This prospective phase III clinical randomized study was conducted at the Clinical Oncology Department in Assiut

University Hospital from 2014 to 2017. The Ethics Committee of Faculty of Medicine, Assiut University approved this protocol before data collection. Sixty female patients with pathologically confirmed early breast cancer (clinical stage I, II, IIIA according to AJCC) [14], were included in the study. Patients eligible for the study were between 18 and 70 years of age, in good general condition, had undergone primary surgery (lumpectomy with free surgical margins or mastectomy plus axillary-node dissection including at least 10 lymph nodes), all patients had at least one axillary lymph node positive for cancer on histological examination. Complete staging workup was done including chest radiography, abdominal ultrasonography, computed tomography, or both, and bone scan when indicated. Assessment of the left ventricular ejection fraction with echocardiography was mandatory.

Study design

Patients were classified into two groups; the first group received intravenous infusion of TAC (docetaxel 75mg/m², Adriamycin 50mg/m² and cyclophosphamide 500mg/m²). The second group received intravenous infusion of FAC (5-Fluorouracil 500mg/m², Adriamycin 50mg/m² and cyclophosphamide 500mg/m²) every three weeks for six cycles. Patients on TAC received premedication dexamethasone 8mg p.o. every 12 hours for six doses starting the day before chemotherapy to prevent docetaxel-related hypersensitivity and fluid retention. Antiemetic drug was recommended for both groups.

The primary end point was DFS, defined as the time from randomization to the date of clinical relapse. Second end point was OS, defined as the time from randomization until death.

Evaluation

Toxicity was assessed before each cycle and evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Eventsv4.0 (NCI-CTCAE).

On day 21 of each cycle, complete blood cell count and clinical assessments, including those for toxic effects were performed. Follow-up visits took place every 3 months during the period of the study.

Chest radiography and abdominal ultrasonography were performed every 6months mammography was repeated annually during the follow-up period.

Statistics

The statistical analysis was done with the Statistical Package for the Social Sciences, version 16 (SPSS, Inc., Chicago, IL, USA). The descriptive analysis was done. The Kaplan–Meir survival curves were used for estimation of DFS and OS. P values less than 0.05 was considered significant.

3. Results

A total of sixty patients were randomly enrolled in our study and all of them completed six cycles of chemotherapy successfully. The baseline demographic data of our patients were summarized in Table 1. The mean age in the TAC group was 46.4±9.8years, and 45.7±10.3 years in the FAC group. No significant difference was noticed between the study groups in terms of age, tumor characters, menopausal status and the type of surgery. Table 2 shows the toxicity of the treatment in both groups, the most common toxicity was nausea and vomiting. Almost all patients had alopecia. The incidence of grade 2-3 anemia was higher in the TAC group than in the FAC group (23.3% versus 13.3%, P<0.04). As regarding to the neutropenia, it occurred more in the TAC group (13.3% versus 6.7%, P<0.04). The incidence of grade 3 febrile neutropenia in the TAC group was 10% versus 3.3% in the FAC group (P=0.372).

After 30 month of follow up of patients, the median estimated rate of DFS for patients in the TAC group was 24 month compared to 20 month for patients in the FAC group which was statistically significant (CI, 0.49 to 7.17; P <0.04) Table 3 and figure 1. In terms of OS, no significant difference between the two treatment groups, the median estimated rate of OS in the TAC arm was 25 month compared to 24 month in the FAC arm (CI, 2.84 to 5.27; P= 0.522)Table 4 and figure 2. Table 5 shows the analysis of the impact of the prognostic factors on the DFS and OS revealed that there was no significant difference as regarding the number of involved axillary lymph nodes (p=0.485),menopausal status (P=0.684), hormone-receptor status (P=0.795) and HER2/neustatus (P=0.509).

Table 1: Patients and disease characteristics of the studied groups

Character	*TAC (N=30)*	*FAC (N=30)*	*P value*
Age			
Mean age (year)	46.4±9.8	45.7±10.3	P=0.378
Tumor size-no. (%)			
≤2cm	6(20.0)	4(13.33)	P=0.592
>2 to 5cm	19(63.33)	22(73.33)	
>5cm	5(16.67)	4(13.33)	
Tumor grade-no. (%)			
Grade 1	1	2	P=0.408
Grade 2	6	4	
Grade 3	23	24	
N stage			
N1(1-3)	10(33.33)	9(30.0)	P=0.372
N2(4-10)	18(60.0)	20(66.67)	
N3(>10)	2(6.67)	1(3.33)	
Histology			
IDC	29(96.67)	30(100.0)	P=0.446
ILC	1(3.33)	0(0)	
Menopausal status-no. (%)			
Premenopausal	18(60.0)	16(53.33)	P=0.273
Postmenopausal	12(40.0)	14(46.67)	
ER/PR status-no. (%)			
ER+/PR+	19(63.33)	17(56.67)	
ER+/PR-	5(16.67)	8(26.67)	P=0.583
ER-/PR+	3(10)	3(10.0)	
ER-/PR-	3(10)	2(6.67)	
Her 2-neu-no. (%)			
Positive	19(63.33)	18(60.0)	P=0.336
Negative	11(36.67)	12(40.0)	
Surgery-no. (%)			
Breast-conserving surgery	5(16.67)	6(20.0)	P=0.362
Mastectomy	25(83.33)	24(80.0)	

Table 2: Treatment Toxicity

Toxic Effect	*TAC(N=30) no.(%)*	*FAC (N=30) no.(%)*	*P- value*
Hematologic			
Anemia	7(23.33)	4(13.33)	P<0.04*
Leukopenia	5(16.67)	3(10.0)	P=0.0224
Thrombocytopenia	2(6.67)	0(0)	P=0.371
Neutropenia	4(13.33)	2(6.67)	P<0.04*
Febrile neutropenia	3(10.0)	1(33.3)	P-0.372
Neutropenic infection	1(3.33)	0(0)	P=0.694
Nonhematologic			
Nausea and vomiting	27(90.0)	28(93.33)	P=0.254
Diarrhea	5(16.67)	3(10.0)	P=0.335
Alopecia	30(100.0)	30(100.0)	P=1
stomatitis	3(10.0)	5(16.67)	P=0.0224
Irregular menses	18(60.0)	16(53.33)	P=0.846
Amenorrhea	13(43.33)	12(40.0)	P=0.684
Nail disorder	3(10.0)	1(3.33)	P=0.372

Table 3: Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
group	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
1	22.100	1.411	19.334	24.866	24.000	1.095	21.853	26.147
2	18.759	1.290	16.230	21.287	20.000	2.355	15.385	24.615
Overall	20.458	.974	18.548	22.367	23.000	.843	0.49	7.17
a. Estimation is limited to the largest survival time if it is censored.								

Table 4: Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
Group	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
1	22.800	1.403	20.050	25.550	25.000	1.369	22.316	27.684
2	21.586	1.465	18.715	24.458	24.000	.663	22.700	25.300
Overall	22.203	1.008	20.228	24.179	24.000	.768	2.84	5.27
a. Estimation is limited to the largest survival time if it is censored.								

Table 5: Disease-free Survival analysis according to the prognostic factors

	No. of all Patients (%)	TAC (N=30) no. (%)	FAC (N=30) no. (%)	P-value
N stage				
N1	19(31.67%)	10(33.33%)	9(30.0%)	
> N1	41(68.33%)	20(66.67%)	21(70.0%)	P=0.485
Menopausal status				
Premenopausal	34(56.67%)	18(60.0%)	16(53.33%)	P=0.684
Postmenopausal	26(43.33%)	12(40.0%)	14(46.67%)	
ER/PR status				
Positive	55(91.67%)	27(90.0%)	28(93.33%)	P=0.795
Negative	5(8.33%)	3(10.0%)	2(6.67%)	
HER2/neu status				
Positive	37(61.67%)	19(63.33%)	18(60.0%)	P=0.509
Negative	23(38.33%)	11(36.67%)	12(40.0%)	

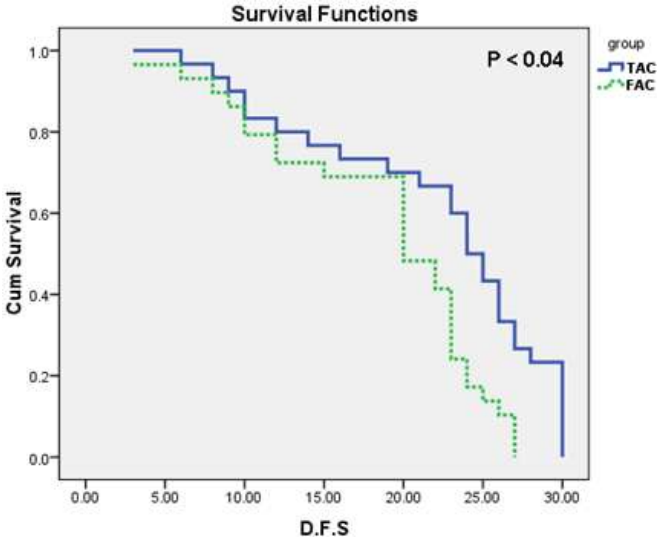

Figure 1: Kaplan-Meier curve for disease free survival

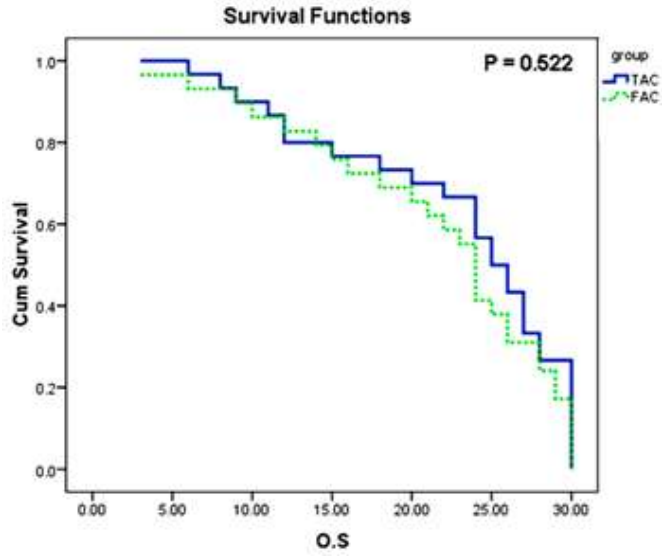

Figure 2: Kaplan-Meier curve for over-all survival

4. Discussion

A recent therapeutic advance for the adjuvant treatment of breast cancer was the use of taxanes [paclitaxel (P) or docetaxel (T)]. Several randomized clinical trials (RCTs) evaluate the taxanes with anthracycline-based regimens. In the present evidence review, trials of taxanes represented the largest number of RCTs (fifty-five trials in ninety-three publications) but the EBCTCG was the most completed one [4].The hazard ratios (HRs) for DFS and OS of many of these trials showed that taxane-based therapy was associated with significant reduction in the risk of recurrence and death. This meta-analysis indicated that taxane-based adjuvant chemotherapy was more efficacious in improving DFS and OS when compared with taxane-free therapy [11,15-21].

In 2004, docetaxel was approved in combination with doxorubicin and cyclophosphamide for patients with node-positive operable breast cancer [22, 23].

Our clinical randomized phase III trial comparing the TAC with the FAC as adjuvant treatment for patients with node-positive early breast cancer showed that, there was improvement in the median DFS for patients in the TAC group compared to the median DFS for patients in the FAC group (CI, 0.49 to 7.17; P <0.04).

These results are similar to the final results from BCIRG 001trial which showed TAC is superior to FAC, estimated 5-year DFS was 75% with TAC and 68% with FAC (HR, 0.72; 95% CL, 0.59-0.88; P=0.01); survival was 87% with TAC and 81% with FAC (HR, 0.70; 95% CL, 0.53-0.91;P= 0.008)[11]. However in terms of OS, the present study showed that there was no significant difference between the two groups (P=0.522) which differ from the results of the previous trials this may be due to the short duration of follow-up of our study [11]. The 10-year updated results of the Eastern Cooperative Oncology Group (ECOG) 1199 trial which compared patients with node-positive or high risk node-negative breast cancer who received 4 cycles of Adriamycin and cyclophosphamide (AC) followed by either paclitaxel or docetaxel, either weekly or every 3 weeks showed that, incorporation of weekly paclitaxel and docetaxel every 3 weeks was associated with significant improvement in DFS and marginal improvement in OS, compared with paclitaxel every 3 weeks [24].

Jones et al 2009 reported that at a median follow-up of 7 years of women with stage I to III breast cancer, the DFS and OS were improved with docetaxel and cyclophosphamide (TC) compared with Adriamycin and cyclophosphamide (AC) [25].

After a median follow-up of 84 month of 1,016 patients with operable breast cancer who were assigned to four 3-week cycles of AC ordocetaxel and cyclophosphamide (DC),the US Oncology Research phase III trial found that there was significant improvement in the DFS (HR, 0.74; P = 0.033) and OS (HR, 0.69; P = 0.032) [25].

The results of analysis of the impact of the prognostic factors as number of axillary lymph node, menopausal status, ER/PR status and HER2/neuon the DFS indicated that there was no significant improvement in DFS in the TAC arm compared to the FAC arm this maybe due to the small number of patients and the short duration of follow-up. These results are consistent with the results of the BCIRG001 that did not find any correlation between the benefit in DFS and the nodal, hormone receptor, and HER2/neu status and adjuvant docetaxel [11, 13, 26]. Martin et al 2005 and Roche et al 2006 demonstrated that the benefits of taxanes may be lower, if not negligible, for N4+ [11, 27] and for ER- positive patients [28-32].

Hayes et al reported that increase in the taxanes response in ER negative patients [33]. Other previous studies demonstrated that taxanes and anthracycline are more effective in triple negative breast cancer (TNBC) [33-35].

Drug-related toxicities, such as anemia, neutropenia, febrile neutropenia and other non- hematological toxicities were reported in this study and in other previous studies [36].TAC was associated with marked toxicities as anemia and neutropenia (P<0.04) and were manageable with standard supportive measures.

5. Conclusion

In patients with node-positive early breast cancer TAC provides improvement in DFS with manageable toxicity compared with FAC. However, further follow-up is needed to demonstrate its effect on the OS.

References

[1] Mohammah H , Allyne M, Rafael Lozano et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. The Lancet 2011; 6736:61351-61352.
[2] Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin 2017; 67:7–30. 2.
[3] Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, et al. (eds). SEER Cancer Statistics Review, 1975–2011, National Cancer Institute. Bethesda, MD. Based on November 2013 SEER data submission, posted to the SEER web site, April 2014. http://seer.cancer.gov/csr/1975_2011/. [Last accessed 7/28/2015.]
[4] Early Breast Cancer Trialists′ Collaborative G, Peto R, Davies C, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomized trials. Lancet 2012; 379:432-444. Available at: http//www.ncbi.nim.nih.gov/pubmed/22152853.
[5] Ghersi D, Wilcken N, Simes RJ. A systematic review of taxane containing regimens for metastatic breast cancer. Br J Cancer. 2005; 93(3): 293–301.
[6] Nowak AK, Wilcken NR, Stockler MR, Hamilton A, Ghersi D. Systematic review of taxane-containing versus non-taxane-containing regimens for adjuvant and neoadjuvant treatment of early breast cancer. Lancet Oncol. 2004; 5(6):372–80.
[7] Taxotere (docetaxel) [package insert]. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2010.
[8] Jones SE, Erban J, Overmoyer B, et al. Randomized phase III study ofDocetaxel compared with paclitaxel in metastatic breast cancer. J ClinOncol. 2005; 23(24):5542–51.
[9] Ringel I, Horwitz SB. Studies with RP 56976 (taxotere): A semisyntheticanalogue of taxol. J Natl Cancer Inst. 1991; 83(4):288–91.
[10] Us Food and Drug Administration. taxotere. http://www.accessdata.fda. gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetail. Accessed Jan 6, 2012.
[11] Martin M, Pienkowski T, Mackey J, et al: Adjuvant docetaxel for node positive breast cancer. N Engl J Med 352:2302-2313, 2005.
[12] Jones SE, Erban J, Overmoyer B, Budd GT, Hutchins L, Lower E, et al. Randomized phase III study of docetaxel compared with paclitaxel in metastatic breast cancer. J ClinOncol. 2005; 23:5542–51.
[13] Nabholtz JM, Pienkowski T, Mackey J, etal. Phase III trial comparing TAC (docetaxel,doxorubicin, cyclophosphamide) with FAC(5-fluorouracil, doxorubicin, cyclophosphamide)in the adjuvant treatment of nodepositive breast cancer (BC) patients: interimanalysis of the BCIRG 001 study. Proc AmSocClinOncol 2002; 21:36a. Abstract.
[14] AJCC (American Joint Committee on Cancer) Cancer Staging Manual, 8th edition, Amin MB, Edge SB, Greene FL et al. (Eds), Springer, Chicago 2017.
[15] De Laurentiis M, Cancello G, D'Agostino D, Giuliano M, Giordano A, et al. (2008) Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. J ClinOncol 26: 44–53.
[16] Ferguson T, Wilcken N, Vagg R, Ghersi D, Nowak AK (2007) Taxanes for adjuvant treatment of early breast cancer. Cochrane Database Syst Rev. CD004421.
[17] Gianni L, Baselga J, Eiermann W, GuillemPorta V, Semiglazov V, Lluch A, et al. European Cooperative Trial in Operable Breast Cancer Study Group. Feasibility and tolerability of sequential doxorubicin/paclitaxel followed by cyclophosphamide, methotrexate, and fluorouracil and its effects on tumor response as preoperative therapy. Clin Cancer Res 2005; 11:8715-21.
[18] Henderson IC, Berry DA, Demetri GD, Cirrincione CT, Goldstein LJ, Martino S, et al. Improved outcomes from adding sequential Paclitaxel but not from escalating Doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J ClinOncol 2003; 21:976-83.
[19] Sparano JA, O'Neill A, Schaefer PL, Falkson CI, Wood WC. Phase II trial of doxorubicin and docetaxel plus granulocyte colony-stimulating factor in metastatic breast cancer: Eastern Cooperative Oncology Group Study E1196. J ClinOncol 2000; 18:2369-77.
[20] Evans TR, Yellowlees A, Foster E, Earl H, Cameron DA, Hutcheon AW, et al. Phase III randomized trial of doxorubicin and docetaxel versus doxorubicin and cyclophosphamide as primary medical therapy in women with breast cancer: An Anglo-Celtic Cooperative Oncology Group study. J ClinOncol 2005; 23:2988-95.
[21] 18. Martin M, Segui MA, Anton A, Ruiz A, Ramos M, Adrover E, et al. Adjuvant docetaxel for high-risk, node-negative breast cancer. N Engl J Med 2010; 363:2200-10.
[22] Taxotere (docetaxel) [package insert]. Bridgewater, NJ: Sanofi-Aventis US. LLC; 2010.
[23] Us Food and Drug Administration. taxotere. http://www.accessdata.fda. gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.DrugDetails. Accessed Jan 6, 2012.
[24] Sparano JA ZF, Martino S, et al. Ten year update of E 1199: Phase III study of doxorubicin-cyclophosphamide followed by paclitaxel or docetaxel given every 3 weeks or weekly in patients with axillary node- positive or high risk node-negative breast cancer [abstract]. San Antonio Breast Cancer Symposium. Oral Presentation Abstract S3-03.2014.
[25] Jones S, Holmes FA, O'Shaughnessy J, Blum JL, Vukelja SJ, McIntyre KJ, et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow up of US Oncology Research Trial 9735. J ClinOncol. 2009; 27:1177–83.

[26] Andre F, Broglio K, Roche H, et al: Estrogen receptor expression and efficacy of docetaxel-containing adjuvant chemotherapy in patients with node positive breast cancer: Results from a pooled analysis. J ClinOncol 26:2636- 2643, 2008
[27] Roche H, Fumoleau P, Spielmann M, et al: Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: The FNCLCC PACS 01 Trial. J ClinOncol 24:5664-5671, 2006
[28] Buzdar AU, Singletary SE, Valero V, et al: Evaluation of paclitaxel in adjuvant chemotherapy for patients with operable breast cancer: Preliminary data of a prospective randomized trial. Clin Cancer Res 8:1073-1079, 2002
[29] Henderson IC, Berry DA, Demetri GD, et al: Improved outcomes from adding sequential paclitaxel but not from escalating doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer. J ClinOncol 21:976-983, 2003
[30] Fountzilas G, Skarlos D, Dafni U, et al: Postoperativedose-dense sequential chemotherapywith epirubicin, followed by CMF with or withoutpaclitaxel, in patients with high-risk operable breastcancer: A randomized phase III study conducted bythe Hellenic Cooperative Oncology Group. Ann Oncol16:1762-1771, 2005.
[31] Goldstein LJ, O'Neill A, Sparano J: E2197: Phase III AT (doxorubicin/docetaxel) v AC (doxorubicin/ cyclophosphamide) in the adjuvant treatment of node-positive and high risk node-negative breast cancer. J ClinOncol 23:16s, 2005 (suppl; abstr 512)
[32] Crown J, Francis P, Di Leo A, et al: Docetaxel (T) given concurrently with or sequentially to anthracycline-based (A) adjuvant therapy (adjRx) for patients (pts) with node-positive (N_) breast cancer (BrCa), in comparison with non-T adjRx: First results of the BIG 2-98 Trial at 5 years median follow-up (MFU). J Clin Oncol18s, 2006 (suppl; abstr LBA519).
[33] Hayes DF, Thor AD, Dressler LG et al; Cancer and Leukemia Group B (CALGB) Investigators. HER2 and response to paclitaxel in node-positive breast cancer. N Engl J Med 2007; 357:1496-1506.
[34] Bilici A, Arslan C, Altundag K. Promising therapeutic options in triple-negative breast cancer. JBUON 2012; 17:209-222.
[35] Berry DA, Cirrincione C, Henderson IC et al. Estrogen-receptor status and outcomes of modern chemotherapy for patients with node-positive breast cancer. JAMA 2006;295:1658-1667
[36] Ferguson T, Wilcken N, Vagg R, Ghersi D, Nowak AK (2007) Taxanes for adjuvant treatment of early breast cancer. Cochrane Database Syst Rev. CD004421.