Study Reference Quality Rating	Description of Treatment Arms	CONSORT Numbers Retention	Secondary Malignancies	Comments	Primary Abstractor Initials	Dual Abstractor Initials	isAnthracycline	isCyclophosphamide	isTaxane
EN# **Author Year** **All related ENrs** Trial name, if any If an ancillary article, note followup time or subanalysis. Quality Rating	**Intervention description:** Intervention description (note drugs, dosage, timeline, # of courses) **Control description:** Control description (note drugs, dosage, timeline, # of courses)	**N recruited or assessed for eligibility**: **N eligible**: Total: IG: CG: **N excluded**: Total: IG: CG: **N run-in**: NA if no run-in period Total: IG: CG: **N randomized:** Total: IG: CG: **N Analyzed:** Total: IG:	**Number of patients:** **Number of cancers:** **Cancer types:** **Deaths related to SM:**			*Include date data was checked*			
EN#961 **Fisher (1999)** NSABP B25 Trial (Based on B22 trial - EN#1876; some of the basic study criteria based on earlier NSABP trials, such as EN#1877) **Good**	**Intervention description:** **IG1:** Doxorubicin 60 mg IV every 21 days x 4 courses + cyclophosphomide 2400 mg IV on day 1 of course 1 and course 2 (no cyclo during cycles 3-4) **IG2:** Doxorubicin 60 mg IV every 21 days x 4 courses + cyclophosphomide 2400 mg IV on day 1 of course 1-4 **Control description:** Doxorubicin 60 mg IV every 21 days x 4 courses + cyclophosphomide 1200 mg IV every 21 days x 4 courses *(same as one of the B22 groups)* *All patients >50 years also recievend tamoxifen 20mg/d on Day 1 of Cylce 1 and continuing for 5 years. G-CSF 5 ug/kg was also given to patients on Day 2 of each cycle and continued until a threshold was reached; G-CSF dose adjustments made based on sepsis	**N recruited or assessed for eligibility:** NR **N eligible**: NR **N excluded**: Total: 34 CG: 12 IG1 13 IG2 9 **N run-in**: NA **N randomized:** Total: 2548 patients CG 850 IG1 848 IG2 850 **N analyzed: DFS, OS** Total: 2545 patients CG 849 IG1 847 IG2 849 **N Analyzed: toxicity group** Total: 2534 patients CG: 842 IG1: 845 IG2: 847 **Lost to Followup**: 3.9% **Withdrew consent (XX mo), n (%): NR**	**Acute myeloid leukemia** Total: 0.59% (15/2534) CG: 0.48 % (4/842) IG1: 0.59% (5/845) IG2: 0.71% (6/847) **Myelodysplastic syndrome (MDS)** Total: 0.28% (7/2534) CG: 0% (0/845) IG1: 0.59% (5/842) IG2: 0.24% (2/847) **First Reported Treatment Failure - SM** Total: 2.29% (58/2545) CG: 1.77% (15/849) IG1: 2.24% (19/847) IG2: 2.83% (24/849)		MSW (3/24)		TRUE	FALSE	FALSE
EN#970 **Bergh (2000)** Scandinavian Breast Group (SBG) 9401 study **Fair**	**Intervention description:** **IG1: Tailored FEC**: all patients randomized to this group start on Step 1; based on haematological toxicity, dose adjustments were made - escalation, reduction, or unaltered. Step -2: fluorouracil 600 mg IV + epirubicin 38 mg IV + cyclophosphomide 450 mg IV Step -1: fluorouracil 600 mg IV + epirubicin 60 mg IV + cyclophosphomide 600 mg IV Step 1: fluorouracil 600 mg IV + epirubicin 75 mg IV + cyclophosphomide 900 mg IV Step 2: fluorouracil 600 mg IV + epirubicin 90 mg IV + cyclophosphomide 1200 mg IV + mesna 720 mg IV Step 3: fluorouracil 600 mg IV + epirubicin 105 mg IV + cyclophosphomide 1500 mg IV + mesna 900 mg IV Step 4: fluorouracil 600 mg IV + epirubicin 120 mg IV + cyclophosphomide 1800 mg IV + mesna 1080 mg IV **IG2: high-dose FEC+CTb**: fluorouracil 600 mg IV + epirubicin 60 mg IV + cyclophosphomide 600 mg IV x 2 courses ***followed by*** fluorouracil 600 mg IV + epirubicin 60 mg IV + cyclophosphomide 1200 mg IV + 5 ug/kg G-CSF ***followed by*** high dose chemotherapy after 3-4 weeks (cyclophosphomide 6000 mg + thiotepa 500 mg + carboplatin 800 mg) **Both groups underwent locoragional radiation therapy and were given tamoxifen non-concurrently with chemotherapy at 20 mg/day for 5 years* **Control description:** N/A (compared two intervention groups)	**N recruited or assessed for eligibility:** NR **N eligible**: NR **N run-in**: NA **N randomized:** Total: 525 patients IG1: 251 IG2: 274 **N excluded/ineligible:** Total: 4 IG1: 2 IG2: 2 **N Analyzed (ITT)** Total: 525 IG1: 251 IG2: 274 **Lost to Followup (XX mo), n (%):** Total: 4/525 after 43 months **Withdrew consent (XX mo), n (%): NR**	**Acute myeloid leukemia** IG1: 1.20% (3/251; one each occuring at 14, 15 and 33 months after completion of tx) IG2: NR **Myelodysplastic syndrome (MDS)** IG1: 0.73% (2/274; one each occuring at 27 and 30 months after completion of tx) IG2: NR **Other secondary cancers** IG1: Contralateral BC: 3.59% (9/251) Rectal carcinoma: 0.40% (1/251) Basal carcinoma of the skin: 0.40% (1/251) IG2: NR	Timeline of second solid cancers is unclear. Does not report on SM's occuring in the high-dose CTCb group	MSW (3/25)		TRUE	FALSE	FALSE
EN#974 **Chaplain (2000)** **Fair +**	**Intervention description:** mitoxantrone or anthracycline-containing regimens **Control description:** NA	**N recruited or assessed for eligibility:** 3540 patients **N excluded**: 447 patients 195 women with metastesis; 119 women with unknown surgical treatment; 133 who were older than 85 years of age **N randomized:** NA **N Analyzed:** 3093 patients ***N surgery plus chemotherapy***: 49 patients ***N surgery plus RT plus chemo:*** 960 patients ***N Recieving anthracyclines*** **:** 341 patients **Lost to Followup (XX mo), n (%):** NA **Withdrew consent (XX mo), n (%):** NA	**NLAH/RAEB+ observed:** Anthracycline group 0.29% (1/341) No chemotherapy group: 0.01% (2/2084) **Relative Risk of NLAL/RAEB+** Anthracycline group: 0.095 (95% CI, 0.010-0.90; p=.04)	Doesn't break out leukemia with the anemia group	MSW (3/26)		TRUE	FALSE	FALSE
EN#1028 **Schrama (2002)** (Parent article is EN#1873 - Rodenhuis, 1998; EN#1028 presents updated long-term results) **Fair+**	**Intervention description:** Pre-surgery: FEC (5-fluorouacil 500 mg IV + epirubicin 120 mg IV + cyclophosphomide 500 mg IV) x 3 courses Post-surgery: FEC x 1 course + filgrastim 300 ug + peripheral-blood progenitor cell (PBPC) collection ***followed by*** high-dose chemotherapy after 3 weeks (cyclophosphomide 6 g + thiotepa 480 mg + carboplatin 1600 mg, divided over 4 days) + PCPC support (anti-emetics and antibiotics) **Control description:** Pre-surgery: FEC (5-fluorouacil 500 mg IV + epirubicin 120 mg IV + cyclophosphomide 500 mg IV) x 3 courses Post-surgery: FEC x 1 course	**N eligible**: 97 patients (patients who underwent 3 courses of FEC pre-surgery) **N excluded**: 5 *PBPC unsuccessful: 1* *Unresponsiveness to FEC: 4* **N randomized:** Total: 81 IG: 41 CG: 40 **N Analyzed:** Total: 81 IG: 41 CG: 40 **Lost to Followup (XX mo), n (%):** Total: NR **Withdrew consent:** 17/81 *Patient refusal: 1* *Patient refusal for HD chemo, if randomized to that arm: 11* *Patient refusal for HD chemo, after randomization: 5*	**Myleodysplastic syndrome:** IG: 4.9% (2/41) CG: 0/40 **Solid Tumors:** IG: 4.9% (2/41); basal cell carcinoma, tubular/tubulovilleus adenoma of the colon CG: 2.5% (1/40); tubular/tubulovilleus adenoma of the colon		MSW (4/1)		TRUE	FALSE	FALSE
EN#1035 **Bernard-Marty (2003)** (Parent article - EN#1846 Piccart, 2001) **Good**	**Intervention description:** **IG1:** EC (epirubicin 60 mg/m2 IV on day 1 and cyclophosphomide 600 mg/m2 IV on day 1) cycles every 21 days **IG2:** HEC (epirubicin 100 mg/m2 IV on day 1 and cyclophosphamide 830 mg/m2 IV on day 1) cycles every 21 days **Control description:** **CG:** CMF (cyclophosphomide 100 mg/m2 orally days 1-14; methotrexate 40 mg/m2 IV days 1 and 8; 5-fluorouracil 600 mg/m2 IV days 1 and 8) for six cycles (every 28 days)	**N recruited or assessed for eligibility:** NR **N eligible**: NR **N run-in**: NA **N randomized:** 804 patients **N excluded:** 27 patients CG: 12 *?=inadequate disease stage; 1=inadequate cardiac/bone marrow function; 2=other ineligibility; 2=withdrawal* IG1: 5 *2=inadequate disease stage; 1=inadequate cardiac/bone marrow function; 1=other ineligibility; 1=withdrawal* IG2: 10 *5=inadequate disease stage; 1=inadequate cardiac/bone marrow function; 2=other ineligibility; 2=withdrawal* **N Analyzed:** Total: 777 patients CG: 255 patients IG1: 267 patients IG2: 255 patients **Lost to Followup:** 2.96% (23/777; median 32.3 months) CG: 0.39% (1/255) IG1: 3.37% (9/267) IG2: 5.10% (13/255) **Withdrew consent:** 0.64% (5/777) CG: 0.78% (2/255) IG1: 0.37% (1/267) IG2: 0.78% (2/255)	**Solid Tumors** **CG: 4.31% (11/255)** Contralateral breast: 7 Colorectal carcinoma: 2 Thyroid: 1 Melanoma: 1 **IG1: 3.00% (8/267)** Contralateral breast: 4 Uterus (adenocarcinoma): 1 Thyroid: 1 Lung: 1 Melanoma: 1 **IG2: 4.31% (11/255)** Contralateral breast: 5 Ovary (epithelial): 2 Cervix (squamous): 1 Thyroid: 1 Lung: 1 Glioblastoma: 1 **Other Malignancies** **CG: 0/255** **IG1: 0.37% (1/267)** Chronic lymphocytic leukemia: 1 **IG2: 1.96% (5/255)** AML: 3 Lymphoma: 1 Chronic lymphocytic leukemia: 1	**Data not abstracted:** mean age, age range, mean delay and delay range for each type of secondary malignancy (not broken out by chemo tx); details and characteristics of patients developing AML	MSW (4/2)		TRUE	FALSE	FALSE

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EN#1042 **Crump (2003)** National Cancer Institute of Canada Clinical Trials Group (NCIC-CTF) Adjuvant Chemotherapy Trial **Fair**	**Intervention description:** Women had been in trials with one of the following regimens… **CEF:** cyclophosphamide 700 mg/m2, 900 mg/m2 or 1100 mg/m2 + epirubicin 70 mg/m2 + fluorouracil 500 mg/m2 **CEF + G-CSG:** Cyclophosphamide 700 mg/m2, 900 mg/m2 or 1100 mg/m2 + epirubicin 70 mg/m2 + fluorouracil 500 mg/m2 + G-CSF every 2 weeks x 12 cycles **CMF** **AC:** doxorubicin 60 mg/m2 + cyclophosphamide 600 mg/m2 every 3 weeks x 4 cycles **Control description:**	**N recruited or assessed for eligibility:** NR **N eligible**: 1,545 women CEF: 34.89% (539/1545) CEF+G-CSF 6.28% (97/1545) CMF: 43.88% (678/1545) AC: 14.95% (231/1545) **N excluded**: NR **N run-in**: NA **N randomized:** NR **N Analyzed:** 1451 (based on Table 2) CEF: 34.60% (502/1451) CEF+G-CSF: 4.34% (63/1451) CMF: 45.76% (664/1451) AC: 15.30% (222/1451) **Lost to Followup (XX mo), n (%): NR** **Withdrew consent (XX mo), n (%): NR**	**Incidence of Leukemia** **Overall 0.65% (10/1545)** CEF: 1.30% (7/539) CMF: 0.15% (1/678) AC: 0.43% (1/231) **Leukemia-Related Deaths** **Overall: 60% (6/10)** CEF: 66.67% (4/6) CMF: 16.67% (1/6) AC: 16.67% (1/6)	**Data not abstracted:** interval to diagnosis; cumulative risk; leukemia by RT therapy	MSW (4/2)		TRUE	FALSE	FALSE
EN#1106 **Campone (2005)** French Adjuvant Study Group (FASG) **Fair**	**Intervention description:** Epirubicin-based treatment FEC 50: 59% of patients FEC 75: 7% FEC 100: 19% Epirubicin-vinorelbine: 9% Weekly single agent epirubicin: 6% **Control description:** Patients not receiving adjuvant epirubicin	**N recruited or assessed for eligibility:** NR **N eligible**: NR **N excluded**: NR **N run-in**: NA if no run-in period **N randomized:** NR **N Analyzed:** Total: 3653 IG: 2603 CG: 1050 **Lost to Followup (XX mo), n (%):** Total: IG: CG: **Withdrew consent (XX mo), n (%):** Total: IG: CG:	**Incidence of Leukemia:** 0.31% (8/2603) **Incidence of myelodysplastic syndrome:** 0% (0/2603) **Leukemia-related deaths**: 62.5% (5/8)	**Data not abstracted:** patient age of leukemia cases; onset period; cumulative dose; 9 year cumulative incidence of secondary leukemia; incidence rates of seconday leukemia by epirubicin dose	MSW (4/7)		TRUE	FALSE	FALSE
EN#1131 **Praga (2005)** **Fair +** Analysis of multiple trials; we have already abstracted some - need to pull others and determine whether to use this pooled analysis	The trials contained 44 different treatment arms, and these arms were pooled into 5 groups **Intervention description:** Epirubicin-containing chemotherapy regimens (epirubicin dose/cycle of ≤100mg/m2 or epirubicin dose/cycle of >100mg/m2) **Control description:** Non-epirubicin-containing treatment (chemotherapy not including epirubicin, hormone therapy without chemotherapy or no chemotherapy or hormone therapy)	**N recruited or assessed for eligibility:** **N eligible**: 10,111 patients (all those randomized across 19 trials) **N excluded**: Total: IG: CG: **N run-in**: NA if no run-in period **N randomized:** NA **N Analyzed:** 9,796 patients IG: 7,110 CG: 2,686 **Lost to Followup (XX mo), n (%):** NR **Withdrew consent (XX mo), n (%):** NR	**Incidence of AML/MDS:** Total: 0.31% (30/9796) IG (total): 0.39% (28/7110) *IG (epirubicin ≤100 mg/m2 per cycle): 11 cases* *IG (epirubicin >100 mg/m2 per cylce): 17 cases* CG: 0.07% (2/2686) *CG (chemo w/o epirubicin): 1 case* *CG (hormone therapy): 1 case* *CG (surgery with/out RT): 0 cases* **Timing to AML/MDS diagnosis** Total: median 33 months (range: 8-126 months) IG: median 29.5 months (range: 8-126) CG: median 73 months (range: 72-74) **AML/MDS-related deaths** **Deaths within 1 month of AML/MDS dx:** Total: 16.7% (5 deaths/30 diagnoses) IG: 14.3% (4/28) CG: 50% (1/2)	**Data not abstracted:** age at first adjuvant tx for patients developing AML/MDS; epirubicin/cyclophosphomide dose; yes/no to tamoxifen, RT, G-CSF; prior breast cancer recurrence; AML/MDS rate by risk factors (age, RT, tamox, G-CSF); cumulative probability of AML/MDS at 3, 5, 8 years We have already abstracted some of the original studies for this analysis (Piccart; Bernard-Marty; Levine; Crump) - **PULL OTHERS TO REVIEW**	MSW (4/8)		TRUE	FALSE	FALSE
EN#1141 **Venturini (2005)** **Good**	**Intervention description:** **IG:** FEC14 (fluorouracil 600 mg/m2 + epirubicin 60 mg/m2 + cyclophosphamide 600 mg/m2) every 14 days x 6 courses, with the addition to filgrastim **Control description:** **CG**: FEC21 (fluorouracil 600 mg/m2 + epirubicin 60 mg/m2 + cyclophosphamide 600 mg/m2) every 21 days x 6 courses	**N recruited or assessed for eligibility:** **N eligible**: **N run-in**: NA if no run-in period **N randomized:** 1,214 patients IG: 604 patients CG: 610 patients **N ineligible** 40 patients IG: 23 patients CG: 17 patients **N Analyzed:** 1,214 patients IG: 604 patients CG: 610 patients **Lost to Followup:** 10.8% (132/992 living patients) IG: CG: **Withdrew consent (XX mo), n (%):** Total: IG: CG:	**Incidence of Any Second Primary Cancer (after 10.4 years):** Total: 4.7% (57/1214) IG: 4.8% (29/604) CG: 4.6% (28/610) **Incidence of Second Primary Breast Cancer (after 10.4 years):** Total: 2.1% (26/1214) IG: 2.0% (12/604) CG: 2.3% (14/610) **Incidence of Second Primary Non-Breast Cancer (after 10.4 years):** Total: 2.6% (31/1214) IG: 2.8% (17/604) CG: 2.3% (14/610)		MSW (4/8)		TRUE	FALSE	FALSE
EN#1214 **Ferguson (2007)** **Good** Systematic review - pull original articles	**Intervention description:** Any chemotherapy regimen containing taxanes **Control description:** Any chemotherapy regimen that did not contain a taxane	**N recruited or assessed for eligibility:** NA **N eligible**: NA Total: IG: CG: **N excluded**: NA **N run-in**: NA if no run-in period **N randomized:** NA **N Analyzed:** NA **Lost to Followup (XX mo), n (%):** NA **Withdrew consent (XX mo), n (%):** NA	Based on Analysis 9.4 (page 53) **Incidence of Secondary Leukemia/MDS:** Total: 0.34% (48/14149) IG: 0.38% (25/7093) CG: 0.33% (23/7056)	Reports median f/u for the different studies, but the analysis does not indicate when the secondary malignancies occurred. One of the 7 included studies is only an abstract; have pulled the other 6 studies for review	MSW (4/8)		FALSE	FALSE	FALSE
EN#1263 **Francis (2008)** **Good**	**Intervention description:** **Control description:**	**N recruited or assessed for eligibility:** **N eligible**: Total: IG: CG: **N excluded**: Total: IG: CG: **N run-in**: NA if no run-in period Total: IG: CG: **N randomized:** Total: IG: CG: **N Analyzed:** Total: IG: CG: **Lost to Followup (XX mo), n (%):** Total: IG: CG: **Withdrew consent (XX mo), n (%):** Total: IG: CG:	**Number of patients:** **Number of cancers:** **Cancer types:** **Deaths related to SM:**				FALSE	FALSE	FALSE
EN#1265 **Goldstein (2008)** **Good**							FALSE	FALSE	FALSE
EN#1273 **Liu (2008)** **Fair**							FALSE	FALSE	FALSE
EN#1399 **Martin (2010)** (Parent article EN#1874 Martin, 2006) **Good**							FALSE	FALSE	FALSE
EN#1463 **Kaplan (2011)** **Fair**							FALSE	FALSE	FALSE

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EN#1586 Shulman (2012) (Parent article - EN#1040 Citron, 2003) Fair+							FALSE	FALSE	FALSE
EN#1587 Simone (2012) Fair -							FALSE	FALSE	FALSE
EN#1598 Vici (2012) Fair							FALSE	FALSE	FALSE