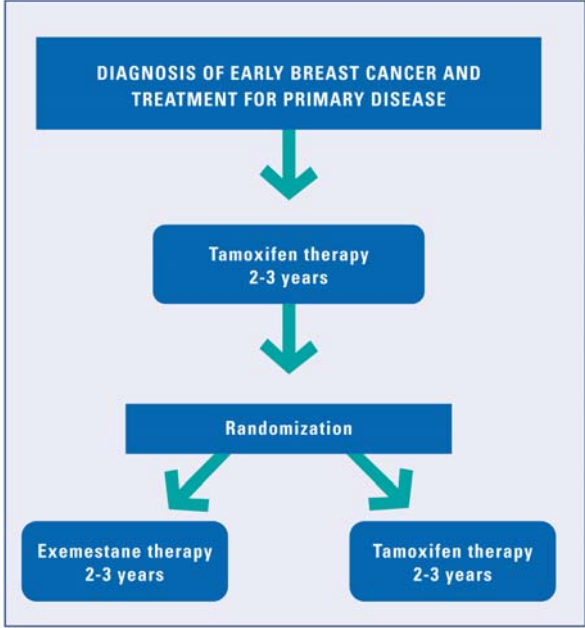


Intergroup Exemestane 031 Trial (IES 031 Trial)
As published in the *New England Journal of Medicine**

Trial Design:	Randomized phase III double-blind trial in postmenopausal women with estrogen receptor (ER)-positive breast cancer to test whether, after 2 – 3 years of adjuvant tamoxifen, switching to AROMASIN was more effective than continuing tamoxifen for the remainder of the 5 years of adjuvant hormonal therapy.
Objectives:	<ul style="list-style-type: none"> • Primary: Compare disease-free survival defined as time from randomization to recurrence of breast cancer at any site, second primary breast cancer, or death from any cause. • Secondary: Compare the regimens in terms of overall survival, the incidence of contralateral breast cancer and long-term tolerability.
Author Conclusions:	Switching to AROMASIN after 2 – 3 years of tamoxifen use results in significant improvement in both disease-free survival and incidence of contralateral breast cancer when compared with the standard 5 years of tamoxifen treatment.
Key Inclusion Criteria:	<ul style="list-style-type: none"> • ER-positive or unknown disease • Adequate therapy for primary disease • Postmenopausal • Having received tamoxifen for 2-3 years • Remaining free from disease following treatment for primary disease
Key Exclusion Criteria:	<ul style="list-style-type: none"> • Significant skeletal, cardiac or endocrine disorders • Hormone replacement therapy within 4 weeks of randomization • Concomitant treatment with systemic corticosteroids for a prolonged period • Clinical evidence of severe osteoporosis and/or history of osteoporotic fracture
Study Subjects:	<ul style="list-style-type: none"> • 4,742 patients from 37 countries and 20 cooperative groups • Average time on tamoxifen prior to switch: 2.4 years • AROMASIN group = 2,380 patients; remaining on treatment: 8.4% • Tamoxifen group = 2,362 patients; remaining on treatment: 8.6% • Median follow-up 30.6 months
Study Schema:	 <pre> graph TD A[DIAGNOSIS OF EARLY BREAST CANCER AND TREATMENT FOR PRIMARY DISEASE] --> B[Tamoxifen therapy 2-3 years] B --> C[Randomization] C --> D[Exemestane therapy 2-3 years] C --> E[Tamoxifen therapy 2-3 years] </pre>

Trial Results:	Disease-free survival rates at 3 years post-randomization: AROMASIN: 91.5%, Tamoxifen: 86.8%, Absolute difference = 4.7% Hazard ratio (unadjusted) = 0.68, Log-rank test: P = 0.00005			
	Events Contributing to Disease-free Survival	AROMASIN	Tamoxifen	Total
	Local recurrence only	21	33	54
	Distant recurrence*	114	174	288
	Contralateral breast primary*	9	20	29
	Intercurrent deaths (without recurrence)	39	39	78
	Total	183	266	449
	*Includes patients who additionally reported local relapse			
Statistically Significant Adverse Events:	Continuation of tamoxifen was associated with a greater incidence of thromboembolic events (2.4% vs. 1.3%), gynecological symptoms (9.0% vs. 5.8%), vaginal bleeding (5.6% vs. 4.0%), and muscle cramps (4.4% vs. 2.8%) while AROMASIN was associated with a greater incidence of arthralgia (5.4% vs. 3.6%) and diarrhea (4.3% vs. 2.3%). Non-breast secondary primary cancers before distant relapse were also significantly higher in the tamoxifen group (53 vs. 27, P=.003).			
Principal Investigator:	R. Charles Coombes, MD Head of Department, Cancer Medicine – Imperial College School of Medicine Director, Cancer Unit – Hammersmith Hospital London, England			
AROMASIN Product Information:	<u>Indications</u> <ul style="list-style-type: none"> <i>EU (June 1999)</i>: Treatment of advanced breast cancer (ABC) in postmenopausal women whose disease has progressed following antiestrogen therapy. <i>US (Oct 1999)</i>: Treatment of ABC in postmenopausal women whose disease has progressed following tamoxifen therapy. <i>Japan (July 2002)</i>: Postmenopausal breast cancer (Precautions for indication: The effectiveness and the safety of this drug as the first-line hormone therapy and the postoperative adjuvant therapy have not been established). <u>Dosing</u> <ul style="list-style-type: none"> AROMASIN (25 mg) is taken once daily after a meal. <u>Side Effects</u> <p>AROMASIN is well tolerated and side effects associated with the treatment are generally predictable and manageable. Given its potent suppression of estrogen, AROMASIN use is associated with low-grade nausea (18%) and hot flashes (13%). In comparative studies with megestrol acetate, patients treated with megestrol acetate experienced a lower incidence of these effects. Patients treated with AROMASIN experienced a lower incidence of fatigue, diarrhea, constipation, undesirable weight gain and shortness of breath than those treated with megestrol acetate.</p>			

* Coombes RC. Exemestane improves disease-free survival in postmenopausal patients with early breast cancer after two to three years of tamoxifen: a double blind randomized trial. *N Engl J Med.* (issue): 2004.