

HT-1

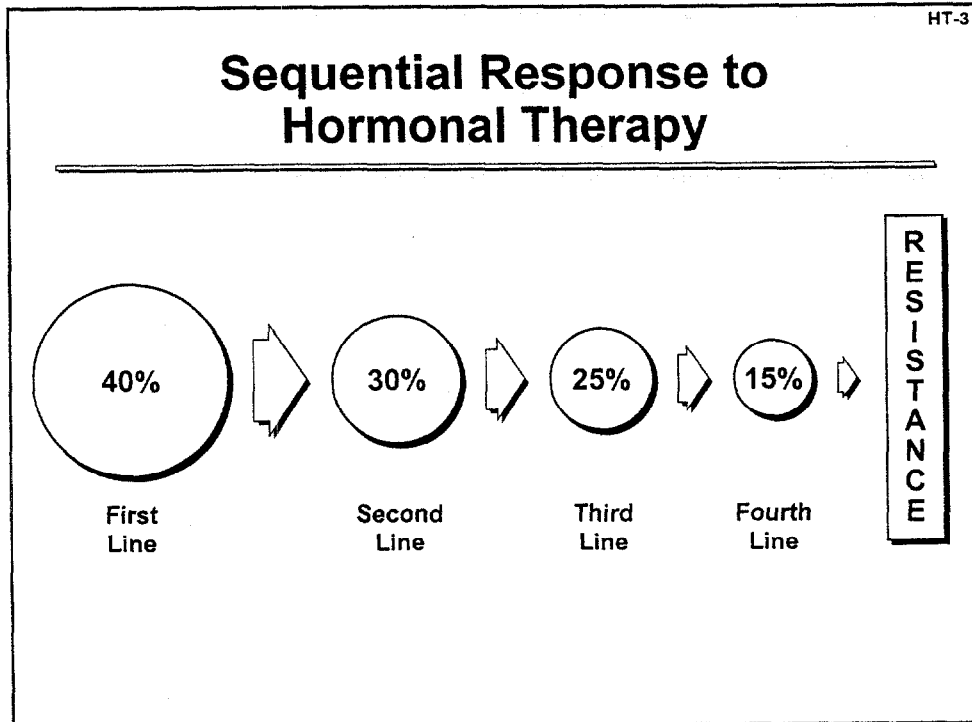
Hormonal Therapy of Breast Cancer

**Harold A. Harvey, MD
Professor of Medicine
Penn State College of Medicine
Hershey, Pennsylvania**

HT-2

Characteristics of Hormone Dependent Breast Cancer

- **Functional ER/PR**
- **Histologic differentiation**
- **Low S phase, diploid**
- **Long disease-free interval**
- **Metastasis to favorable sites**
- **Indolent clinical course**
- **More prevalent in older patients**
- **Sequential responses to endocrine therapies**



HT-4

Number of Breast Cancer Patients Eligible for Therapy

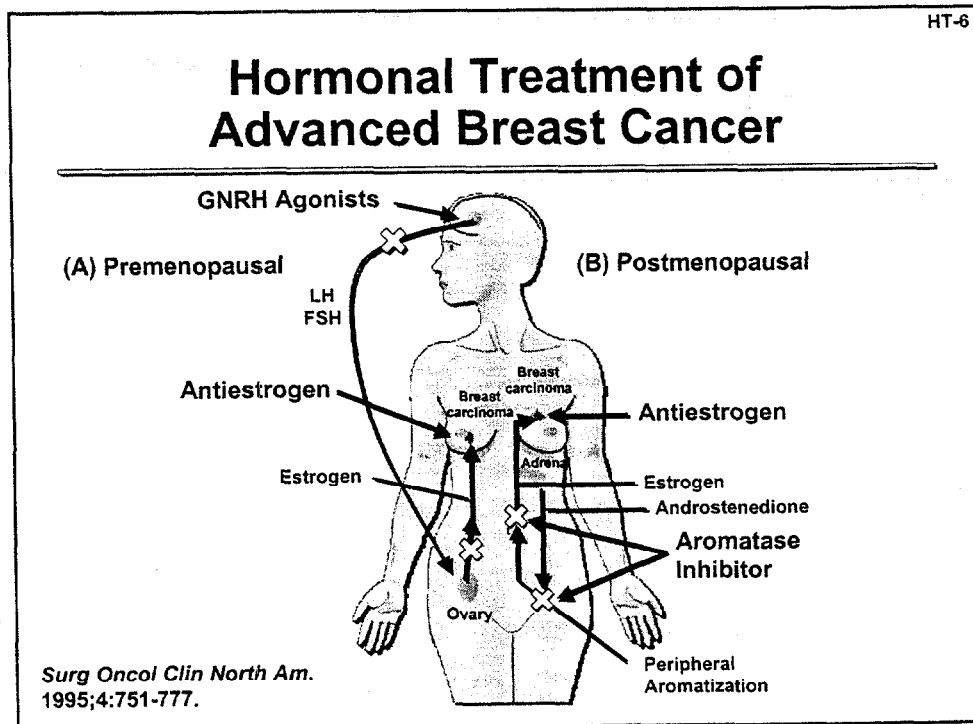
Advanced premenopausal/ER+	41,700
Advanced premenopausal/ER-	19,000
Advanced postmenopausal/ER+	200,800
Advanced postmenopausal/ER-	28,800
Early premenopausal/ER+	140,400
Early premenopausal/ER-	29,700
Early postmenopausal/ER+	509,600
Early postmenopausal/ER-	59,700
Total	1,029,700

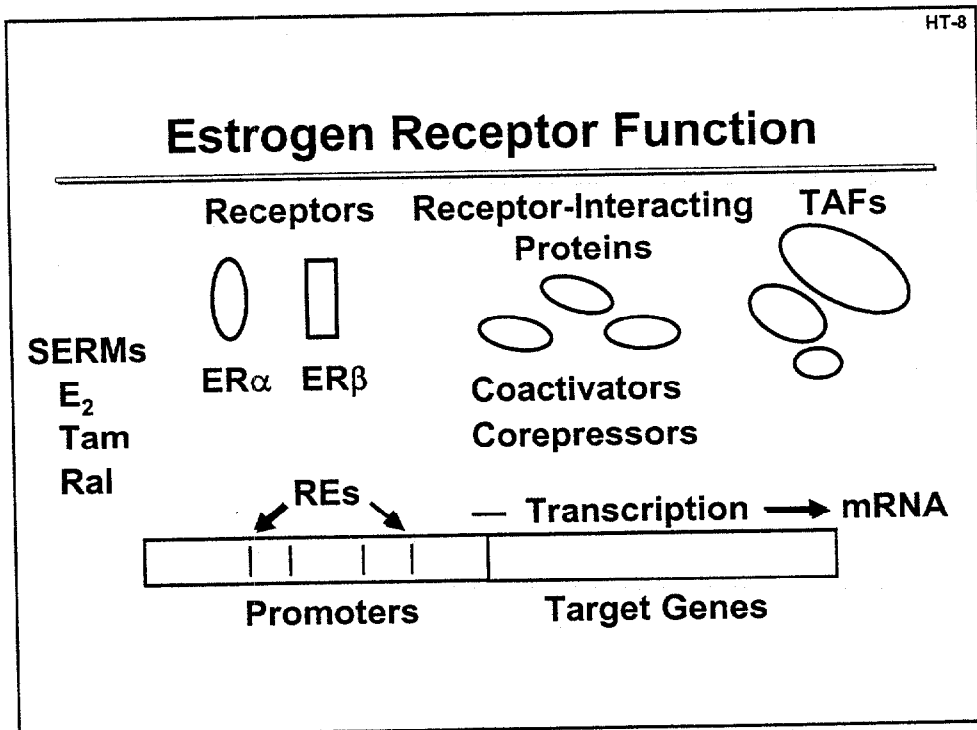
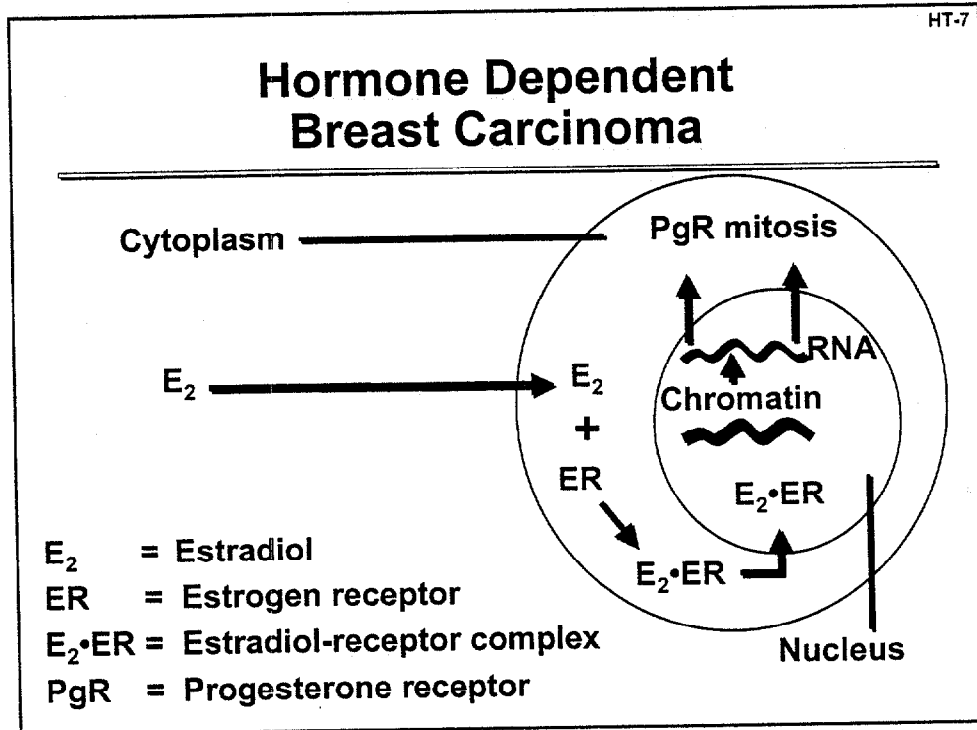
US and Europe Approximation.

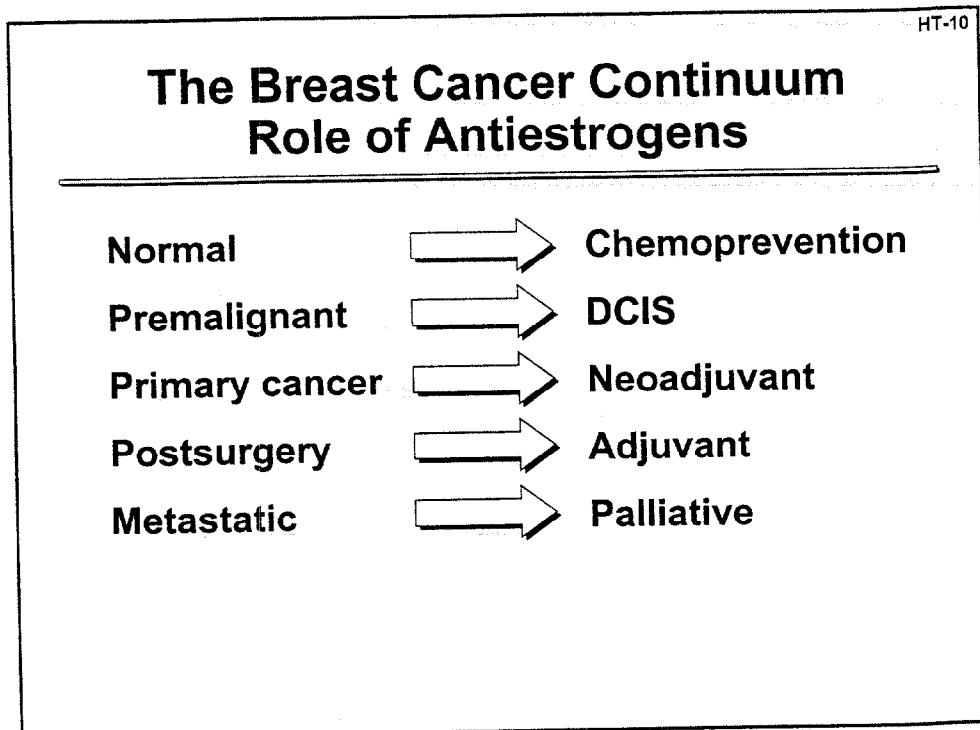
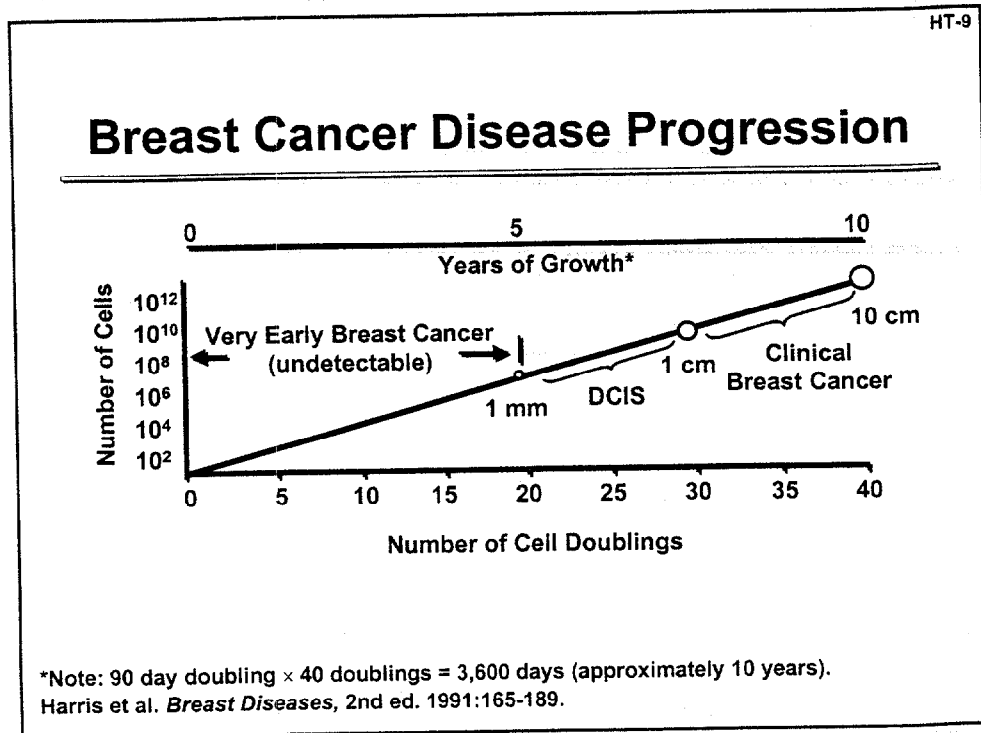
HT-5

Current Endocrine Therapies for Breast Cancer

- Ovarian ablation
 - Surgical (oophorectomy)
 - Radiation
- LHRH agonists
- Antiestrogens
- Aromatase inhibitors (nonselective and selective)
- Progestins
- Androgens
- Others: estrogens, pure antiestrogens, LHRH antagonists, glucocorticoids








HT-11

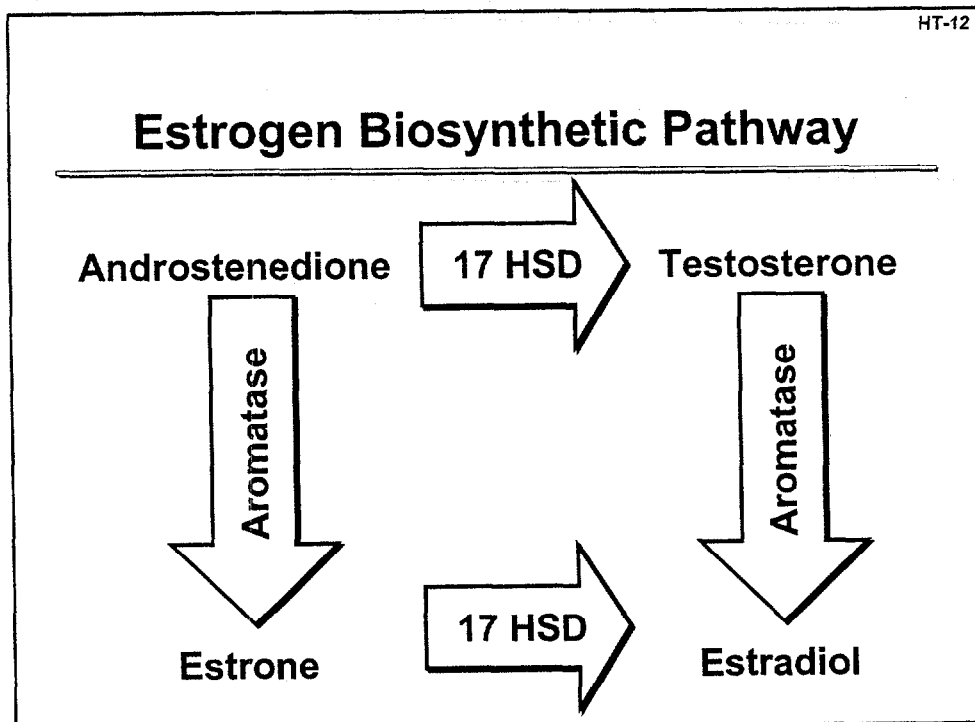
Alternatives After Anti-estrogen Therapy

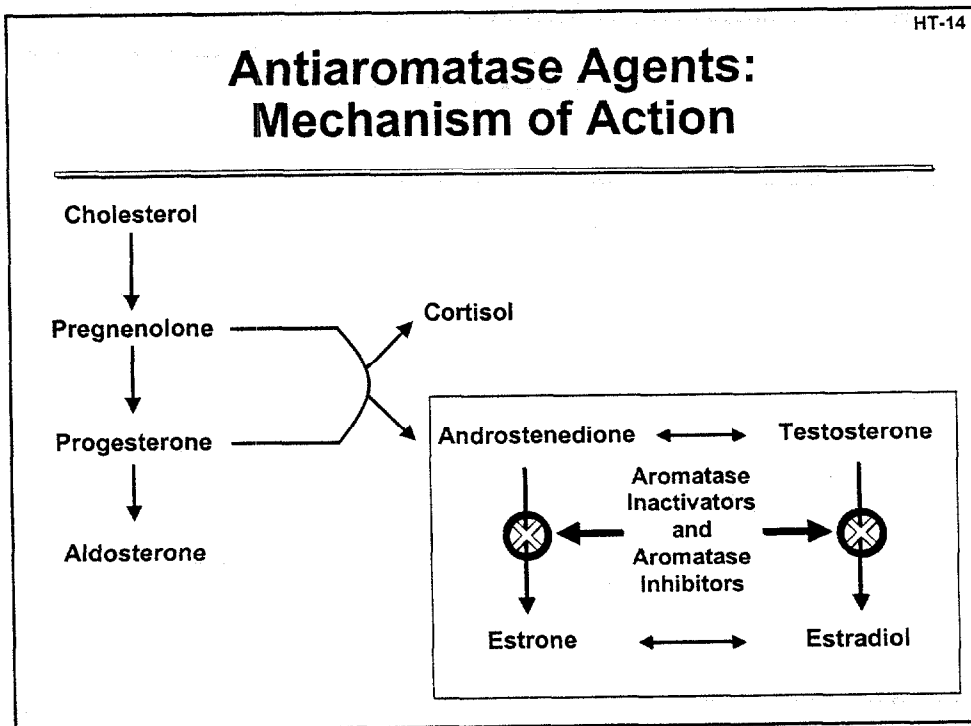
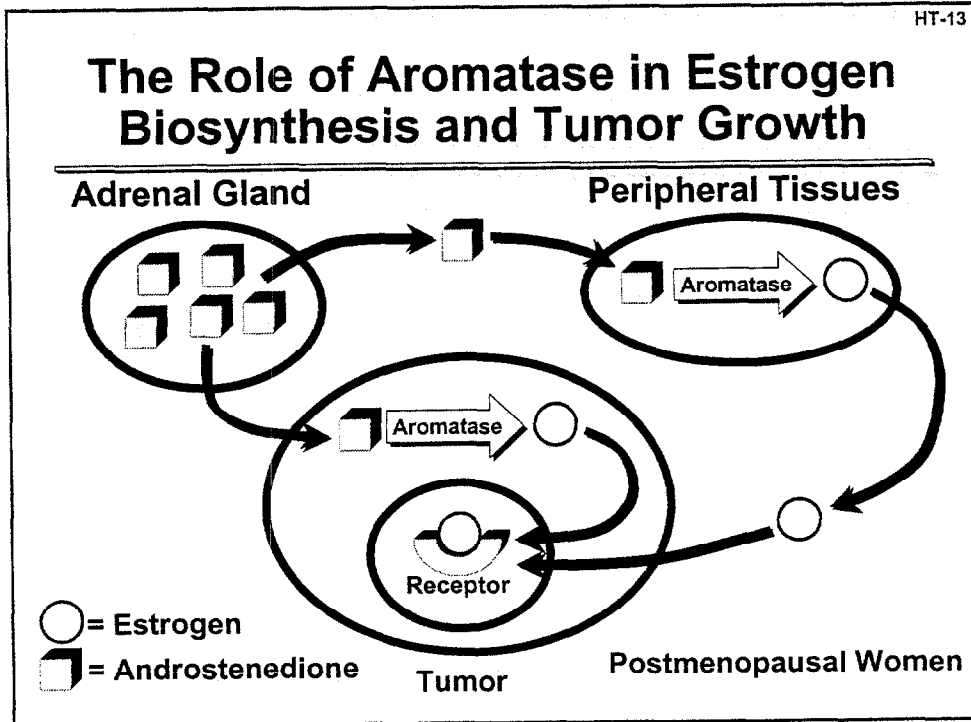
Blockade of estrogen receptor (anti-estrogen therapy)

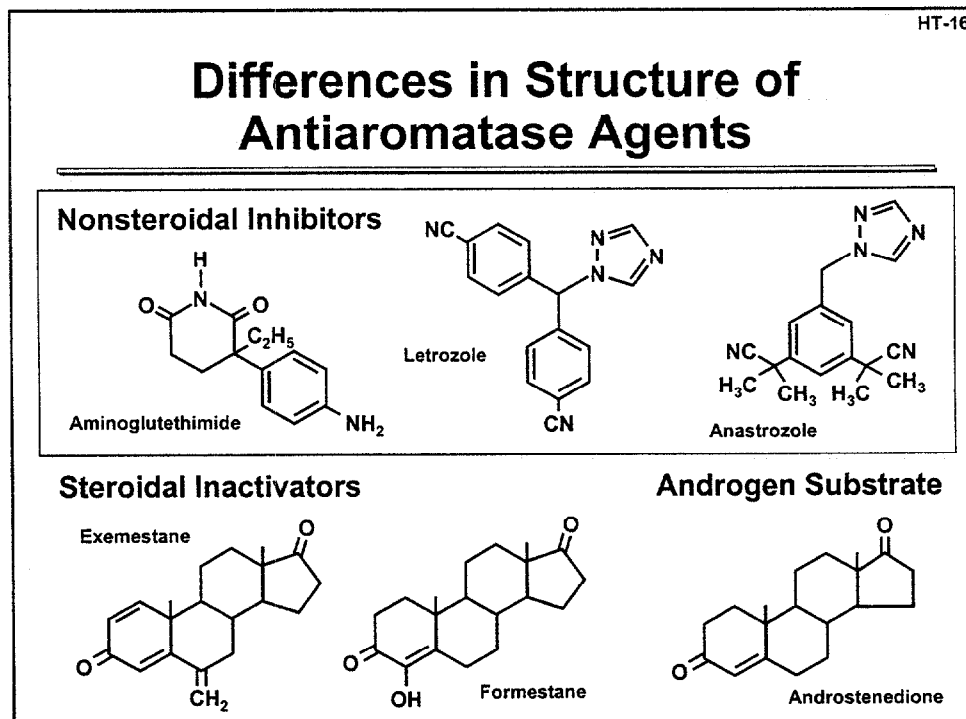
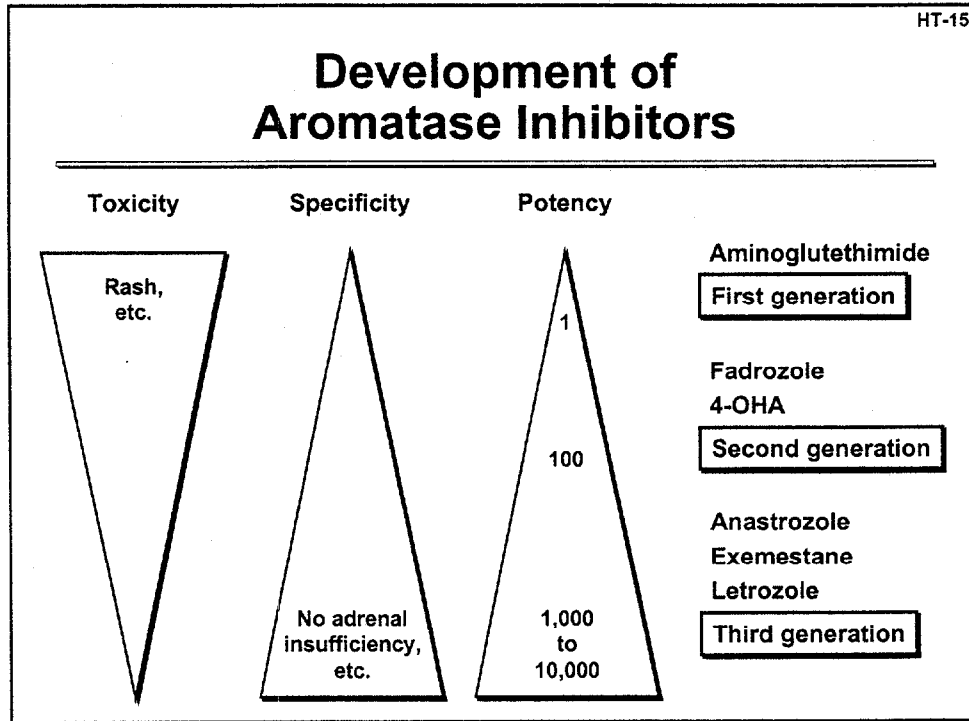


Inhibition of estrogen synthesis (aromatase inhibition)

? Same or better







HT-17

Quality of Life in Patients With Metastatic Breast Cancer

- Metastatic breast cancer cannot be cured
- Quality of life and duration of remission are the most important parameters of therapeutic success in women with advanced disease
- Aromatase inhibitors offer an option for postmenopausal women who no longer respond to antiestrogen therapy
- Aromatase inhibitors (eg, letrozole) are as effective as progestins (eg, megestrol acetate) as second-line therapy, but have better side-effect profiles, offering improved quality of life

HT-18

Antiaromatase Agents Versus Megestrol Acetate (MA)

	Anastrozole Arimidex® 1 mg versus MA	Letrozole Femara® 2.5 mg versus MA	Exemestane Aromasin® 25 mg versus MA
No. of patients	263 vs 253	174 vs 189	366 vs 403
CR + PR, %	AN = MA	LET > MA	EXE = MA
Duration clinical benefit	Not Reported	LET > MA	EXE > MA
TTP	AN = MA	LET = MA	EXE > MA
TTF	Not Reported	LET > MA	EXE > MA
Overall survival	AN > MA	LET = MA	EXE > MA
	(Pooled Data)		

* >, Difference statistically significant in favor of first agent.

=, Difference not statistically significant.

Kaufmann. *J Clin Oncol.* 2000; Buzdar et al. *Cancer.* 1998; Dombernowsky et al. *J Clin Oncol.* 1998.

HT-19

Aromatase Inhibitors: Rationale for First-Line Use

- Selective AIs, anastrozole and letrozole, represent a significant advantage over existing second-line endocrine therapies in postmenopausal women with advanced breast cancer
- Rapidly becoming established as the treatments of choice in this patient population
- These results provide a rationale for studying aromatase inhibitors as first-line endocrine therapy

HT-20

First-Line Trials of Anastrozole Versus Tamoxifen (027 and 030): Randomization

Randomized 1:1 (double blind, double dummy)

Anastrozole 1 mg/day
plus tamoxifen
placebo daily

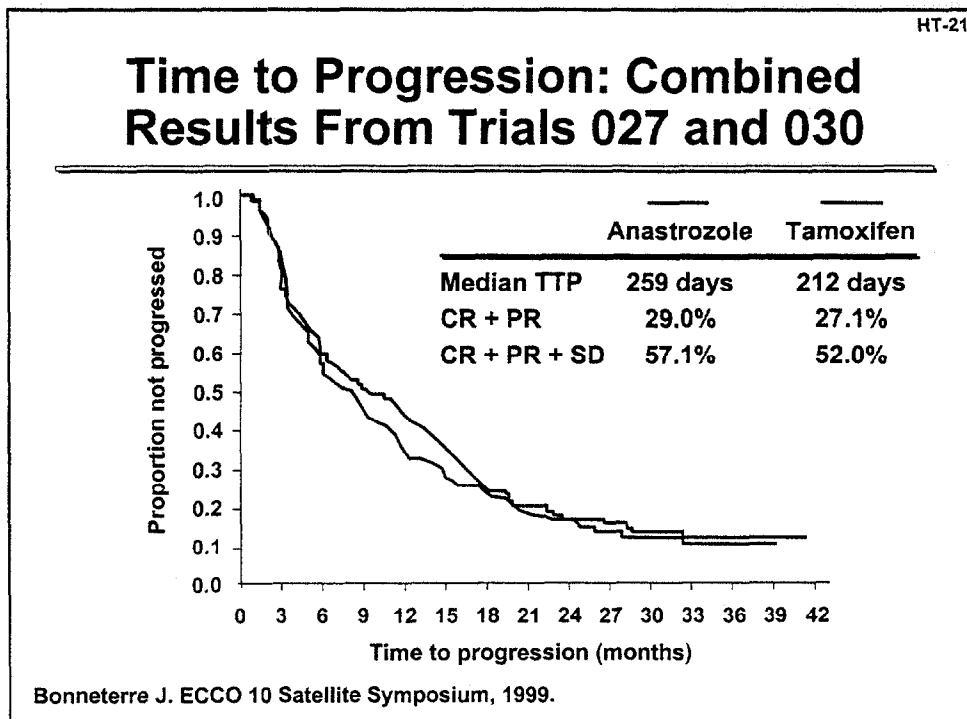
Tamoxifen 20 mg/day
plus anastrozole
placebo daily

↓
For study endpoints

↓
Objective progression

↓
Treatment may stop/standard treatment initiated

↓
Patients followed for death details



- HT-22
- ### Anastrozole as First-Line Therapy for Advanced Breast Cancer: Summary
- At least as effective as tamoxifen (time to progression and objective response)
 - Fewer thromboembolic events and less vaginal bleeding
 - First aromatase inhibitor to demonstrate at least equivalence to tamoxifen

