

Hormonal Therapy for the Prevention of or Treatment of Early Stage Breast Cancer

Kevin R. Fox, M.D.

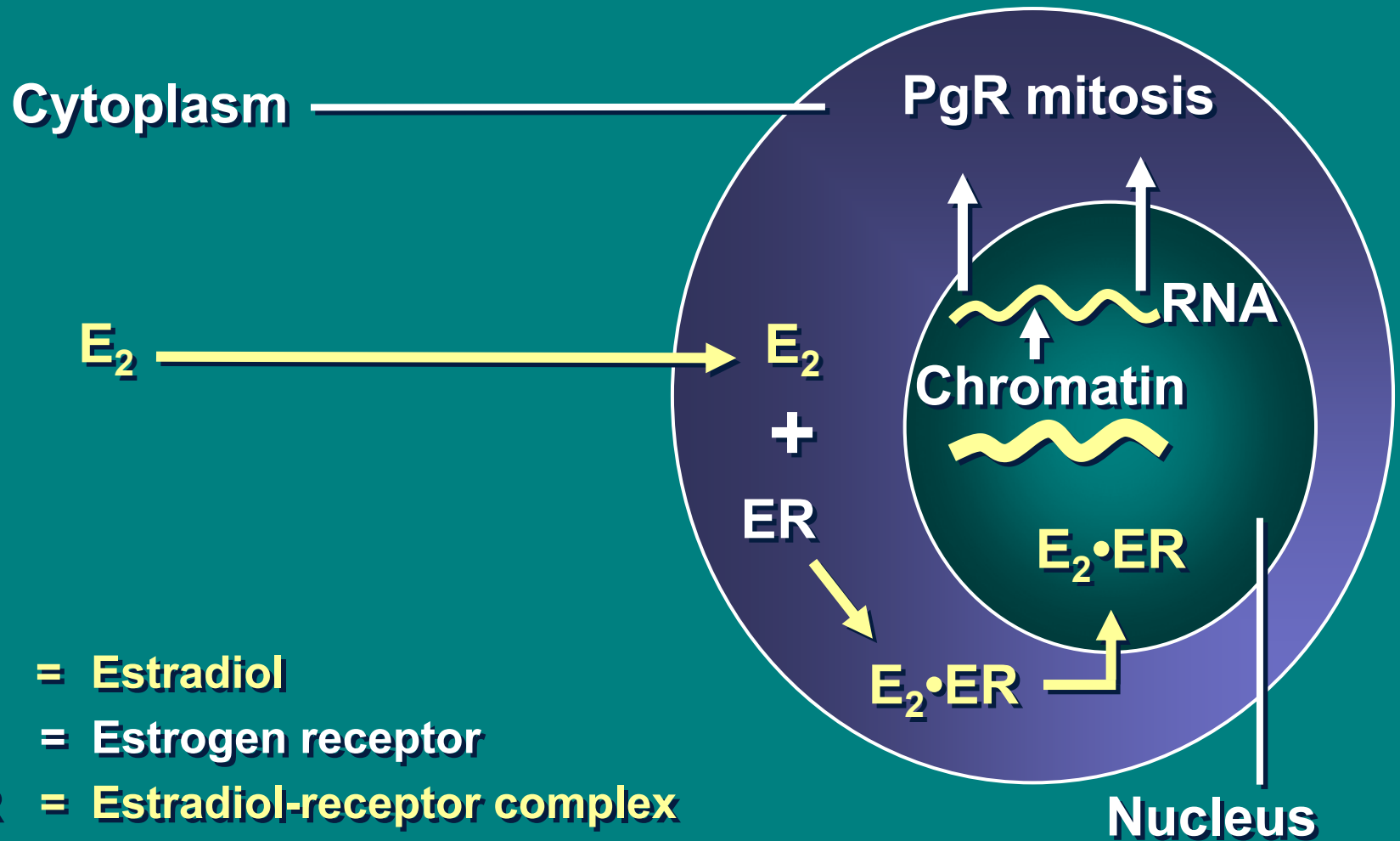
Hormonal Therapy

Antihormonal Therapy

Basic Principles

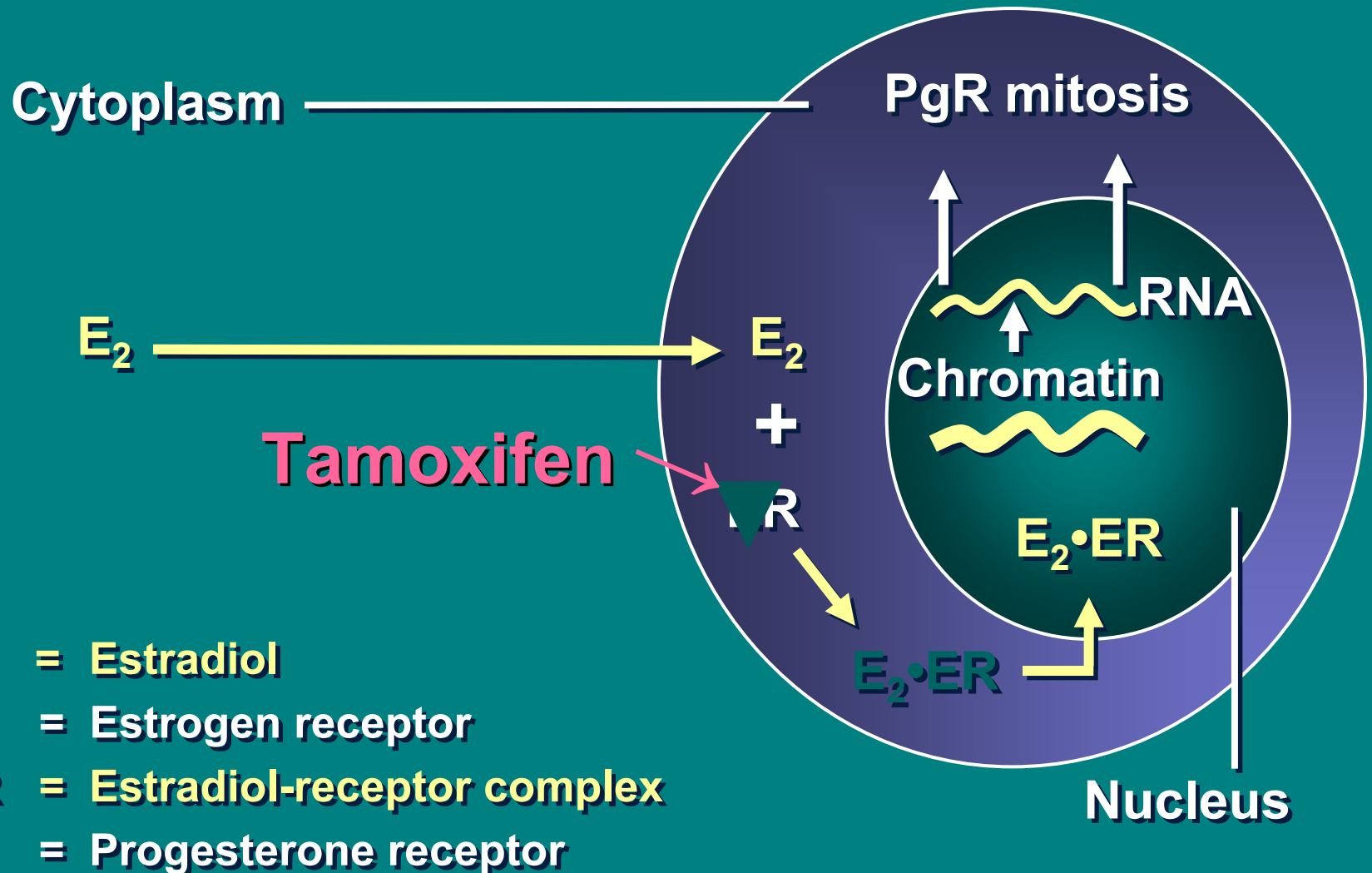
- Most breast cancers are dependent on estrogen for development and growth
- By opposing the function of estrogen, or by preventing estrogen from being made, breast cancer can be prevented
- In the same way, breast cancers that have already developed can be stopped, sometimes permanently

Hormone-Dependent Breast Carcinoma



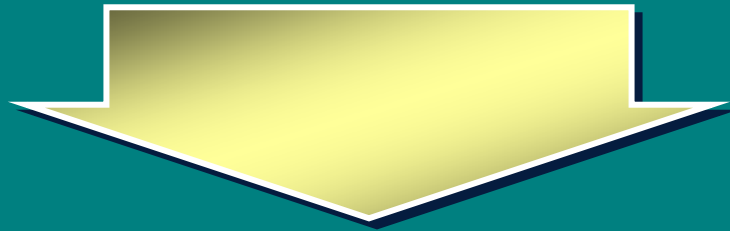
- E₂** = Estradiol
- ER** = Estrogen receptor
- E₂•ER** = Estradiol-receptor complex
- PgR** = Progesterone receptor

Hormone-Dependent Breast Carcinoma



Alternatives?

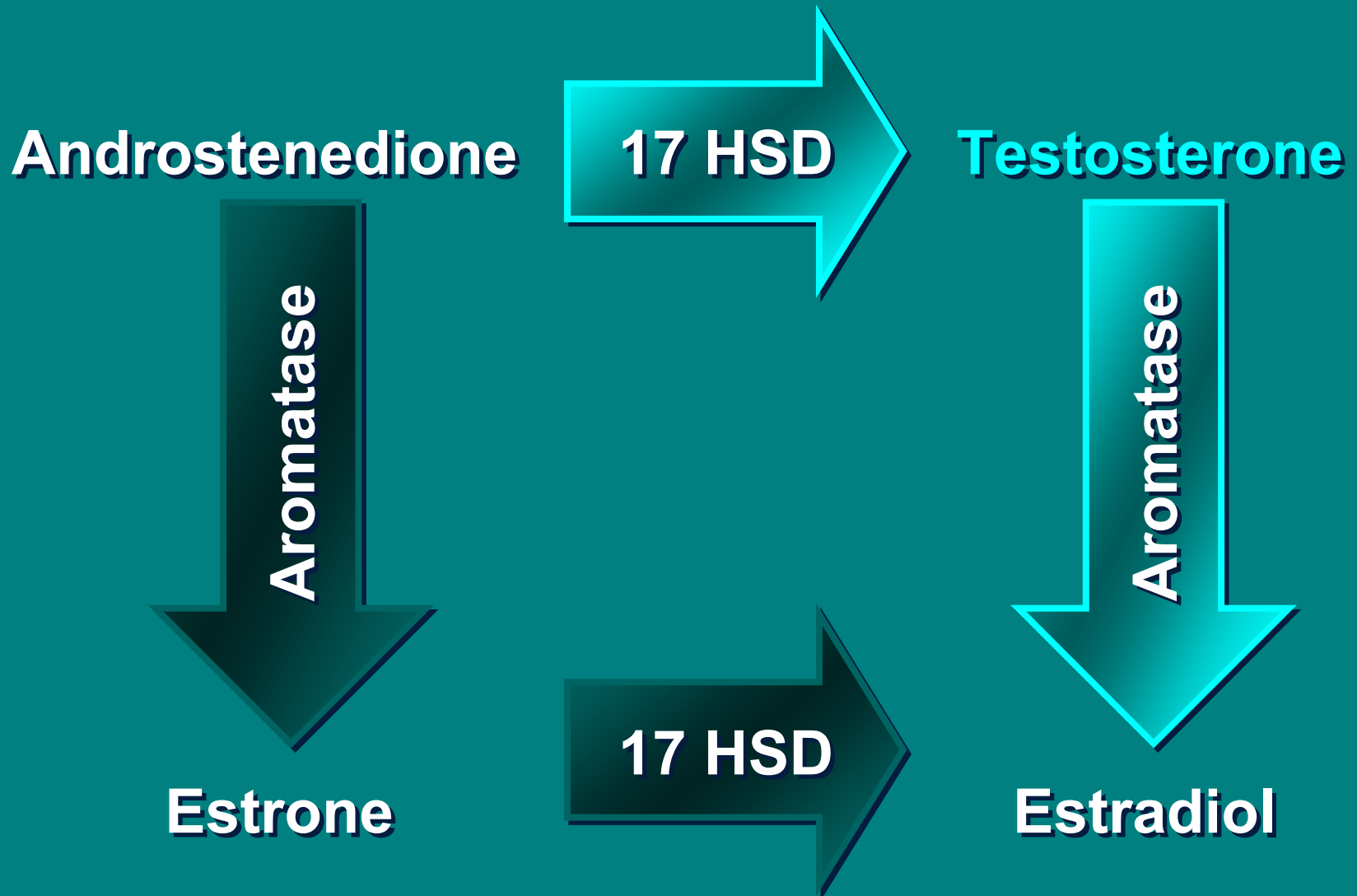
Blockade of estrogen receptor (antiestrogen therapy)



Inhibition of estrogen synthesis (aromatase inhibition)

Anastrozole
Letrozole
Exemestane

Estrogen Biosynthetic Pathway



Breast Cancer Prevention

- Remove the ovaries (premenopausal women)
- Tamoxifen (premenopausal and postmenopausal women)
- Raloxifene (only postmenopausal women)
- About 50% effective
- Remove the breasts (prophylactic mastectomy)
- About 90% effective

Breast Cancer Treatment: Goals of “Adjuvant Therapy” of Early Stage Breast Cancer

- Surgery to remove the cancer and lymph node(s)
- Medical treatment to prevent recurrence and cure the patient
 - Chemotherapy
 - Hormonal Therapy
 - Immunotherapy (herceptin)
 - Radiation therapy

Breast Cancer Treatment: Goals of “Adjuvant Therapy” of Early Stage Breast Cancer

- Surgery to remove the cancer and lymph node(s)
- Medical treatment to prevent recurrence and cure the patient
 - Chemotherapy
 - **Hormonal Therapy (if ER or PR positive)**
 - Immunotherapy (herceptin)
 - Radiation therapy

Where are we now?

Premenopausal women

- Tamoxifen is the standard of care
- Five years of treatment is recommended

Postmenopausal women

- Tamoxifen is effective, but aromatase inhibitors are the standard of care
- Five years of treatment is recommended
- They work a little better than tamoxifen
- These drugs don't work in premenopausal women
- They shouldn't be given at the same time as tamoxifen

Recent Adjuvant Endocrine Therapy Trials

Type of Trial	Trial Design	Trial Name
Initial Adjuvant	Tamoxifen	ATAC (N = 9366)
	AI	BIG 1-98 (N = 6193)
Initial and Sequencing	Tamoxifen AI	BIG 1-98 (N = 6193)
	Tamoxifen	
	AI Tamoxifen	
	AI	
Sequencing	Tamoxifen AI	ABCSG 8 (N = 3224)
	Tamoxifen	
Switching	2-3 Years of Prior Tamoxifen Tamoxifen	ARNO 95 (N = 979)
	2-3 Years of Prior Tamoxifen AI	ITA (N = 488) IES (N = 4742)
Extended Adjuvant	5 Years of Tamoxifen	MA.17 (N = 5157)
	5 Years of Tamoxifen Placebo	ABCSG-6A (N = 856) NSABP B-33 (N = 1598)

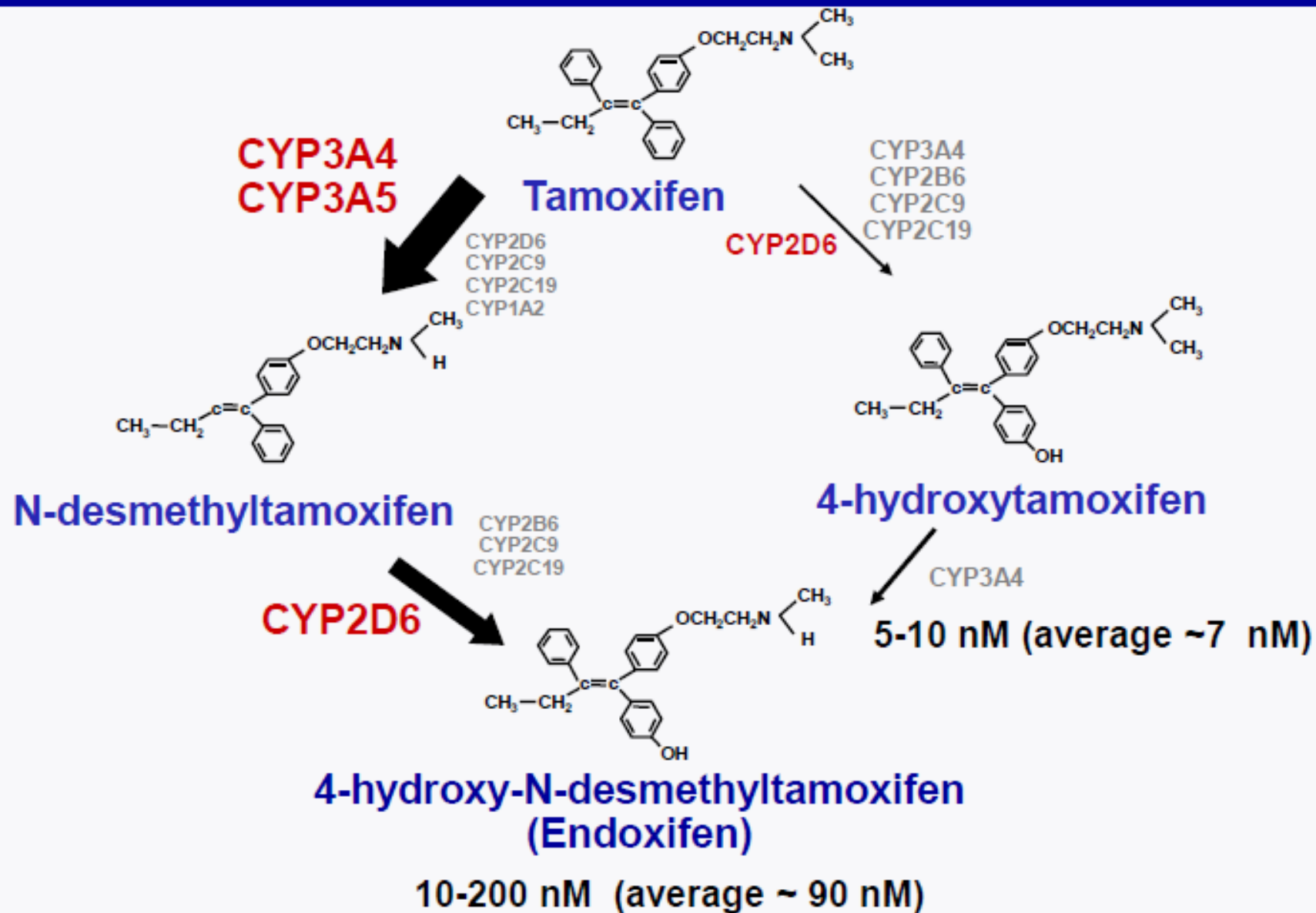
ABCSG = Austrian Breast and Colorectal Cancer Study Group; ARNO = Arimidex-Nolvadex; ATAC = Arimidex, Tamoxifen, Alone or in Combination; BIG = Breast International Group; IES = Intergroup Exemestane Study; ITA = Intergruppo Tamoxifen Anastrozole.

What now?

Premenopausal women?

- Should we give tamoxifen and stop the ovaries from working at the same time?
- Should we give aromatase inhibitors instead of tamoxifen?
- Are there dangerous interactions between tamoxifen and other drugs?

Tamoxifen Biotransformation



**Do we have enough evidence
that we should not co-
prescribe potent CYP2D6
inhibitors and tamoxifen?**

**Do we have enough evidence
that we should not co-
prescribe potent CYP2D6
inhibitors and tamoxifen?**

Not at all

Consider

- The reason for CYP2D6 inhibitor use
- The alternatives
 - Endocrine therapy alternatives
 - Alternatives for hot flash management
 - Call your psychiatrist

Postmenopausal women?

- Which aromatase inhibitor is best?
- How long should the drug be taken? Is five years enough? How about more?

Thanks