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SERMs

Selective Estrogen Receptor Modulator

→ A group of drug which are synthetic, non steroidal with tissue selective estrogenic & Antiestrogenic Action (Agonist or Antagonist at Estrogen Receptor)

→ Drugs - Tamoxifen, Raloxifene, Toremifene

TAMOXIFEN:

- MOA:
  - competitive Inhibitor of estradiol binding to estrogen Receptor. This will induce conformational change in Receptor, HSP dissociate, Inhibit ER dimerization.

⇒ Potent ER Antagonist at - Breast, blood vessel.

⇒ Potent ER Agonist - uterus, bone.

Pharmacological Action

1) Antiestrogenic effect
   - Inhibit breast cancer cell
   - Hot flushes.

2) estrogenic effect.

→ ↑ bone mineral density

- Reduce LDL, total
- venous.

PK - oral, long duration of Action.
Biphasic thalf: 10hours, 7 days.

Uses:
→ Pre of postmenopausal breast cancer
→ Prophylaxis of breast cancer in high Risk-factor female
→ Postmenopausal osteoporosis.
→ Hch. infertility (Alternative to clomiphene)
→ ↓CAD.

ADR:
- Hot flashes, vaginal bleed, menstrual irregularities, venous thromboembolism, depression

RALOXIFENE
- Developed for Rx of prophylaxis of postmenopausal osteoporosis, later for breast cancer.

Estrogenic → bone, CVS.
Antiestrogenic → breast, endometrium
- Has distinct DNA

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Uses:

→ Oskoporosis
→ Rx of prevention of vertebral fracture forcibly.
→ Prevention of breast cancer
→ .

SERD

- Selective estrogen Receptor Down Regulator
  - Fulvestrant
- Pure estrogen Antagonist.

AROMATASE INHIBITORS:

- Anastrozole, Letrozole, Exemestane

MOA

→ Aromatisation of "A Ring of testosterone & Androstenedione by Aromatase enzyme is the first key step of estrogen synthesis in body. This is imp in breast cancer

- Aromatase Inhibitor Reversibly Aromatisation allows body, Resulting in total estrogen depletion

- Proliferation of estrogen dependent breast cancer cell suppressed

→ It delay Recurrence of early Breast cancer
→ No Risk of endometrial hyperplasia, thromboembolism

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Comparison

Tamoxifen	Letrozole
→ selective Action is tissue	• Near total estrogen depriva
✓→ Used in premenopausal breast Ca	• Not used
→ Less effective in ER Ca Recurrence during pregnancy	• More effective • Absent
→ Endometrial Ca, VTE Risk	• ~~Accelerates~~
→ No bone loss.	• ~~No effect~~. Accelerates
→ Improve lipid profile	• No effect.

Female Infertility drug:

- Clomiphene citrate, Gonadotropin. (GnRH Analogue (Antagonist & Agonist).

MIFEPROSTONE: — Antiprogestin

→ Progestrone Receptor Modulator

→ A 19 nor steroidal with potent Antiprogestin, Antiglucocorticoid, Anti Androgenic Actions.

MOA:

→ Partial Agonist And competitive Antagonist at progestrone Receptor.

→ In follicular phase, it slow down follicle development

→ Cause decidual breakdown, detachment of the blastocyst and cervical softening

→ In luteal phase, if pregnancy occurs

→ By Increasing prostaglandin Release, it stimulate uterine contraction induce menstruation, thus Induce Abortion.

PK → Oral, Liver metabolism, biliary excretion.

Uses

1 → MTP upto 7 week with misoprostol. induction of labour.
2 → Cervical Ripening - 24-30 hrs before surgical Abortion.
3 → Post-coital contraceptive. - 600mg single dose.
4 → one a month contraceptive.
5 → Induction of labour
6 → Cushing syndrome - Due to Antiglucocorticoid Activity
7 → Endometriosis, fibroid.
8 → Meningioma
9 → Breast cancer.

ADR → GI, bleeding, Uterine cramps, failed Abortion

Name one pure Progesterone Antagonist

⇒ Onapristone