ANTI - NEOPLATIC DRUGS III

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Objectives

- 1- Hormones
- 2- Tyrosine-kinase inhibitors
- 3- Monoclonal antibodies
- 4- Others

5-Hormones

- Several types of hormone-dependent cancer (especially breast, prostate, and endometrial cancer) respond to treatment with their corresponding hormone antagonists.
- Estrogen antagonists are primarily used in the treatment of breast cancer, whereas androgen antagonists are used in the treatment of prostate cancer.

Antiestrogen: Tamoxifen

- Tamoxifen (Nolvadex) is a selective estrogen receptor modulator (SERM)
- used to treat all stages of hormone receptor-positive breast cancer in females and males.
- Indications:
- first choice for pre-menopausal women and is still a good choice for post-menopausal women who can't take an aromatase inhibitor.

- **Advantages of tamoxifen:**
- While tamoxifen blocks (antagonist) estrogen's action on breast cells, it also activates (agonist) estrogen's action in bone and liver cells.
- So, tamoxifen can: stop osteoprosis after menopause & lower cholesterol levels.
- **Dose**: one tablet daily for 5 years after surgery

- **Tamoxifen adverse effects:**
- Thrombosis: deep venous thrombosis
- Endometrial cancer

Aromatase inhibitors

- **MOA:**
- Aromatase inhibitors (AIs) lower estrogen levels by inhibition an enzyme in fat tissue (called aromatase) from changing other hormones (STEROIDS) into estrogen.
- **Indication:**
- Aromatase inhibitors are a class of drugs used in the treatment of breast cancer in postmenopausal females and in males.

- **Members:**
- Letrozole
- Anastrozole
- **Dose**: one tablet daily for 5 years after surgery

Antiandrogens

- Antiandrogen medications can be used as hormone therapy to treat prostate cancer
- Flutamide: potent ANDROGEN antagonist
- Cyproterone acetate (CPA): weak antiandrogenic activity
- Indications of CPA: 1- Moderate to severe acne related to androgen-sensitivity (with or without seborrhea)
- 2- Hirsutism, in females of reproductive age

6-Tyrosine-kinase inhibitors

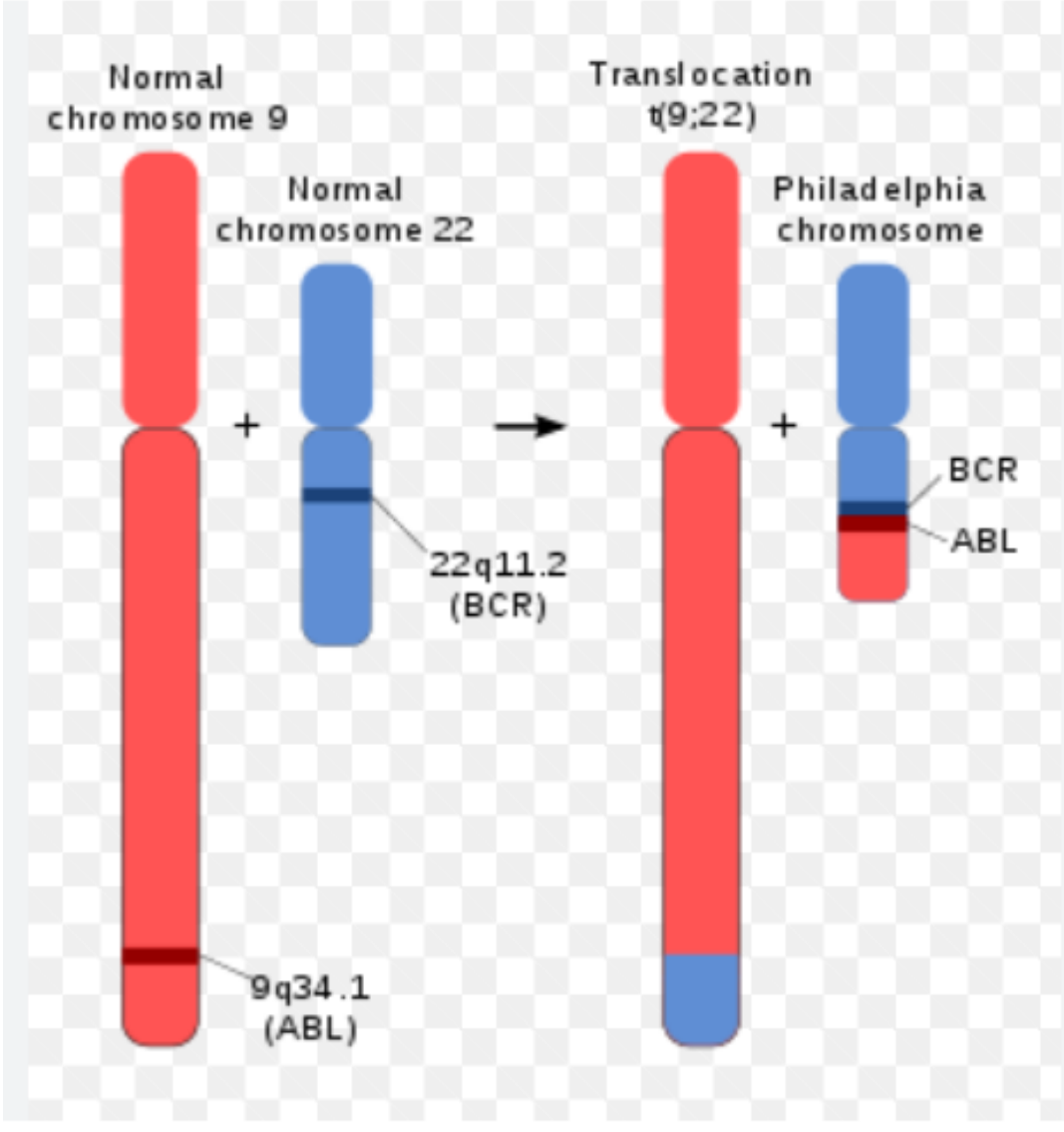
- A substance that blocks the action of enzymes called tyrosine kinases.
- Tyrosine kinases are a part of many cell functions, including cell signaling, growth, and division.
- These enzymes may be too active or found at high levels in some types of cancer cells, and blocking them may help keep cancer cells from growing.

Imatinib

- **inhibits the bcr-abl tyrosine kinase**, the constitutive abnormal tyrosine kinase created by the Philadelphia chromosome abnormality in chronic myeloid leukemia (CML).

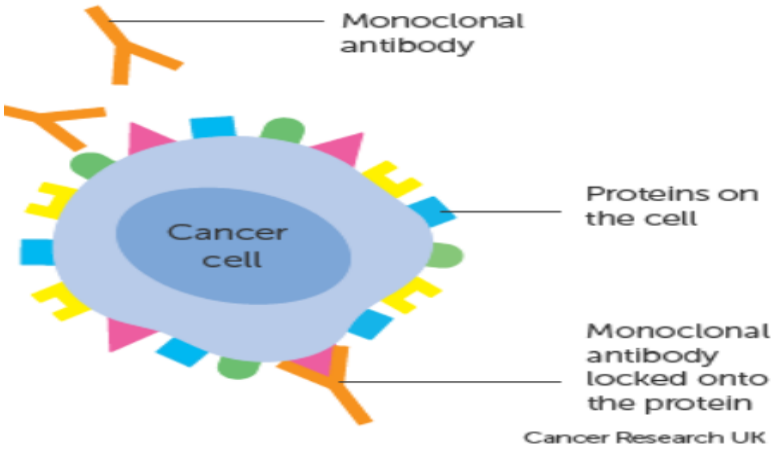
Philadelphia chromosome

- An abnormality of chromosome 22 in which part of chromosome 9 is transferred to it. Bone marrow cells that contain the Philadelphia chromosome are often found in chronic myelogenous leukemia and sometimes found in acute lymphocytic leukemia.


Normal
chromosome 9
Normal
chromosome 22
+
22q11.2
(BCR)
9q34.1
(ABL)
Translocation
t(9;22)
Philadelphia
chromosome
+
BCR
ABL

7- Monoclonal antibodies

- Lab-made antibodies that are clones or exact copies of a specific antibody.
- These antibodies find and kill specific cancer cells.



- **Trastuzumab** (Herceptin) blocks HER2 protein.
- HER2 helps breast cells grow.
- **Rituximab**: CD4 protein on B-cell non-Hodgkin's lymphoma and acute leukemia.

- **Dostarlimab** blocks protein (programmed cell death receptor-1, or PD-1)
- Produced 100% cure rate in colorectal cancer cases

8- Others

- **Bortezomib** is used to treat multiple myeloma (a type of cancer of the bone marrow) & mantle cell lymphoma (a fast-growing cancer)
- **MOA: inhibition of proteasome functions in cancer cells**

References

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Thanks!