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 females
•A good choice for post-menopausal females when aromatase inhibitors are contraindicated.

- **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 osteoporosis after menopause & lower cholesterol levels.
- **Dose**: one tablet daily for 5 years after surgery

- **Tamoxifen adverse effects:**
- Serious:
- Thrombosis: deep venous thrombosis (DVT)
- Endometrial cancer
- **Common but not serious**: hot flashes, joint and muscle pain

Aromatase inhibitors

- **Mechanism of action:**
- Aromatase inhibitors (AIs) lower estrogen levels by inhibition an enzyme in fat tissue (called aromatase) from changing other hormones (STEROIDS) into estrogen.
- **Indication:**
- Breast cancer in postmenopausal females and in males.

- **Members of aromatase inhibitors:**
- Letrozole
- Anastrozole
- **Dose**: one tablet daily for 5 years after surgery
- **Adverse effects:**
- Joint pain, fatigue, hot flashes
- **Contraindications**: allergy to AIs (anaphylaxis), pregnancy

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.

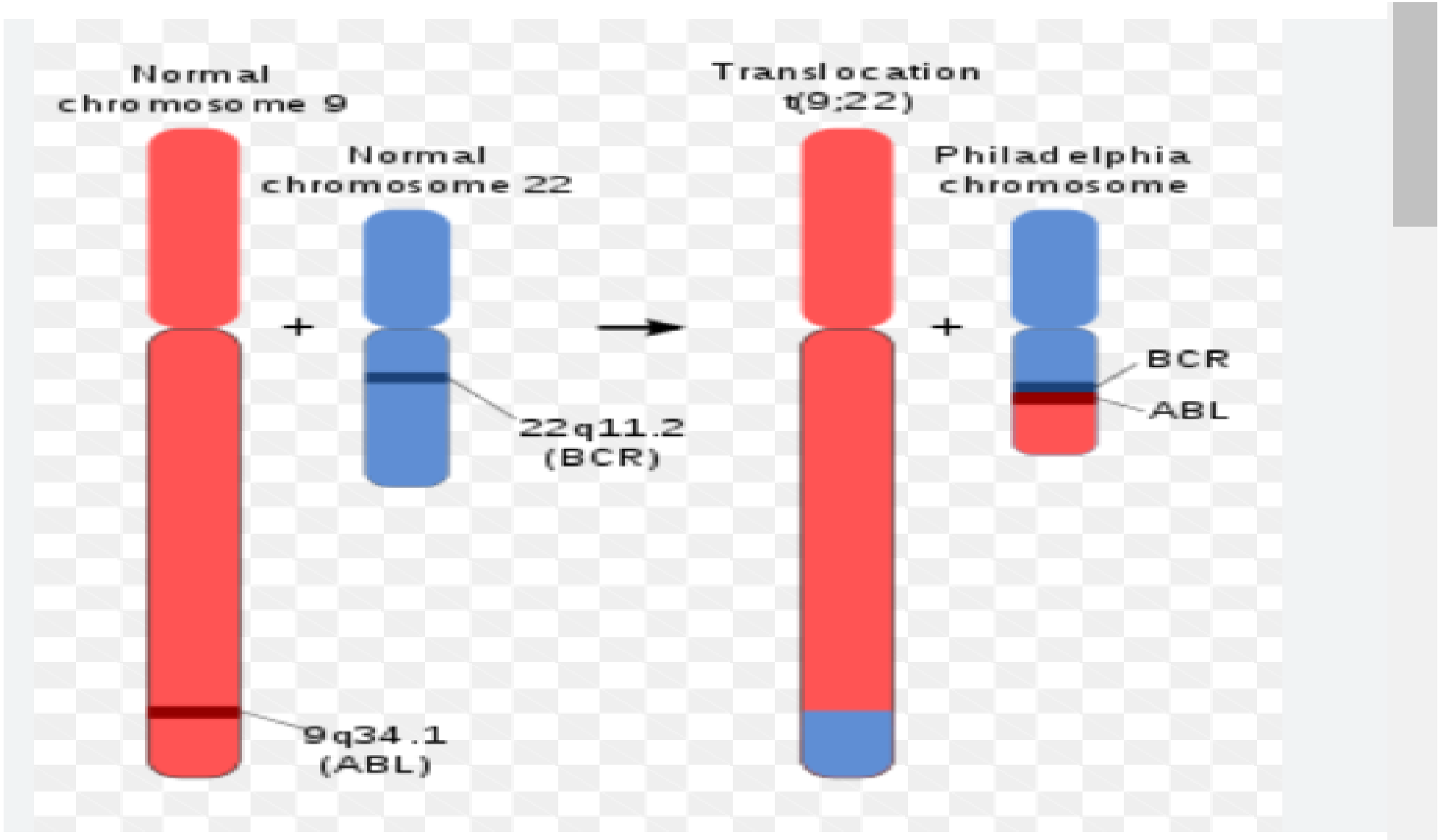
Imatinib

- **Mechanism of action:**

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

•**Adverse effects**:

•Fluid retention

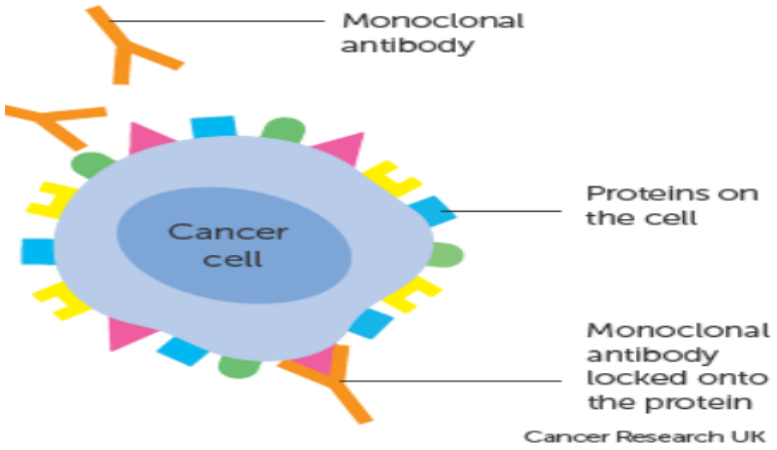

Normal
chromosome 9
Normal
chromosome 22
22q11.2
(BCR)
9q34.1
(ABL)
Translocation
t(9;22)
Philadelphia
chromosome
BCR
ABL

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.

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: proteasome inhibitors

- **Bortezomib, carfilzomib**
- **Indications:**
- multiple myeloma (a type of cancer of the bone marrow) & mantle cell lymphoma (a fast-growing cancer)
- **Mechanism of action:**
- Inhibition of proteasome functions in cancer cells: accumulation of unfolded and misfolded proteins inside cells: apoptosis

References

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Thanks