Therapy of cancer disease

This study material is recommended specifically for practical courses from Pharmacology II for students of general medicine and stomatology. These brief notes could be used to prepare for the lesson and as a base for own notes during courses. Addititonal explanations and information are given in single lessons.

Cytostatics

Definition

chemiotherapeutics =

chemoprotectives –

Cytostatics

Cancer disease

Classification:

1. *Benign*

2. *Malign*

Cytostatics

Cabcerogenesis

- process of change of somatic cell to cancer cell

- 3 phases: initiation
  promotion
  progression

Cytostatics

Exogenous factors involved in cancerogenesis

1.

-
-
-
-

Cytostatics

Endogenous factors involved in cancerogenesis

2.

Cytostatics

Modes of action

Target sites:

-
-
-
-

Adverse effects

1. Early

-
-
-
-

Nežádoucí účinky cytostatik

2. Delayed

-
-
-
-
-
-
-

Adverse effects

Adverse effects

Adverse effects

Adverse effects

Adverse effects

Analgesics

- basic analgesics are NSAIDs
- in strong pain opioids
- bone pain – kalcitonin, bisphosphonates
- combination with corticoids and psychoactive agents (antidepressants, neuroleptics, anxiolytics)

Adverse effects

Bisphosphonates

-

ibandronate

clodronate

pamidronate

zoledronate

Cytostatics

Particularity of cancer pharmacotherapy

- DDF
- „nonspecificity“ of target site
- combination with othrt types of therapy
- dosing, administration routes and combinations

Cytostatics

Classification

with regard to cell cycle

- cycle specific/nonspecific
- phase specific/nonspecific

Cytostatics

Classification

- monoclonal antibodies and other drugs of „biological“ (targeted) therapy
- alkylating
- platin cytostatics
- cytotoxic antibiotics
- antimetabolites
- herbal alkaloids
- hormones
- others

Alkylating cytostatics

Mode of action

- **alkylation** of cellular structures, namely DNA → loss of function and cellular death

Alkylating cytostatics

- **β-chloretylamines (N-yperite derivatives):** chlorambucil, melphalan

- **oxazaphosphorines:** cyclophosphamide, ifosfamide

- **methanesulphonic acid derivatives:** busulphan

Alkylating cytostatics

nitrosourea derivatives: lomustine, carmustine, fotemustine, streptozocine

triazenes: procarbazine, dacarbazine

platin compounds: cisplatin, carboplatin, oxaliplatin

mitomycin

Intercalating agents

MofA

- bounds between DNA strands with **non-covalent** binding (Van der Waals forces, hydrogen bonds)

doxorubicine

daunorubicine

mitoxantrone

Antimetabolites

Folic acid antagonists

MofA: dihydrofolate reductase inhibition

methotrexate

Antimetabolites

Purine antagonists

6-merkaptopurine

6-thioguanine

azathioprine

cladribine

fludarabine

Antimetabolites

Pyrimidine antagonists

cytarabine

5-fluorouracil

gemcitabine

Herbal alkaloids

irinotecan, topotecan

MofA: topoisomerase I inhibition

Herbal alkaloids

etoposid, teniposid

MofA: topoisomerase II inhibition

Herbal alkaloids

Vinca alkaloids

MofA: destruction of mitotic spindle

vincristine

vinblastine

vindesine

vinorelbine

Herbal alkaloids

Taxans

MofA: inhibition of tubulin depolymerization = block of mitotic spindle

paclitaxel

docetaxel

Hormones and theit antagonists

Androgens
Antiandrogens
Oestrogens
Antioestrogens
Gestagens

Gonadoliberin inhibitors
Aromatase inhibitors
Glucocorticoids
Octreotide
Estramustine, prednimustine

Others

bleomycine, (peplomycine)

MofA: ROS production→ DNA fragmentation

AE: pyretic reactions, pulmonary fibrosis

- low myelosuppression

hydroxycarbamid

arsenic trioxide

celekoxib

anagrelide

asparaginase