Cancer Pharmacology I, II, and III Questions

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Question 1

Which one of the following drugs is NOT excreted/eliminated by the kidneys?

a) Capecitabine
b) Pralatrexate
c) Pemetrexed
d) Cyclophosphamide
e) Gemcitabine

Answer for Question 1

(E) Gemcitabine

Capecitabine, pralatrexate, pemetrexed, and topotecan are excreted/eliminated by the kidneys. Gemcitabine is metabolized primarily via enzymatic pathways, cytidine deaminase and dCMP deaminase.

Question 2A

A 42 yo white male is diagnosed with stage III colon cancer. He is diabetic and has impaired renal function with a creatinine clearance of 40 mL/min. You plan to treat him with XELOX. How will you dose capecitabine?

a) No dose reduction
b) Reduce the dose by 25%
c) Reduce the dose by 33%
d) Reduce the dose by 50%
e) Should not be given

Answer for Question 2A

(B) Capecitabine and capecitabine metabolites are cleared by the kidneys, and capecitabine should be dose-modified according to creatinine clearance.

No dose reduction is required when CrCl > 50 mL/min

Dose reduction of 25% when CrCl 30-50 mL/min

Contraindicated when CrCr < 30 mL/min

Question 2B

How will you dose oxaliplatin in this patient?

a) No dose reduction
b) Reduce the dose by 25%
c) Reduce the dose by 33%
d) Reduce the dose by 50%
e) Should not be given

Answer for Question 2B

(A) No dose reduction is required. While oxaliplatin is eliminated/cleared by the kidneys, renal dysfunction studies have shown that oxaliplatin is well-tolerated with no increased toxicity with CrCl > 20 mL/min.

No formal studies have been done in patients with CrCr < 20 mL/min.

Question 3

Which one of the following drugs acts by inhibiting microtubule function?

a) **Methotrexate**
b) **Estramustine**
c) **6-Mercaptopurine**
d) **Topotecan**
e) **Irinotecan**

Answer for Question 3

(B) Estramustine

Estramustine is an inhibitor of microtubule function, which is critical for maintaining the spindle apparatus involved in mitosis.

Question 4

The multidrug resistance phenotype is an important mechanism of drug resistance. Which one of the following best describes the mechanism by which this resistance process is mediated?

a) Decreased drug influx
b) Decreased drug efflux
c) Enhanced drug efflux with decreased cellular drug accumulation
d) Enhanced drug influx
e) Enhanced intracellular drug accumulation

Answer for Question 4

(C) Enhanced drug efflux with decreased cellular drug accumulation

The multidrug resistant phenotype is mediated by the P170 glycoprotein, which mediates its effect through enhanced efflux of drug, resulting in decreased intracellular drug accumulation. This resistance mechanism is observed for anthracyclines, taxanes, the camtothecins, and the vinca alkaloids.

Question 5

- A 43 yo white female with advanced breast cancer is started on a combination regimen including 5-fluorouracil, methotrexate, and cyclophosphamide. Within 1 week of receiving her chemotherapy, she experiences severe diarrhea, mouth sores, and myelosuppression.
- Which one of the following enzymes is most likely the cause of her increased toxicity?

a) Thymidylate synthase
b) Thiopurine methyltransferase
c) Dihydropyrimidine dehydrogenase
d) Topoisomerase I
e) Dihydrofolate reductase

Answer for Question 5

(C) Dihydropyrimidine dehydrogenase

This woman most likely has either a partial or complete absence of dihydropyrimidine dehydrogenase (DPD). This enzyme is responsible for catabolizing 5-FU to inactive products, and a pharmacogenetic syndrome has been identified in 3-5% of all cancer patients in which this enzyme is deficient. These patients experience significantly increased toxicity to 5-fluorouracil and other fluoropyrimidine compounds.

Question 6

Which one of the following drugs does not act by inhibiting microtubule function?

a) **Paclitaxel**
b) **Vinblastine**
c) **Docetaxel**
d) **Etoposide**
e) **Vincristine**

Answer for Question 6

(D) Etoposide

Etoposide is a topo II inhibitor and does not inhibit microtubule function.

Question 7

Which one of the following drugs acts by inhibiting topoisomerase II?

a) **5-Fluorouracil**
b) **Doxorubicin**
c) **Vincristine**
d) **Vinorelbine**
e) **Topotecan**

Answer for Question 7

(B) Doxorubicin

Doxorubicin exerts its cyotoxic effects, at least in part, through inhibition of topo II.

Question 8

Which one of the following drugs acts by inhibiting topoisomerase I?

a) Etoposide
b) Vincristine
c) Paclitaxel
d) Docetaxel
e) Irinotecan

Answer for Question 8

(E) Irinotecan

Irinotecan and topotecan are camptothecin analogs that exert their antitumor activity through inhibition of topo I.

Question 9

A deficiency in the catabolic enzyme 6-thiopurine-methyltransferase (TPMT) results in enhanced sensitivity and significant toxicity to which one of the following agents?

a) Methotrexate
b) 6-Mercaptopurine
c) Temozolomide
d) Topotecan
e) Temsirolimus

Answer for Question 9

(B) 6-Mercaptopurine

A partial or complete deficiency of TPMT results in excessive, severe toxicity, in the form of myelosuppression, GI toxicity, and neurotoxicity in response to treatment with the thiopurines, 6-mercaptopurine or 6-thioguanine.

Question 10

Grapefruit juice can alter the metabolism of which of the agents?

a) Erlotinib
b) Sunitinib
c) Sorafenib
d) Lapatinib
e) None of the above
f) All of the above

Answer for Question 10

(F) all of the above

Grapefruit juice and/or products can alter the metabolism of all of the small molecule tyrosine kinase inhibitors.

Question 11

A drug-drug interaction occurs between coumadin and which of the following agents?

a) Capecitabine
b) Tamoxifen
c) Etoposide
d) Flutamide
e) Bicalutamide
f) All of the above

Answer for Question 11

(F) all of the above

Coumadin can interact with a wide range of anticancer and hormonal agents, including capecitabine, cyclophosphamide, ifosfamide, etoposide, imatinib, dasatinib, nilotinib, erlotinib, tamoxifen, bicalutamide, flutamide, nilutamide

Question 12

The metabolism of which of the following drugs is altered in the presence of St. John's Wort?

a) Erlotinib
b) Vemurafenib
c) Sunitinib
d) Ixabepilone
e) Irinotecan
f) All of the above

Answer for Question 12

(F) All of the above

The metabolism of the small molecule inhibitors that are metabolized by liver CYP3A4 microsomal enzymes are altered in the presence of St. John's Wort. The metabolism of other drugs such as irinotecan, ixabepilone, and the mTOR inhibitors is also affected by St. John's Wort.

Question 13

All DPD mutations result in the DPD deficiency phenotype

a) True
b) False

Answer for Question 13

(B) False

Not all mutations in the DPD gene result in the DPD deficiency phenotype. Moreover, up to 40-50% of patients who experience excessive, severe toxicity and who are felt to have DPD deficiency will not have mutations in the DPD gene.

Question 14

Bevacizumab exerts its antitumor effects, in part, by binding to which of the VEGF ligands

a) VEGF-A
b) VEGF-B
c) VEGF-C
d) PlGF
e) All of the above

Answer for Question 14

(A) VEGF-A

Bevacizumab binds only to VEGF-A (all 6 isoforms). In contrast, ziv-aflibercept, binds to VEGF-A, VEGF-B, and PlGF.

Question 15

The TS ternary complex is made up of thymidylate synthase (TS), 5,10-methylenetetrahydrofolate, and which 5-FU metabolite?

a) FdUTP
b) FUTP
c) FdUMP
d) FdUDP
e) None of the above

Answer for Question 15

(C) FdUMP

FdUMP is the 5-FU metabolite that forms the ternary complex with TS and the reduced folate 5,10-methylenetetrahydrofolate

Question 16

Treatment with cetuximab is associated with which electrolyte abnormality?

a) **Hypophosphatemia**
b) **Hyponatremia**
c) **Hypouricemia**
d) **Hypomagnesemia**

Answer for Question 16

(D) Hypomagnesemia

Treatment with the anti-EGFR antibodies cetuximab and panitumumab is associated with a magnesium wasting from the renal tubules, which then leads to hypomagnesemia

Question 17

Which of the following anticancer agents is not associated with SIADH?

a) Cisplatin
b) Vincristine
c) Cyclophosphamide
d) Cytarabine
e) Vinblastine

Answer for Question 17

(D) Cytarabine

SIADH has been associated with cyclophophamide/ifosfamide, cisplatin/carboplatin, vinca alkaloids (vincristine, vinblastine, vinorelbine), and melphalan.

Question 18

The TS ternary complex is composed of thymidylate synthase (TS), FdUMP, and which reduced folate

a) 5-Formyltetetrahydrofolate
b) 5-Methyltetrahydrofolate
c) 5,10-Methylenetetrahydrofolate
d) Folic acid
e) Tetrahydrofolate

Answer for Question 18

(C) 5,10-Methylenetetrahydrofolate

When leucovorin (5-formyltetrahydrofolate) is administered with 5-FU, it is taken up in cells via the reduced folate carrier and then metabolized to various reduced folate forms, the most important of which is 5,10-mehtylenetetrahydrofolate. This is the specific reduced folate that forms a ternary complex with TS and the 5-FU metabolite FdUMP.

Question 19

Imatinib inhibits all of the following except:

a) c-Kit
b) Bcr-Abl
c) Bcr-Abl T315I mutation
d) Platelet-derived growth factor

Answer for Question 19

(C) Bcr-Abl T315I mutation

Imatinib inhibits Bcr-Abl, platelet-derived growth factor (PDGF), and c-Kit. It is unable to inhibit the T315I gatekeeper mutation. Dasatinib and nilotinib are able to overcome resistance to imatinib by being active against Bcr-Abl mutations, but they are also inactive against the T315I mutant. Only pomatinib has activity against the T315I mutant.

Question 20

Crizotinib inhibits all of the following except:

a) ALK
b) c-Met
c) RON
d) ROS1
e) EGFR

Answer for Question 20

(D) EGFR

Crizotinib inhibits multiple receptor tyrosine kinases, including ALK, RON, ROS1, and c-Met.