

MedCh 562 – Oncology agents - Midterm 2 - Key

Student name: _____

Problems 1-20 worth 4 points each, while problems 21-23 worth 6 or 7 points each.

1. The taxanes are an important group of anticancer agents. All of the following are true about the taxanes except for one thing. Which is not true?

- A. They include the agents paclitaxel, docetaxel, and cabazitaxel
- B. They are all poorly water soluble
- C. They all tend to cause some hearing loss
- D. They can all cause some myelosuppression
- E. They all interfere with the mitotic spindle (microtubules)

2. Ixabepilone (Ixempra) was approved in 2007 and the package insert (label) includes the following: Approved for advanced breast cancer (commonly with capecitabine) for patients who have been previously treated with anthracyclines or who cannot tolerate additional anthracyclines. Administration is IV only and formulated with Cremophor/ethanol. What is true about this agent?

- A. It is used first line
- B. It is poorly water soluble
- C. It can cause cardiotoxicity
- D. A and B
- E. B and C

3. Irinotecan (Camptosar) is a useful agent for treating colorectal cancer (CRC). All of the following are true about this agent except one thing. Which is not true?

- A. Genetic testing for the UGT1A1 gene is required before its use
- B. It's a prodrug
- C. Severe diarrhea can be a side effect
- D. Peripheral neuropathy is a major side effect
- E. It is part of the regimen called FORFIRI

4. Doxorubicin, daunorubicin and idarubicin are all anthracycline anticancer agents. What is true about these agents?

- A. They are all topoisomerase II inhibitors
- B. They can all generate reactive oxygen species (ROS)
- C. They can all cause extravasation injury if administered incorrectly
- D. A, B, and C
- E. A and B

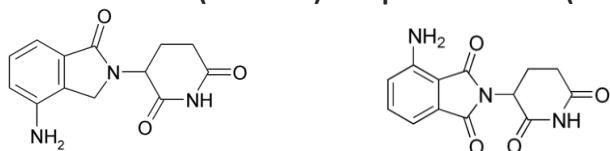
5. Etoposide is a useful anticancer agent. All of the following are false about etoposide except for one thing. Which is true?

- A. It interferes with the mitotic spindle (microtubules)
- B. It causes cardiotoxicity
- C. It will not cause myelosuppression
- D. It can form reactive oxygen species (ROS)
- E. It inhibits topoisomerase II

6. Dactinomycin is a macrolide antibiotic type of anticancer agent. What is true about this agent?

- A. It can intercalate into DNA
- B. It is very potent and dosed at the mcg/kg level
- C. It will not form reactive oxygen species
- D. A and B
- E. B and C

7. Lenalidamide (Revlimid) and pomalidamide (Pomalyst) are shown below. What is true about them?



- A. They are both immunomodulator type of drugs and possess some antiangiogenic properties
- B. They can both be assumed to be teratogenic (cause birth defects)
- C. They are both good substrates for CYP3A4
- D. A, B, and C
- E. A and B

8. Imatinib (Gleevec) is an older but interesting cell growth inhibitor. All of the following are true about this agent except one thing. Which is not true?

- A. It targets a tyrosine kinase activated by the Philadelphia (bcr/abl) chromosome translocation
- B. It's activity is vulnerable to a mutation (threonine 315 to isoleucine) in the target enzyme
- C. It will not cause QT prolongation
- D. It can be given orally
- E. It interferes with the binding of ATP

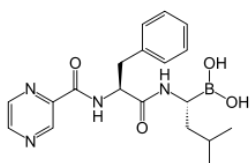
9. Erlotinib (Tarceva) is a useful agent and information from its package insert (label) includes the following: **Approved for advanced or metastatic non-small cell lung cancer after platinum and docetaxel therapy. Also approved for advanced or metastatic pancreatic cancer, in combination with gemcitabine. Administered PO and fasting. Strong inhibitors and inducers of CYP3A4 should be avoided.** What is true about this agent?

- A. It has full approval for both metastatic non-small cell cancer and metastatic pancreatic cancer
- B. It is likely metabolized by CYP3A4 to a fair degree
- C. It has not yet shown overall survival benefit
- D. A and B
- E. A, B, and C

10. Temsirolimus (Torisel) is a useful anticancer agent for renal cell carcinoma. It is administered IV and is formulated in ethanol/vitamin E/ polyethylene glycol. What is true about this agent?

- A. Premedication is advised
- B. It's an mTOR inhibitor
- C. Extravasation injury is a concern
- D. A and B
- E. A, B, and C

11. Bortezomib (Velcade) is a useful anticancer agent for treating multiple melanoma. What is true about this agent?

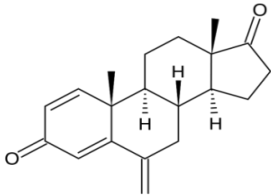


- A. The boron atom is critically important to its mechanism of action
- B. It won't cause myelosuppression or peripheral neuropathy
- C. It inhibits the activity of proteasomes
- D. A and B
- E. A and C

12. Bicalutamide (Casodex) is an antihormonal agent useful for treating prostate cancer. All of the following are true about this agent except one thing. Which is not true?

- A. It inhibits the formation of androgens
- B. It binds to the androgen receptor (AR) in an antagonist way
- C. It can be given orally
- D. It can cause some loss or degradation of the androgen receptor (AR)
- E. It can cause some liver and lung toxicity

13. Exemestane (Aromasin) is shown below and is useful for treating breast cancer. What is true about this agent?



- A. It binds the estrogen receptor antagonistically
- B. It is useful only for HER2 positive cancer
- C. It can inhibit CYP19 (CYP19A1)
- D. It will not cause osteoporosis with extended use
- E. It is administered IV

14. The glucocorticoids (prednisone, prednisolone, dexamethasone) are often given as part of chemotherapy. What is true about these agents?

- A. They can all be administered orally
- B. They are all immunosuppressive
- C. They have good anticancer activity, but we don't understand the mechanism(s) well
- D. A and B
- E. A and C

15. Imagine a fictitious monoclonal antibody drug called "Colomumab" that was recently approved that targets the EGFR-1 receptor on colon cancer cells. What is true about this agent?

- A. It's a humanized antibody
- B. It could be useful for treating colorectal cancer (CRC) if the cancer cells are KRAS positive
- C. It won't cause any immune reactions (allergic reactions)
- D. A and B
- E. A and C

16. Bevacizumab (Avastin) is a monoclonal antibody approved for treating colorectal cancer (CRC) along with FOLFOX and FOLFIRI. What is true about bevacizumab?

- A. It can cause cardiotoxicity and/or gastrointestinal perforation
- B. It binds the VEGF receptor
- C. It is humanized so it won't cause any immune (allergic) reactions
- D. A and B
- E. B and C

17. Axicabtagene ciloleucel (Yescarta) is a CAR-T cell therapy recently approved for a variety of B cell lymphomas. What is true about this agent?

- A. It targets the CD-19 antigen
- B. Its use can lead to opportunistic infection(s)
- C. Before its use, patients are treated with a lymphodepleting regimen
- D. A, B, and C
- E. A and C

18. Tocilizumab (Actemra) is a useful supportive agent. What is true about this agent?

- A. It is useful to reduce cytokine release syndrome (CRS)
- B. It targets IL-6
- C. It is useful both IV and oral
- D. A, B, and C
- E. A and B

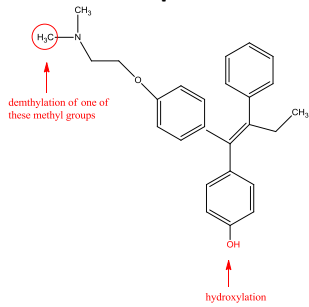
19. As a class, the bisphosphonates are useful and interesting agents. All of the following are true about them except one thing. What is not true about the bisphosphonates?

- A. They were originally developed to treat osteoporosis
- B. They are mimics of pyrophosphate, a natural molecule in bone, but are much more stable
- C. Chronic use can lead to tumor metastasis
- D. Chronic use can lead to osteonecrosis of the jaw (ONJ)
- E. The most recently approved agents have very long half-life values

20. GM-CSF (Sargramostim, Leukine) and G-CSF (Filgrastim, Neupogen) are both useful supportive agents. What is true about these agents?

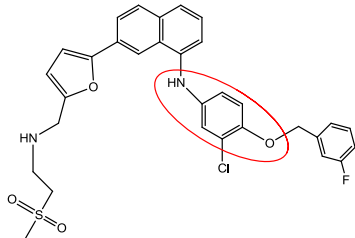
- A. They both can stimulate granulocytes including neutrophils
- B. Excessive use can lead to higher death rates due to myocardial infarction and stroke
- C. They both can help faster rebound from the neutrophil nadir
- D. A and B
- E. A and C

21. (6 pts) Tamoxifen (Novadex) is shown below and is an old anticancer drug useful for treating breast cancer. Answer the questions below about tamoxifen which short answers.



- State the enzymes involved in the bioactivation of tamoxifen. **CYP3A4 and CYP2D6.**
- With a circle or arrow, indicate the positions that are modified by bioactivation. **As above.**
- Is tamoxifen a true prodrug? Yes or **No**? What is the name of the molecule formed by bioactivation? **Endoxifen.**

22. (7 pts) Lapatinib (Tykerb) is shown below. It is useful for treating HER2 positive breast cancer. Answer the following questions below with short answers.



- State its exact mechanism of action including the molecule it interferes with. **It's a tyrosine kinase inhibitor (TKI) and interferes with the binding of the ATP molecule. Also accept if they say ATP analog.**
- Lapatinib can cause hepatotoxicity (liver toxicity). State how in one sentence it is believed to cause hepatotoxicity, and circle the important portion of the molecule believed to be involved. Be specific. **It can form a quinone imine, but also accept quinone, hydroquinone, imine quinone or anything similar.**
- Does this molecule need to enter cancer cells to work? **Yes** or No?
If yes, explain why in one sentence. **As this agent is a tyrosine kinase inhibitor it must enter the cancer cells to reach the kinase.**

23. (7 pts) Pembrolizumab (Keytruda) is a useful agent that was recently approved for metastatic melanoma. Its mechanism of action involves the PD-1 receptor. Answer the following questions about this agent with short answers.

- State its exact mechanism of action in 1-2 sentences. **It binds the PD-1 receptor on cancer cells and prevents binding of the PD-1 ligand on cancer cells to the PD-1 receptor. This activates the T- cells.**
- The BRAF mutation (at V600) is activating, yet Keytruda is useful for treating metastatic melanoma with this mutation. Explain this in one sentence. **BRAF is a kinase enzyme that is independent of the PD-1 receptor.**
- Can this agent cause immune reactions (allergic reactions) upon administration and even after administration? **Yes** or No? If yes, explain in 1-2 sentences. **It is possible for all MAB agents to cause immune reactions during administration as the body can recognize them as foreign. And this agent can turn on T-cells and actually cause severe immune reactions some time after administration because the T cells are over-activated.**