

Sample Exam & Answer Key
(Correct answers highlighted in yellow)

Medicinal Chemistry 562

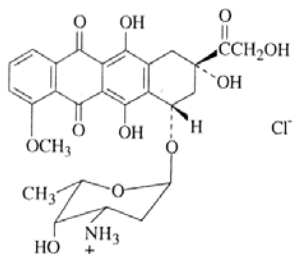
Final Examination

December 14, 2016

NAME: _____

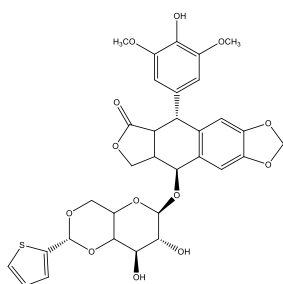
Questions 1-26 are multiple choice. (3 points each)

1. Shown below is the structure of doxorubicin (Adriamycin) which is useful for many types of cancer. Which of the following is true about this agent?



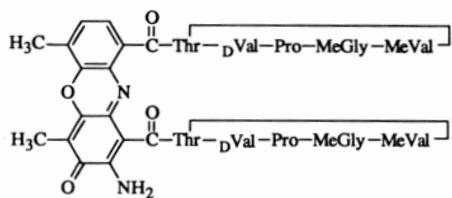
- A. It's an anthracycline type of drug.
- B. It intercalates into DNA, inhibits Topo II, and forms reactive oxygen species (ROS).
- C. It can cause myelosuppression and cardiotoxicity.
- D. A and B.
- E. A, B, and C.

2. Shown below is the structure of Teniposide (Vumon or VM26) and is formulated in Cremophor/ethanol. Which of the following is true about this agent?



- A. It inhibits Topo I and Topo II.
- B. It can cause myelosuppression.
- C. Administration of it should follow premedications such as antihistamines and/or corticosteroids.
- D. A and B.
- E. B and C.

3. Shown below is the structure of dactinomycin (Cosmegen) which is a very potent agent and is dosed at very low levels (micrograms/kg). Which of the following is true about this agent?



- A. It can be expected to form reactive oxygen species (ROS).
- B. It can cause extravasation injury if administered improperly.
- C. It inhibits Topo I.
- D. A and B.
- E. B and C.

4. Pomalidomide (Pomalyst) is a useful agent for treating multiple myeloma. Which of the following is true about this agent?

- A. It is structurally similar to thalidomide.
- B. It can be assumed to be teratogenic (cause birth defects).
- C. It is an immunomodulating agent.
- D. A and B.
- E. A, B, and C.

5. The vinca alkaloids are a useful type of anti-cancer agents. Which of the following is true about these agents?

- A. They all function by targeting the microtubules (i.e. they are anti-mitotic agents).
- B. Paclitaxel and docetaxel are examples of vinca alkaloids.
- C. They do not cause myelosuppression or peripheral neuropathy.
- D. A and B.
- E. B and C.

6. Abraxane (nab-paclitaxel) is a newer formulation of paclitaxel. As discussed in class, which of the following is true about this agent?

- A. It is formulated by pre-binding the paclitaxel to serum albumin.
- B. It causes fewer (or less severe) infusion reactions compared to the Taxol formulation of paclitaxel.
- C. It would not be expected to cause myelosuppression.
- D. A and B.
- E. A and C.

7. The following is in the package insert (label) for Panitumumab (Vectibix): Approved for use in treating colorectal cancer (CRC), as a single agent for the treatment of epidermal growth factor receptor (EGFR-1) expressing tumors*, with disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens (i.e. FOLFOX or FOLFIRI). Which of the following is true about this agent?

- A. It can be used first line.
- B. It can be used only for CRC patients who over-express EGFR-1 on their tumors.
- C. It can be used in combination with FOLFOX or FOLFIRI in CRC patients.
- D. A and B.
- E. B and C.

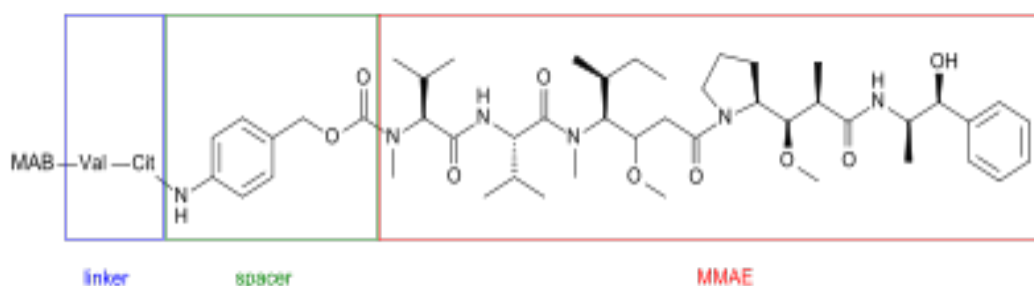
8. The following is in the package insert (label) for Atezolizumab (Tecentriq): Used for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. Targets PD-L1. Accelerated approved in May 2016. As discussed in class, which of the following is true about this agent?

- A. It cannot be used first line.
- B. Overall survival data will be needed for the company to obtain full approval of this agent.
- C. Too much blockade of its target can lead to too much immunostimulation.
- D. A and B.
- E. A, B, and C.

9. The agent trastuzumab emtansine (Kadcyla) is useful for treating HER2+ breast cancer. As discussed in class, which of the following is true about this agent?

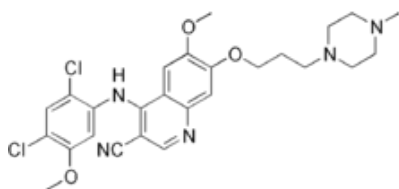
- A. It contains a humanized antibody and targets EGFR-2
- B. It's an antibody conjugate that contains a toxic payload.
- C. Unlike trastuzumab, this agent will not cause cardiotoxicity.
- D. A and B.
- E. A and C.

10. Shown below is an agent discussed in class. If the agent was named Excelimab, which of the following would be true about this agent?



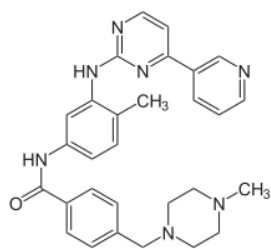
- A. It is a chimeric antibody (part mouse and part human).
- B. The toxic payload is in the far right box (MMAE).
- C. The toxic payload (MMAE) targets the microtubules and is therefore antimetabolic.
- D. A and B.
- E. A, B, and C.

11. Shown below is the structure of bosutinib (Bosulif). As discussed in class, which is true for this agent?



- A. It's a tyrosine kinase inhibitor.
- B. It prevents the binding of ATP to the enzyme active site.
- C. It can overcome the T315-I mutation at (threonine 315 to isoleucine).
- D. A and B.
- E. A, B, and C.

12. Shown below is imatinib (Gleevec) which is useful for Ph+ chronic myelogenous leukemia (CML) and Ph+ acute lymphocytic leukemia (ALL). As discussed in class, which is true about this agent?



- A. It's a serine kinase inhibitor.
- B. Although quite effective, resistance to the agent can develop quickly.
- C. It prevents binding of ATP to the kinase active site.
- D. A and B.
- E. B and C.

13. Gefitinib (Iressa) got accelerated approval by the FDA in 2003 for treatment of non-small cell lung cancer (NSCLC). It was later withdrawn from the market in 2012. Which of the following is true about this agent?

- A. It's a tyrosine kinase inhibitor.
- B. It never showed an improvement in overall survival (OS).
- C. It targets the VEGF receptor.
- D. A and B.
- E. A and C.

14. FDA approved carbozantinib (Cabometyx) and the package insert (label) states the following: For the treatment of advanced renal cell carcinoma (RCC) in patients who have received prior anti-angiogenic therapy. Targets tyrosine kinase activity of MET, VEGFR-1, -2 and -3, AXL, RET, ROS1, TYRO3, MER, KIT, TRKB, FLT-3, and TIE-2. As discussed in class, which is true about this agent?

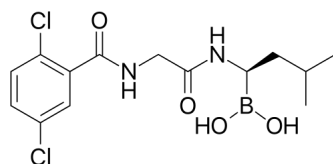
- A. It can be used first line.
- B. It hits multiple targets and can be expected to possess extra side effects.
- C. It showed overall survival (OS) benefit for patients.
- D. A and B.
- E. B and C.

15. Shown below is the structure of Idelalisib (Zydelig) which is useful for treating for chronic lymphocytic leukemia (CLL) in combination with rituximab. As discussed in class, which is true about this agent?



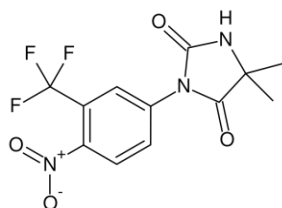
- A. It's phosphoinositide 3-kinase (PI3K) inhibitor.
- B. Its mechanism of action is independent of the binding of ATP.
- C. It can be used as sole therapy.
- D. A and B.
- E. A, B, and C.

16. Shown below is the structure of ixazomib (Ninlaro) which is used in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma. It is administered PO without food and is metabolized extensively by CYP3A4. As discussed in class, which is true about this agent?



- A. It's a proteasome inhibitor.
- B. Absorption is less variable in the absence of food.
- C. Try to avoid use with strong CYP3A4 inducers.
- D. A and B.
- E. A, B, and C.

17. Shown below is the structure of nilutamide (Nilandron) which is useful for hormone dependent prostate cancer. Which is true about this agent?



- A. It 's an anti-androgen that inhibits androgen biosynthesis.
- B. It can be expected to have some liver and/or lung toxicity.
- C. It can cause some destruction of the androgen receptor (AR).
- D. A and B.
- E. B and C.

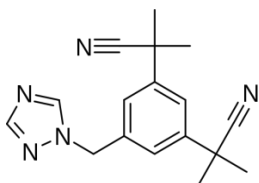
18. Abiraterone acetate (Zytiga) has been approved for metastatic, castrate resistant prostate cancer. It is administered PO daily. As discussed in class, which is true about this agent?

- A. It's an anti-androgen and irreversibly inhibits CYP17A.
- B. Its bioavailability is quite low (<10%).
- C. Repetitive dosing with food (or overdosing) can lead to hypertension and congestive heart failure.
- D. A and B.
- E. A, B, and C.

19. Tamoxifen is an older agent but has been used extensively to treat estrogen receptor positive (ER+) breast cancer. It is dosed PO and some QT prolongation could be associated with use of the agent. As discussed in class, which is true about this agent?

- A. It is metabolized to an active metabolite (endoxifen).
- B. Polymorphic metabolism is not an issue with the agent.
- C. Tamoxifen and endoxifen inhibit the enzyme CYP19A.
- D. A and B.
- E. A, B, and C.

20. Anastrozole (Arimidex) is a useful agent for treating ER+ breast cancer. The package insert (label) includes a number of uses but includes the following: For adjuvant treatment of postmenopausal women with hormone receptor-positive early breast cancer. As discussed in class, which is true about this agent?



- A. It inhibits estrogen biosynthesis by inhibiting CYP19A.
- B. It can cause loss of bone density.
- C. It can be used as a sole agent following surgery in breast cancer patients.
- D. A and B.
- E. A, B, and C.

21. The glucocorticoids are a small group of agents that are commonly used in cancer therapy. As discussed in class, which is true about these agents?

- A. They include dexamethasone, prednisone, and prednisolone.
- B. They possess some immunosuppressant property.
- C. They possess some antimitotic activity.
- D. A and B.
- E. A and C.

22. Granulocyte macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) are used as supportive agents as part of chemotherapy. As discussed in class, which is true about these agents?

- A. Both agents are useful in severe leucopenia caused by certain anti-cancer agents.
- B. Both agents stimulate neutrophils and macrophages.
- C. Any drugs that can cause myeloproliferation (e.g. corticosteroids, lithium) can exaggerate the effects of GM-CSF and G-CSF.
- D. A and B.
- E. A, B, and C.

23. Epoetin (Epoen, Procrit) and darbopoetin (Aranesp) are used as supportive agents as part of chemotherapy. As discussed in class, which is true about these agents?

- A. Both simulate the production of platelets.
- B. Darbopoetin has a longer half-life than epoetin.
- C. Both can cause unexpected death (e.g. from myocardial infarction or stroke).
- D. A and B.
- E. B and C.

24. Bisphosphonates are supportive agents that are used as part of chemotherapy. As discussed in class, which is true about these agents?

- A. They mimic the structure of pyrophosphate.
- B. They incorporate into bones and make them harder and resistant to fractures.
- C. They all have rather short half-life values.
- D. A and B.
- E. B and C.

25. Granisetron (Kytril) and palonsetron (Aloxi) are both anti-emetics that are frequently used in chemotherapy. Which is true about these agents?

- A. They are both serotonin (5-HT₃) receptor antagonists.
- B. They both help reduce nausea and vomiting.
- C. They are not metabolized by any of the CYP enzymes.
- D. A and B.
- E. A, B, and C.

26. Mercaptoethane sulfonate (MesNa), N-acetyl cysteine (NAC) and Amifostine (Ethyol) are all chemoprotectants. As discussed in class, which is true about these agents?

- A. MesNa is useful to protect from hemorrhagic cystitis (bladder toxicity).
- B. NAC is useful to protect nephrotoxicity (renal toxicity or kidney toxicity).
- C. Ethyol is useful to protect against ototoxicity (hearing loss) and kidney toxicity.
- D. A and B.
- E. A, B, and C.

Questions 27-36 are True/False. (2 points each)

True or False Questions

27. Humanized monoclonal antibodies (umabs) never cause immune reactions.

- A. True
- B. False**

28. The QT interval for cardiac re-polarization is a little longer in men than in women.

- A. True
- B. False**

29. Dosing of several cancer chemotherapy every 3 weeks is more a function of neutrophil recovery than drug half-life.

- A. True**
- B. False

30. Antimitotic cancer drugs always interfere with the microtubules (mitotic spindle).

- A. True**
- B. False

31. In general, one should always consider that anthracycline drugs can cause myelosuppression and cardiotoxicity.

- A. True**
- B. False

32. In general, immunomodulatory agents do not cause myelosuppression but they can cause teratogenic effects (birth defects).

- A. True**
- B. False**

← 2 points were awarded for either answer on Question 32.

33. In general, QT prolongation is not a concern with the tyrosine kinase inhibitor (TKI) drugs.

- A. True
- B. False**

34. Dexrazoxane (Zincard or Totect) is useful to protect against cardiotoxicity caused by anthracyclines or to protect from extravasation injury.

- A. True**
- B. False

35. A monoclonal antibody (MAB) that targets EGFR-1 can be ineffective if activating mutations occur in downstream targets such as KRAS or BRAF.

- A. True**
- B. False

36. Palliative therapy is defined as care or therapy for a patient who is at end stage and is expected not survive long.

- A. True**
- B. False

3 extra points

Remember: You will be awarded 2 extra points if you fill out and return the course evaluation form.