Pharmacology Update 2018/2019

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Disclosures

No conflicts to disclose

Objectives

- **Identify new drugs/agents that have been FDA approved for cancer treatment in 2018 and thus far in 2019.**
- **Recognize how new drugs/agents are given generic names.**
- **Identify how to gain information about new drugs based on the generic naming system**

Progress in Cancer Therapy 2018/19

- **New FDA Approved Cancer Treatment Agents**
  - **22 total: 13 solid tumor & 9 hematologic**
    - **2 radiopharmaceutical agents**
    - **1 androgen receptor inhibitor**
    - **1 cytotoxin**
    - **1 asparagine specific enzyme**
    - **17 Molecularly Targeted/Immunotherapy**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Progress in Cancer Therapy 2018/19

- **New FDA Approved Cancer Treatment Agent Indications**
  - **26 drugs with 45 new indications**
    - **34 solid tumor indications**
    - **11 hematologic indications**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Trends

Progress in Cancer Therapy 2018/19

- **Immunotherapy and Molecular Therapies**
  - **Subcutaneous formulations of monoclonal antibodies**
  - **Expanded indications**
    - **Neoadjuvant/adjuvant**
    - **Metastatic and locally advanced treatment**
    - **Maintenance after primary treatment**
    - **New generations of drugs to treat drug resistance**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Progress in Cancer Therapy 2018/19

- **Biosimilars**
  - **A biological product that is approved based on a showing that it is highly similar to an already-approved biological product, known as a reference product.**
  - **The biosimilar also must show it has no clinically meaningful differences in terms of safety and effectiveness from the reference product.**
  - **Only minor differences in clinically inactive components are allowable in biosimilar products.**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Progress in Cancer Therapy 2018/19

- **Radiolabeled pharmaceutical agents**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Progress in Cancer Therapy 2018/19

- **Cellular Gene Therapies**
  - **2017: "The U.S. Food and Drug Administration issued a historic action today making the first gene therapy available in the United States, ushering in a new approach to the treatment of cancer and other serious and life-threatening diseases."**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

Progress in Cancer Therapy 2018/19

- **Tumor Agnostic Drugs: Drugs designed to treat genomic alterations; not tumor histology specific**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

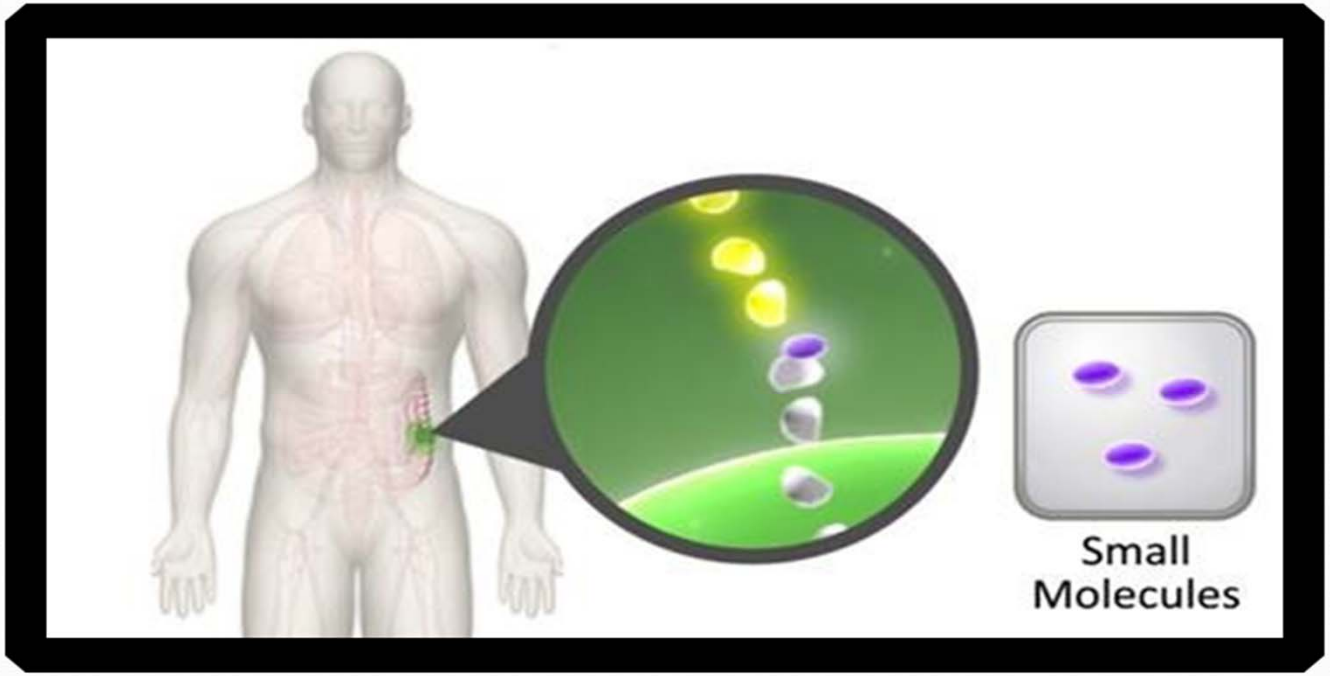
Tips for Learning about New Cancer Therapies

- **Know the type of drug/agent**
  - **Small molecule, monoclonal antibody, gene therapy, vaccine, cytotoxic**
- **Know the generic name**
- **Know the target and what is does normally in the body/what other FDA approved drugs are similar**
- **Know if the drug is genomically specific**

I know the generic name; but how do I pronounce it and how do I learn more??

- **http://www.cancer.gov/dictionary**
- **http://www.mycancergenome.org/content/molecular-medicine/overview-of-targeted-therapies-for-cancer/**
- **Reference list at end of slide set**

Once potential targets are identified, then drugs are designed to best attack the target



http://www.cancer.gov/cancertopics/understandingcancer/targetedtherapies

Small Molecules

- **Majority are oral, although a few are IV or subcutaneous. Implications for orals:**
  - **Adherence**
  - **Possible drug/food , drug/drug interactions**
  - **Patient education regarding taking medication correctly**

- **Targets vary**

http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/naming-biologics/monoclonal-antibodies.page

Small Molecules
Naming Conventions

- **tinibs:**
  - **tyrosine kinase inhibitors**
    - **erlotinib, sunitinib, ponatinib, imatinib, dasatinib, ibrutinib, dacomitinib, lorlatinib, larotrectinib, gilteritinib, erdafitinib**

- **rafenibs/metanibs**
  - **RAF/RAS/MEK inhibitors**
    - **sorafenib, dabrafenib, trametinib, vemurafenib, encorafenib, binimetinib**

- **paribs**
  - **PARP inhibitors**
    - **olaparib, rucaparib, niraparib, talazoparib**

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dacomitinib (VIZIMPRO®) Pfizer (first line tx metastatic non-small lung cancer with EGFR exon 19 deletion or exon 21 L858R substitution mutations)

www.vizimpro.com

lorlatinib (LORBRENA®) Pfizer (ALK positive metastatic NSCLC whose disease has progressed on crizotinib and at least one other ALK inhibitor for metastatic disease or whose disease has progressed on alectinib or ceritinib as the first ALK inhibitor for metastatic disease)

www.lorbrena.com

larotrectinib VITRAKVI® Loxo Oncology and Bayer

Tumor Agnostic: (Adult and pediatric pts with solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion without a known acquired resistance mutation, that are either metastatic or where surgical resection is likely to result in severe morbidity and who have no satisfactory alternative txs or whose cancer has progressed following tx)

www.vitrakvi.com

gilteritinib XOSPATA® Astellas Pharma(adult pts with relapsed or refractory AML with a FLT3 mutation)

www.xospata.com

erdafitinib BALVERSA ™ Janssen Pharmaceutical Companies (locally advanced or metastatic urothelial carcinoma, with susceptible FGFR3 or FGFR2 genetic alterations, that has progressed during or following platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy)

www.BALVERSA.com

encorafenib BRAFTOVI™and binimetinib MEKTOVI® Array BioPharma (combination treatment for unresectable or metastatic melanoma with a BRAF V600E or V600K mutation)

www.braftovi.com and www.mektovi.com

talazoparib TALZENNA ™ Pfizer Inc.(a poly [ADP-ribose] polymerase [PARP] inhibitor, for patients with deleterious or suspected deleterious germline BRCA-mutated [gBRCAm], HER2 negative locally advanced or metastatic breast cancer.)

www.talzenna.com

Small Molecules
Naming Conventions

- **lisibs:**
  - **PI3 kinase inhibitors**
    - **idelalisib, copanlisib, duvelisib**
- **denibs:**
  - **Isocitrate dehydrogenase IDH enzyme inhibitors**
    - **enasidenib (IDH2), ivosidenib (IDH1)**
- **degibs:**
  - **Sonic hedgehog pathway inhibitors**
    - **sonidegib, vismodegib, glasdegib**

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duvelisib (COPIKTRA™) Veristem (relapsed/refractory chronic lymphocytic lymphoma or small lymphocytic lymphoma after at least 2 prior therapies. Also, relapsed/refractory follicular lymphoma after at least 2 prior therapies.)

www.copiktra.com

ivosidenib TIBSOVO® Agios (adults with relapsed or refractory AML with a susceptible IDH1 mutation)

www.tibsovo.com

glasdegib DAURISMO ™ Pfizer (in combination with low-dose cytarabine for newly diagnosed AML in pts who are 75 y/o or older or who have co-morbidities that preclude intensive chemotherapy)

www.daurismo.com

Small Molecules
Naming Conventions

- **ciclibs:**
  - **Cyclin dependent kinase (CDK) 4 & 6 inhibitors**
    - **palbociclib, ribociclib, abemaciclib**

- **zomibs:**
  - **Proteasome inhibitors**
    - **bortezomib, carfilzomib, ixazomib**

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Small Molecules
Naming Conventions

- **toclax:**
  - **BCL-2 inhibitors**
    - **venetoclax**

- **inostats:**
  - **Histone deacetylase inhibitors (HDAC inhibitors)**
    - **vorinostat, belinostat, panobinostat**

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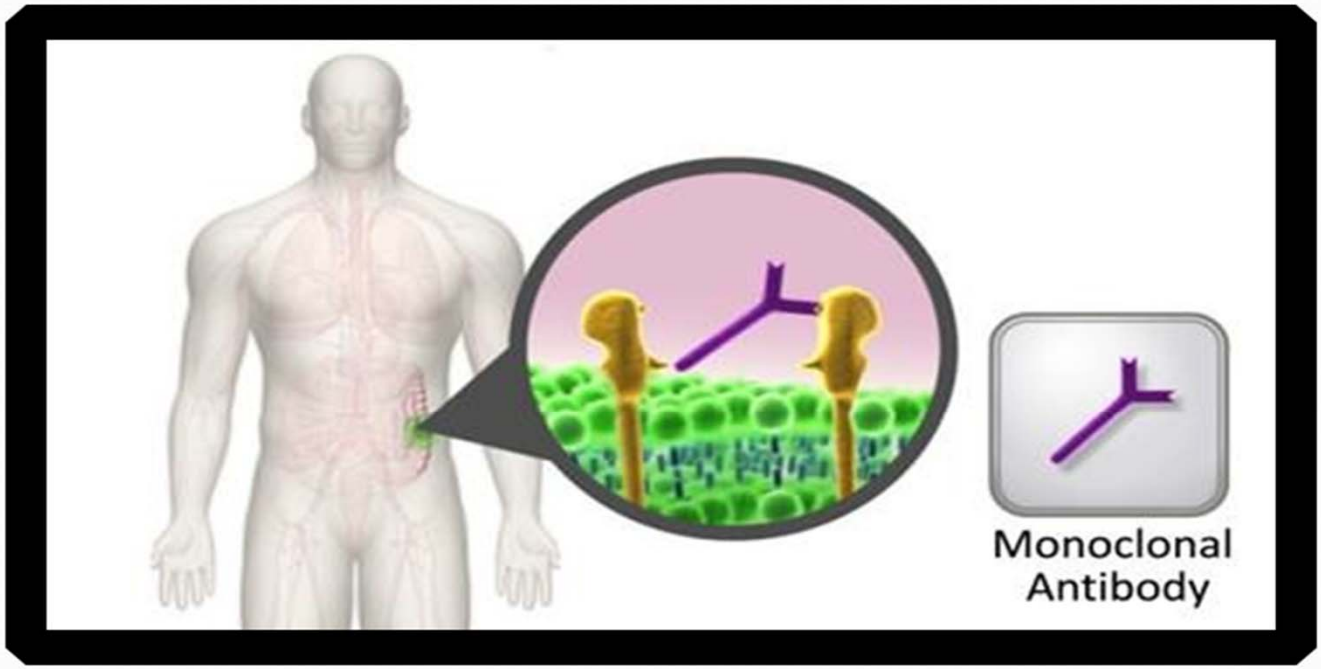

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Monoclonal Antibody Naming Conventions

Monoclonal antibody = mab

- tositu**mo**mab and iodine 131
  - **mo = mouse**
- ritu**xi**mab
  - **xi = chimeric or cross between mouse and human**
- trastu**zu**mab, bevaci**zu**mab
  - **zu = humanized**
- panitum**u**mab
  - **u = fully human (may also leave out the u)**

http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/naming-biologics/monoclonal-antibodies.page

What does the name mean?

t or tu = tumor

trastuzumab

ci = circulatory

bevacizumab

li or l = immunomodulator

ipilimumab

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What does the name mean?

- **One or two words added to name indicates it is a conjugated monoclonal antibody. May be combined with:**
  - **Radioactive particle: ibritumomab tiuxetan**
  - **Drug (antibody-drug conjugate): ado-trastuzumab emtansine**

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What does the name mean?

- **Biosimilars have the reference product generic name as the "core" with "4 lower case letters devoid of meaning" attached by a hyphen as a suffix:**
  - **bevacizumab-awwb Mvasi™**
  - **trastuzumab-dskt Ogivri™**
  - **trastuzumab-pkrb Herzuma®**
  - **rituximab-abbs Truxima®**

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trastuzumab-pkrb Herzuma® Celltrion (biosimilar to trastuzumab for HER2-overexpressing breast cancer)

www.Herzuma.com

trastuzumab and hyaluronidase-oysk injection™ Herceptin Hylecta Genentech (subcutaneous combination of trastuzumab, a HER2/neu receptor antagonist, and hyaluronidase, an endoglycosidase, for the treatment of HER2 overexpressing breast cancer)

www.Herceptin Hylecta.com

rituximab-abbs TRUXIMA® Celltrion (CD20-positive B-cell non –Hodgkin Lymphoma as single agent or in combination with chemotherapy)

www.truxima.com

What does the name mean?

- **In 2017, the FDA made the decision to name all new biologics (not just biosimilars) with"4 lower case letters devoid of meaning" attached by a hyphen as a suffix:**
  - **There was concern that the suffix on biosimilars would serve as a barrier to their use; creating a misimpression that they were inferior to the reference (originator) products**
  - **Resulted in the FDA deciding to attached the suffix to all new biologics; not just biosimilars**
  - **Change in naming advances patient safety and creates a high quality, competitive market**
  - **FDA does not intend to modify the proper names of biological products that have already been licensed or approved under the Public Health Service Act without an FDA-designated suffix in their proper names.**

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mogamulizumab-kpkc Poteligeo® Kyowa Kirin, Inc.(for adult patients with relapsed or refractory mycosis fungoides [MF] or Sézary syndrome [SS] after at least one prior systemic therapy)

www.poteligeo.com

moxetumomab pasudotox-tdfk (LUMOXITI™) AstraZeneca (CD22-directed cytotoxin indicated for adult patients with relapsed or refractory hairy cell leukemia [HCL] who received at least two prior systemic therapies, including treatment with a purine nucleoside analog [PNA])

www.lumoxiti.com

cemiplimab-rwlc LIBTAYO® Regeneron Pharmaceuticals Inc. (for patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation)

www.libtayo.com

Living Drugs/ Genetically Engineered Cells

leucel

- **Cellular therapies; "living drugs"**
- **Intravenous; currently must be given at approved centers**
- **Precision: Cells from patient, genetically engineered and given back to pt**
- **Examples**
  - **sipuleucel-T, tisagenlecleucel, axicabtagene ciloleucel**

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Radiolabeled Pharmaceutical Agents

- **lutetium Lu 177 dotatate, LUTATHERA® Advanced Accelerator Applications USA, Inc. (a radiolabeled somatostatin analog, for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults)**

- **iobenguane I 131 AZEDRA® Progenics (adult and pediatric pts 12 and older with iobenguane scan-positive, unresectable, locally advanced or metastatic paragangliomas or pheochromocytomas that require systemic anticancer therapy)**

http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm

The Others

tagraxofusp-erzs ELZONRIS™ Stemline Therapeutics (a CD123-directed cytotoxin for blastic plasmacytoid dendritic cell neoplasm in adult and pediatric pts 2 y/o and older)

www.elzonris.com

calaspargase pegol-mknl ASPARLAS™ Servier (a component of a multi-agent chemotherapeutic regimen for ALL in pediatric and young adult pts age 1 month to 21 years. An asparagine specific enzyme; allows for a longer interval between doses compared to other pegasparagase products)

www.asparlas.com

apalutamide ERLEADA™ Janssen (treatment of patients with non-metastatic castration-resistant prostate cancer)

www.erleada.com

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- http://www.vitrakvi.com
- http://www.xospata.com
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