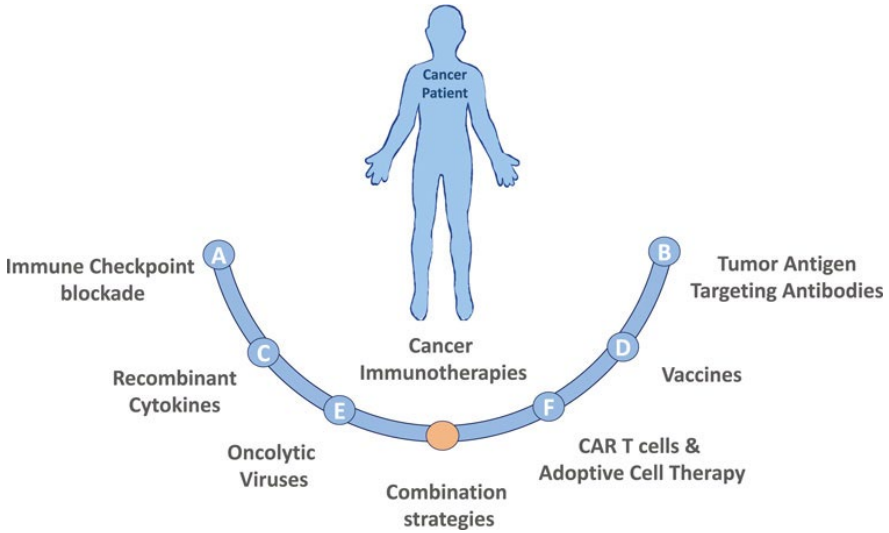
# Advanced Oncology Certified Nurse Practitioner

## REVIEW COURSE 2024

**October 10-12, 2024 | Houston, TX**

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®




# Immunotherapy

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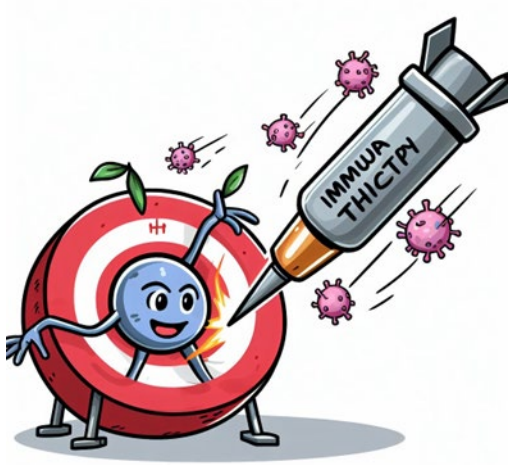
October 11, 2024



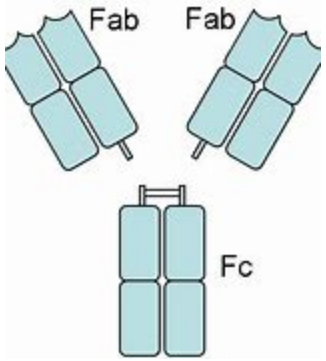

# Monoclonal Antibodies

First developed in 1986- to prevent organ transplant rejection

# Functional domains of monoclonal antibodies:

- 2 antigen-binding fragments (Fabs)
  - Binds to specific antigen targets

- 1 crystallizable fragment (Fc)
  - Binds to immune effector cells → phagocytosis; stimulation of cytokine release→ destruction of cell expressing the antigen
  - Binds to complement → complement cascade



# Naming of Monoclonal Antibodies (suffixs)

- “mab”- indicates monoclonal antibody class
  - “umab”- completely human
  - “zumab”-mostly human, some mouse
  - “ximab”- chimeric; part mouse, part human
  - “momab”-entirely mouse (better at finding targets ?hypersensitivity)

- Developed 2022 and onward
  - “ tug”-unmodified
  - “bart”-engineered constant region
  - “mig”- bi/multispecific
  - “ment”- variable region fragments

# Rituximab

- **Treatment of…:** First for cancer txmt (CD20-positive lymphoma= low-grade follicular & DLBCL)

- **What is it**: Chimeric immunoglobulin G1-kappa monoclonal antibody

- **Target:** CD20 antigen on pre-B and mature B cells; Fab portion binds to immune effector cells→ cell lysis→ release of cytokines ( TNF & IL-6)→ infusion related reactions

# Rituximab (continued)

- **Side-effects:**
  - 77% of patients—infusion-related reactions with 1st dose
    - Symptoms: Mild--chills, rigors, n/v, pruritus, rash, myalgia; Severe—hypotension, dizziness, bronchospasm, anaphylaxis
    - Associations: bowel obstruction, renal failure, cardiac arrythmias, severe mucocutaneous rx, multifocal leukoencephalopathy (progressive)
  - Fatal reactions usually within 24 hours--≈80% associated with 1st infusion

- **Precautions:**
  - *Premedicate*: acetaminophen and antihistamine 30-60 minutes prior (prednisone if…)
  - ↑ *risk of TLS:* newly dx non-HL
  - *Up-to-date* immunizations: non-live vaccines at least 4 weeks prior to treatment

- **Contraindications:**
  - Active infections
  - Live viral vaccines not recommended prior to or during treatment

# Ofatumumab & Obinutuzumab

- **Treatment of…:**
  - **Ofatumumab:** CLL =>previously untreated, relapsed/refractory, recurrent or progressive
  - **Obinutuzumab**: untreated CLL, relapsed/refractory follicular lymphoma (stage II bulky, III, or IV follicular lymphoma
- **What is it**: monoclonal antibody (completely/mostly human)
- **Target:** CD20 antigen on pre-B, mature B cells, and malignant B cells; engage antibody-dependent cell-medicated cytotoxicity and antibody-dependent cellular phagocytosis → activations of intracellular death signaling pathways and the complement cascade

# Ofatumumab & Obinutuzumab (continued)

- **Side effects:** cough, nausea, diarrhea, infusion-related reactions and TLS, severe/life threatening thrombocytopenia with 1st cycle, ↑ risk of infection, Hep B reactivation (fulminant hep, hepatic failure or death), progressive multifocal leukoencephalogpathy (John Cunningham virus)
- **Precautions:**
  - *Premedicate*: hydration, glucocorticoid, antihyperuricemics, acetaminophen, and antihistamine
  - *Hold* antihypertensive meds for preexisting cardiac or pulmonary conditions
  - *Hold* meds that increase risk of bleeding
  - *Screen* for hepatitis prior to treatment
- **Contraindications:**
  - Avoid live vaccines during treatment

# Alemtuzumab

- **Treatment of**: B-cell CLL
- **What is it**: humanized monoclonal antibody
- **Target**: CD52 antigen

# Alemtuzumab (continued)

- **Side effects:** n/v/d, insomnia myelosuppression, prolonged and sever lymphopenia→ ↑ risk of opportunistic infections, infusion related reactions
- **Precautions:**
  - *Premedicate:* glucocorticoids, acetaminophen
  - *Prophylaxis:* P.jirovecii pneumonia & herpes virus
- **Contraindications:**??

# Daratumumab (SubQ form dara + hyaluronidase-fhj)

- **Treatment of**… MM (monotherapy)
- **What is it**:  monoclonal antibody (completely human)
- **Target**: binds to CD38 inhibiting growth of CD38- expressing tumors

# Daratumumab (continued)

- **Side-effects**: ocular changes (acute myopia/narrowing of the anterior chamber angle→ ophthalmic consult, neutropenia, thrombocytopenia
- **Precautions:**
  - *Premedicate*: corticosteroids, acetaminophen, and antihistamines (Inhaled bronchodilators and steroids for COPD)
  - *Posttransfusion*: steroids (potential anaphylactic infusion reactions)
  - *Discontinue* posttransfusion meds after 3-4 doses if no reaction
  - Antiviral prophylaxis 1 week prior & continue for 3 months post treatment
  - *Type & screen* prior to treatment (d/t interference w cross-matching for up to 6 months)
  - *Contraception* for at least 3 months after treatment
- Contraindications:

# Panitumumab

- **Treatment of** … wild-type RAS (KRAS and NRAS) metastatic colorectal cancer (in combination with FOLFOX)—1st line or monotherapy for disease progression prior to  fluoropyrimidine, oxaliplatin & irinotecan

- **What is it**: immunoglobulin G1 monoclonal antibody (completely human) EGFR antagonist

- **Target**: binds to EGFR preventing initiation of cell signaling w/cell division

# Panitumumab (continued)

- **Side-effects:** photosensitivity (90%-- 15% grade 3 or higher), soft tissue toxicities, infusion-related rxs (4%), interstitial lung disease (1%), diarrhea, dehydration→ renal failure, ocular toxicities (keratitis, corneal ulceration, ulcerative keratitis)
- **Precautions:**
  - *Monitor* for soft tissue toxicities (infection-necrotizing fasciitis, bullous mucocutaneous skin disease, sepsis, death).
  - *Monitor* electrolytes frequently for 8 weeks after completion
  - *Careful*-> increased mortality and severe toxicity with panitumumab, bevacizumab & chemotherapy
- Contraindications:

# Trastuzumab approved 1998

- **Treatment of**… HER2 overexpressing breast cancer or metastatic gastric and GE junction adenocarcinoma
- **What is it**: immunoglobulin G1 fully humanized monoclonal antibody
- **Target**: binds with extracellular HER2 protein

# Trastuzumab (continued)

- **Side-effects:** cardiomyopathy (asymptomatic);infusion-related reactions (40%), pulmonary toxicity, neutropenia
- **Precautions:**
  - *Premedicate*: antihistamines & corticosteroids
  - *Baseline:* echocardiogram (LVEF measurement) prior to treatment and every 3 months, then every 6 months x 2 years after treatment
  - *Hold:* for  4 weeks if ≥ 10-16% decrease in LVEF (measure LVEF q 4 weeks if treatment held)
- **Contraindications:**
  - Fatal toxicities during pregnancy or within 7 months prior to conception

# Pertuzumab

- **Treatment of**…HER2-positive metastatic breast cancer (no prior anti-HER2 therapy or chemo), HER2-positive locally advanced inflammatory or early-stage breast cancer at high risk for recurrence

- **What is it:** fully humanized monoclonal antibody HER2 antagonist

- **Target:** HER family members (EGFR, HER3, HER4), mediates antibody-dependent cell-mediated cytotoxicity

# Pertuzumab (continued)

- **Side-effects:** Left ventricular dysfunction (↓LVEF and CHF); anaphylaxis (2-8%), hyperuricemia, acute renal failure, hyperphosphatemia, neutropenia (grade 3-4), n/v/d, alopecia, fatigue, rash and PN
- **Precautions:**
  - *Monitor*: LVEF 50% at baseline & every 3 months (↑ risk w/chest XRT & anthracyclines)
  - *Monitor* for severe hypersensitivity & observe for 30 minutes after transfusion
  - TLS with higher tumor burden/bulky disease
- Contraindications:

# Cetuximab

- **Treatment of**… squamous cell carcinoma of H & N (w/xrt- locally or regionally advanced; w/5FU recurrent loco regionally advanced or metastatic); wild type KRAS EGFR expressing metastatic colorectal cancer

- **What is it**: chimeric immunoglobulin G1 monoclonal antibody

- **Target:** extracellular EGFR on healthy (skin, hair follicle) and malignant cells (colon, head and neck cancer). High affinity for EGFR vs EGFR ligand. Possible recruitment of immune effector cells through anti-body dependent cellular cytotoxicity and complement activation

# Cetuximab (continued)

- **Side-effects:** severe/fatal infusion rxs (70% 1st treatment), anaphylactic rxs (h/o tick bites, red meat allergies, immunoglobulin E antibodies, cardiac arrest, sudden death, interstitial lung disease, electrolyte imbalance, dermatologic toxicities (acneiform rash, telangiectasias, xerosis, hyperpigmentation, infectious sequelae,) photosensitivity
- **Precautions:**
  - *Initiate* 1 week prior to XRT
  - *Ensure* infusion completed 1 hour prior to chemo
- Contraindications:

# Isatuximab

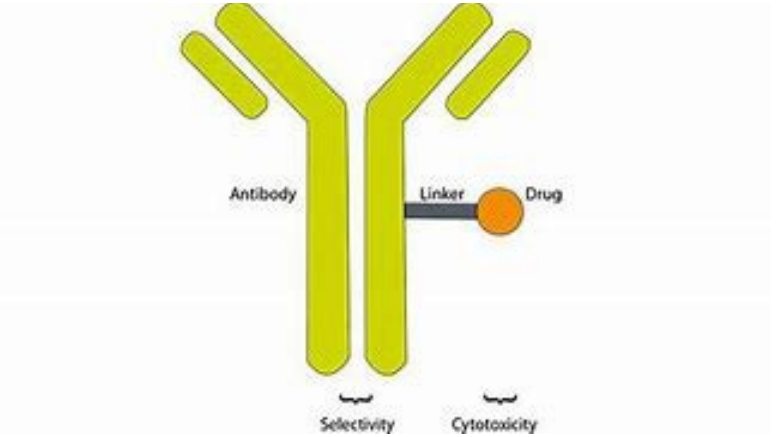
- **Treatment of**… MM (in combination with dex and pomalidomide) in those previously treated…
- **What is it**: monoclonal antibody (chimeric)
- **Target**: binds to CD38 expressed on surface of hemopoietic and MM cells→ induces apoptosis & activates immune effector mechanisms

# Isatuximab (continued)

- **Side-effects:** infusion related reactions

- **Precautions:**
  - *Premedicate*: dexamethasone, acetaminophen, $H_2$ antagonist, and diphenhydramine

- **Contraindications:**




# Antibody-Drug Conjugates

Monoclonal antibody attached by a linker to a cytotoxic drug/radioisotope (payload)

# Antibody-Drug Conjugates

- Increases the effectiveness of drug/radioisotope while ↓ toxicity
- Cleavable-Payload  released in response to tumor-associated factors/conditions
- Uncleavable- relies on lysosomal degradation  of antibody-linker
- “fab” portion ➔specific target antigen on tumor cell surface➔ delivers toxin/radioisotope to target cell ➔ kills it
- Administered by IV

# Ado-trastuzumab emtansine (Kadcyla/ T-DM1)

- **Treatment of**… HER2 positive early-stage breast cancer (invasive residual disease)

- **What is it:** HER2-targeted monoclonal antibody (mostly human) attached to microtubular inhibitor emtansine

- **Target**:

# Ado-trastuzumab emtansine (continued)

- **Side-effects**: thrombocytopenia (83%→15% ≥ grade 3), elevated LFTs (98%→ 8% grade 3-4), heart failure (1.8%), grade 3 interstitial lung disease, xrt pneumonitis, infusion related reactions (1.6%), fatal hemorrhage (grade 3=1.8%), PN, fatigue, nausea, constipation, headache, musculoskeletal pain
- **Precautions**:
  - *Assess* platelets prior to each treatment (100k/$mm^3$ at initiation, 50k/$mm^3$ subsequent)
  - *Assess* LFTs prior to treatment (risk of hepatotoxicity/liver failure)
  - *Assess* LVEF at baseline and q 3 months
  - *Assess* for respiratory symptoms
- Contraindications:

# Fam-trastuzumab deruxtecan-nxki (Enhertu)

- **Treatment of**…: Unresectable/ metastatic HER2-positive breast cancer or locally advanced/metastatic HER2 positive gastric/GE junction adenocarcinoma
- **What is it**: humanized anti-HER2 antibody and topoisomerase inhibitor conjugate

- **Target**:

# Fam-trastuzumab deruxtecan-nxki (continued)

- **Side-effects**: neutropenia, myelosuppression, elevated LFTs, constipation, decreased appetite, diarrhea, abdominal pain, alopecia, headache, upper respiratory infection, musculoskeletal pain, fatigue, nausea
- **Precautions:**
  - *Premedicate*: Antiemetics
  - *Monitor* for neutropenia at baseline and prior to each dose
  - *Assess* LVEF at baseline and during treatment
- **Contraindications**: None

# Sacituzumab govitecan-hziy (Trodelvy)

- **Treatment of**…: metastatic triple negative breast cancer (2 prior therapies), locally advanced/metastatic urothelial cancer (prior txmt—platinum-based, PD-L1 or Pd-1)

- **What is it**: combines monoclonal antibody with cytotoxic agent

- **Target:**

# Sacituzumab govitecan-hziy

- **Side effects**: severe/life threatening neutropenia, severe diarrhea, hypersensitivity and infusion reactions, n/v, alopecia, anemia, decreased appetite, fatigue, rash, abdominal pain
- **Precautions**:
  - *Premedicate*: Antiemetics
  - *Hold* for absolute neutrophil count <1,500/$mm^3$
  - *Consider* granulocyte-CSF for 2$^{nd}$ prophylaxis
- **Contradictions:**

# Tisotumab vedotin-tftv

- **Treatment of**…: recurrent metastatic cervical cancer w/progression after chemo
- **What is it**: tissue factor-directed antibody & microtubule inhibitor conjugate
- **Target**:

# Tisotumab vedotin-tftv

- **Side effects**: changes in corneal epithelium and conjunctiva (60%), PN (42%), hemorrhage (62%- hematuria, vaginal, epistaxis), pneumonitis (1.3%), nausea, fatigue, alopecia, elevated creatinine, rash, decreased leukocytes, increased serum coags
- **Precaution**s:
  - *Monitor* for vision changes→slit lamp exam at baseline, prior to each dose and PRN (onset 1.2 months- usually improves or resolves)
  - *Monitor* for new or worsening pulmonary symptoms

- **Contraindications**: do not give with concurrent stron CYP3A4 inhibitors

# Enfortumab vedotin-ejfv

- **Treatment of**…: locally advanced/metastatic urothelial cancer (prior txmt PD-1/PD-L1 & platinum containing chemo) or cisplatin ineligble
- **What is it**: a human immunoglobulin GI directed against nectin-4
- **Target**: microtuble-disrupting agent→ attaches to the antibody with a protease-cleavable linker

# Enfortumab vedotin-ejfv

- **Side effects:** hyperglycemia (14%)→ DKA, pneumonitis (3.1%-- onset 2.9 months), PN (52%), ocular disorders (40%), cutaneous reactions (55%-- during 1st cycle: Stevens-Johnson syndrome/ toxic epidermal necrolysis),

- **Precautions:**
  - *Monitor* BG--. Hold if ≥ 250 mg/dL
  - *Monitor* for cutaneous reactions
  - *Assess* venous access (extravasation→ fever, increased temperature, edema, etc.)
  - *Caution*: dual P-glycoprotein & CYP3A4 inhibitors increase toxicity

- **Contraindications:**

# Brentuximab vedotin (2011) (Adcetris)

- **Treatment of** …: stage III or IV classical Hodgkin lymphoma (w/doxorubicin, vinblastine & dacarbazine, or after auto HSCT consolidation, or after failure of 2 multiagent chemo regimens), untreated systemic anaplastic large cell lymphoma, primary cutaneous large cell lymphoma

- **What is it**: chimeric immunoglobulin G1 monoclonal antibody

- **Target**: CD30 (TNF receptor) conjugated to the microtubule-disrupting agent MMAE (binds to tubulin preventing cell replication= cell death)

# Brentuximab vedotin (continued)

- **Side effects:** infusion reactions (19%- chills, dyspnea, fever, cough, nausea, pruritus), PN, neutropenia, TLS, bone marrow suppression, fatigue, n/v/d, fever, cough, rash, upper respiratory infection
- **Precautions**:
  - *Premedicate* with acetaminophen, antihistamine and corticosteroid if previous infusion reaction
  - Growth factor support for prior grade 3-4 neutropenia
- **Contraindications**: do not use in combination with Bleomycin

# Gemtuzumab ozogamicin (2000->withdrawn 2010-> reapproved 2018) (Mylotarg)

- **Treatment of**…: newly dx'd CD33-positive ALL

- **What is it**: CD33-Directed monoclonal antibody linked to N-acetyl gamma calicheamicin

- **Target**: CD33

# Gemtuzumab ozogamicin (continued)

- **Side effects**: Hemorrhage (21%), death (3%), hepatotoxicity, QT prolongation

- **Precautions**:
  - *Premedicate*: Corticosteroid, antihistamine and acetaminophen
  - *Observe* for at least 1 hour post infusion
  - TLS prophylaxis
  - *Monitor* platelet counts, LFTs, total bili

- **Contraindications:**

# Inotuzumab ozogamicin (2017) (Besponsa)

- **Treatment of**…: relapsed/refractory CD22 positive B-cell precusor ALL
- **What is it**: CD22-directed antibody-drug conjugate
- **Target**: CD22

# Inotuzumab ozogamicin (continued)

- **Side effects**: neutropenia & thrombocytopenia (50%), infection, infusion reactions (1st dose), QTc prolongation, hepatotoxicity, SOS, pyrexia, nausea, fatigue, headache

- **Precautions**:
  - *Premedicate* with corticosteroid, antipyretic and antihistamine
  - *Observe* for 1hour post infusion
  - *Obtain* ECG and electrolytes at baseline, during treatment (more often if on meds)
  - *Monitor* bilirubin

- **Contraindication**:

# Polatuzumab vedotin-pliq

- **Treatment of**…: relapsed/refractory DLBCL
- **What is it:** antibody drug conjugate of CD79b-directed monoclonal antibody and MMAE
- **Target:**

# Polatuzumab vedotin-piq (continued)

- **Side effects**: PN (cumulative), myelosuppression (neutropenia, anemia, thrombocytopenia, febrile neutropenia), TLs, hepatotoxicity,

- **Precautions**:
  - *Premedicate*: antihistamine & antipyretic
  - *Observe* for 90 minutes post transfusion of 1$^{st}$ dose
  - *Monitor* CBC
  - CSF as need
  - *Consider* prophylaxis for P. jirovecii pneumonia and herpes simplex
  - *Monitor* for neurologic or behavioral changes
  - *Monitor* LFTs and bilirubin
  - *Contraception* during treatment

- **Contraindications:**

# Belantamab mafodotin-bimf

- **Treatment of** …: multiple myeloma
- **What is it**: antibody drug conjugate
- **Target**: B-cell maturation antigen on myeloma cell and monomethyl auristatin F

# Belantamab mafodotin-blmf (continued)

- **Side effects**: infusion reactions (18%), ocular toxicity (77%), thrombocytopenia

- **Precaution:**
  - *Assess* visual acuity and slit lamp exam baseline and prior to each dose and w/each visual symptom
  - Lubricant eye drops 4 times daily; no contacts during therapy
  - *Obtain* CBC at baseline and throughout treatment
  - *Contraception* during treatment & female =up to 4 months, males= up to 6 months

- **Contraindication**:

# Loncastuximab tesirine-lpyl

- **Treatment of**…: refractory DLBCL
- **What is it**: a monoclonal antibody targeting CD19 conjugated to an alkylating agent
- **Target:**

# Loncastuximab tesirine-lpyl (continued)

- **Side effects**: pleural effusion, asites, peripheral edema, pericardial effusion, myelosuppression, neutropenia, thrombocytopenia, anemia, febrile neutropenia, fatal infections, dermatologic reactions
- **Precautions:**
  - *Premedicate* dexamethasone 4 mg BID for 3 days prior to treatment (rec)
  - *Monitor* CBC
  - Growth factor support PRN
  - *Monitor* for new/worsening signs/symptoms of infection
  - *Minimize* exposure to sunlight (sunscreen, protective clothing)
  - If treatment delay > 3 weeks (d/t toxicity) dose reduction by 50%
- **Contraindications:**

# Ibritumomab tiuxetan

- **Treatment of**…: refractory, low-grade, or follicular B-cell non-Hodgkin lymphoma & untreated follicular non-Hodgkin lymphoma

- **What is it**: a CD20-directed monoclonal antibody conjugated to the yttrium-90 radioisotope.

- **Target**:

# Ibritumomab tiuxetan (continued)

- **Side effects**: rare but fatal infusion-related rxs with 24 hours of rituximab (80% w/1st infusion), cytopenias lasting up to 12 weeks, severe cutaneous and mucosal rxs (4d – 4 months), 2nd primary malignancies (AML, MDS)

- **Precautions:**
  - *Monitor* closely for extravasation
  - *Avoid* live vaccines following txmt
  - *Use* contraception during and up to 12 months after therapy

- **Contraindications:**
  - 25% or > lymphoma-involved bone marrow
  - Impaired bone marrow reserve

# Moxetumomab pasudotox-tdf

- **Treatment of**…: relapsed or refractory hairy cell leukemia
- **What it is**: s a CD22-directed antibody conjugated to a cytotoxic agent
- **Target**: Binding to CD22 on the surface of B cells inhibits protein synthesis and apoptosis

Discontinued

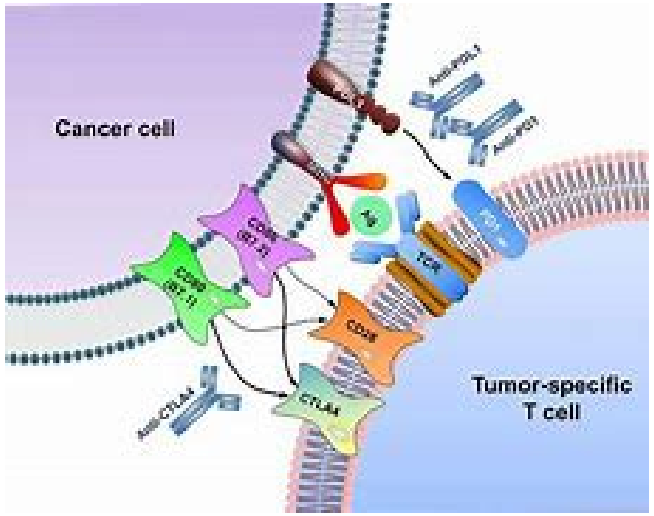
# Moxetumomab pasudotox-tdf

- **Side effects:** capillary leak syndrome (s hypoalbuminemia, hypotension, fluid overload, and hemoconcentration), life-threatening hemolytic uremic syndrome (microangiopathic hemolytic anemia, thrombocytopenia, and progressive renal failure)

- **Precautions**:
  - Assess weight, blood pressure, H/H, Cr , WBC, plts & albumin prior to each dose
  - Maintain daily hydration of 3L
  - IVF during administration
  - Low dose ASA 1$^{st}$ week of every cycle
  - Premedicate: acetaminophen, antihistame and $H_2$ antagonist prior to each infusion w/ isotonic fluids
  - Assess for nephrotoxicity prior to each infusion and PRN—delay until recovered
  - Electrolytes prior toeach dose and mid cycle

Discontinued

- **Contraindications:**

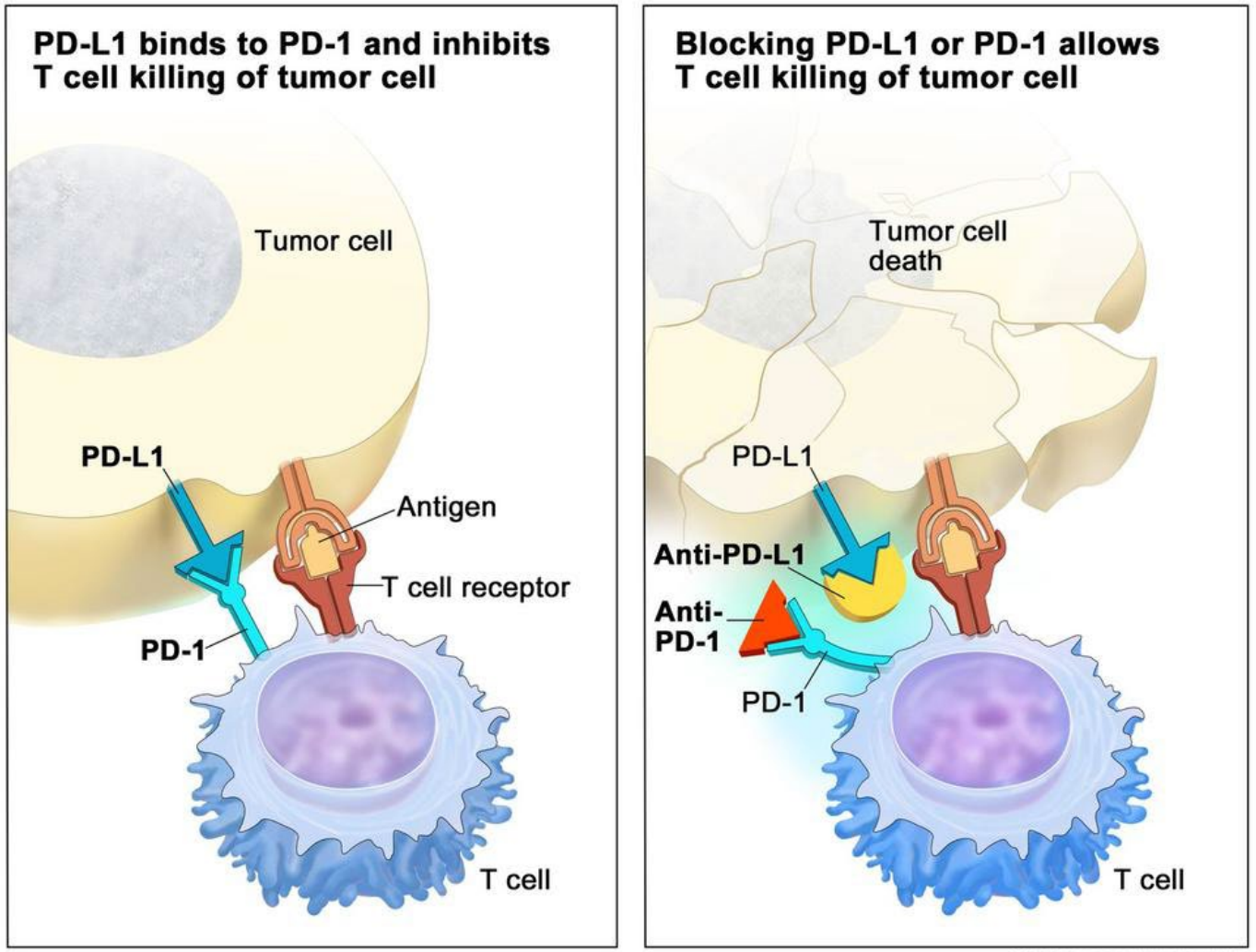



# Immune Checkpoint Inhibitors (ICI)

# Immune Checkpoint Inhibitors

- Monoclonal antibodies that block specific inhibitory molecules involved in regulation of certain immune system checkpoint pathways
- Blocking of checkpoints activates T-cells and increases immune surveillance
- Prevent autoimmunity & Keeps immune system at homeostasis
  - ICIs:
    - cytotoxic T-lymphocyte antigen 4 (CTLA-4)
    - Programmed cell death protein 1 (PD-1)
    - Programmed cell death-ligand 1 (PD-L1)

# Immune Checkpoint Inhibitors (ICI)Mechanism of Action




National Cancer Institute, [Immune Checkpoint Inhibitors – NCI (cancer.gov)]

# Immunotherapy Drugs

| Year of FDA Approval | Drug | Mechanism of Action | Diseases Treated |
|---|---|---|---|
| **2016** | Atezolizumab | Binds to PDL-1 selectively preventing the interaction between PD-1 and B7.1 receptors on T-cells | NSCLC, SCLC, Basal cell carcinoma<br>Melanoma, Urothelial carcinoma<br>Hepatocellular carcinoma |
| **2018** | Cemiplimab- | Binds to PD-1 and blocks its interactions with the ligands PD-L1 and PD-L2, releases PD-1 pathway-mediated inhibition of immune responses | Cutaneous small cell carcinoma<br>Basal cell carcinoma, NSCLC |
| **2016** | Durvalumab | It blocks the interaction between PD-L1 and PD-1 as well as CD80 (B7.1) on T-cells.<br>enhances anti-tumor immune responses, allowing T-cells to kill tumor cells | Urothelial carcinoma<br>NSCLC , SCLC |
| **2015** | Nivolumab | Engineered IgG4 monoclonal antibody.<br>Regulates T cell activation by blocking PD-1 | Advanced melanoma<br>Esophageal, urothelial carcinoma<br>SCC, HCC, HL, HNSCC, NSCLC, RCC |
| **2016** | Pembrolizumab | Engineered IgG4 monoclonal antibody.<br>Regulates T cell activation by blocking PD-1 | Advanced melanoma<br>Cervical cancer, Endometrial cancer,<br>Espohageal carcinoma, Gastric carcinoma<br>Mesothelioma, Breast Cancer<br>Large B-cell lymphoma, Hodgkin lymphoma<br>MSI-high/MMR-deficient/TMB-high cancers<br>NSCLC, CRC, SCC, HCC, HNSCC, RCC, CSCC, SCLC, MCC |
| **2017** | Avelumab | Binds to PD-L1 inhibiting its interaction with the PD-1 receptor prevents the inhibition of CD8+ T cells | Renal Cell cancer<br>Merkel cell carcinoma<br>Urothelial carcinoma |
| **2010** | Ipilumumab | Expressed on the surface of activated T-cells.<br>Blocks cytotoxic T lymphocyte -antigen-4. Inhibits T-cell mediated response | Advance melanoma, Renal cell cancer<br>Hepatocellular cancer, NSCLC<br>Colorectal cancer, mesothelioma |

# ICI (immune-related adverse events)

- Can affect any organ
- Incidence of irAEs higher with ipi (anti- CTLA-4) than monotherapy PD-1 or PD-L1
- irAEs increase with ICIs in combination (w/chemo)
- Reactions can begin during treatment or weeks/months after
- Early identification critical for early intervention
- **advise female patients of childbearing age to use contraception during treatment and up to 5 months after therapy

# CTLA-4 inhibitors

Cytotoxic T lymphocyte associated antigen-4

- **Side effects:**
- **Precautions**:
  - *Monitor* LFTs prior to each dose
  - Neurologic exam before each dose
  - Low grade irAEs= supportive care
  - Moderate ->severe irAEs= drug interruption, high dose steroids→ taper
  - *Baseline* labs: CMP, CBC w/diff, TSH, free T4, LFTs, amylase, & lipase
- **Contraindications:**

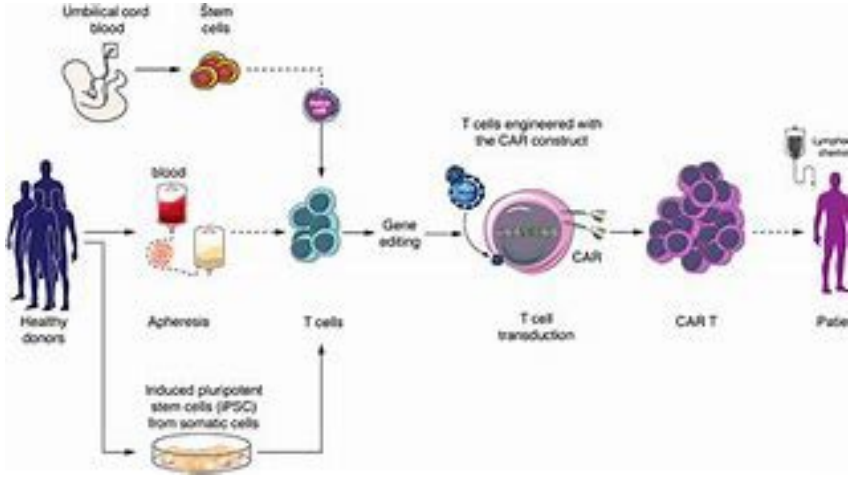
# PD-1 & PD-L1

- PD-1=Expressed when T-cells activated
- PD-L1= expressed on tumor cells and tumor infiltrating immune cells → contributes to inhibition of antitumor immune response in microenvironment

- PD-L1 binds to PD-1 and shuts off the T-cells so healthy tissue is not damaged
- Upregulated--Used by tumor cells to block the immune system

# Things to Consider

- Immunotherapy is a “living drug”; the adaptive immune response may persist for years –thus adverse effects may be seen months after therapy is discontinue
- ICI related symptoms often mimic symptoms of malignancy making evaluation prior to initiation of treatment imperative. (Deligiori, et al. 2020)
- Symptoms of ICI induced endocrine toxicities are diverse and non- specific requiring a high index of suspicion. (Wright, Powers, & Johnson, 2021)




# Chimeric Antigen Receptor T-Cell Therapy (CAR-T)

# CAR-T

- Genetic modification of patient's immune cells to target antigen on malignant cells
- CAR-T cell therapies→
  - Target CD19 on B cells
    - Tisangenlecleucel
    - Lisocabtagene marlaeucel
    - Axicabtagene ciloleucel
  - Target B-cell maturation antigen
    - Idecabtagene vicleucel
    - Ciltacabtagen autoleucel

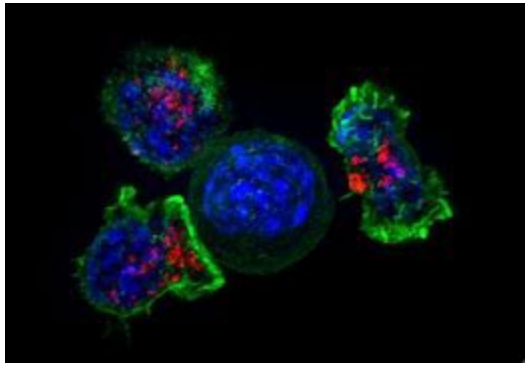
# CAR-T

- **Side effects**: cytokine release syndrome (CRS- grade 3=48%, median onset 3 days, resolves in 8 days), neurotoxicity- grade 3 = 31%, median onset 5-8 days, resolves in 5-17 days); infections (48% grade 3); prolonged cytopenia, infection febrile neutropenia
- **Precautions:**
  - *Consider* seizure prophylaxis for those at higher risk
  - Patient remains near institution for 4 weeks after infusion
  - *Watch* for reactivation of Hep B, C, or HIV
  - NO GM-CSF in first 21 days after infusion
  - *No live* vaccines for at least 6 weeks
  - *Lifetime* monitoring for second malignancies
- **Contraindications:**

# Cancer Vaccine Therapy

# Sipuleucel-T

- **Treatment of**…:symptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer.
- **What is it**: an autologous cellular immunotherapy
- **Target**: Dendritic cells, T cells and B cells linked to CM-GSF
- **Treatment Process**: patients' immune cells (leukapheresis 3 days prior to infusion)→ cells  along with peripheral mononuclear bloods cells are reinfused in patient, 3 doses approximately 2 weeks apart
- **Side effects**: infusion-related reactions (71%), chills, fever, fatigue back pain, joint pain, headache nausea
- **Premedication:** acetaminophen & diphenhydramine; observe 30 minutes after infusion



# Oncolytic Viral Therapy

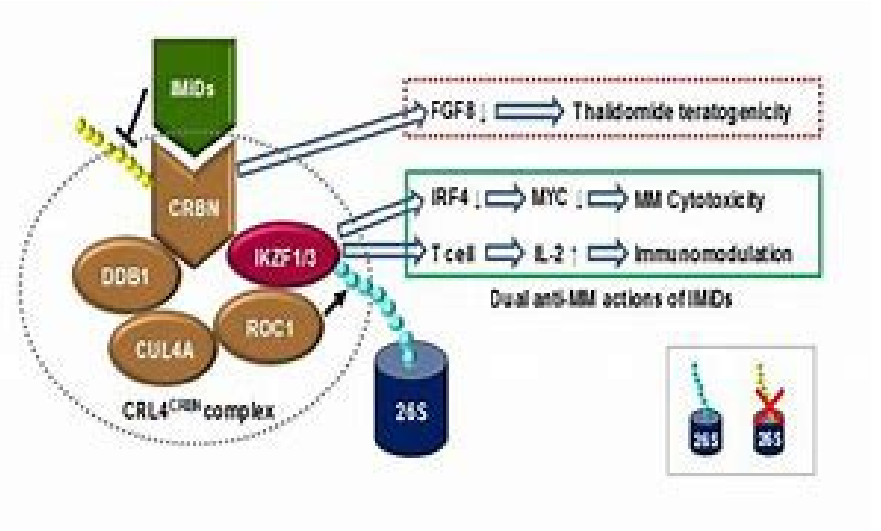
# Talimogene laherparepvec

- **Treatment of**…:locally advanced unresectable cutaneous, subcutaneous, and nodal lesions of recurrent melanoma after surgery.
- **What is it**: genetically modified herpes virus
- **Target**: inject into tumor to produce immune stimulatory protein GM-CSF→lysis of tumor → release of tumor-derived antigens→ antitumor immune response
- **Precautions**: contact precautions
- **Side effects**: flu-like symptoms, pain at injection site, tumor necrosis, open wounds, cellulitis, bacterial infections

# Biospecific T-cells Engagers

# Bispecific T-cell Engagers

- **Treatment of**:Ph-negative relapsed or refractory B-cell precursor ALL
- **What is it:**
  - Blinatumomab (2014)– CD19-directed; B-cell ALL
  - tebentafusp-tebn (2022)– binds toCD3 on T-cells; metastatic uveal melanoma
- **Target**: connect to T cells by binding to an antigen on the T cell and and antigen on a cancer cell
- **Side effects:** fever, peripheral edema, nausea, headache,TLS. hypokalemia, tremor, rash, constipation, neurotoxicities (seizures, speech disorder, confusion,change in consciousness, disorder of coordination/ balance)
- **Precautions**: monitor CBC, AST, ALT, total bili, & gamma-glutamyl transferease at baseline and during therapy




# Immunomodulatory Drugs

# Immunomodulatory Drugs

- **Class:** Thaliomide
  - Lenalidomide- MM, maintenance after HSCT, MCL (relapsed)
  - Pomalidomide- MM,  AIDS related Kaposi sarcoma
- **Mechanism of Action:** not fully understood (immunomodulatory, anti-inflammatory and antiangiogenic)
- **Precautions**:
  - *Do* pregnancy testing 4 weeks prior to txmt and every 4 weeks- regular menses; every 2 weeks-irregular menses; contraception!!; males = latex/synthetic condoms ==during and up to 28 days after treatment
  - CBC  weekly for 8 weeks then monthly
  - *Avoid* drugs that may cause drowsiness
  - *Monitor* for PN
  - *Monitor* LFTs, thyroid function
  - *Monitor* Viral load after 1 and 3 months then every 3 months
- **Contraindication**: pregnancy

# Immunomodulatory Drugs

- **Side effects:** thromboembolism, neutropenia, drowsiness, orthostatic hypotension, somnolence, PN, syncope, bradycardia, Stevens-Johnson syndrome, toxic epidermal necrolysis, seizures, TLS, hypersensitivity rxs, hepatotoxicity w/hepatic failure, 2nd primary malignancies (MDS, AML, nonmelanoma skin cancers, increased viral load, tender lymphadenopathy, low-grad fever, rash, thyroid disorders

# Biosimilars

"not generics"

Similar in potency and toxicity

4-letter suffix (meaningless letters)

Not interchangeable

# References (select)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# Thank you!

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