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# Current Advances in Immunotherapy

## Implications for Navigation and Clinical Management

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Presented at the Oncology Nurse Advisor Navigation Summit
June 2018

# Disclosures

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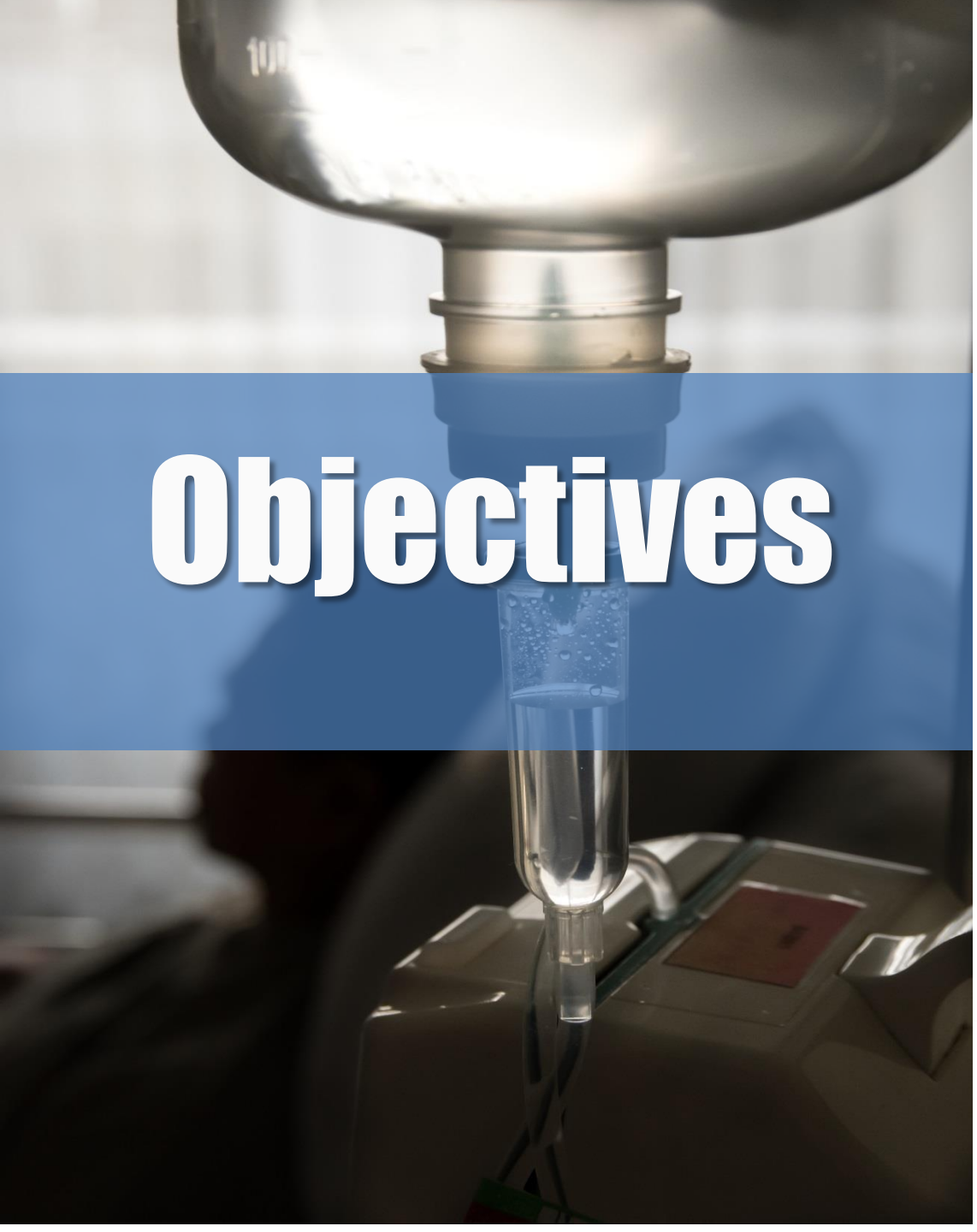
Research funding from
Genentech 2017- Present


Consulting for Premier Inc.
February 2018 - Present



# Objectives

## Objective 01

Provide an overview of the types of immunotherapeutic agents and the unique immune related adverse events (irAEs) associated with these therapeutic approaches

## Objective 02

Discuss the important role of nurse navigators in supporting patients on immunotherapy as they transition within and between healthcare settings

## Objective 03

Identify important and unique considerations for the navigation of patients undergoing immunotherapy

# QUIZ

AVRS Question 1:
How many of you have cared for a patient receiving immunotherapy?

- Yes
- No
- Uncertain

# What Is Immunotherapy and Why Is it Important?

Treatment that maximizes the immune systems innate responses to eradicate cancer

While seemingly new, immunotherapy has been in development for over a century

Coley first tested immunotherapy principles by injecting streptococcal organisms into a patient with inoperable sarcoma, resulting in regression of cancer growth

Immunotherapy has the power to regress and eliminate cancer growth using the body's own immune system

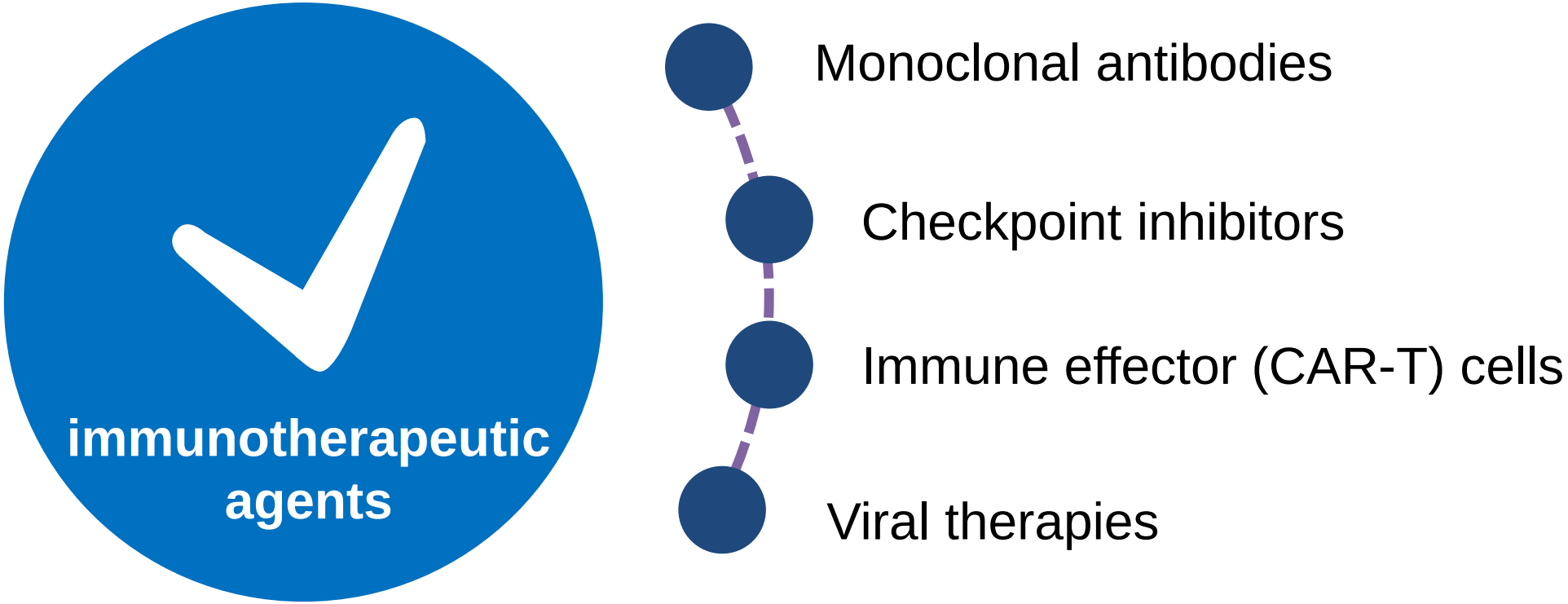
# QUIZ

AVRS Question 2: Which of the following are the categories of immunotherapy?

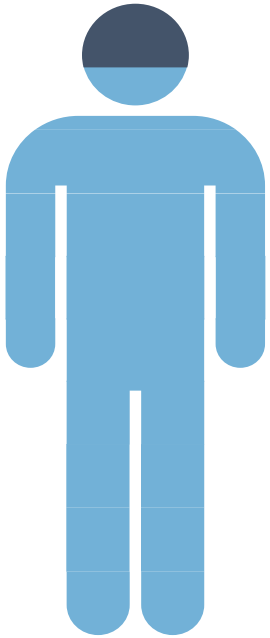
1. Viral oncolytic therapy, checkpoint inhibitors, T-cells, and monoclonal antibodies
2. Monoclonal antibodies, targeted therapies, CAR-T cells, and checkpoint inhibitors
3. Targeted therapies, hormonal therapies, checkpoint inhibitors, and CAR-T cells
4. CAR-T cells, monoclonal antibodies, targeted therapies, and hormonal therapies

# Classes of Immunotherapeutic Agents

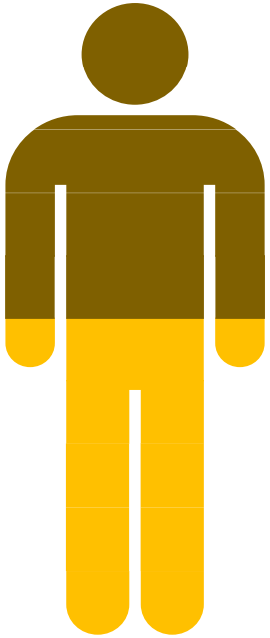
**Immunotherapy is generally defined as consisting of four classes of agents:**



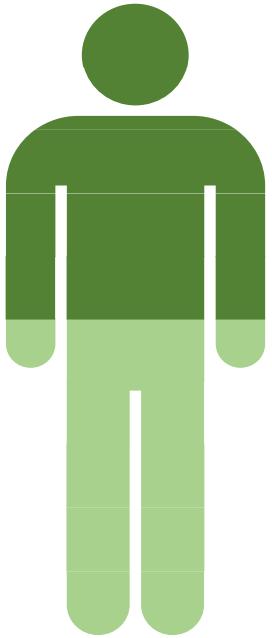
# The Monoclonal Antibodies (mAbs/moAbs)



**anti-VEGF**: (Bevacizumab (Avastin®) a humanized monoclonal antibody that blocks angiogenesis by binding to vascular endothelial growth factor (VEGF) preventing it from uniting with receptors (clinical indications include colorectal cancer, non-small cell lung cancer, and breast cancer)



**anti-CD20**: (Ritumiximab (Rituxan®) a chimeric murine/human monoclonal antibody that binds to B cells expressing CD20 to induce cell death (clinical indications include NHL and CLL)



**anti-EGFR**: (Cetuximab (Erbitux®) a recombinant human/mouse chimeric monoclonal antibody that blocks EGFR from connecting with its ligand EGF reducing malignant cell proliferation (Clinical indications: colorectal cancer and squamous cell head and neck cancer)

Sample Targets

How they work: bind to and block signaling pathways on the surface of cells that leads to inhibition of proliferation, activation of apoptosis, and re-sensitization of malignant cells to cytotoxic agents.

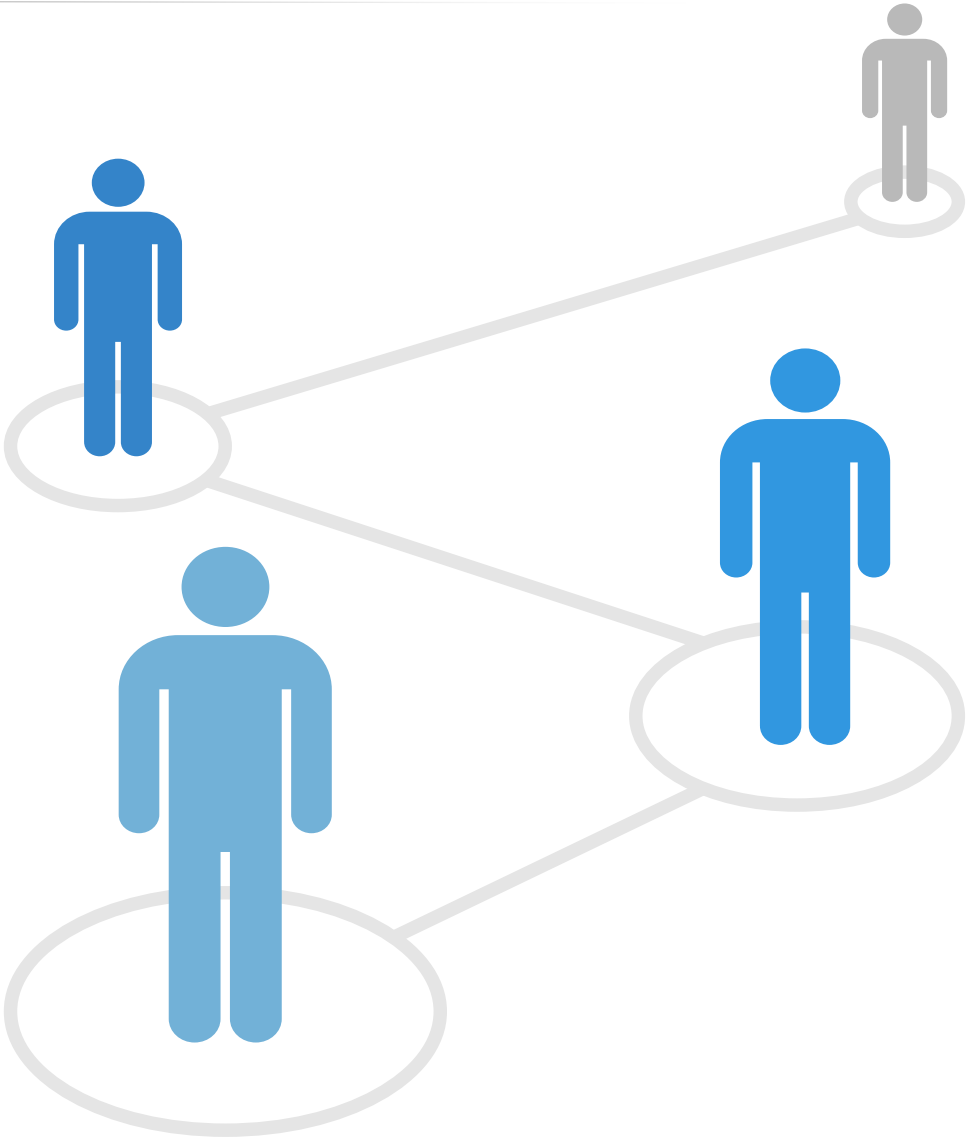
# QUIZ

AVRS Question3: Which of the following cells are the primary beneficiary of checkpoint inhibition?

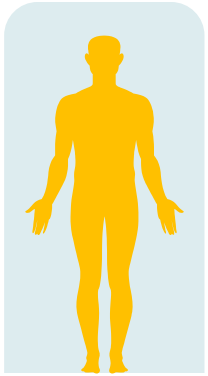
1. B cells
2. NK cells
3. T cells
4. CD34 cells

# The Checkpoint Inhibitors

- Checkpoint inhibitors have been defined as “taking the breaks off the immune system”
  - A series of pathways in the immune system regulate the activation of T-cell responses
  - By inhibiting the immune systems natural checkpoint, this therapeutic approach allows for T-cell activation leading to tumor regression

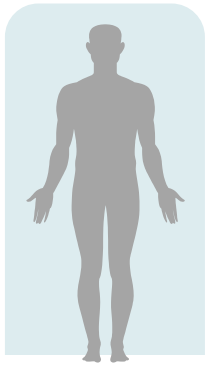


# Checkpoint Targets



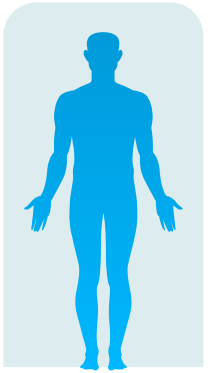
## Anti-CTLA 4

CTLA-4:  CTLA is a T-cell receptor that engages with B7 to prevent overactivation. By inhibiting CTLA-4, T-cell activation is less inhibited, which results in anti-tumor responses (e.g Ipilimumab)



## Anti-PD-1

PD-1: PD-1 binds to the PD-L1 ligand to disrupt immune surveillance and antitumor response.  Inhibiting PD-1 promotes T-cell activation resulting in enhanced tumor surveillance and elimination (e.g. nivolumab, pembrolizumab)



## Anti-PD-L1

PD-L1: A receptor located on the surface of tumor cells which binds to PD-1 and B7 receptors to protect tumor from T-cell mediated immunosurveillance. Inhibition of PD-L1 results in resumed immunosurveillance (e.g. atezolizumab, avelumab, durvalumab)

# QUIZ

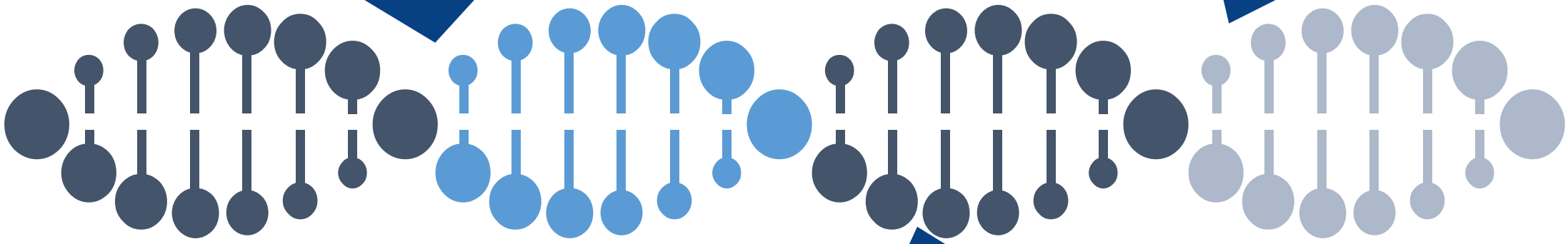
AVRS Question 4: Immune effector cells target which of the following surface antigens?

1. CD19
2. CD24
3. CD72
4. CD90

# Immune Effector Cells

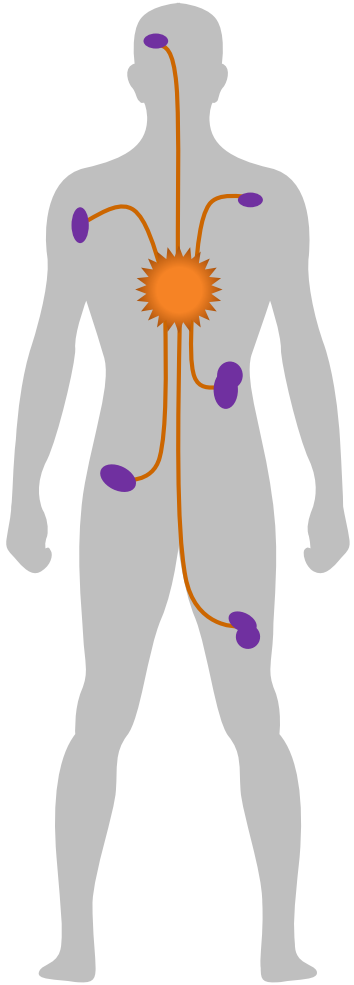
Immune effector cells refer to the class of cellular therapies that involve therapeutically reprogramming T-cells to target tumors.

Chimeric antigen receptor (CAR) T cells target the CD19 antigen which is highly expressed in B-cell malignancies.



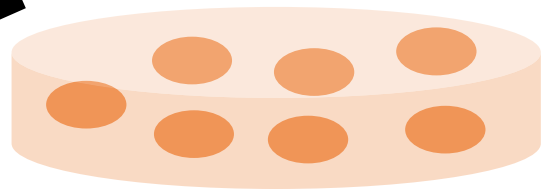
CAR-T cell therapies have been FDA approved for the treatment of relapsed or refractory B-cell acute lymphoblastic leukemia in pediatric and young adult patients (tisagenlecleucel, (Kymriah™), as well as relapsed or refractory large B-cell lymphomas in adult patients (axicabtagene ciloleucel (Yescarta™).

# Chimeric Antigen Receptor T-Cell Therapy: How it works



Blood sample

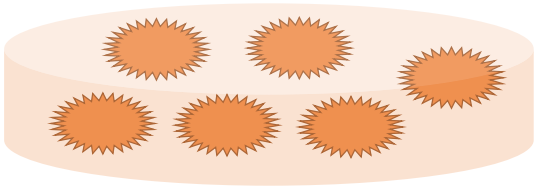
T-cells are collected from the patient through apheresis



T-cells are reengineered in a laboratory

After the reengineering, the T-cells are known as “Chimeric antigen receptor (CAR) T-cells”

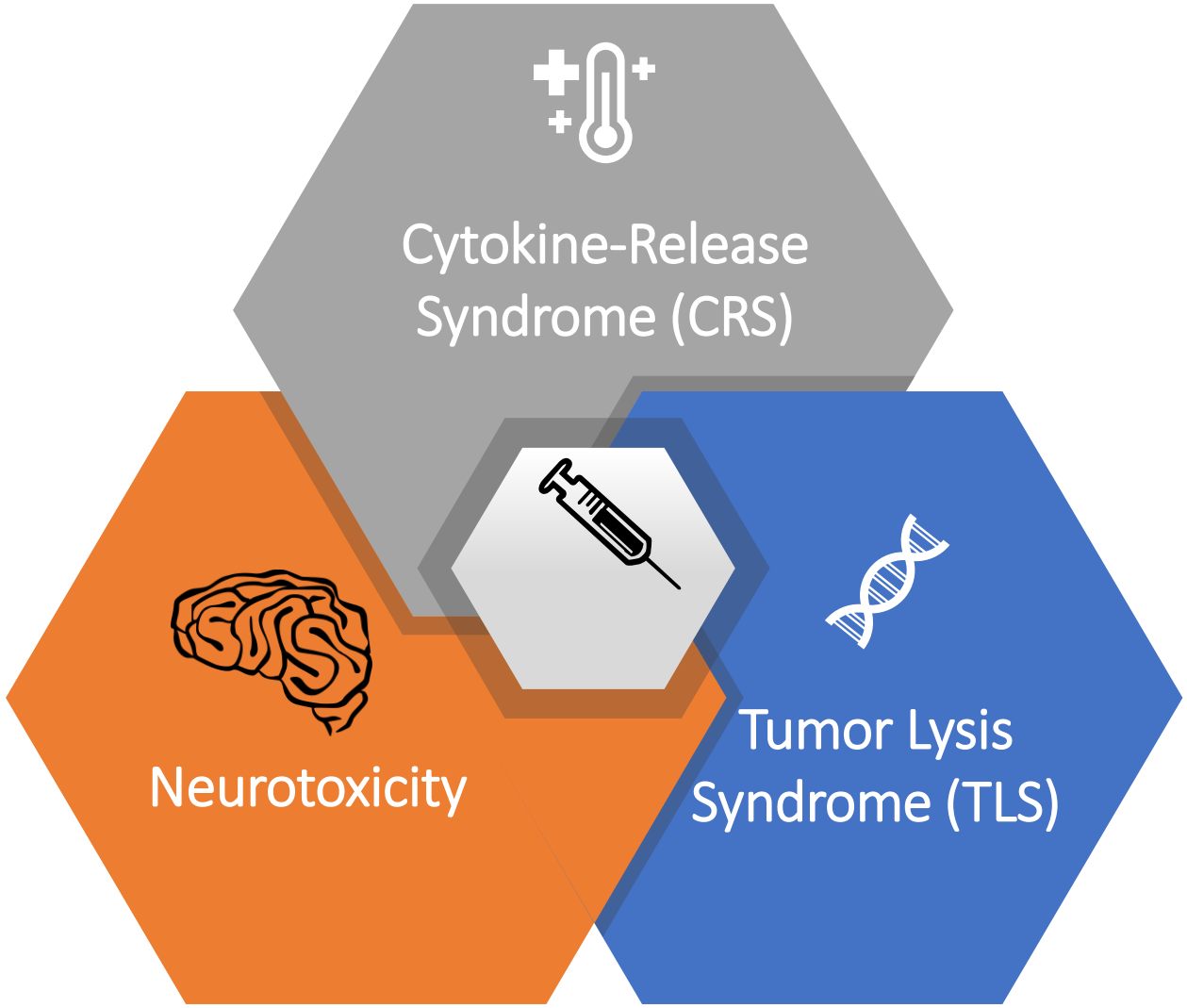
The reengineered cells are then multiplied



In the hospital setting the CAR T-cells are then infused into the patient

Modified T-cells recognize and kill tumor

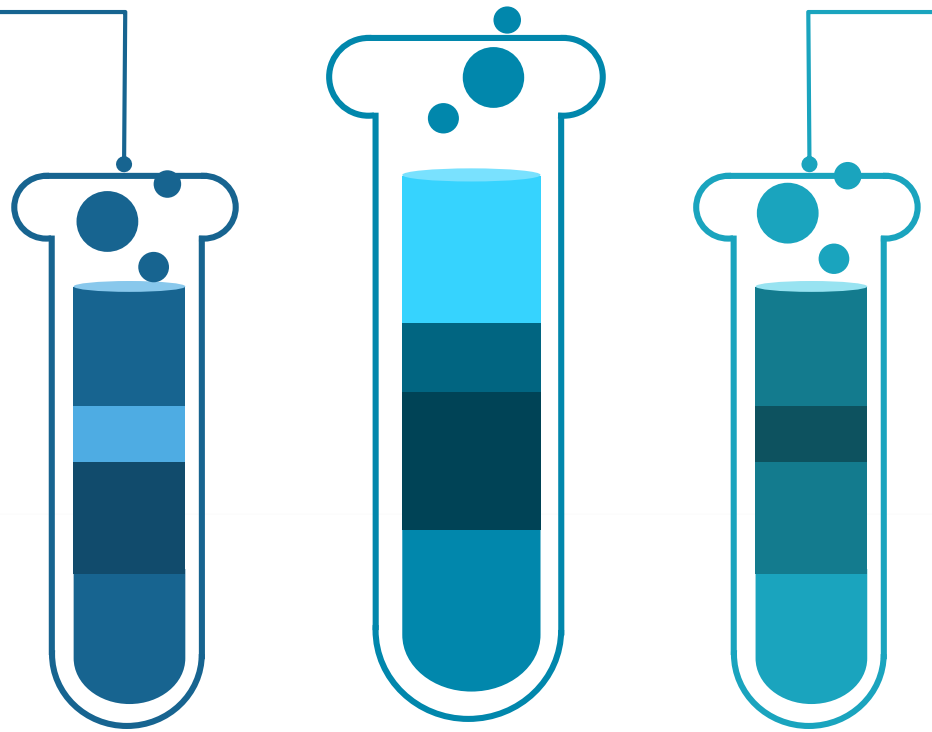
# Side Effects of CAR-T Cell Therapy



# Oncolytic Viral Therapies

The use of viruses, both nonpathogenic (harmless to humans) and pathogenic (requiring genetic modification for use), to induce apoptosis among malignant cells

Currently one FDA approved agent, talimogene laherparepvec (Imlygic®) for the treatment of multiple myeloma



Indications for safe handling as the virus can shed though body fluids, specifically drainage from the injection site

# Benefits and Challenges of Immunotherapy

## Benefits

Remarkable tumor response observed in diverse malignancies

Ability to extend potentially curative treatment to patients

Reduction in standard toxicities observed with chemo or radiotherapy

Potential for enduring immune response

## Challenges

Unique toxicities, some of which may be fatal

Immunotherapy has not proven effective for some tumor types or in some individuals

High cost of treatment

# QUIZ

AVRS Question 6: Many irAEs are caused by excessive release of:

1. T cells
2. B cells
3. Cytokines
4. NK cells

# Immune Related Adverse Events (irAEs)

Immunotherapies have demonstrated both similar toxicity manifestations, as well as unique toxicities, however their underlying pathophysiologic mechanisms are distinct

Immune-related adverse events (irAEs) often result from Tcell activation, resulting in a release of cytokines that cause inflammation to surrounding tissues, both malignant and healthy

irAEs are therefore often inflammatory in nature and can occur in tissues throughout the body

# QUIZ

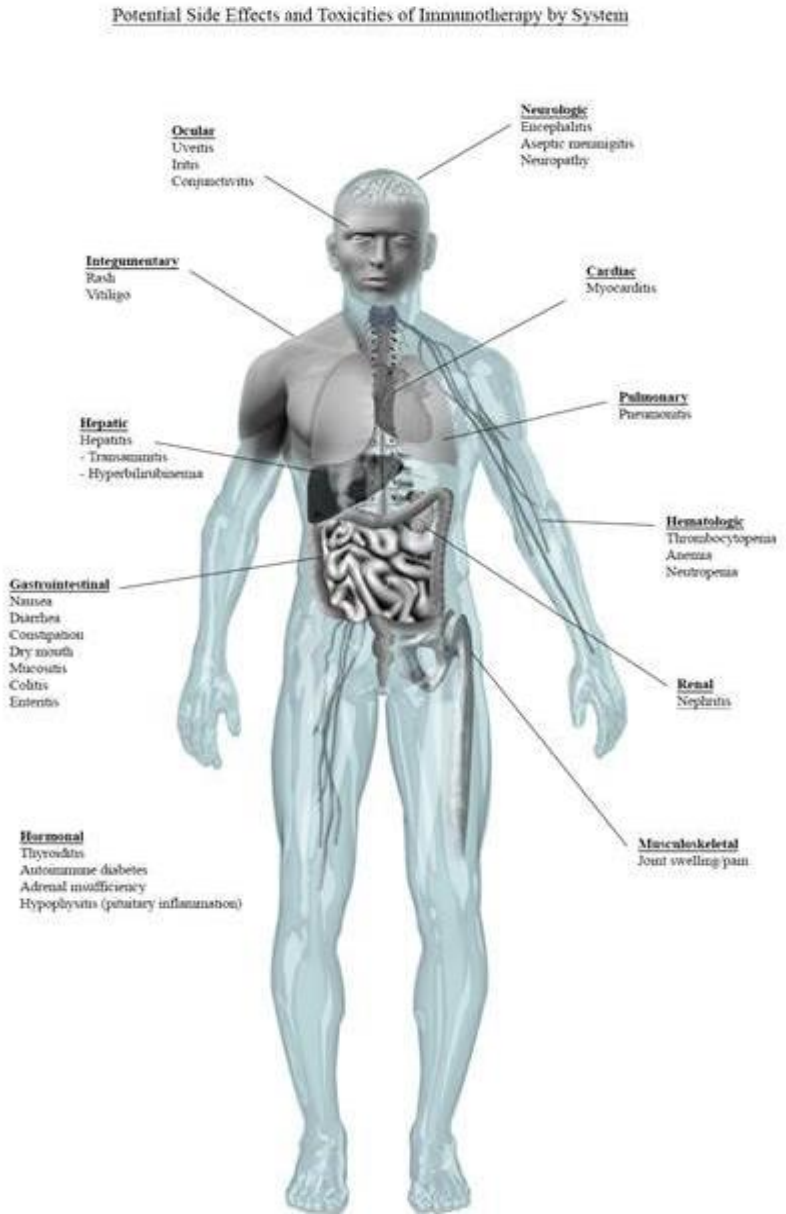
AVRS Question 7: Which of the following is a potentially fatal adverse event of CAR-T therapy?

1. Pneumonitis
2. Colitis
3. Hepatitis
4. Neurotoxcitiy

# Immunotherapies and their common toxicities

- CAR-T cell therapy: Cytokine release syndrome (CRS) and neurotoxicity
- Viral therapies: localized injection site irritation, flu-like symptoms
- Checkpoint inhibitors: Inflammatory responses including pneumonitis, hypophysitis, colitis, nephritis
- Monoclonal antibodies: allergic type reactions and flu-like symptoms

# Toxicities of Immunotherapy by System



# QUIZ

AVRS Question 8: Unlike chemotherapy and radiotherapy induced toxicities, irAEs may require primary management with:

1. Antibiotics
2. Narcotics
3. Steroids
4. Diuretics

# Toxicity Management

- While diarrhea associated with chemo or radiotherapy may be safely managed with loperamide, immune-mediated toxicities resulting in diarrhea often require treatment with steroids to reduce the inflammation causing the toxicity

- It is important for patients and nurses alike to understand that immunotherapy is NOT chemotherapy, and that its side effects may require early identification and unique management to prevent potentially terminal progression

# Why Navigation Is Fundamental to Safe Care for Individuals Receiving Immunotherapy

- Immunotherapy is distinct from other types of cancer treatment, and so are its side effects, so consistent education is pivotal to patients being able to safely advocate
- Many immunotherapy agents are delivered in the ambulatory setting so patients will need care coordination for follow-up in the event an acute toxicity occurs
- Patients may experience long term sequelae that may need immediate and unique management
- Patients should be supported throughout their care transitions to optimize outcomes

# Important Considerations for Individuals Considering Immunotherapy

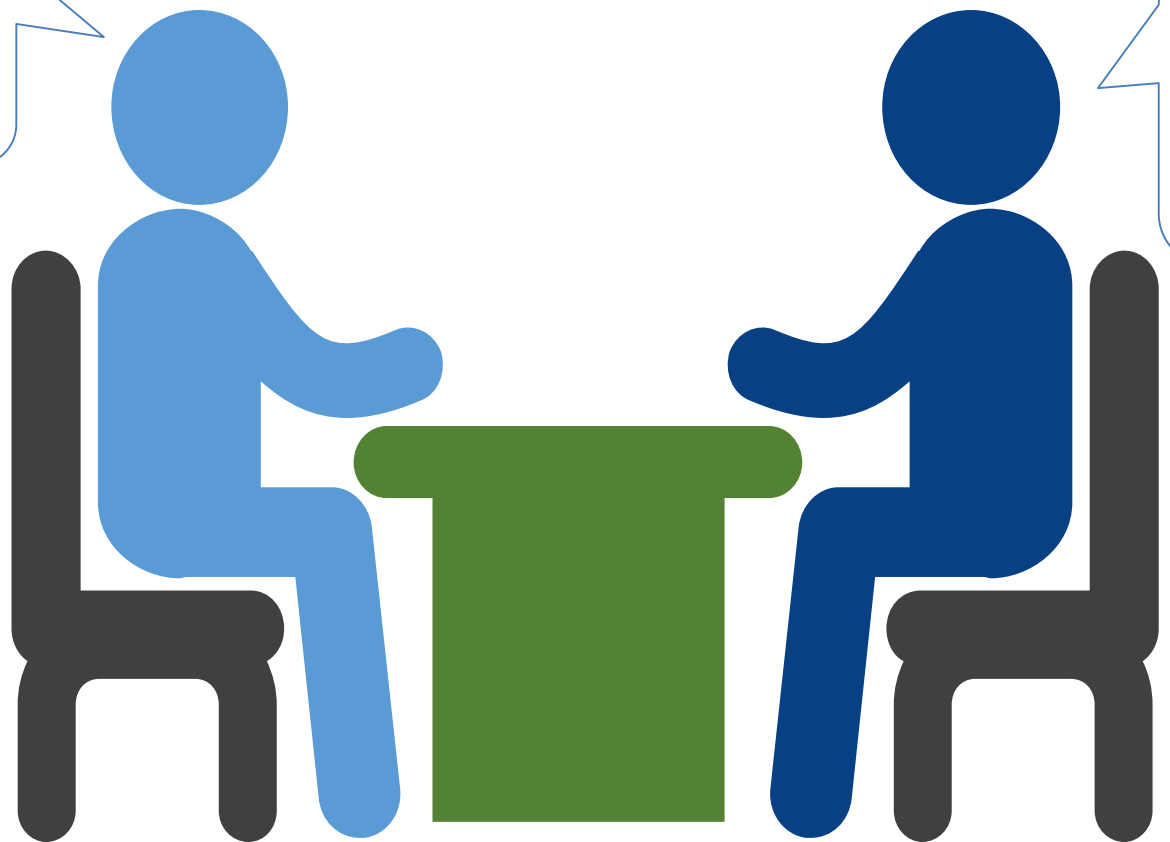
Immunotherapy does NOT work for everyone

Immunotherapy costs can be significant and insurance approval may be challenging

Immunotherapies may result in late effects

Immunotherapy may result in long term immunogenicity

Immunotherapy may be used alone or in combination with other immunotherapeutic agents or cancer treatment types



# Resources to Support Individuals Receiving Immunotherapy & Their Navigators

- Immunotherapy Pocket Card
- Toxicity Guidelines from ASCO/NCCN, SITC, ESMO
- Immunotherapy education from the Oncology Nursing Society

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# Thank you.

# Q & A

What's on your mind?