Two Sides of the Coin of Oncology Nursing:

Digging Deeper and Knowing When to Call for Help When Managing Patients Receiving Bispecific Antibodies

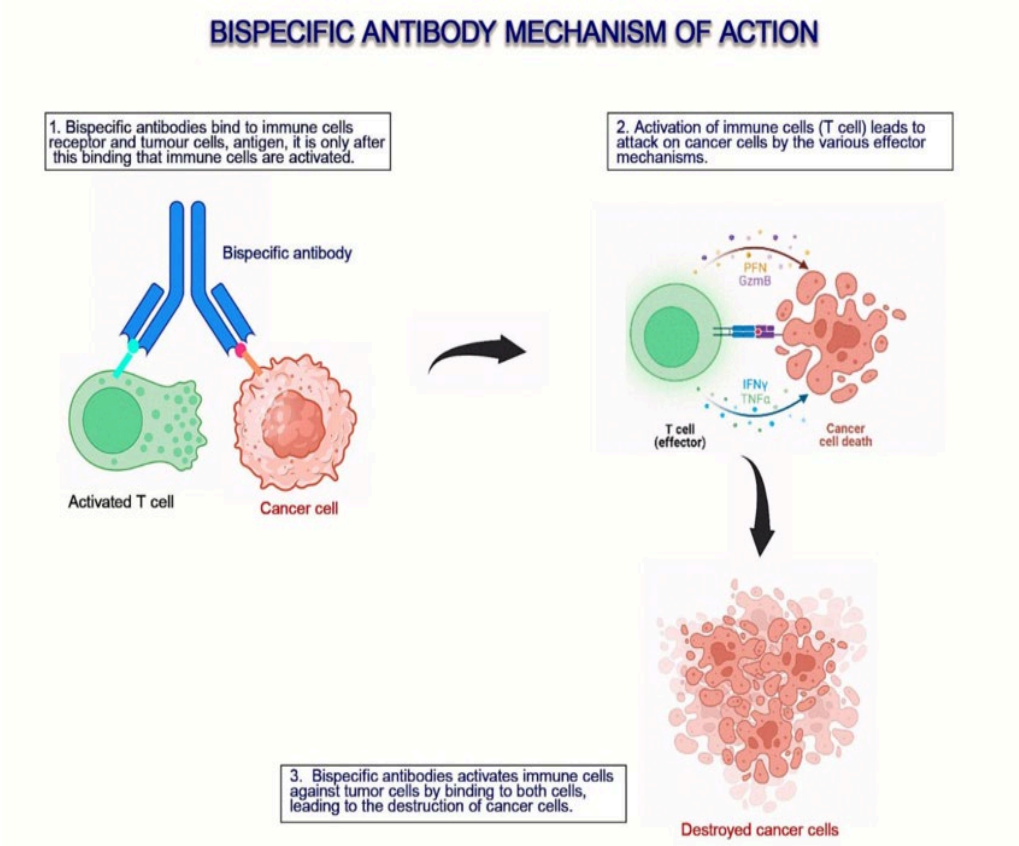
Elizabeth Romano, MSN, AGNP
Hematology Oncology of Indiana

Disclosures

- There are no relevant financial relationships to disclose.

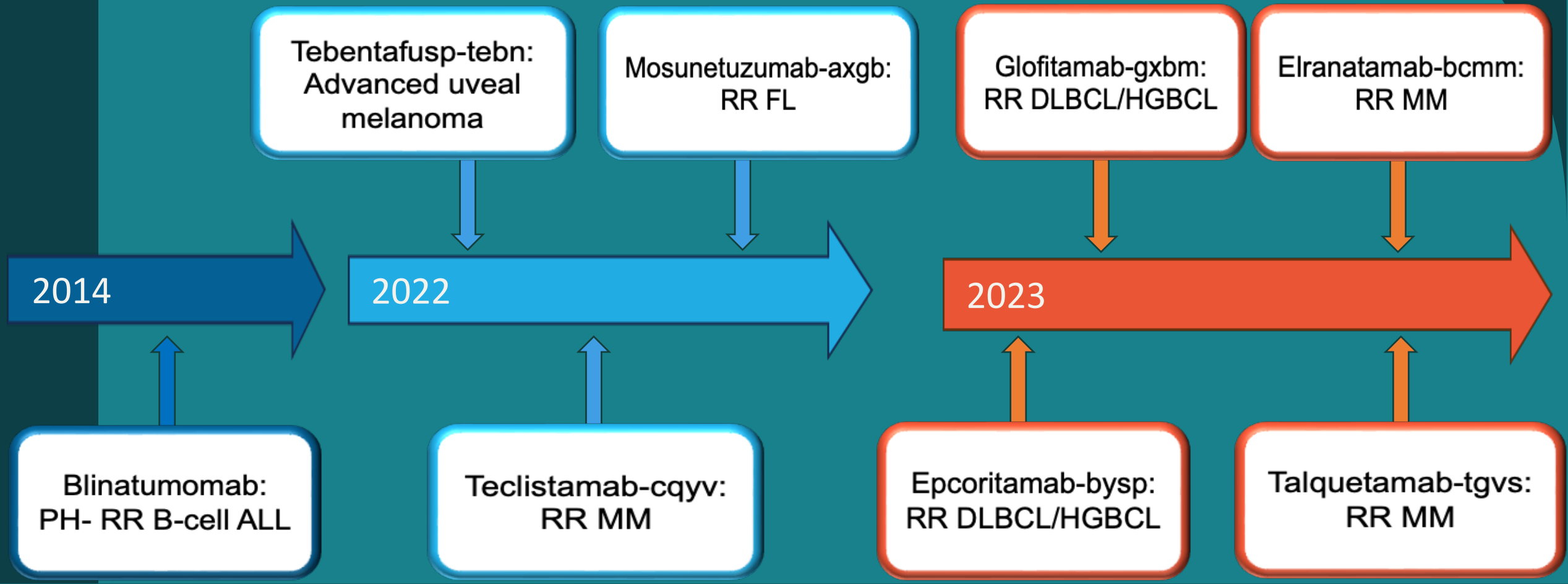
Bispecific Overview

- Bispecific antibodies are monoclonal antibodies with two distinct binding domains that can bind to two antigens or two epitopes of the same antigen simultaneously to effect response.
- Bispecific T cell engagers link endogenous T cells to tumor-expressed antigens, activating the cytotoxic potential of a patient's own T cells to eliminate cancer without genetic alteration or expansion/manipulation of T cells.
- Effective in treating hematological malignancies such as leukemia, lymphoma and multiple myeloma.
- Shown to have 60-83% efficacy in clinical trials.



Einsele H, Borghaei H, Orlowski RZ, et al. *Cancer*. (2020).
Wang, X., Zhao, A., Zhu, J., & Niu, T. (2024).
Zhou S, Liu M, Ren F, Meng X, Yu J. *Biomark Res*. (2021).

Timeline of Bispecifics



ALL: acute lymphoblastic leukemia, DLBCL: diffuse large B-cell lymphoma, FL: follicular lymphoma, HGBCL: high grade B-cell lymphoma, MM: Multiple myeloma, RR: relapsed refractory

Omer MH, Shafqat A, Ahmad O, Alkattan K, Yaqinuddin A, Damlaj M. (2023).

Side Effects

- Related to the mechanism of action for each individual drug.
- Infection, cytopenias, fatigue, musculoskeletal pain, and rash can occur.
  - Check CBC w/ differential, IgG levels, blood cultures as needed
  - May require antibiotics, antivirals, antifungals, or IVIG

- Two serious side effects include:

1. Cytokine release syndrome (CRS): a systemic inflammatory response that results in activation or engagement of endogenous or infused T cells.
2. Immune effector cell–associated neurotoxicity syndrome (ICANS): life-threatening phenomenon related to disruption of blood-brain barrier by inflammatory cytokines released during treatment.

Lee D, et al. Biol Blood Marrow Transplant. (2019).

CRS

- Symptoms of CRS may include fever, hypotension, tachycardia, hypoxia, and chills.
- Can be associated with organ dysfunction (cardiac, hepatic, and/or renal dysfunction).
- Typical onset is 2-3 days after infusion, however, may occur as early as hours after infusion and as late as 10-15 days post-infusion.
- Timing, frequency, severity vary between products.
- Healthcare workers and caregivers must identify the following symptoms that require immediate attention:
  - Dyspnea/hypoxia
  - Fever (100.4F/38C)
  - Very low blood pressure
  - Dizziness/lightheadedness
  - Headache
  - Chills/shaking
  - Confusion
  - Severe nausea, vomiting, diarrhea
  - Severe muscle or joint pain

Lee D, et al. Biol Blood Marrow Transplant. (2019).

Determining Grade of CRS

ASTCT Grading of CRS				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
Fever	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C	Temperature ≥38°C
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
Hypoxia	None	Requiring low flow oxygen	Requiring high-flow oxygen	Requiring positive pressure

- Grade is determined by the most severe event
- Fever is defined as temperature ≥ 38°C not attributable to any other causes. In patients who have CRS and receive antipyretic or anticytokine therapy (e.g., tocilizumab or steroids), fever is no longer required to grade subsequent CRS severity and should be driven by hypotension and/or hypoxia
- Low-flow oxygen: ≤ 6 L/min; low-flow nasal canula, blow-by
- High-flow oxygen: >6 L/min; high-flow nasal canula, nonrebreather mask, or Venturi mask
- Positive pressure: CPAP, BiPAP, intubation and mechanical ventilation

Lee D, et al. Biol Blood Marrow Transplant. (2019).

Management Grade 1 (Outpatient)

Work Up

- Blood culture
- Urine culture
- Chest X Ray
- Cardiac telemetry
- Pulse oximetry

Supportive Care

1. Acetaminophen
2. Dexamethasone 4-12 mg PO/IV
3. IV fluids
4. Start levetiracetam 500 mg PO BID if at higher risk of seizure

*If neutropenic → oncologic emergency, febrile neutropenia

1. Start broad spectrum antibiotics
2. Consider daily GCSF

Treatment

Consider tocilizumab 8 mg/kg (max 800 mg) x 1 for fever lasting >3 days

Lee D, et al. Biol Blood Marrow Transplant. (2019).

ICANS

- Typically occurs concurrently with CRS or shortly after resolution of CRS but can also occur with a delayed onset occurring up to one month after infusion.
- Time of onset, severity, and duration can vary between products.
- Healthcare workers and caregivers must identify the following symptoms that require immediate attention:
  - Altered or decreased consciousness
  - Seizures
  - Difficult speaking and understanding
  - Loss of balance
  - Delerium
  - Confusion
  - Agitation

Rees J. Management of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). (2022).

Determining ICE Score

ICE Encephalopathy Assessment (0-10 scale)		
Orientation	Orientation to year, month, city, hospital	4 points
Naming	Ability to name 3 objects (e.g. point to clock, pen, button)	3 points
Following Commands	Ability to follow simple commands (e.g. “show me 2 fingers” or “close your eyes and stick out your tongue”)	1 point
Writing	Ability to write a standard sentence (e.g. “Our national bird is the bald eagle”)	1 point
Attention	Ability to count backwards from 100 by 10	1 point

Rees J. Management of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). (2022).

Determining ICANS Grade

ASTCT Grading of ICANS				
	Grade 1	**Grade 2**	**Grade 3**	**Grade 4**
ICE Score	7-9	3-6	0-2	0
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient unarousable; stupor or coma
Seizure	n/a	n/a	Any clinical seizure focal or generalized that resolves rapidly or nonconclusive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min); or repetitive clinical or electrical seizures without return to baseline in between
Motor findings	n/a	n/a	n/a	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/ cerebral edema	n/a	n/a	Focal/local edema on imaging	Diffuse cerebral edema on neuroimaging; decerebrate or decorticate posturing; or cranial nerve VI palsy; or papilledema; or Cushing's triad

Rees J. Management of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). (2022).

Management ICANS

ICANS Grade	No Concurrent CRS	Additional Therapy if Concurrent CRS
1	• Supportive care • Add levetiracetam 500 mg PO BID seizure prophylaxis	• Administer tocilizumab 8 mg/kg (max 800 mg) x 1 IV over 1 hour • Consider dexamethasone if refractory to first dose of tocilizumab
2	• Supportive care • Dexamethasone 10 mg IV x 1-2 doses and reassess, every 6-12 hours as needed • Rapidly taper steroid once symptoms improve to grade 1	• Consider ICU transfer • Tocilizumab • If refractory to 1st dose tocilizumab, consider dexamethasone 10 mg IV, every 6-12 hours as needed • Continue until grade 1 or less then taper

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Management ICANS

ICANS Grade	No Concurrent CRS	Additional Therapy if Concurrent CRS
3	• ICU care recommended • Neuroimaging every 2-3 days if symptoms persist • Dexamethasone 10mg IV every 6-12 hours • Continue until grade 1 or less then taper	• Tocilizumab as per grade 1 • If refractory to 1st dose of tocilizumab, give dexamethasone 10mg every 6-12 hours • Continue until grade 1 or less then taper steroids
4	• ICU care, possible mechanical ventilation • Treatment of status epilepticus • High-dose corticosteroids (methylprednisolone 1000mg 1-2 times per day x 3 days), followed by rapid taper	• Tocilizumab as per grade 1 • High-dose corticosteroids (methylprednisolone 1000mg 1-2 times per day x 3 days), followed by rapid taper

Rees J. Management of Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS). (2022).

Frequency of CRS and ICANS

- CRS and ICANS are serious complications
- Incidences reported vary between products
- Most reported cases are grade 1 or grade 2
- Very few, if any, cases reported with grade 3 or grade 4 depending on product

General Management

- Bring patient in for clinic visit for the following side effects:
  - Fever (≥100.4°F/38°C)
  - Mild chills/shaking (rigors)
  - Mild muscle or joint pain or weakness
  - Asymptomatic hypotension
  - Decreased oxygen saturation
  - Headache

General Management

- Send patient to the ER or direct admit for the following side effects:
  - Difficulty breathing
  - Confusion, aphasia, tremors
  - Severe nausea/vomiting/diarrhea
  - Severe muscle or joint pain or weakness
  - Symptomatic hypotension (SBP <90 mmHg or <75% of patient baseline)
  - Severe dizziness/lightheadedness

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