Bispecific Antibodies: A Review for Non-Oncology Clinicians

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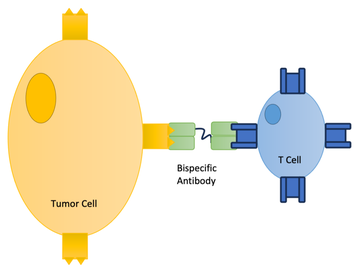
Background

- Bispecific antibodies (BsAbs) have two different binding sites used to engage effector cells and/or cytokines to tumors
- First agent, blinatumomab, received accelerated FDA approval in 2014 for B-cell acute lymphoblastic leukemia
  - 9 approved as of 2024, primarily for heme
  - Emerging evidence for solid tumor and other pathologies
- Unique immune mediated side effect profile, including cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), and cytopenia



Objective

- Summarize structure, mechanism, indications, and major toxicities of bispecific antibodies
- Provide strategies for practical recognition and initial management of treatment-related complications in primary care, emergency, and inpatient settings

Methods

- PubMed literature search for terms related to BsAb history, structure, mechanism, indications, toxicities and management
- Inclusion of relevant articles as of January 2025
- Emphasis on clinically actionable data and recognition and management of toxicities for non-oncology settings

Key Findings

Toxicity	Key Symptoms	Timing
CRS	Fever ± hypotension, hypoxia	Early (1–2 days)
ICANS	Confusion, aphasia, seizures	With/after CRS
Cytopenia	Fatigue, bleeding, infection	Variable

CRS

- Fever to be treated as CRS until proven otherwise
- Reference American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading

→ **Management**
- Mild (Grade 1): Antipyretics, fluids, monitor
- Moderate–Severe (≥Grade 2): Admit, IV fluids, oxygen, ICU if unstable

ICANS

- Reference Immune Effector Cell-Associated Encephalopathy (ICE) scoring system and ASTCT Consensus Grading for Adults

→ **Management**
- Mild (Grade 1): monitor
- Moderate (Grade 2): admit, dexamethasone
- Severe (Grade 3/4): ICU, dexamethasone, antiepileptics as needed

Infection & Hematologic Risk

- Neutropenia, anemia, and thrombocytopenia possible
- PJP, HSV, VZV prophylaxis recommended
- Continue influenza and COVID vaccines

→ **Management**
- G-CSF for neutropenia <1000/mm
- Transfuse if clinically indicated

Clinical Approach

For patients on BsAb therapy presenting with fever, hypotension, hypoxia, or altered mental status consider CRS, ICANS, or pathology secondary to cytopenia.

- Initial Management:
  - Obtain vitals, CBC CMP, lactate, infectious workup
  - Start IV fluids and oxygen if needed
  - Consult oncology
- Admit for:
  - Neurological symptoms
  - Oxygen requirement
  - Hemodynamic instability

Conclusion

- BsAbs are rapidly expanding class of immunotherapies
- Patients on BsAb therapy will present with increasing frequency to non-oncology settings, including primary care, emergency, and inpatient settings
- Most dangerous complications are CRS, ICANS
- Early recognition and supportive care are critical
- Non-oncology providers should have a low threshold to escalate care and consult oncology for these patients

Disclosures

- None at this time