Let's Bispecific About T-Cell Engager Therapies Handout

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Bispecific T-cell engagers are antibodies that are capable of binding two antigens at the same time. This allows T-cells and cancer cells to be brought into close proximity so that T-cells can become activated to kill the tumor cells.

The use of bispecifics for hematologic malignancies is rapidly expanding. In 2022 and 2023, six bispecific T-cell engagers have been FDA approved for hematologic malignancies based on phase I/II trial data. These agents are recommended in the NCCN guidelines for patients with relapsed or refractory disease. In general, overall response rates to bispecifics are very promising for patients with relapsed or refractory disease that have already undergone multiple lines of therapy.

Agent	Indication	Target	Route
Blinatumomab	ALL	CD19	IV continuous infusion
Teclistamab	Multiple myeloma	BCMA	Subcutaneous
Talquetamab	Multiple myeloma	GPRC5D	Subcutaneous
Elranatamab	Multiple myeloma	BCMA	Subcutaneous
Epcoritamab	DLBCL	CD20	Subcutaneous
Glofitamab	DLBCL	CD20 bivalent	IV intermittent infusion
Mosunetuzumab	Follicular lymphoma	CD20	IV intermittent infusion

Common toxicities:

All of the bispecifics are associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Each agent has different strategies to mitigate and manage CRS and ICANS such as giving the patient premedications, utilizing a step-up dosing strategy, and hospitalizing the patient for strict monitoring.

CRS is non-antigen specific inflammation that occurs when a large number of immune cells become activated and release cytokines.

Symptoms: hallmark sign of CRS is a fever.[1,2] Other symptoms include a rash, myalgias, rigors, headache, and flu-like symptoms. More severe symptoms include hypotension, hypoxia, disseminated intravascular coagulation, and multi-organ failure. CRS associated with bispecifics is typically much less severe than CRS associated with CAR-T.

ICANS:[3] Neurologic symptoms that occur after the use of immunotherapy. The mechanism is not fully understood.

Symptoms: headache, tremors, fatigue, aphasia, seizures, cerebral edema, coma

CRS and ICANS Characterization for Each Bispecific[4–11]

	CRS					ICANS		
	Any grade (%)	Grade 3-4 (%)	Median time to onset	Median duration	Patients with >1 CRS event (%)	Any grade (%)	Grade 3-4 (%)	Median time to onset
Blinatumomab	14.2	4.9	NR	NR	NR	NR	NR	NR
Teclistamab	72.1	0.6	2 days	2 days	33.3	3.0	NR	3 days
Talquetamab	77	3	2 days	2 days	31.9	NR	NR	NR
Elranatamab	56.3	0	2 days	2 days	15.1	3.4	0	2.5 days
Epcoritamab	49.7	2.5	0.8 days	2 days	16	6.4	0.6	NR
Glofitamab	65.6	2.6	13.8 hrs	30.5 hrs	34	8.4	3	NR
Mosunetuzumab	44	2	5-27 hrs	3 days	NR	5.5	0	NR

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