Two for the Price of One: Review of Bispecific Antibodies in Lymphoma & Multiple Myeloma

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Objectives

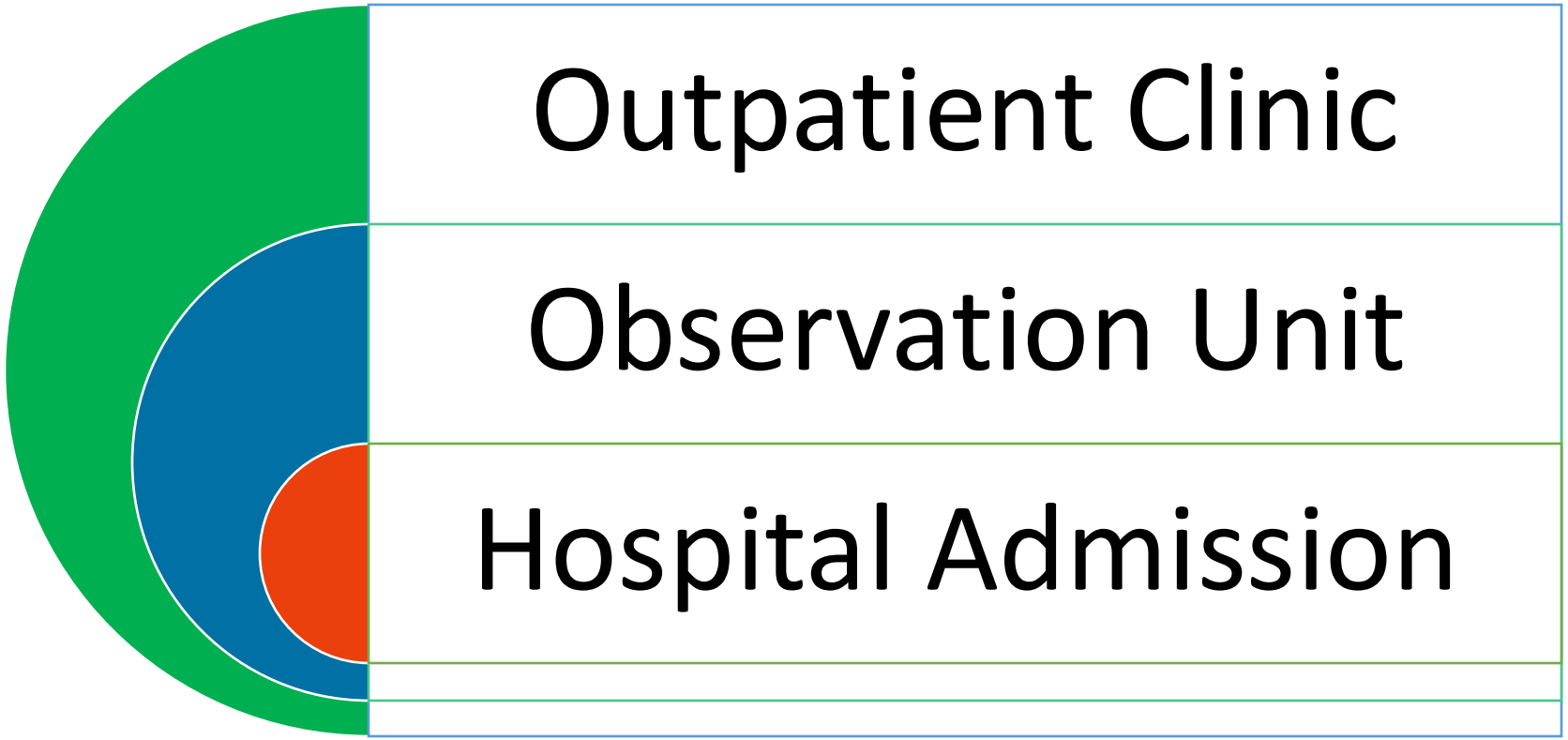
- Explore available Bispecifics (BsAbs) at different institutions
- Understand common supportive care practices for patients receiving BsAbs
- Examine common barriers and future direction with BsAbs

BsAbs in Hematology – Overview

BsAbs	Targets	Disease	Indication
Blinatumomab^	CD19; CD3	Acute Lymphoblastic Leukemia	MRD-positive CD19-positive; R/R CD19-positive
Teclistamab-cqyv	BCMA; CD3	Multiple Myeloma	R/R with at least four prior lines of therapy (including proteasome inhibitor, immunomodulatory agent, and an anti-CD38 mab)
Elranatamab-bcmm			
Talquetamab-tgvs	GPRC5D; CD3		
Mosunetuzumab-axgb	CD20; CD3	Follicular Lymphoma	R/R with at least two prior lines of therapy
Epcoritamab-bysp	CD20; CD3	Diffuse Large B-cell Lymphoma Follicular Lymphoma	
Glofitamab-gxbm	CD20; CD3	Diffuse Large B-cell Lymphoma	

**Minimal residual disease (MRD); Relapsed or refractory (R/R); B-cell maturation antigen (BCMA); G protein-coupled receptor class C group 5 member D (GPRC5D)
^FDA approved in both adults and pediatric patients

What setting are BsAbs agents given/started in each institution?



What baseline laboratory data is collected prior to initiation of BsAbs therapy?

CBC	CMP	IgG
CD4	CMV	TLS Labs

What infectious prophylaxis is initiated upon BsAbs administration?

Microbial	Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
Bacterial	• Levofloxacin 500 mg daily when ANC <500 and continue until neutrophil recovery	• Ciprofloxacin 500 BID OR • Cefdinir 300 BID (if cipro contraindication) until ANC recovery	• Levofloxacin 500 mg daily with start of treatment and continued until neutrophil recovery or longer case by case basis
Fungal	• Fluconazole starts on admission and continues until neutrophil recovery • Mold active agents considered in certain scenarios	• Fluconazole when ANC <500 and continue until neutrophil recovery • Rarely mold coverage, unless prolonged steroid use/previous history of fungal infection	• Fluconazole only when ANC <500 and continue until neutrophil recovery • Only consider mold active agents when prolonged neutropenia
Pneumocystis jirovecii pneumonia (PJP)	• TMP-SMZ 1 DS tablet MWF OR • Atovaquone 1500 mg daily started on admission and continued until CD4 >/= 200/mm3	• CD4 count at baseline, then every 3 months • TMP-SMZ 1 DS MWF only if CD4 <200 until recovery • Atovaquone/Pentamidine as alternative, if low counts with TMP-SMZ	• TMP-SMZ 1 DS tablet MWF or atovaquone 1500 mg daily starts on admission throughout BsAb therapy • Pentamidine as alternative

What infectious prophylaxis is initiated upon BsAbs administration?

Microbial	Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
Hepatitis B Virus (HBV)	• Tenofovir 300 mg daily or entecavir 0.5 mg daily if HBsAg or HBcAb-IgG (+)	• Monitor for HBV reactivation • Only continue prophylaxis if prior CART/Auto or B-Cell depleting therapies	• Tenofovir 300 mg daily or entecavir 0.5 mg daily if HBsAg or HBcAb-IgG (+)
Herpes simplex virus (HSV)	• Acyclovir 400-800 mg BID or valacyclovir 500 mg BID starts on admission and throughout therapy	• Acyclovir 400 BID or valacyclovir (≥ 365 days post CART/AUTO) • Acyclovir 800 BID or valacyclovir 500 BID (≤365 post CART/AUTO)	• Acyclovir 400-800 mg BID or valacyclovir 500 mg daily-BID starts on admission and throughout therapy
Cytomegalovirus (CMV)	CMV IgG checked at baseline during initiation of BsAb. Then PCR checked as indicated for fevers, GI or pulm complaints.	CMV at baseline (if not available), then as clinically indicate. Prophylaxis not indicated	CMV at baseline (if not available), then as clinically indicate. Prophylaxis not indicated

What is the role of IVIG Replacement to prevent infectious complications?

- **Patients on bispecific antibodies with hypogammaglobulinemia should be aggressively managed with IVIG replacement**

How does the oncology team manage CRS/ICANS?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• Guideline for CRS/ICANS management was created by pharmacist/physicians	• Guideline for CRS/ICANS management was created by pharmacist/physicians • Recent with solid tumor agent, nursing guideline for management guided by BsAb-specific supportive plan with all medications needed	• Guideline for CRS/ICANS management was created by pharmacist/physicians

- **Individualized approach for individual drugs**

What is the typical LOS of your BsAbs patients?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)

Depends on BsAb
 	
• Myeloma BsAbs:
  • Teclistamab/Talquetamab: step-up dosing schedule is days 1, 3, 5 and discharge 48 hours after final step-up dose (7 days)
  • Elranatamab: Discharged 24 hours after second ramp up
 	
• Lymphoma BsAbs:
  • Epcoritamab (LBCL): Admit on C1D15 for 24 hours
  • Glofitamab: Admit on C1D8 for 24 hours, if any CRS then readmit for C1D15 dose as well
	Depends on BsAbs
	
	• Myeloma BsAbs: Admission duration is patient specific (~7-9 days)
	• Lymphoma BsAbs:
	  • Epcoritamab (LBCL): Admit C1D15 for 24-hour observation
	  • Glofitamab: C1D8 24-hour observation and readmit for D15 if pt experiences CRS with D8 dose
	  • Mosunetuzumab – all doses outpatient
		• Depends on BsAb
		• Admission may be extended as clinically indicated
		
		• Myeloma BsAbs:
		  • Teclistamab or Talquetamab: step-up dosing schedule is days 1, 3, 5 and discharge 48 hours after final step-up dose (7 days)
		  • Elranatamab: Discharged 24 hours after second ramp up dose

Plan for outpatient administration: • Most BsAbs inpatient per package insert recommendation except Mosunetuzumab • Infusion/injections of BsAbs occur at MCI infusion center • Goal to administer first therapeutic dose (step-up dose #3) as outpatient in patients with low risk of CRS	OP Admin (IPOP area): • Usually re-starts of therapy if previous low CRS and patient deemed fit (patient specific) • Moving towards IP/observation admission with solid tumor and in near future other agents	Process for outpatient administration: • Myeloma BsAb typically follow label recommendation • First 0.8 mg/kg talquetamab (biweekly schedule) given as outpatient with infusion center visit 24 and 48 hours • Subsequent doses outpatient

How often dose nursing team monitor for BsAbs toxicity?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• RN staff monitor for symptoms of CRS/ICANS every 4 hours • ICE score performed every shift	• RN staff monitor for symptoms of CRS/ICANS every 4 hours	• RN staff monitor for symptoms of CRS/ICANS every 4 hours (including vitals and ICE assessment) • Long term complications are monitored at each infusion center visit and provider visits

How are patients triaged when CRS/ICANS occurs in the inpatient and outpatient setting?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• Keep 2 vials of tocilizumab on hand for each patient • "Smart-zone" alerts flag patients on BsAb • Tocilizumab order set entered as PRN to avoid delays in administration • Over-night APPs facilitate around the clock monitoring for CRS/ICANS • Tocilizumab doses are approved by the physician on BMT service	• No tocilizumab vial procured for patients receiving BsAbs <u>Inpatient:</u> • Order set inpatient for CRS/ICANS management • On call fellow manages overnight events/escalates to attending as needed. Usually, one dose approved overnight then other doses reviewed in AM <u>Outpatient:</u> • Patient's call triage number which is then transferred to the on-call provider for further guidance on their symptom management • All patients have an active alert on EPIC to call Heme/ONC when admitted to the hospital	• No tocilizumab vial procured for patients receiving BsAbs • Individualized approach in line with institutional SOP • Outpatient 24 hour on call • Patient Education including patient wallet card (helpful for admission to outside hospital)

What role does pharmacy and/or nursing play regarding patient counseling?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• Nurse educator, APRN and physician provide education in the pre-admission visit and at each appointment • Inpatient nurses, pharmacist and APRN provide education on an as-needed basis • Inpatient pharmacist educates at discharge	• APRN in the pre-admission visit, and at each appointment visit • Oncology TOC pharmacist at discharge • New process with solid tumor BsAb with pharmacist counseling before admission	• Outpatient pharmacist provides education prior to admission and is available as a resource throughout outpatient treatment • Inpatient pharmacist provides education on admission

How are BsAb and CART sequenced at each institution?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• Previous lines of therapy • Performance status • Social support, care taker, transportation • Patient preference • Patient eligibility (disease status/response to previous agents)	• Data reviews completed to review patients are good candidates • Previous lines of therapy, current target marker for BsAb therapy (CD20, BCMA, CD3), aggressiveness of the disease • Consider social support, caretaker, transportation • It depends on previous lines of therapy or psychosocial social support • Preference of the patient, time toxicity (frequent appts, prolonged hospitalization, follow up labs, imaging)	• Patients are screened for eligibility for CAR-T based on clinical and social factors • BsAbs are typically able to be used in a wider range of patients with poor PS, comorbidities, etc. • Early data suggests patients who get early CAR-T may still have a response to bispecific antibodies later in time

What obstacles does your team currently face with BsAbs therapy?

Baptist Hospital of Miami	Memorial Hospital West	University of Miami (Myeloma)
• Approval of BsAb as outpatient to assure continuation of therapy • Approval of necessary infectious prophylaxis medications	• Outpatient authorization by the time of the scheduled inpatient admission • Imperative to request OP and IP approval at the same time, to ensure pt can receive BsAb therapy once they are discharged. • Utilize a pre-services auth email group for updates on OP approval prior to admission • Epic group chat to inform authorization team of new BsAb therapy	• Imperative to request OP and IP approval at the same time, to ensure pt can receive BsAb therapy once they are discharged. • Patient access to safe use of therapies in areas away from academic medical centers

Questions

- Thank you for your attention