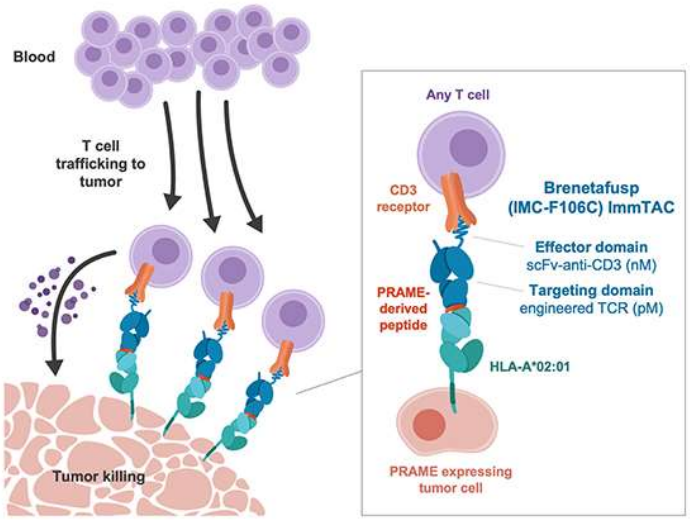
Brenetafusp (non-FDA approved)

- Targets PRAME
  - Preferentially Expressed Antigen in Melanoma
  - High PRAME levels seen in melanoma (>90%)
  - Phase ½ trial brenetafusp had promising efficacy and few adverse events
  - Phase 1 study (IMC-F106C-101)
    - DCR was 56%
    - 28% pts showed tumor reduction
    - 42% pts showed molecular response



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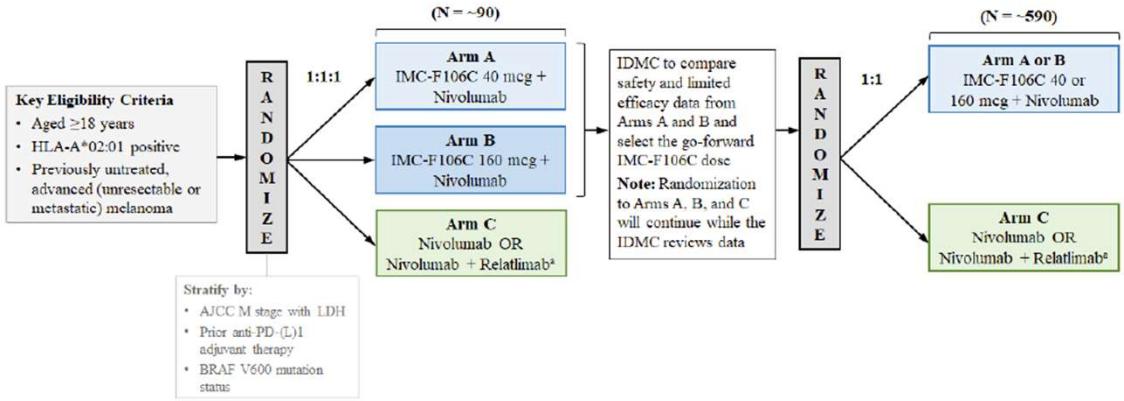
Immunocore Trial: Phase 3

PI: Dr. Domingo Musibay



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Financial "Toxicity"

- Blinatumomab $154k per cycle (28 days)
- Annual Cost: Epcoritamab $211k, Glofitamab $347k Tesclistamab $372k
- Total cost of Bispecifics vs CAR T still being assessed (outpatient utilization will affect this)

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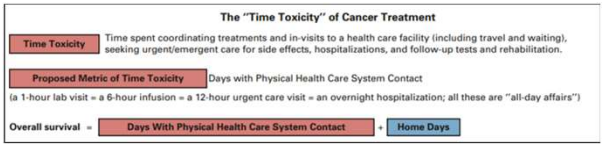
Financial "Toxicity"



- Move Bispecifics ramp-up to outpatient or home hospital setting?
  Example: >$165K billed to Medicare for teclistamab IP ramp-up (Medicare reimbursed $23.5k for DRG)
- Use dexamethasone ($1.18/10 mg IV vial) vs tocilizumab ($2500/800 mg IV dose) for CRS?
- Prioritize fixed duration therapy?

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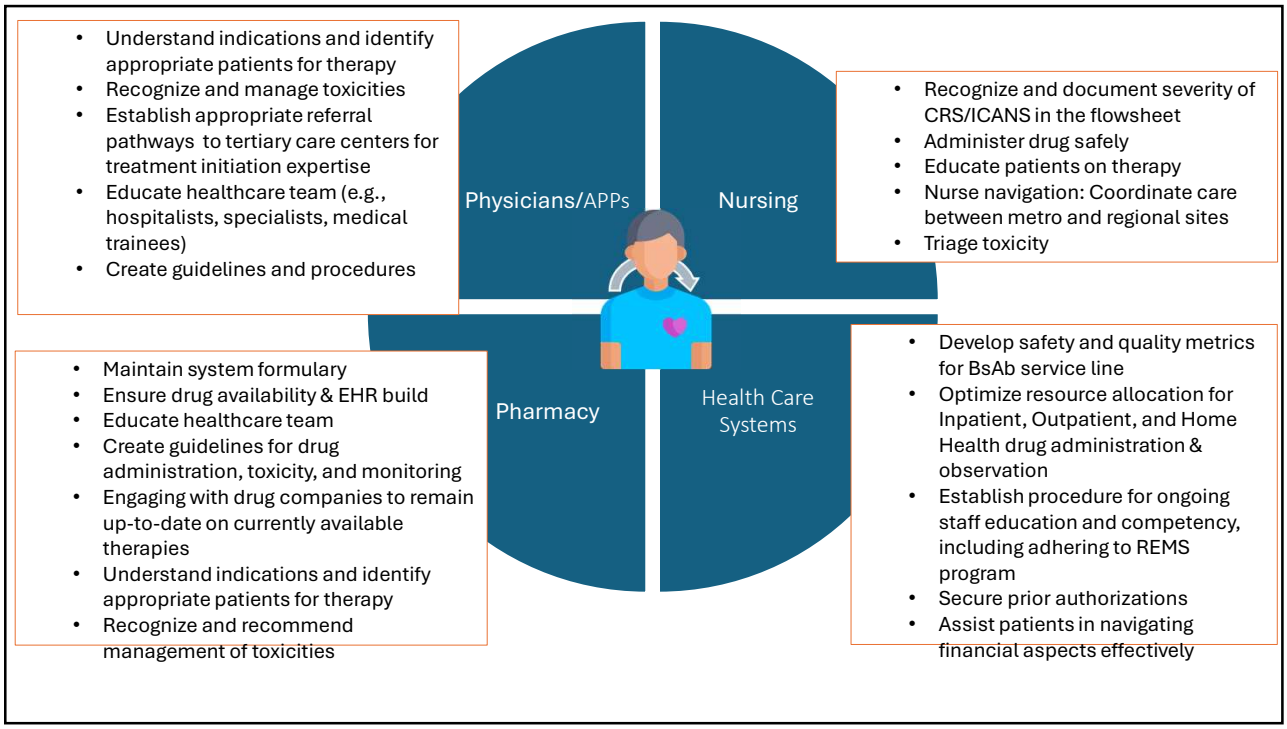

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Teclistamab (Tecvayli®) Tip Sheet

Indications	R/R multiple myeloma, after ≥4 lines of therapy
Target Antigens	BCMA on plasma cells
Black Box Warnings/REMS	REMS: ICANS and CRS. **Provide patient w/ wallet card** • Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during and for 48 hours after completion of TECVAYLI step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms until neurologic toxicity resolves
Dosing	Step-up (subcutaneous): • Day 1 step-up dose = 0.06 mg/kg • Day 4 step-up dose = 0.3 mg/kg • Day 7 treatment dose = 1.5 mg/kg Wait 2-4 days in between the first 3 doses (up to 7 days to allow for toxicity resolution) Maintenance Dose: 1.5 mg/kg weekly until progression/toxicity (may switch to every 2 weeks if patient has achieved and maintained a CR for ≥6 months)
Post Dose Monitoring Requirements	Administer the first 3 doses in the **inpatient unit** – expect at 6-day hospitalization at minimum (discharge on day 7) – administer doses on days 1,3,5 (≥48 hours after each dose). • If the patient experience Grade ≥2 CRS, hospitalize for subsequent dose.
Dose Delays	If teclistamab is held for >7 days, see PI for restarting after dose delay
Pre- and Post-Medications	Administer dexamethasone, diphenhydramine, and APAP prior to first 3 doses, for dose delay, and then as needed if patient experiences CRS (see PI)
Inpatient Observation CRS and ICANS post Dose Monitoring Recommendations	Baseline vital signs (temperature, pulse, & respiration, BP, O2 sat) upon transfer from AHCI to inpatient unit and every four hours thereafter until discharge. CRS/ICANS • Monitor every 8-hour shift • Increase monitoring to every 2-4 hours with symptoms • Use **Neurotoxicity/CRS Assessment flowsheet** for scoring • Ensure baseline writing sample is available in the chart – should be titled, "ICE Score Handwriting Assessment" • The handwriting sample shall consist of the same simple sentence, such as "Jack walks the dog to the lake." The patient shall write this sentence during every ICANs check, and the handwriting should be compared to the original scanned copy • Nursing Shift Summary Note - may use **.CRSICANSSCORE** - to pull last score into your note. Utilize bispecific hypersensitivity order set for reactions
CRS Frequency & Onset (Median)	Overall CRS incidence: 72% • Grade 3 CRS occurred in 0.6% • Recurrent CRS occurred in 33% Timing of CRS • 42% after dose 1, 35% after dose 2, 24% for dose 3, <3% after dose 3 • Time to onset was 2 days (range 1-6) with a median duration of 2 days (range: 1 to 9)

Visit Allina AKN for managing toxicity associated with Bispecific T-Cell

Allina Resources

Management of CRS/ICANS

Drug-specific tip sheet

- REMS Requirement
- Dose, route, ramp-up
- Timing/severity of CRS/ICANS
- Pre-/post-medication
- Site of administration & monitoring

Allina Health

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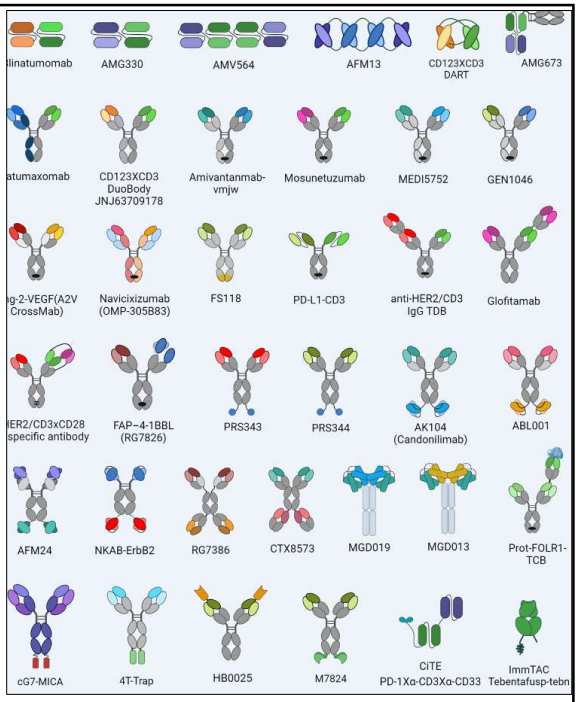
Future of BsAbs: Investigational Pipeline

Linvoseltamab	• Target/MOA: BCMAxCD3 (Myeloma)
Odronextamab	• Target/MOA: CD20xCD3 (B-cell Lymphomas)
Forimtamig	• Target/MOA: GPRC5dxCD3 (2+1 binding) (Myeloma)
Cevostamab	• Target/MOA: FcRH5xCD3 (Myeloma)
SUBQ blinatumomab	• Target/MOA: CD19xCD3 BiTE® (ALL)



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Summary of TCE BsAbs

- "New" class of drugs with good efficacy in heavily pre-treated disease, may be moving closer to frontline and in novel combinations
- Step-up dosing and inpatient observation have improved safety
- All have risk for infection, especially those that target BCMA
- CRS and ICANS should be recognized and managed appropriately per institutional guidelines
- Multidisciplinary collaboration necessary to improve outcomes

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