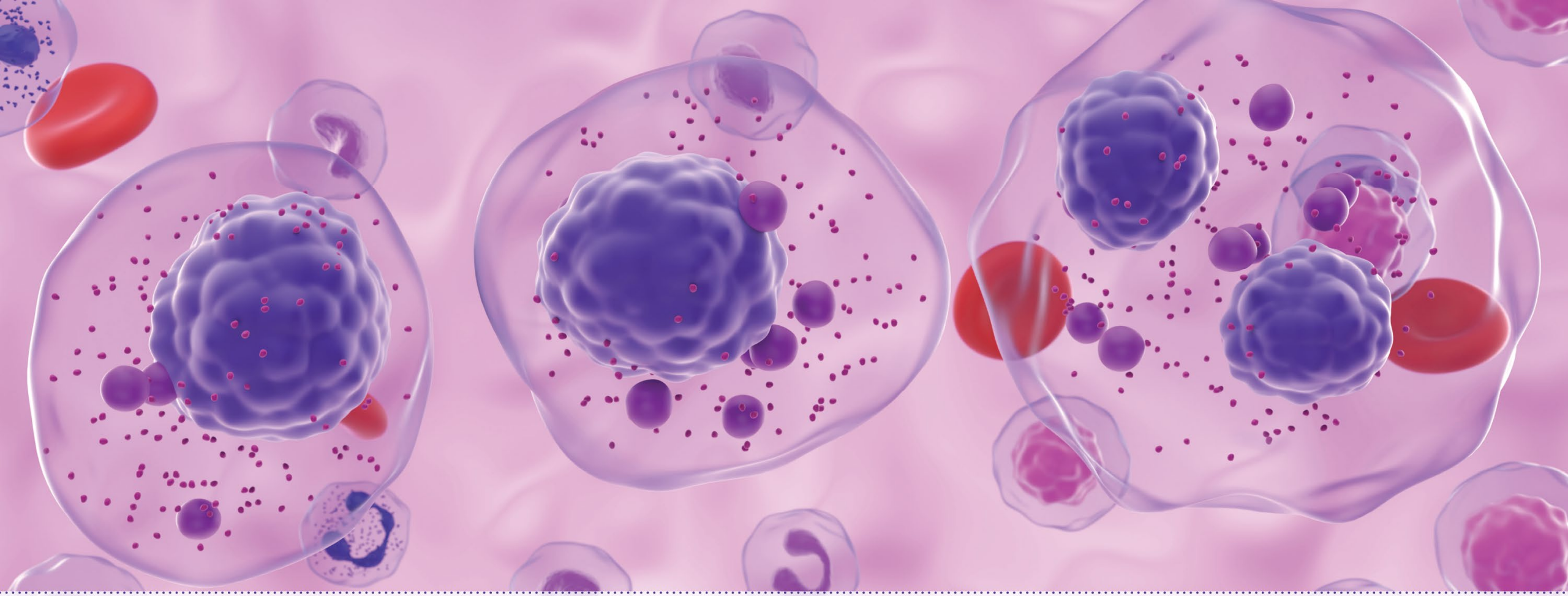

SUSTAIN

Systematic Uptake and Standardization of Treatment Advances Through an Integrated Network for BISPECIFIC ANTIBODY THERAPY

Provided by UK HealthCare

The France Foundation

Today's Faculty

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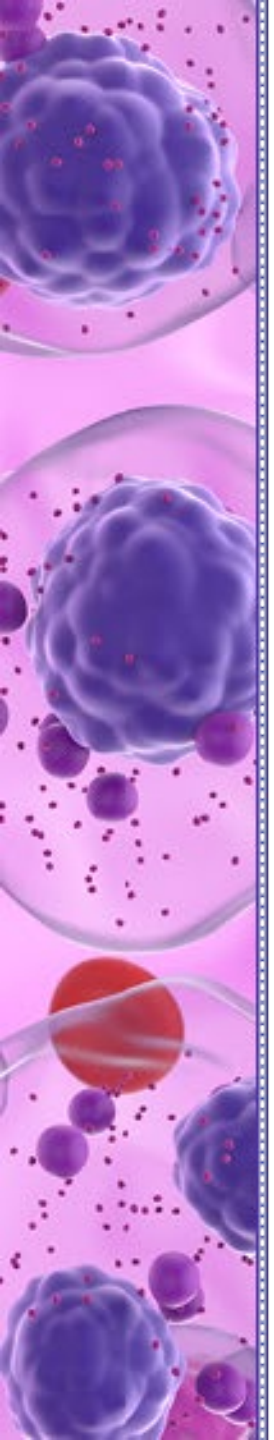

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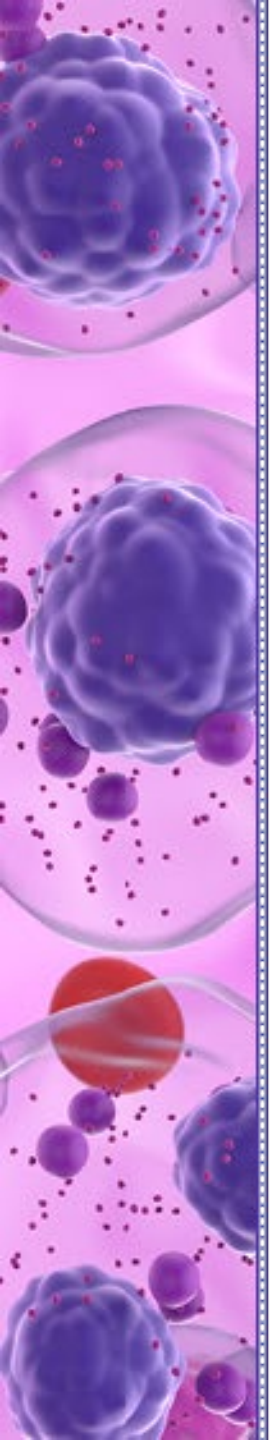

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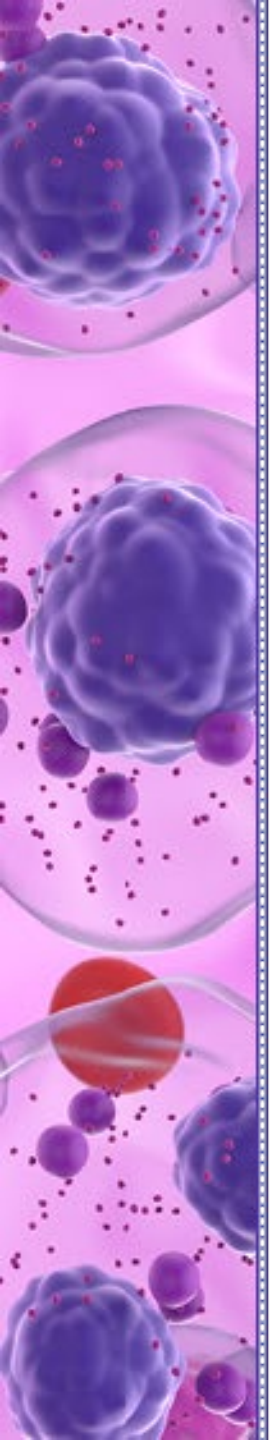
Educational Support

This activity is supported by an independent medical educational grant from Johnson & Johnson.



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- **1.00** *AMA PRA Category 1 Credit*™

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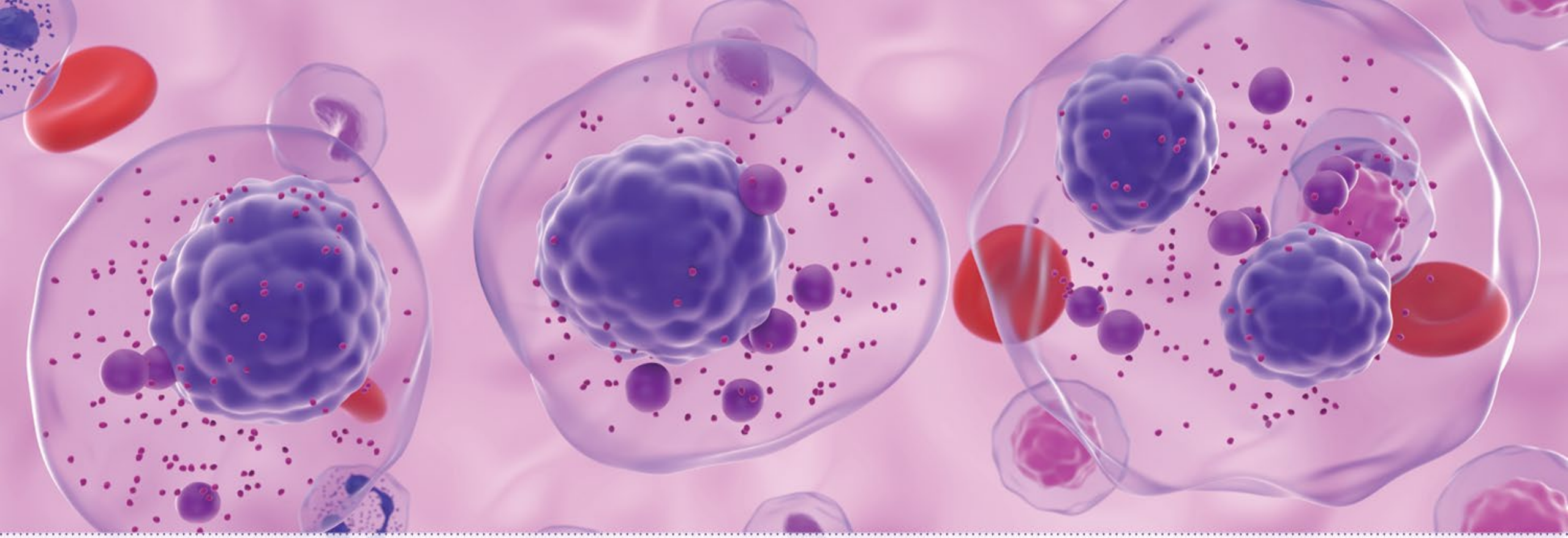
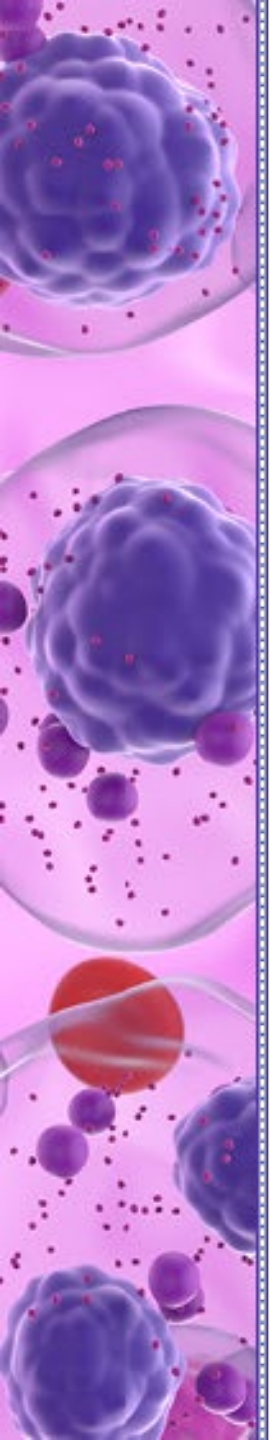
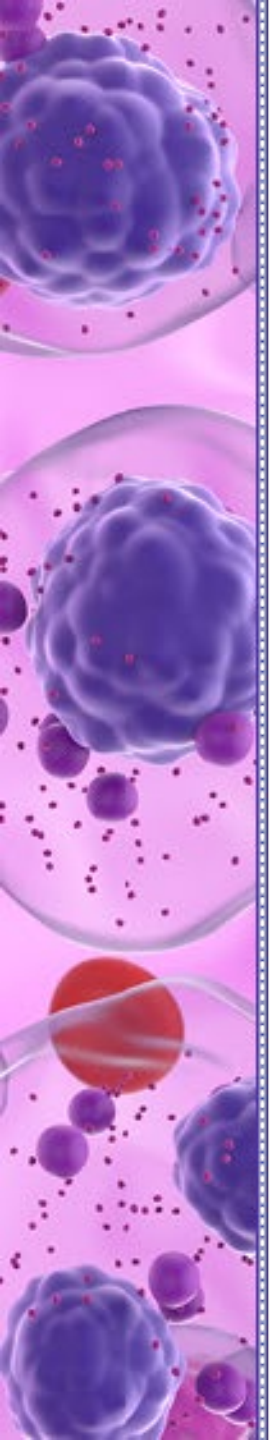


Session 5: Infection Prevention and Management During BsAb Therapy



Curriculum Learning Objective

- Develop and implement site-specific protocols for safe BsAb administration, including patient selection criteria, pre-medication regimens, dose escalation procedures, and post-infusion monitoring
- Educate multidisciplinary teams on BsAb pharmacology, recognition and grading of adverse events, and appropriate interventions, including when to escalate care
- Train providers in appropriate patient selection criteria, risk stratification, and patient/caregiver education regarding expectations, monitoring requirements, and symptom reporting

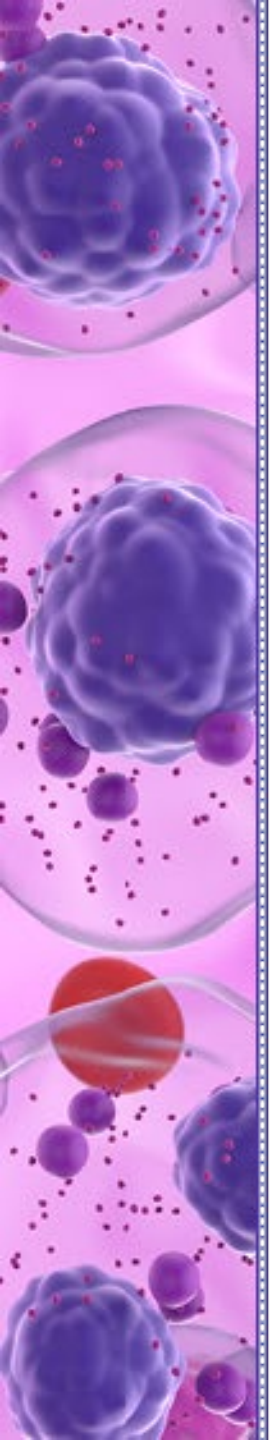


Session Objectives

1. Provide appropriate prophylaxis to patients receiving BsAbs to prevent infection during treatment
2. Develop protocols to monitor and manage patients who develop infections and/or cytopenias during treatment with BsAbs
3. Develop a comprehensive monitoring and management plan for patients receiving bispecific antibody therapy

Knowledge Check!

Look for a brain symbol in the top right corner of the screen to find the answers to the “What Do You Know?” questions



What Do You Know?

Which treatment-related factor most increases risk for opportunistic infections during BsAb therapy?

A. Recurrent prolonged high-dose corticosteroids for CRS/ICANS requiring slow taper

B. IL-6 blockade for CRS with transient hypogammaglobulinemia during early cycles

C. Brief grade 3 lymphopenia during step-up dosing

D. Antiviral prophylaxis for herpesvirus given throughout maintenance therapy

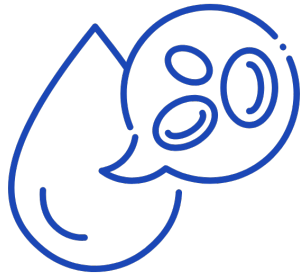
Adverse Events Associated With BsAbs

BsAbs are associated with potentially serious and fatal adverse events, including:

ECHO #3 and 4 reviewed how to identify and manage CRS and ICANS!

Cytokine release syndrome (CRS)

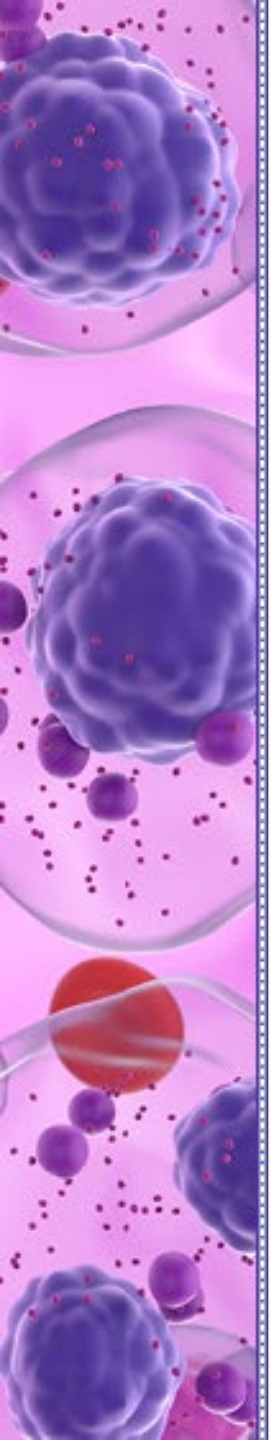
Immune effector cell-associated neurotoxicity syndrome (ICANS)



Cytopenias

Infection

Biltibo E, et al. *Am Soc Clin Oncol Educ Book*. 2026;46(3):e517460; Ludwig H, et al. *Lancet Oncol*. 2023;24(6):e255-e269; van de Donk NWCJ, Zweegman S. *Lancet*. 2023;402(10396):142-158; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025.

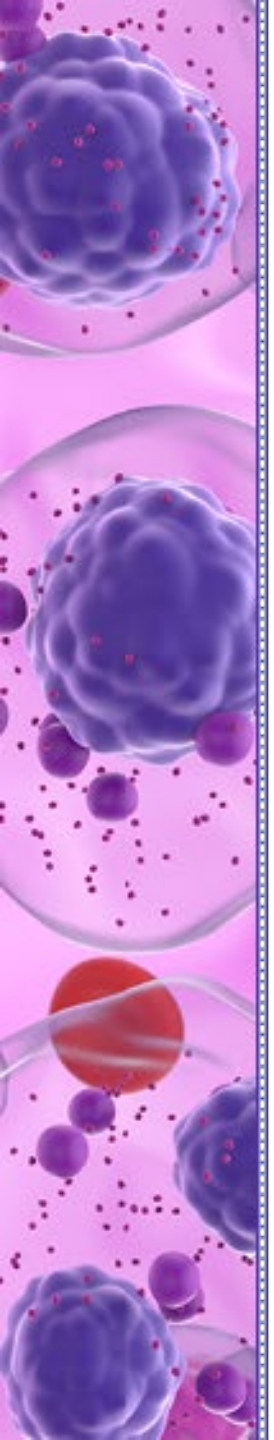


Risk Factors for Infections

Domain	Risk Factors
Patient specific	• Age • Comorbidities • Previous frequent episodes of infections • Lymphopenia • Neutropenia • Hypogammaglobulinemia
Disease related	• Refractory or poorly controlled disease
Treatment related	• High dose and long duration of corticosteroids, leading to immunosuppression • TNF-α inhibition • Cytokine release syndrome • Bacterial and granulomatous infections, including tuberculosis • Proteasome inhibitors • CD38 antibodies • Virus reactivation (VZV, CMV) • Fluconazole increases risk for mold infections
Comments	• Biological age is a stronger health predictor than chronological age • Previous infections are key in assessing infection risk • BCMA-targeting therapies cause significant depletion of B cells and plasma cells • CRS is more linked to bacterial infections than viral or fungal ones

BCMA = B-cell maturation antigen; BMPC = bone marrow plasma cell; CMV = cytomegalovirus; CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; TNF = tumor necrosis factor; VZV = varicella zoster virus

Ludwig H, et al. *Lancet Oncol*. 2023;24(6):e255-e269; van de Donk NWCJ, Zweegman S. *Lancet*. 2023;402(10396):142-158.



Risk Factors for Cytopenias

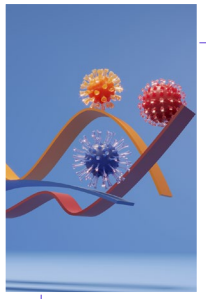
Cytopenias are a risk factor and a consequence of infections

	Causes of Cytopenias
Patient specific	• Reduced bone marrow function • High baseline BMPC infiltration • Older age
Disease related	• Refractory or poorly controlled disease
Treatment related	• Multiple previous lines of therapy • BCMA-targeted therapy • Intensity of lymphodepletion therapy

BCMA = B-cell maturation antigen; BMPC = bone marrow plasma cell

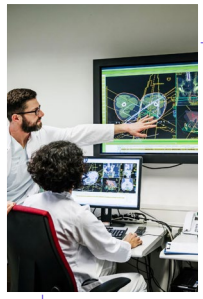
Ludwig H, et al. *Lancet Oncol*. 2023;24(6):e255-e269; van de Donk NWCJ, Zweegman S. *Lancet*. 2023;402(10396):142-158.

Timing of Infections and Cytopenias in Patients on BsAbs



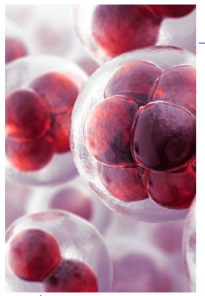
Highest risk of infection is early during step-up dosing and the first few cycles

- Infections can still occur anytime during treatment



Some patients may have more than 1 infection during therapy

- Constant monitoring vigilance is necessary
- May require dose interruptions



BCMA-directed therapies have been associated with an increased infection risk relative to CAR-T therapy

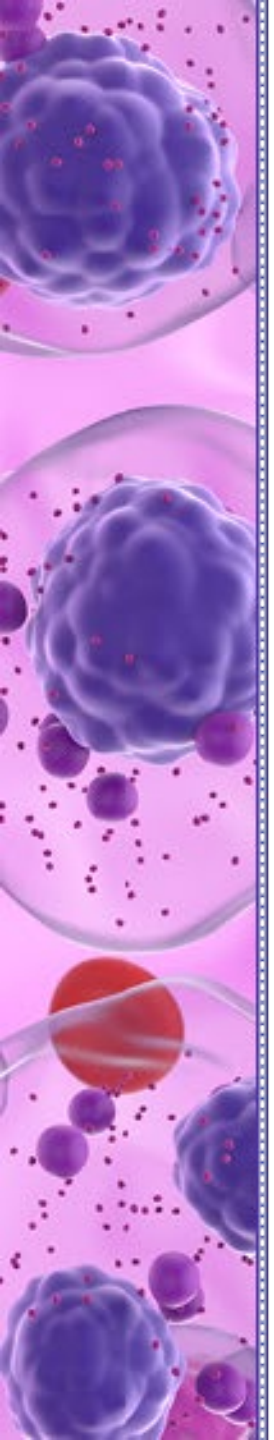
- Caused by B cell and plasma cell depletion

It is important to differentiate the symptoms of CRS from infection

Onset of cytopenias may not occur until ~2-4 months after treatment initiation

- Constant vigilance is required
- May require dose interruptions

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025; Alshammari F, et al. *Hematology*. 2025;30(1):2448898; Nath K, et al. *Blood Cancer J*. 2024;14(1):88.



Preventing Infections During Treatment

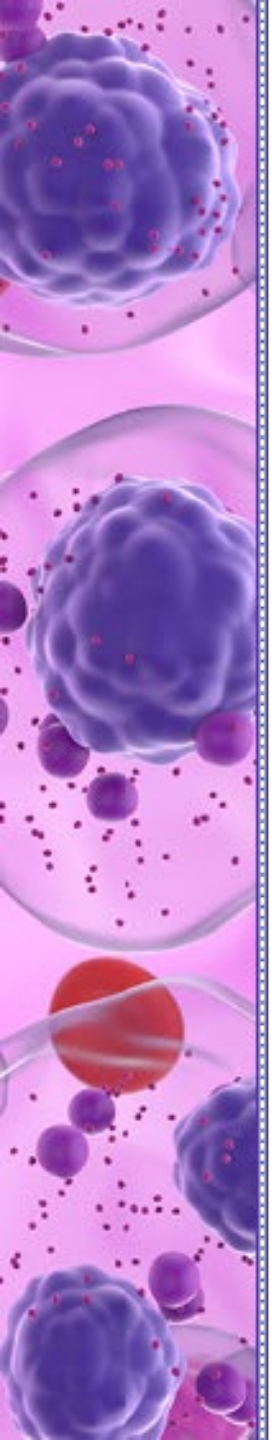
- Patients should undergo baseline screening for HBV, HCV, HIV, with further assessment for other infections as needed:
  - Screening for cytomegalovirus, and Epstein-Barr virus infections can be ordered if clinically indicated
- Preventive measures include vaccination and prophylaxis, with mandatory vaccines for influenza, pneumococcal disease, herpes zoster, and COVID-19

	Prophylaxis Recommendations
Viral Infections	• Antiviral against HSV/VZV for all patients
Bacterial Infections	• Recommended if prolonged neutropenia, high risk of infections, history of recurrent bacterial infections • Prophylaxis with levofloxacin until no longer neutropenic
Fungal Infections	• PJP prophylaxis for all patients

HSV = herpes simplex virus; PJP = pneumocystis jirovecii pneumonia

Ludwig H, et al. *Lancet Oncol*. 2023;24(6):e255-e269; Raje N, et al. *Blood Cancer J*. 2023;13(1):116; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025

Laboratory Monitoring for Infections and Cytopenias



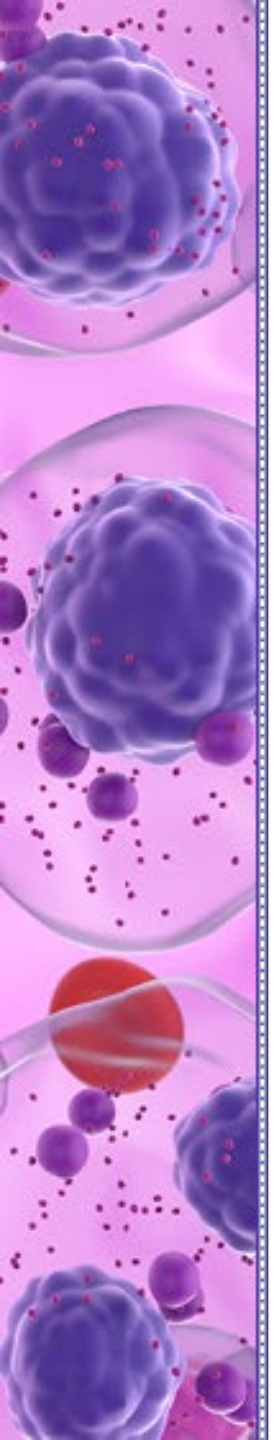
Monitor patient symptoms and clinical presentation

Check CBC, CMP, and IgG at every visit or more frequently as needed

Perform cultures and tests, depending on the infection site

- Imaging can be used for further confirmation

Raje N, et al. *Blood Cancer J*. 2023;13(1):116; Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025



Managing Infections (1/2)

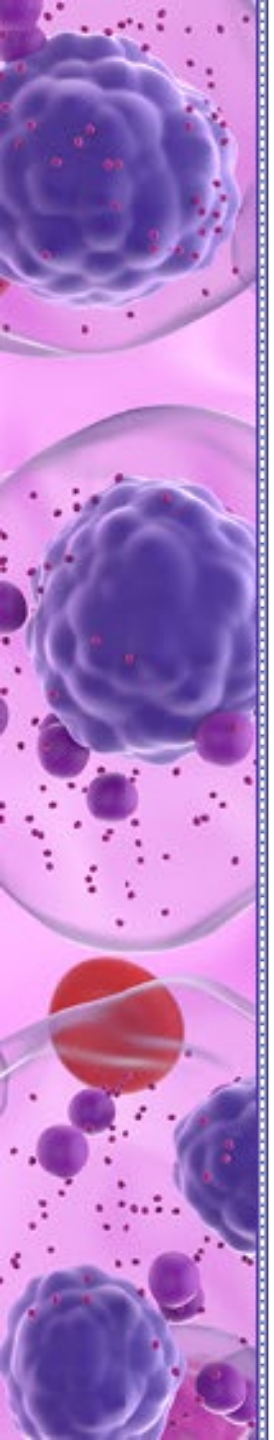
Treatment principles:

- Follow neutropenic fever protocols
- Escalate based on severity and local epidemiology

Severity	Actions for Teclistamab
All Grades	• Withhold BsAbs in patients with active infection during step-up dosing
Grade 3	• Withhold subsequent BsAb doses administered after step-up dosing until infection improves to Grade ≤ 1
Grade 4	• Consider permanent discontinuation of BsAb • If not permanently discontinued, withhold subsequent BsAb doses administered after step-up dosing until infection improves to Grade ≤ 1

Severity	Actions for Elranatamab
Grade 3	• Withhold until infection improves to Grade ≤ 1 or baseline
Grade 4	• Consider permanent discontinuation of BsAb • If not permanently discontinued, withhold subsequent BsAb doses administered after step-up dosing until infection improves to Grade ≤ 1

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025



Managing Infections (2/2)

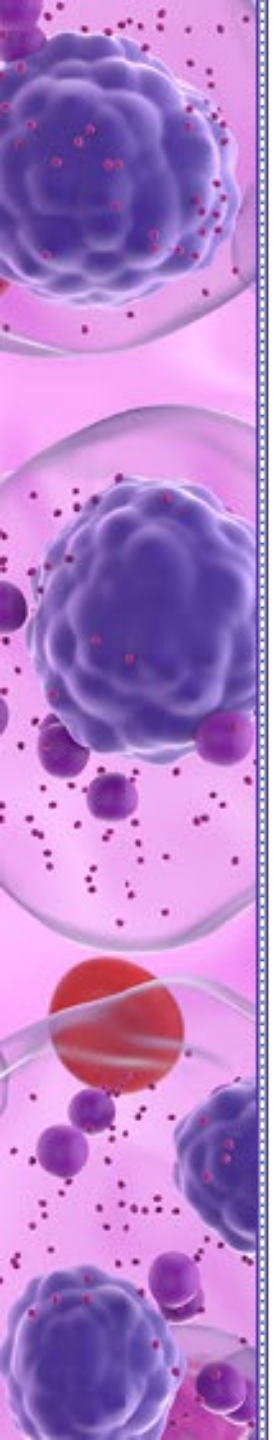
Treatment principles:

- Follow neutropenic fever protocols
- Escalate based on severity and local epidemiology

Severity	Actions for Talquetamab
All Grades	• Withhold in the step-up phase until infection resolves
Grade 3	• Withhold during the treatment phase until infection improves to Grade ≤ 1 within 28 days
Grade 4	• Consider permanent discontinuation of BsAb • If not permanently discontinued, withhold subsequent doses administered after step-up dosing schedule until infection improves to Grade ≤ 1

Severity	Actions for Linvoseltamab
Grade 2 or 3	• Withhold subsequent BsAb doses administered after step-up dosing schedule until infection improves to Grade ≤ 1
Grade 4	• Consider permanent discontinuation of BsAb • If not permanently discontinued, withhold subsequent doses administered after step-up dosing schedule until infection improves to Grade ≤ 1

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025



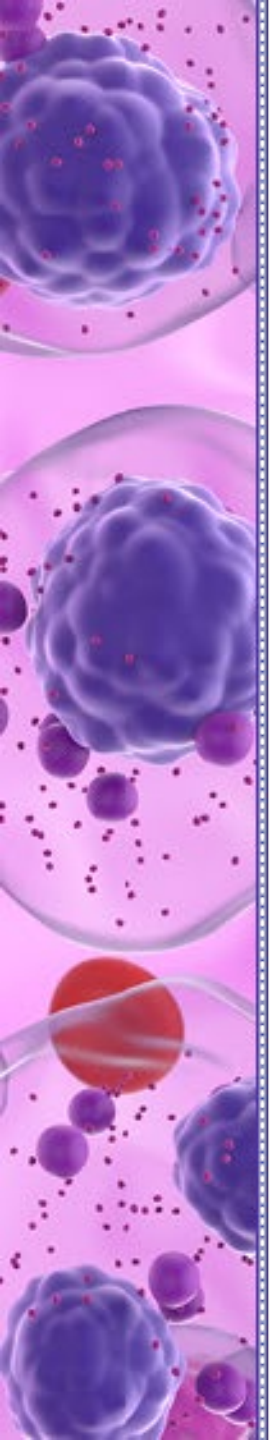
Managing Cytopenias

Severity	Actions for Teclistamab*, Elranatamab, Talquetamab, Linvoseltamab
Absolute neutrophil count (ANC) < 0.5 x 10^9/L	• Withhold until ANC is ≥ 0.5 x 10^9/L
Febrile neutropenia	• Withhold until ANC is ≥ 1 × 10^9/L and fever resolves
Hemoglobin < 8 g/dL	• Withhold until hemoglobin is ≥ 8 g/dL
Platelet count* < 25,000/mcL or Platelet count 25,000-50,000/mcL with bleeding	• Withhold until platelet count is ≥ 25,000/mcL and no evidence of bleeding

IVIG may be indicated in some patients with cytopenias

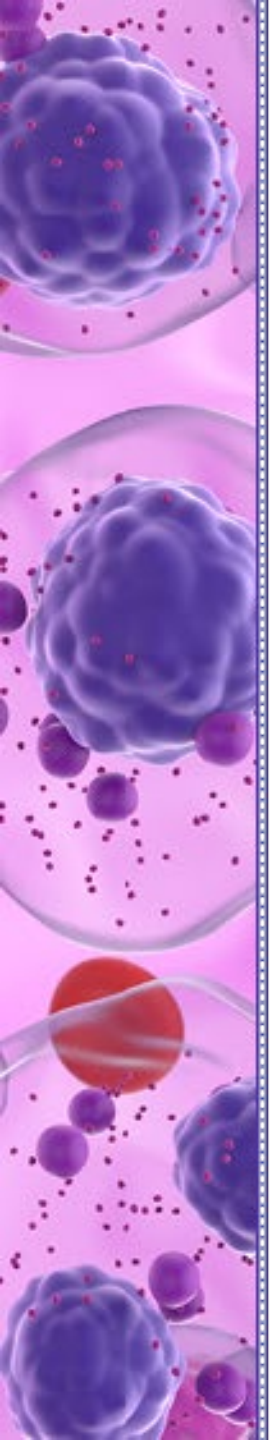
*In combination with daratumumab therapy, withhold teclistimab until platelet count is ≥ 50,000/mcL and no evidence of bleeding.

Teclistamab-cqyv (Tecvayli) [prescribing information]. Janssen Biotech, Inc; March 2026; Elranatamab-bcmm (Elrexfio) [prescribing information]. Pfizer Inc; July 2025; Talquetamab-tgvs (Talvey) [prescribing information]. Janssen Biotech, Inc; August 2023. Linvoseltamab-gcpt (Lynozyfic) [prescribing information]. Regeneron Pharmaceuticals, Inc; July 2025



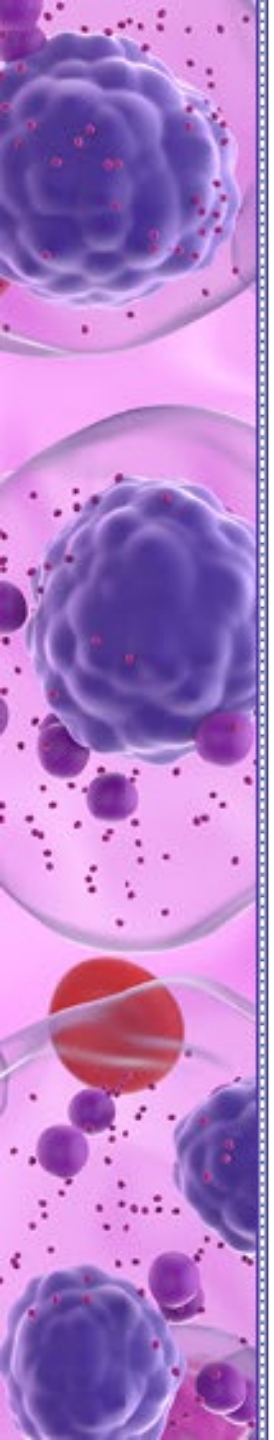
Role of the Pharmacy

- Review patient's home medication regimen
  - Consider withholding antihypertensives for 1-2 days following step-up doses
  - Clinically significant drug interactions with BsAbs are rare
- Collaborate in the development of institutional protocols for infection and cytopenia management



Key Takeaways

- BsAb therapy in multiple myeloma carries highest infection risk during early cycles, driven by T-cell redirection–associated immunosuppression and cytopenias
- Prolonged systemic corticosteroids for CRS/ICANS substantially increases risk for opportunistic and invasive infections
- Febrile or subtle infectious presentations require prompt diagnostic evaluation with early broad-spectrum empiric therapy in high-risk patients
- Prevention strategies include antiviral/PJP prophylaxis, immunoglobulin monitoring with IVIG replacement when indicated, and temporary treatment interruption for ≥ grade 3 infections.



What Did You Learn?

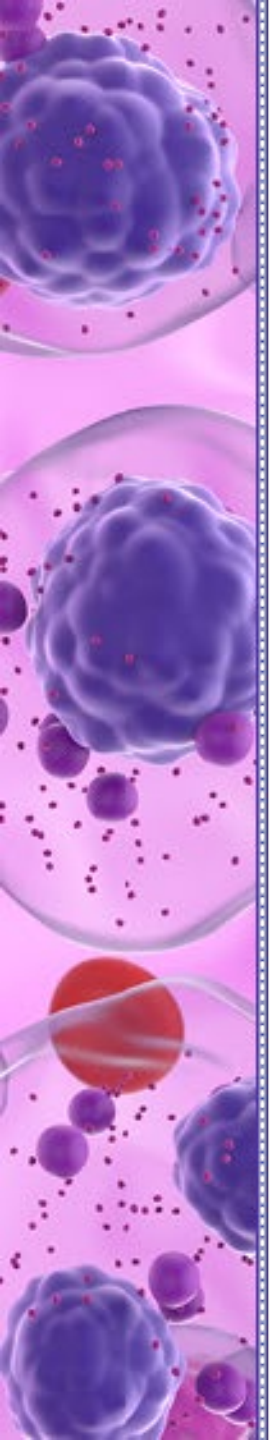
Which treatment-related factor most increases risk for opportunistic infections during BsAb therapy?

A. Recurrent prolonged high-dose corticosteroids for CRS/ICANS requiring slow taper

B. IL-6 blockade for CRS with transient hypogammaglobulinemia during early cycles

C. Brief grade 3 lymphopenia during step-up dosing

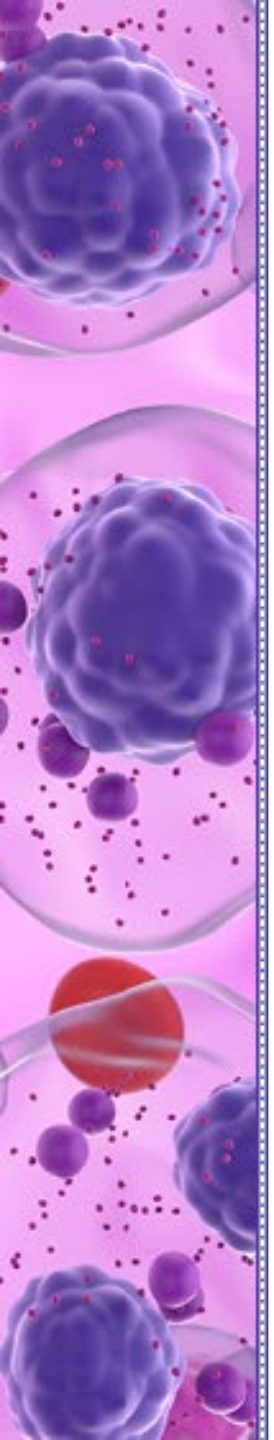
D. Antiviral prophylaxis for herpesvirus given throughout maintenance therapy



Ask the Audience!

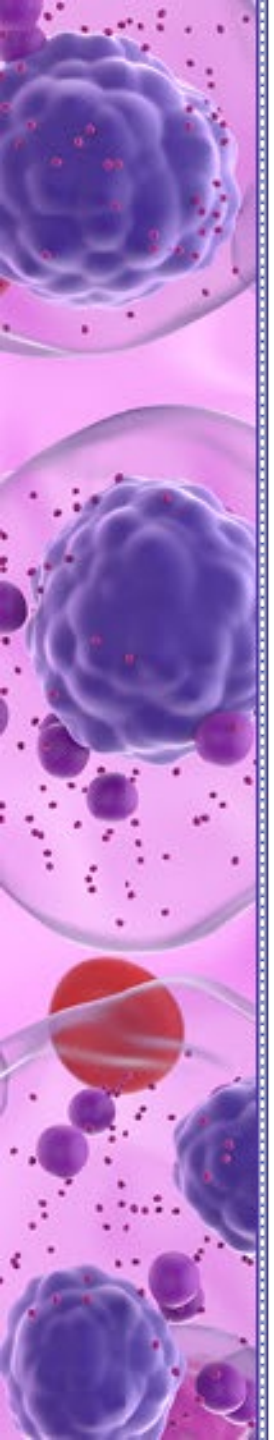
Please unmute or use the chat feature to discuss with your colleagues.

What are your top 3 concerns on recognizing, assessing, and managing BsAb-related infections in your clinical practice?



Case Studies

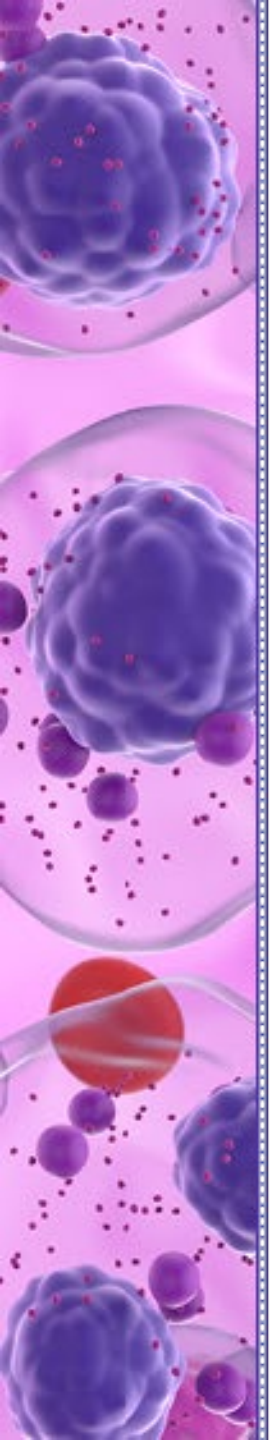
Please come off mute or use the chat feature to ask questions about your patient cases and discuss answers with your colleagues.



Remember Our Case From ECHO #2…

- Elderly woman with lambda light chain MM and renal involvement on a background of CKD and HFpEF
- Initial low-burden disease with high-risk cytogenetics; achieved renal/hematologic response to CyBorD, but limited by toxicity
- Progressed in 2022; declined transplant; re-treatment and subsequent therapies (DRd → DPd → selinexor/dex) led to transient or modest responses
- Course complicated by heart failure (bortezomib intolerance), worsening renal function, and cytopenias
- Developed relapsed/refractory disease; not a CAR-T candidate → planned for bispecific antibody (teclistamab) with need for careful cardiorenal optimization

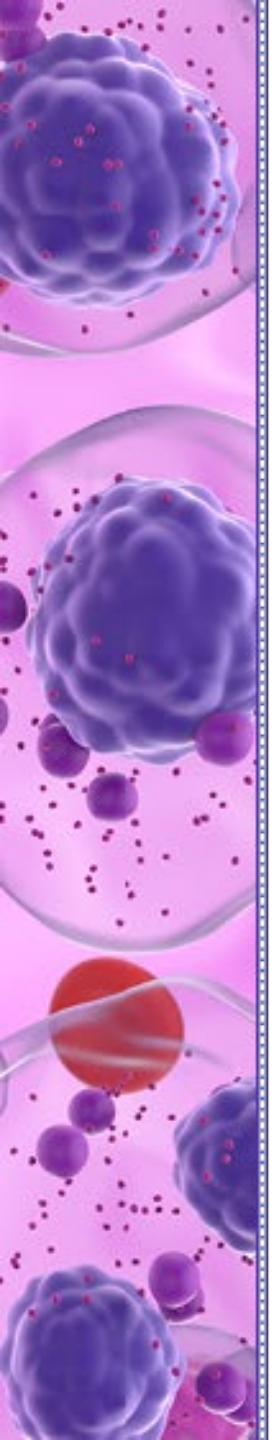
CKD = chronic kidney disease; CyBorD = cyclophosphamide, bortezomib, dexamethasone; DPd = daratumumab, pomalidomide, dexamethasone; DRd = daratumumab, lenalidomide, dexamethasone; HFpEF = heart failure with preserved ejection fraction



What Happened Next?

- **3/31/2025-4/26/2025: Admitted for teclistamab**
  - Patient continued to have issues with volume overload
  - She had marked improvement in serum-free lambda light chain
  - Patient transitioned to intermittent dialysis
  - **Day 15 dose remained on hold**
- **5/6/2025: Patient tolerated dialysis well**
  - Discussed patient restarting teclistamab cycle 1
- **05/18/2025: Restarted teclistamab C1D1**
- **She had recurrent infections:**
  - 06/04/2025-06/08/25: Admitted for *pseudomonas* pneumonia
  - 6/14/2025: TP 5.4, SPEP: no monoclonal ab, IgG < 44, IgA < 5, IgM < 7
  - 07/04/2025-07/09/2025: Admitted for acute respiratory failure with hypercapnia secondary to pneumonia
    - Patient was started on cefepime, sputum culture positive for *pseudomonas*, which was sensitive to cephalosporin
    - 03/13/26-present: admitted with AHRF requiring intubation
    - Positive for rhinovirus

AHRF = acute hypoxemic respiratory failure; C1D1 = cycle 1 day 1; Ig = immunoglobin; SPEP = serum protein electrophoresis; TP = total protein



To Claim Credit

1. Go to https://cme.cecentral.com/content/sustain-5-infection-prevention-and-management-during-bsab-therapy and “Take Course” then “Start Course”
2. Enter attendance code **ROZFEZ** when prompted
3. Complete the evaluation
4. Appropriate credit will be issued automatically
5. Download certificate (optional)
6. Complete commitment to change survey (optional)

IMPORTANT! The deadline to claim credit online is **September 8, 2026.**

For questions, please contact support@cecentral.com