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Practice patterns, gaps, and priorities in infection management for patients receiving bispecific antibodies and CAR-T cell therapy – Results from the E-Impact survey of the EHA-SWG Infections in Hematology

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Abstract

Bispecific antibodies (BsAbs) and chimeric antigen receptor T-cell (CAR-T) therapies have transformed the treatment of hematologic malignancies, but infectious complications remain a leading cause of morbidity and mortality. We conducted a multicenter international survey across 101 institutions—predominantly academic tertiary hospitals (80.2%)—to characterize contemporary prevention and management practices. We assessed antimicrobial prophylaxis, infection surveillance, and management of therapy-induced immunodeficiency for patients receiving BsAbs and/or CAR-T. Practices were highly heterogeneous. Viral infections were most frequently reported with BsAbs (69.3%), whereas bacterial infections predominated after CAR-T (52.8%). Anti–Pneumocystis Jirovecii prophylaxis was nearly universal (93.5% BsAbs; 97.5% CAR-T), but antibacterial and antifungal prophylaxis varied widely and were omitted in 37.6% and 38.7% of BsAb centers, respectively. CMV monitoring strategies differed markedly; one-third of BsAb centers did not routinely monitor CMV-DNA. Most respondents identified better guidelines (72.3% BsAbs; 52.8% CAR-T), improved diagnostic tools, and multidisciplinary approaches as priorities. These findings underscore substantial practice variation and the urgent need for harmonized, evidence-based guidance, particularly in light of recent data highlighting prolonged hypogammaglobulinemia, infection burden per patient-month with continuously dosed BsAbs, and the potential protective effect of immunoglobulin replacement. Prospective studies are warranted to define optimal prophylaxis, surveillance, and immunoglobulin replacement strategies in these populations.

BULLETS POINTS

- **Distinct infection profiles:** Viral infections dominate in BsAb therapies, whereas bacterial infections are most frequent after CAR-T.
- **Prophylaxis duration lacks consensus:** While PJP and antiviral prophylaxis are nearly universal, stopping criteria vary widely across institutions.
- **Significant CMV surveillance gap:** One-third of BsAb centers do not routinely monitor CMV-DNA, unlike the high vigilance seen in CAR-T programs.
- **Urgent need for standardized guidelines:** Centers highlight a critical need for risk-adapted protocols driven by measurable immune reconstitution rather than fixed timelines.

INTRODUCTION

T cell–redirecting bispecific antibodies (BsAbs) and chimeric antigen receptor T cell (CAR-T) therapies have transformed treatment of B-cell malignancies, reaching responses in relapsed or refractory disease and expanding access to immunotherapy[1–4].

Both modalities cause profound, sometimes prolonged immune dysregulation. B-cell depletion and sustained T-cell engagement lead to persistent B-cell aplasia, hypogammaglobulinemia, and cytopenias, while cytokine-mediated toxicities—cytokine release syndrome (CRS) and immune effector cell–

associated neurotoxicity (ICANS) —often require corticosteroids or IL-6 blockade, further increasing infection risk[5–7].

In CAR-T recipients, infection risk is front-loaded: during the first 30–60 days bacterial pneumonia and bacteremia dominate, driven by lymphodepleting chemotherapy, deep neutropenia, and mucositis. From day 60 to the first 6 months, viral respiratory infections (influenza, SARS-CoV-2, RSV) and herpes virus (HSV/VZV) reactivations prevail, with cytomegalovirus (CMV) events in high-risk patients exposed to prolonged steroids. Late (> 6–12 months) morbidity clusters in those with persistent CD4 lymphopenia and hypogammaglobulinemia—more common after anti-CD19 due to sustained B-cell aplasia[8].

In BsAb recipients, trials and real-world cohorts report frequent upper-respiratory bacterial and viral infections, opportunistic infections—notably Pneumocystis jirovecii pneumonia (PJP) —and reactivations including HSV and VZV, with a signal for CMV reactivation in selected settings. Risk varies by dosing strategy (continuous vs fixed), prior therapy burden, and the depth and duration of hypogammaglobulinemia[5,6,9]. After fixed-duration CD20×CD3 BsAbs, immune reconstitution is slow: B cells and IgM often recover 12–18 months post-treatment, whereas IgG may need 18–24 months, extending susceptibility beyond active therapy[1,10]. Although CAR-T causes more pronounced early severe toxicities, BsAbs may impose a higher cumulative infection burden per patient-month—particularly with continuous dosing—highlighting the need for prophylaxis tailored to exposure length and immune recovery[5,7,9,11].

Consensus guidance recommends systematic prevention for both approaches: universal PJP and herpesvirus prophylaxis, HBV screening and reactivation prevention, consideration of antifungals in high-risk patients, and immunoglobulin replacement for clinically significant hypogammaglobulinemia. Implementation remains heterogeneous, and prospective evidence for optimal prevention is limited[8,10–135–7,12]. To address these gaps, we conducted a multicenter survey to characterize real-world prophylaxis and infection-management practices across institutions with established BsAb and CAR-T programs.

MATERIALS AND METHODS

Study design and population

We performed a cross-sectional, multicenter survey of institutions administering BsAbs and/or CAR-T for hematologic malignancies. The electronic questionnaire was distributed between November 2025 and May 2026; responses were anonymous. The survey was programmed in EFS Fall 2022 (TIVIAN, Cologne, Germany) and hosted at www.clinicalsurveys.net/uc/E_IMPACT/. The study had ethics approval from Hospital General Universitario Gregorio Marañón (Madrid, Spain) and was registered on ClinicalTrials.gov (NCT07609576). Participation was voluntary and survey responses were collected anonymously at the institutional level. Informed consent was waived because no patient-level data were collected and no identifiable personal information was included.

Survey instrument

The survey comprised structured questions on infection prevention and management. We collected center-level characteristics (institution type, availability of multidisciplinary infectious diseases teams, and annual BsAb/CAR-T treatment volumes). We then captured infection epidemiology (most frequent or perceived bacterial, viral, and fungal infections). Antimicrobial prophylaxis practices were assessed (antibacterial, antifungal, anti-PJP, and antiviral), with agents and exposure duration. CMV DNA surveillance strategies and management were recorded. We gathered information on immunodeficiency management, including IgG monitoring, criteria for immunoglobulin replacement, and use of granulocyte colony-stimulating factor (G-CSF). Finally, centers reported unmet needs and the factors most likely to improve infection management (Fig. 1).

Statistical analysis

Descriptive statistics summarized responses as frequencies and percentages. Missing data were handled by excluding non-respondents from denominators for individual questions. Analyses were performed using IBM SPSS Statistics version 31.0.0.

RESULTS

General center information

A total of 101 centers participated from 32 countries. Centers administering BsAbs (101/101; 100%) and those delivering both BsAbs and CAR-T (89/101; 88.1%) were included in modality-specific analyses. Most institutions were university or academic tertiary hospitals (81/101; 80.2%), followed by non-university tertiary hospitals (11/101; 10.9%). Multidisciplinary infection teams were available in 84/101 centers (83.2%) (Table 1).

Table 1
Infection management practices and centre characteristics in bispecific antibody and CAR-T therapy.

	Overall		BsAbs		CAR-T	
	n	%	n	%	n	%
General centre information						
Centre type						
University/Academic tertiary hospital	81/101	80.2	-	-	-	-
Non-University/Academic tertiary hospital	11/101	10.9	-	-	-	-
Community hospital	6/101	5.9	-	-	-	-
Other	3/101	3.0	-	-	-	-
Availability of multidisciplinary infection team	84/101	83.2				
Patient volume (BsAbs/CAR-T, 2024)						
Not stated	-	-	2/101	2.0	6/89	6.7
0–5 patients	-	-	29/101	28.7	45/89	50.6
6–10 patients	-	-	27/101	26.7	9/89	10.1
11–25 patients	-	-	16/101	15.8	12/89	13.5
> 25 patients	-	-	27/101	26.7	17/89	19.1
Most frequent infection type	-	-	-	-	-	-
Bacterial	-	-	68/101	67.3	47/89	52.8
Fungal	-	-	27/101	26.7	17/89	19.1
Viral	-	-	70/101	69.3	36/89	40.4
Antimicrobial prophylaxis						
Antibacterial prophylaxis						
No	-	-	80/93	86.0	53/81	65.4
Fluoroquinolones	-	-	16/93	17.2	17/81	21.0
Other	-	-	9/93	9.7	5/81	6.2

BsAbs, bispecific antibodies; **CAR-T**, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **DNA**, deoxyribonucleic acid; **PCR**, polymerase chain reaction; **IgG**, immunoglobulin G; **G-CSF**, granulocyte colony-stimulating factor

	Overall		BsAbs		CAR-T	
	n	%	n	%	n	%
Antibacterial prophylaxis duration						
Until neutropenia resolves	-	-	28/93	30.1	23/81	28.4
While on treatment	-	-	30/93	32.3	14/81	17.3
Fixed duration post-treatment	-	-	4/93	4.3	6/81	7.4
Other	-	-	3/93	3.2	2/81	2.5
Antifungal prophylaxis						
No	-	-	36/93	38.7	16/81	19.8
All patients	-	-	12/93	12.9	19/81	23.5
Severe/prolonged neutropenia	-	-	36/93	38.7	28/81	34.6
High-dose steroids	-	-	29/93	31.2	22/81	27.2
Other	-	-	6/93	6.5	3/81	3.7
Antifungal agent used						
Fluconazole	-	-	19/93	20.4	21/81	25.9
Posaconazole	-	-	26/93	28.0	34/81	42.0
Voriconazole	-	-	7/93	7.5	2/81	2.5
Other	-	-	9/93	9.7	3/81	3.7
Anti-Pneumocystis jirovecii prophylaxis						
No	-	-	6/93	6.5	2/81	2.5
All patients	-	-	67/93	72.0	52/81	64.2
Severe/prolonged neutropenia	-	-	14/93	15.1	6/81	7.4
High-dose steroids	-	-	10/93	10.8	4/81	4.9
Other	-	-	4/93	4.3	2/81	2.5
Antifungal agent used						
Cotrimoxazole	-	-	78/93	83.9	54/81	66.7

BsAbs, bispecific antibodies; **CAR-T**, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **DNA**, deoxyribonucleic acid; **PCR**, polymerase chain reaction; **IgG**, immunoglobulin G; **G-CSF**, granulocyte colony-stimulating factor

	Overall		BsAbs		CAR-T	
	n	%	n	%	n	%
Inhaled pentamidine	-	-	8/93	8.6	8/81	9.9
Other	-	-	3/93	3.2	4/81	4.9
Anti-*Pneumocystis jirovecii* prophylaxis duration						
While lymphopenia present	-	-	33/93	35.5	33/81	40.7
While on treatment	-	-	45/93	48.4	15/81	18.5
While steroids present	-	-	14/93	15.1	9/81	11.1
Fixed duration post-treatment	-	-	13/93	14.0	19/81	23.5
Other	-	-	4/93	4.3	2/81	2.5
Antiviral prophylaxis						
No	-	-	20/93	21.5	8/81	9.9
Acyclovir	-	-	46/93	49.5	33/81	40.7
Valacyclovir	-	-	22/93	23.7	18/81	22.2
Other	-	-	3/93	3.2	0/81	0.0
Antiviral prophylaxis duration						
Until neutropenia resolves	-	-	7/93	7.5	4/81	4.9
While on treatment	-	-	46/93	49.5	17/81	21.0
Fixed duration post-treatment	-	-	12/93	12.9	21/81	25.9
Other	-	-	8/93	8.6	9/81	11.1
CMV-DNA monitored by PCR						
No	-	-	27/81	33.3	12/81	14.8
Weekly	-	-	15/81	18.5	23/81	28.4
Biweekly	-	-	7/81	8.6	7/81	8.6
Monthly	-	-	8/81	9.9	8/81	9.9
If symptomatic	-	-	16/81	19.8	7/81	8.6

BsAbs, bispecific antibodies; **CAR-T**, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **DNA**, deoxyribonucleic acid; **PCR**, polymerase chain reaction; **IgG**, immunoglobulin G; **G-CSF**, granulocyte colony-stimulating factor

	Overall		BsAbs		CAR-T	
	n	%	n	%	n	%
Other	-	-	3/81	3.7	4/81	4.9
CMV management strategy						
Universal	-	-	17/93	18.3	9/81	11.1
Pre-emptive	-	-	47/93	50.5	41/81	50.6
Other	-	-	2/93	2.2	0/81	0.0
Management of immunodeficiency and cytopenias						
IgG monitoring						
No	-	-	8/79	10.1	2/79	2.5
Monthly	-	-	54/79	68.4	44/79	55.7
Every 4 months	-	-	4/79	5.1	5/79	6.3
Only if recurrent infections	-	-	7/79	8.9	6/79	7.6
Other	-	-	3/79	3.8	3/79	3.8
IgG initiation criteria						
If recurrent infections	-	-	33/91	36.3	21/79	26.6
If IgG above certain level	-	-	49/91	53.8	39/79	49.4
Universal prophylaxis	-	-	12/91	13.2	6/79	7.6
G-CSF for bispecific-induced neutropenia						
Routinely	-	-	36/91	39.6	29/79	36.7
If fever/infection	-	-	29/91	31.9	14/79	17.7
Other options	-	-	10/91	11.0	10/79	12.7
Key priorities for infection management						
Better guidelines	-	-	73/101	72.3	47/89	52.8
Improved diagnostic tools	-	-	61/101	60.4	47/89	52.8

BsAbs, bispecific antibodies; **CAR-T**, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **DNA**, deoxyribonucleic acid; **PCR**, polymerase chain reaction; **IgG**, immunoglobulin G; **G-CSF**, granulocyte colony-stimulating factor

	Overall		BsAbs		CAR-T	
	n	%	n	%	n	%
Multidisciplinary approach	-	-	59/101	58.4	43/89	48.3

BsAbs, bispecific antibodies; **CAR-T**, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **DNA**, deoxyribonucleic acid; **PCR**, polymerase chain reaction; **IgG**, immunoglobulin G; **G-CSF**, granulocyte colony-stimulating factor

Infection types differed by modality. In BsAbs programs, viral infections were reported by 70/101 centers (69.3%), bacterial by 68/101 (67.3%), and fungal by 27/101 (26.7%). In CAR-T programs, bacterial infections were most frequent (47/89; 52.8%), followed by viral (36/89; 40.4%) and fungal diseases (17/89; 19.1%) (Table 1).

Antimicrobial prophylaxis

Antibacterial prophylaxis was generally not administered in 80/93 BsAbs centers (86.0%) and 53/81 CAR-T centers (65.4%). When used, fluoroquinolones were most common (17.2% BsAbs; 21.0% CAR-T). Duration strategies varied: until neutropenia resolved (30.1% BsAbs; 28.4% CAR-T), while on treatment (32.3% BsAbs; 17.3% CAR-T), or fixed duration post-treatment (4.3% BsAbs; 7.4% CAR-T).

Antifungal prophylaxis was used in 65/93 BsAbs centers (69.9%) and 60/81 CAR-T centers (74.1%). Indications included severe or prolonged neutropenia (38.7% BsAbs; 34.6% CAR-T) and high-dose corticosteroids (31.2% BsAbs; 27.2% CAR-T). In BsAbs, posaconazole (28.0%) and fluconazole (20.4%) were common; in CAR-T, posaconazole predominated (42.0%).

PJP prophylaxis was administered in 87/93 BsAbs centers (93.5%) and 79/81 CAR-T centers (97.5%). Prophylaxis was universal in 72.0% of BsAbs centers and 64.2% of CAR-T centers; cotrimoxazole was the main agent (83.9% and 66.7%, respectively). Duration varied: maintained during treatment (48.4% BsAbs; 18.5% CAR-T), until lymphopenia resolved (35.5% each), during steroid exposure (15.1% BsAbs; 11.1% CAR-T), or as a fixed post-treatment interval (14.0% BsAbs; 23.5% CAR-T).

Antiviral prophylaxis was provided in 73/93 BsAbs centers (78.5%) and 73/81 CAR-T centers (90.1%), most often acyclovir (49.5% and 40.7%) or valacyclovir (23.7% and 22.2%). Duration approaches included while on treatment (49.5% BsAbs; 21.0% CAR-T), fixed duration post-treatment (12.9% BsAbs; 25.9% CAR-T), or other strategies.

CMV monitoring and management

Routine CMV DNA surveillance was reported by 54/93 BsAbs centers (58.1%) and 69/81 CAR-T centers (85.2%). Monitoring schedules varied: weekly (18.5% BsAbs; 28.4% CAR-T), biweekly (8.6% both), monthly (9.9% both), or only if symptomatic (19.8% BsAbs; 8.6% CAR-T). Pre-emptive therapy was the most common management strategy (50.5% BsAbs; 50.6% CAR-T).

Management of immunodeficiency and cytopenias

Monthly IgG monitoring was performed in 71/79 BsAbs centers (89.9%) and 77/79 CAR-T centers (97.5%). IgG replacement was initiated by threshold in 49/91 BsAbs centers (53.8%) and 39/79 CAR-T centers (49.4%); initiation based on recurrent infections was reported by 36.3% and 26.6%, respectively. Universal prophylactic replacement was uncommon (13.2% BsAbs; 7.6% CAR-T).

G-CSF for treatment-induced neutropenia was administered routinely in 36/91 BsAbs centers (39.6%) and 29/79 CAR-T centers (36.7%), while some limited use to fever or documented infection (31.9% and 17.7%).

The need for clearer guidelines (72.3% BsAbs; 52.8% CAR-T) and more advanced diagnostic tools (60.4% BsAbs; 52.8% CAR-T) emerged as the top priorities for improving infection management.

DISCUSSION

This multicenter survey reveals substantial heterogeneity in infection prevention and management among centers administering BsAbs and CAR-T, despite growing recommendations and experience. Key themes include variability in prophylaxis across pathogens, inconsistent immune monitoring and reconstitution-guided interventions, and differing risk assessments for opportunistic infections. These findings underscore uncertainty around optimal supportive care and the need for standardized, risk-adapted frameworks.

In our cohort, viral infections predominated with BsAbs, whereas bacterial infections were more frequent after CAR-T. This is consistent with reports linking BsAbs to recurrent upper-respiratory viral events and herpesvirus reactivation under sustained B-cell aplasia and hypogammaglobulinemia, while CAR-T programs observe early bacterial infections related to lymphodepletion, mucosal injury, and profound neutropenia[5,6]. Considering time at risk, continuously dosed BsAbs may confer higher infection rates per patient-month than finite regimens, yet fixed-duration schedules still leave a prolonged vulnerability because humoral reconstitution lags: B-cell and IgM recovery at 12–18 months and IgG at 18–24 months after therapy[7,10]. The heterogeneous stopping rules for PJP and antiviral prophylaxis—end of treatment, resolution of cytopenias or lymphopenia, or fixed intervals—likely reflect this uncertainty.

A notable gap is CMV surveillance: approximately one third of BsAb centers do not routinely monitor CMV DNA despite reported events in selected BsAb settings and consensus favoring targeted surveillance in high-risk subgroups (profound lymphopenia, substantial corticosteroids administration, or multiple prior lines)[10,12–14]. Harmonized strategies using quantitative PCR at weekly to biweekly intervals during peak immunosuppression, with predefined thresholds for pre-emptive therapy, could limit clinically significant CMV disease while avoiding excess testing.

Near-universal PJP prophylaxis was reported, but duration varied widely. In light of delayed humoral recovery after BsAbs and late infections post-discontinuation, extending prophylaxis according to

immune-reconstitution markers—CD4 or absolute lymphocyte counts and IgG thresholds of about 400–600 mg/dL—together with clinical risk assessment, appears rational. HSV/VZV prophylaxis should continue throughout persistent immunodeficiency.

Limited use of routine antibacterial prophylaxis aligns with mixed evidence and antimicrobial-resistance concerns. Risk-adapted approaches that incorporate depth and duration of neutropenia, prior invasive infections, mucositis, and local epidemiology are appropriate. Antifungal prophylaxis targeted to severe/prolonged neutropenia or high-dose corticosteroids aligns with consensus; mold-active agents such as posaconazole may be considered in selected CAR-T courses with profound or prolonged neutropenia, whereas universal antifungal prophylaxis is generally unnecessary for BsAb recipients[8,10,11,13].

Evidence supports intravenous or subcutaneous immunoglobulin replacement to reduce severe infections in patients with persistent hypogammaglobulinemia and/or recurrent infections during BsAb therapy[9–11]. A pragmatic approach is monthly IgG monitoring during treatment and for 6–12 months thereafter, initiating replacement at IgG below roughly 400–600 mg/dL or with recurrent or breakthrough infections, followed by periodic reassessment as humoral and B-cell recovery occurs. In high-risk multiple myeloma treated with BCMA-targeted BsAbs, a more proactive, even universal, replacement strategy has been advocated because paraproteins can confound measured IgG and infection risk is high[2,5,15]. Such strategies must be balanced against logistical complexity, costs, and access constraints. G-CSF support for prolonged neutropenia may mitigate bacterial risk. Non-live vaccinations—seasonal influenza, respiratory syncytial virus (RSV), pneumococcal, and SARS-CoV-2 boosters—should be administered and timed outside peak immunosuppression.

Bridging evidence gaps: priorities for harmonized guidance

Duration of PJP and antiviral prophylaxis and timing of immunoglobulin replacement should be linked to measurable biology—B-cell counts, IgG thresholds, and time since last dose—accounting for differences between finite and continuous BsAb dosing. CMV management should adopt risk-stratified surveillance with defined thresholds for pre-emptive therapy; prospective studies are needed to quantify event rates with CD20×CD3 BsAbs and the benefit of surveillance in high-risk cohorts. To compare modalities fairly, infections should be analyzed per patient-month, contrasting BsAb schedules with CAR-T and integrating immune correlates such as IgG trajectories and B-cell reconstitution into registries. Pragmatic trials comparing intensified prevention packages—PJP and HSV/VZV prophylaxis, early immunoglobulin replacement, and risk-adapted CMV monitoring—against standard care would generate practice-ready protocols.

Strengths and limitations

This large, international survey offers a broad view of real-world infection management in BsAb and CAR-T therapy, capturing granular data on antibacterial, antifungal, antiviral, and PJP prophylaxis, CMV surveillance, and immunoglobulin replacement, and enabling cross-platform comparisons across

predominantly academic institutions. Limitations include self-reporting and potential bias toward specialized centers, lack of outcome linkage, variable denominators due to missing responses, and the rapidly evolving therapeutic landscape, all of which may limit generalizability.

CONCLUSIONS

Infection prevention and management for patients receiving BsAbs and CAR-T remain heterogeneous across institutions. Variability in prophylaxis practices, immune monitoring, and CMV surveillance reflects uncertainty in optimal supportive care amid prolonged, modality-specific immune dysfunction. Harmonized, risk-adapted strategies are needed, prioritizing universal PJP and herpesvirus prophylaxis with duration guided by immune recovery, systematic HBV screening and reactivation prevention, individualized antibacterial and antifungal prophylaxis based on neutropenia risk, and structured CMV surveillance with predefined pre-emptive thresholds. Proactive vaccination and immunoglobulin replacement for clinically significant hypogammaglobulinemia should be integrated into routine care. Prospective studies incorporating immune correlates and infection outcomes are essential to establish evidence-based standards and reduce infectious morbidity in these vulnerable populations.

Declarations

Disclosure of Conflicts of Interest

The authors declare no conflict of interest

Data Availability declaration

All data supporting the findings of this study are available within the paper.

Author Contribution

MSI designed the survey and wrote the main manuscript textJSG built the survey, analyzed the data and prepared figure 1 and table 1.All authors reviewed the manuscript.

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Data Availability

All data supporting the findings of this study are available within the paper.

References

1. Giamaiou P, Fioretzaki R, Vassilakopoulos TP, Dimou M (2026) CD20 × CD3 Bispecific Antibodies in B-Cell Non-Hodgkin Lymphomas: Current Evidence, Therapeutic Integration, and Future Directions. Med (Mex) 62(6):1056. https://doi.org/10.3390/medicina62061056
2. Lee H, Neri P, Bahlis NJ (2024) BCMA- or GPRC5D-Targeting Bispecific Antibodies in Multiple Myeloma: Efficacy, Safety, and Resistance Mechanisms. Blood 143(13):1211–1217. https://doi.org/10.1182/blood.2023022499
3. Raje N, Berdeja J, Lin Y, Siegel D, Jagannath S, Madduri D, Liedtke M, Rosenblatt J, Maus MV, Turka A, Lam L-P, Morgan RA, Friedman K, Massaro M, Wang J, Russotti G, Yang Z, Campbell T, Hege K, Petrocca F, Quigley MT, Munshi N, Kochenderfer JN (2019) Anti-BCMA CAR T-Cell Therapy Bb2121 in Relapsed or Refractory Multiple Myeloma. N Engl J Med 380(18):1726–1737. https://doi.org/10.1056/NEJMoa1817226
4. Zhang X, Zhu L, Zhang H, Chen S, Xiao Y (2022) CAR-T Cell Therapy in Hematological Malignancies: Current Opportunities and Challenges. Front Immunol 13:927153. https://doi.org/10.3389/fimmu.2022.927153
5. Reynolds G, Cliff ERS, Mohyuddin GR, Popat R, Midha S, Liet Hing MN, Harrison SJ, Kesselheim AS, Teh BW (2023) Infections Following Bispecific Antibodies in Myeloma: A Systematic Review and Meta-Analysis. Blood Adv 7(19):5898–5903. https://doi.org/10.1182/bloodadvances.2023010539
6. Reynolds GK, Maclean M, Cliff ERS, Teh BW, Thursky KA, Slavin MA, Anderson MA, Hawkes EA (2024) Infections in Patients with Lymphoma Treated with Bispecific Antibodies: A Systematic Review and Meta-Analysis. Blood Adv 8(13):3555–3559. https://doi.org/10.1182/bloodadvances.2024012916
7. Rejeski K, Subklewe M, Aljurf M, Bachy E, Balduzzi A, Barba P, Bruno B, Benjamin R, Carrabba MG, Chabannon C, Ciceri F, Corradini P, Delgado J, Di Blasi R, Greco R, Houot R, Iacoboni G, Jäger U, Kersten MJ, Mielke S, Nagler A, Onida F, Peric Z, Roddie C, Ruggeri A, Sánchez-Guijo F, Sánchez-Ortega I, Schneidawind D, Schubert M-L, Snowden JA, Thieblemont C, Topp M, Zinzani PL, Gribben JG, Bonini C, Sureda A (2023) Yakoub-Agha, I. Immune Effector Cell-Associated Hematotoxicity: EHA/EBMT Consensus Grading and Best Practice Recommendations. Blood 142(10):865–877. https://doi.org/10.1182/blood.2023020578
8. Tabbara N, Dioverti-Prono MV, Jain T (2024) Mitigating and Managing Infection Risk in Adults Treated with CAR T-Cell Therapy. *Hematol. Am. Soc. Hematol. Educ. Program 2024* (1), 116–125.

https://doi.org/10.1182/hematology.2024000535

9. Longhitano AP, Slavin MA, Harrison SJ, Teh BW (2021) Bispecific Antibody Therapy, Its Use and Risks for Infection: Bridging the Knowledge Gap. Blood Rev 49:100810. https://doi.org/10.1016/j.blre.2021.100810
10. Rejeski K, Banerjee R, Hill JA (2026) How We Prevent Infections in Adults Receiving Bispecific Antibody Therapies for Advanced B-Cell Malignancies. *Blood* blood.2025032298. https://doi.org/10.1182/blood.2025032298
11. Raje N, Anderson K, Einsele H, Efebera Y, Gay F, Hammond SP, Lesokhin AM, Lonial S, Ludwig H, Moreau P, Patel K, Ramasamy K, Mateos M-V (2023) Monitoring, Prophylaxis, and Treatment of Infections in Patients with MM Receiving Bispecific Antibody Therapy: Consensus Recommendations from an Expert Panel. Blood Cancer J 13(1):116. https://doi.org/10.1038/s41408-023-00879-7
12. van Besien H, Easwar N, Demetres M, Pasciolla M, Shore T, Leonard J, Barker J, Martin P, Yamshon S (2025) Comparative Infection Risk in CAR T vs Bispecific Antibodies in B-Cell Lymphoma: A Systematic Review and Meta-Analysis. Blood Adv 9(23):6063–6075. https://doi.org/10.1182/bloodadvances.2025016291
13. Ludwig H, Terpos E, van de Donk N, Mateos M-V, Moreau P, Dimopoulos M-A, Delforge M, Rodriguez-Otero P, San-Miguel J, Yong K, Gay F, Einsele H, Mina R, Caers J, Driessen C, Musto P, Zweegman S, Engelhardt M, Cook G, Weisel K, Broijl A, Beksac M, Bila J, Schjesvold F, Cavo M, Hajek R, Touzeau C, Boccadoro M, Sonneveld P (2023) Prevention and Management of Adverse Events during Treatment with Bispecific Antibodies and CAR T Cells in Multiple Myeloma: A Consensus Report of the European Myeloma Network. Lancet Oncol 24(6):e255–e269. https://doi.org/10.1016/S1470-2045(23)00159-6
14. Mohan M, Chakraborty R, Bal S, Nellore A, Baljevic M, D'Souza A, Pappas PG, Berdeja JG, Callander N, Costa LJ (2023) Recommendations on Prevention of Infections during Chimeric Antigen Receptor T-Cell and Bispecific Antibody Therapy in Multiple Myeloma. Br J Haematol 203(5):736–746. https://doi.org/10.1111/bjh.18909
15. Jourdes A, Cellerin E, Touzeau C, Harel S, Denis B, Escure G, Faure E, Jamard S, Danion F, Sonntag C, Ader F, Karlin L, Soueges S, Cazelles C; de La Porte des Vaux, Frenzel C, Lanternier L, Brousse F, Cazaubiel X, Berger T, Collignon P, Blot A, Pieragostini M, Charles A, Chaleteix M, Redor C, Roland A, Cartau V, Macro T, Chalopin M, Vallet T, Perrot N, Martin-Blondel A (2024) G.; G2I and the IFM networks. Characteristics and Incidence of Infections in Patients with Multiple Myeloma Treated by Bispecific Antibodies: A National Retrospective Study. *Clin. Microbiol. Infect. Off. Publ. Eur. Soc. Clin. Microbiol. Infect. Dis. 30* (6), 764–771. https://doi.org/10.1016/j.cmi.2024.02.023

Figures

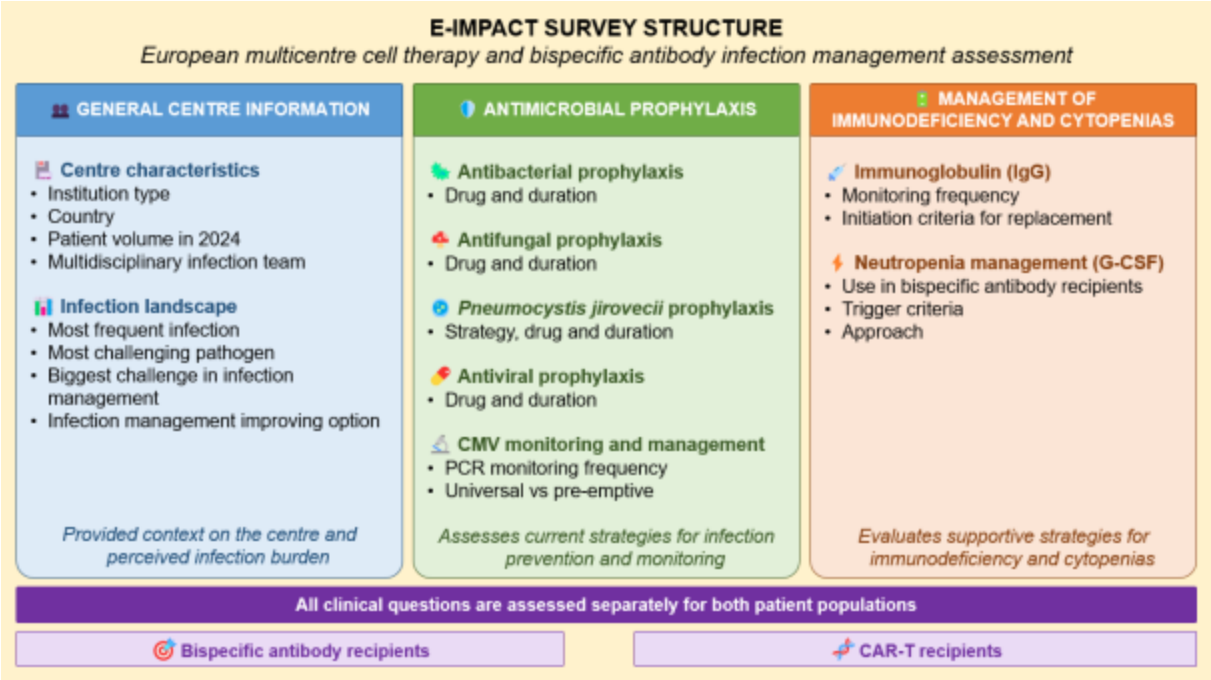


Figure 1

E-IMPACT survey structure for evaluation of infection prevention, monitoring, and management in bispecific antibodies and CAR-T

CAR-T, chimeric antigen receptor T-cell therapy; **CMV**, cytomegalovirus; **PCR**, polymerase chain reaction; **G-CSF**, granulocyte colony-stimulating factor