

# *Os cuidados que devo ter no paciente em tratamento com anticorpos biespecificos e pos CAR-T*

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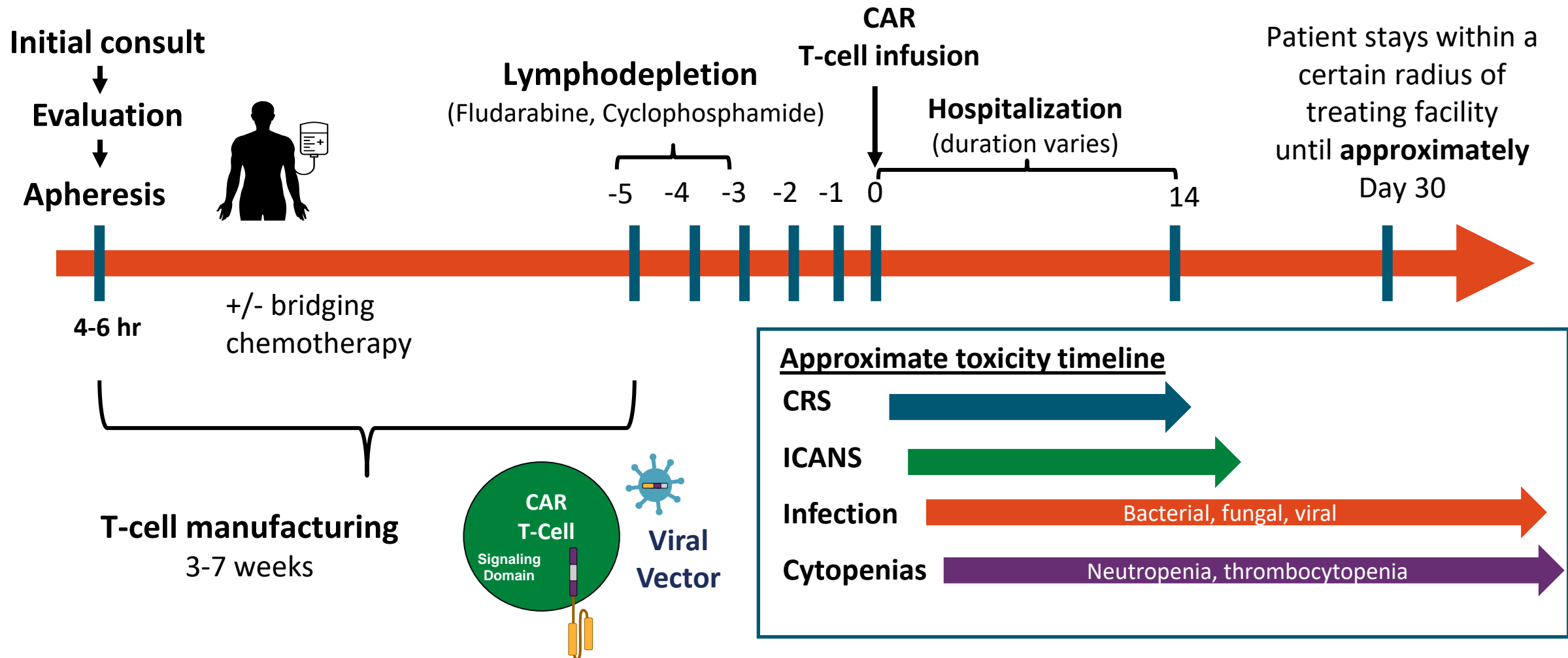
Member of the International Myeloma Working Group



## Disclosure:

- Consultancy: Janssen, Takeda, Amgen, BMS- Celgene, Sanofi, Novartis, Pfizer, Astra Zeneca
  - Research Funding: not applicable
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  - Patents and Royalties: not applicable
  - Membership on an Entity's Board of Directors or Advisory Committees: Board of Directors  
Associação Brasileira de Hematologia e Hemoterapia  
Member of International Myeloma  
Working Group
  - Discussion of off-label drug use: not applicable
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# CAR T-Cell Treatment Schema



# CAR T-Cell Therapy: Toxicities

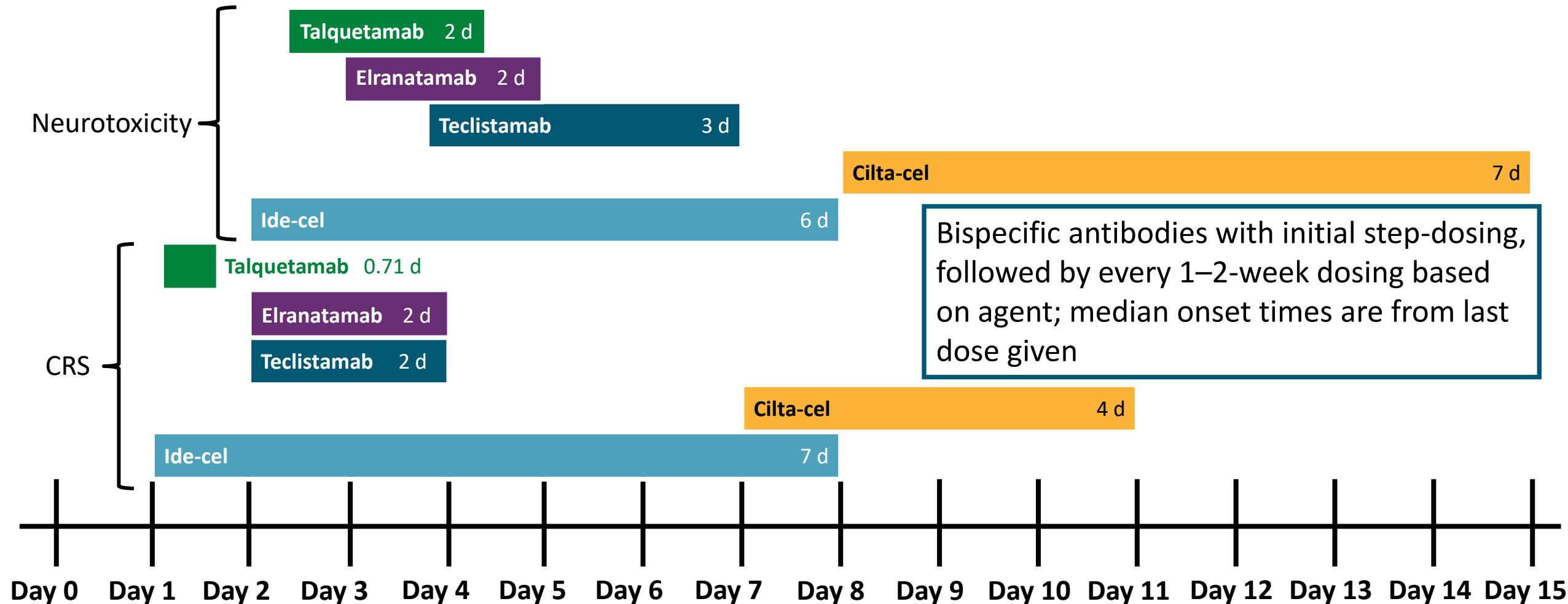
Acute Toxicities <sup>1</sup>	Delayed Toxicities <sup>2,3</sup>
<ul style="list-style-type: none"><li>▪ Cytokine-release syndrome</li><li>▪ Immune effector cell–associated neurotoxicity syndrome</li><li>▪ Cytopenias</li><li>▪ Hemophagocytic lymphohistiocytosis/macrophage activation syndrome</li></ul>	<ul style="list-style-type: none"><li>▪ B-cell aplasia/hypogammaglobulinemia</li><li>▪ Prolonged cytopenias</li><li>▪ Late infections</li><li>▪ Long-term neurologic events/movement and neurocognitive treatment-emergent AEs</li><li>▪ Transient cardiac toxicities</li><li>▪ Secondary malignancies?</li></ul>
Generally managed by <b>treating center HCPs</b>	Generally managed by <b>primary hematologists</b>

# Bispecific Antibodies: Toxicities

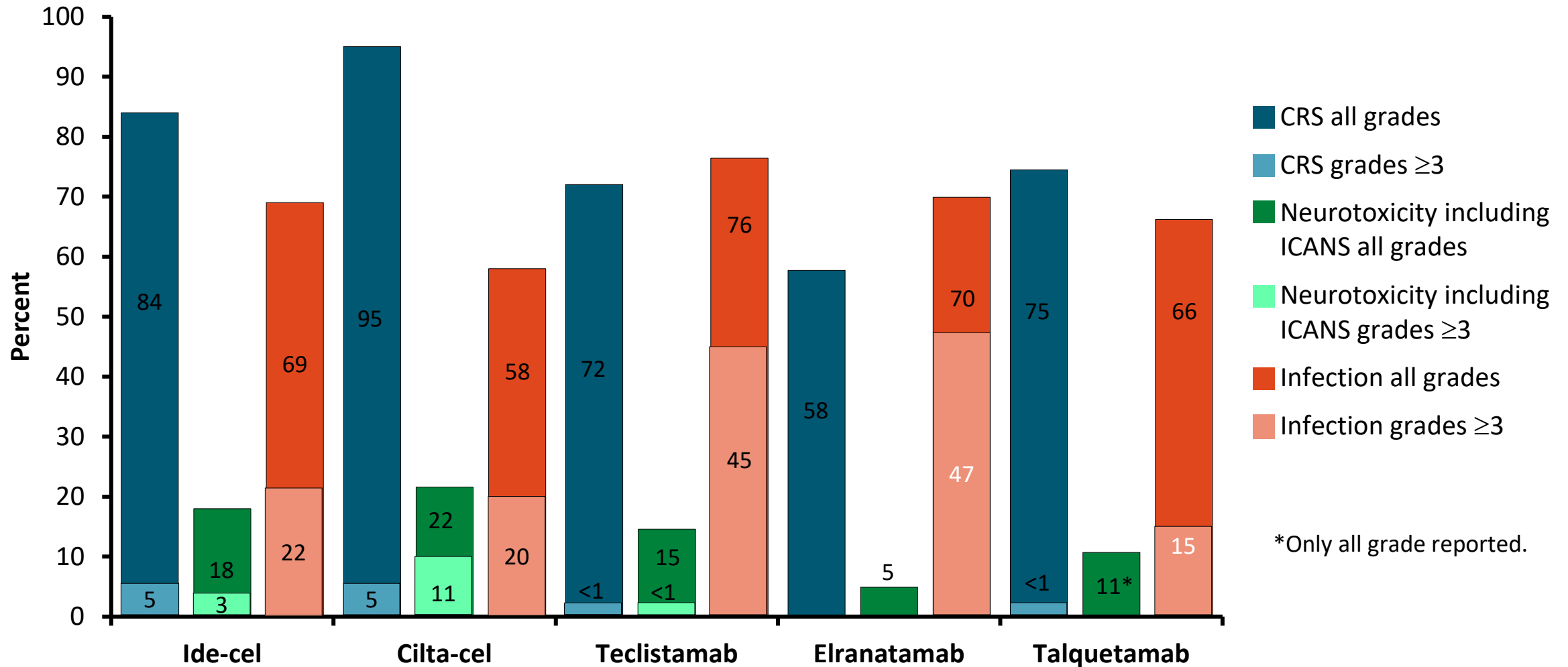
Acute Toxicities	Delayed Toxicities
<ul style="list-style-type: none"><li>▪ Cytokine-release syndrome</li><li>▪ Immune effector cell–associated neurotoxicity syndrome</li><li>▪ Neurologic toxicity</li><li>▪ Infections</li><li>▪ Neutropenia</li><li>▪ Hypersensitivity or injection-site reactions</li></ul>	<ul style="list-style-type: none"><li>▪ Hepatotoxicity</li><li>▪ Cytopenias</li><li>▪ Infections</li><li>▪ ? Neurologic toxicity</li></ul>
<p>Generally managed by treating center HCPs</p>	<p>Generally managed by treating or referral center</p>

- Further long-term follow-up data with bispecific antibodies are necessary

# CRS and Neurotoxicity: Median Time to Onset and Duration by CAR T-Cell or Bispecific Antibody Product



# Summary of Selected AE With CAR T-Cell Therapy and Bispecific Antibodies in R/R MM



Results are from different clinical trials/populations and should not be used for cross-comparison

Ludwig. Lancet Oncol. 2023;24:e255. Munshi. NEJM. 2021;384:705. Martin. JCO. 2023;41:1265. Moreau. NEJM. 2022;387:495.

Tomasson. ASH 2023. Abstr 3385. Schinke. ASCO 2023. Abstr 8036.

Slide credit: [clinicaloptions.com](https://clinicaloptions.com)

# Management of CRS With CAR T-Cell Therapy and Bispecific Antibody Therapy

- **Rule out other etiologies:** infection, heart failure, pulmonary edema, possibly treat for infection

Grade	CAR T-Cell Therapy Supportive Care + Intervention	Bispecific Antibody Therapy Supportive Care + Intervention
1	± tocilizumab*	Withhold until CRS resolution and administer pretreatment medications prior to next dose
2	Tocilizumab ± corticosteroid	Grade 1 interventions + 48-hr hospitalization following next dose according to institutional and manufacturer guidelines
3	Tocilizumab + corticosteroid	<i>First grade 3 occurrence with duration ≤48 hr:</i> grade 2 interventions + ICU/critical care as needed <i>Recurrent grade 3 or grade 3 with duration &gt;48 hr:</i> grade 4 interventions
4	Tocilizumab + high-dose corticosteroid ICU/critical care	Permanently discontinue; provide ICU/critical care as needed

\*High-burden, high-risk products; older; comorbidities; etc.



# Other AE With CAR T-Cell and Bispecific Antibody Therapy

- Cytopenias
  - Common with both CAR T-cell therapy and bispecific antibody therapy
  - Additionally, can be caused by lymphodepletion prior to CAR T-cell therapy
  - Consult hematology/oncology regarding potential growth factors
- Hemophagocytic lymphohistiocytosis/macrophage activation syndrome
  - Rare, and serious complication with CAR T-cell therapy
  - Treatment aimed towards reducing the cytokine hyperactivation
- Hepatotoxicity
  - Monitor liver enzymes

# TALQUETAMAB – MonumenTAL-1

AEs (≥30% in any cohort), n (%)	0.4 mg/kg SC QW (n=143)		0.8 mg/kg SC Q2W (n=145)		Prior TCR (n=51)	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
<b>Nonhematologic AEs</b>						
CRS <sup>b</sup>	113 (79.0)	3 (2.1)	108 (74.5)	1 (0.7)	39 (76.5)	1 (2.0)
Dysgeusia <sup>c</sup>	103 (72.0)	NA	103 (71.0)	NA	39 (76.5)	NA
Infections <sup>d</sup>	84 (58.7)	28 (19.6)	96 (66.2)	21 (14.5)	37 (72.5)	14 (27.5)
Skin related <sup>e</sup>	80 (55.9)	0	106 (73.1)	1 (0.7)	35 (68.6)	0
Nail related <sup>f</sup>	78 (54.5)	0	78 (53.8)	0	32 (62.7)	0
Weight decreased	59 (41.3)	3 (2.1)	60 (41.4)	8 (5.5)	15 (29.4)	0
Rash related <sup>g</sup>	57 (39.9)	2 (1.4)	43 (29.7)	8 (5.5)	18 (35.3)	2 (3.9)
Pyrexia	56 (39.2)	4 (2.8)	40 (27.6)	2 (1.4)	16 (31.4)	0
Dry mouth	38 (26.6)	0	58 (40.0)	0	26 (51.0)	0
Fatigue	35 (24.5)	5 (3.5)	40 (27.6)	1 (0.7)	23 (45.1)	1 (2.0)



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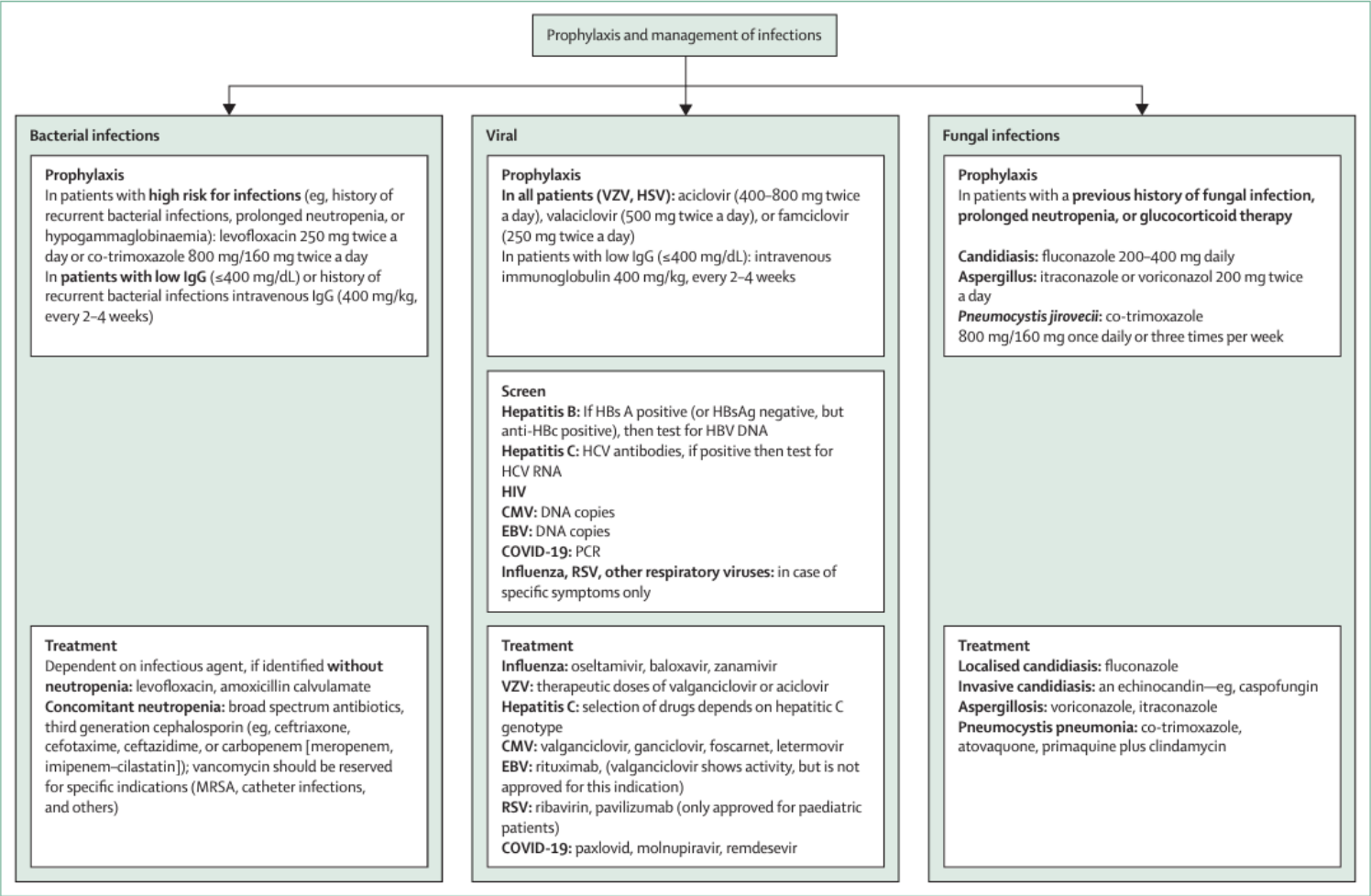


Figure 3: Recommendations for prevention and management of infections  
CMV=cytomegalovirus. EBV=Epstein-Barr virus. HBc=hepatitis core antigen. HBs=hepatitis B surface antigen. HBV=hepatitis B virus. HCV=hepatitis C virus. HSV=herpes simplex virus.  
MRSA=meticillin-resistant *Staphylococcus aureus*. RSV=respiratory syncytial virus. VZV=varicella-zoster virus.



AMC-A-methicillin-resistant *Staphylococcus aureus*; DCV-respiratory syncytial virus; VZV-varicella zoster virus.



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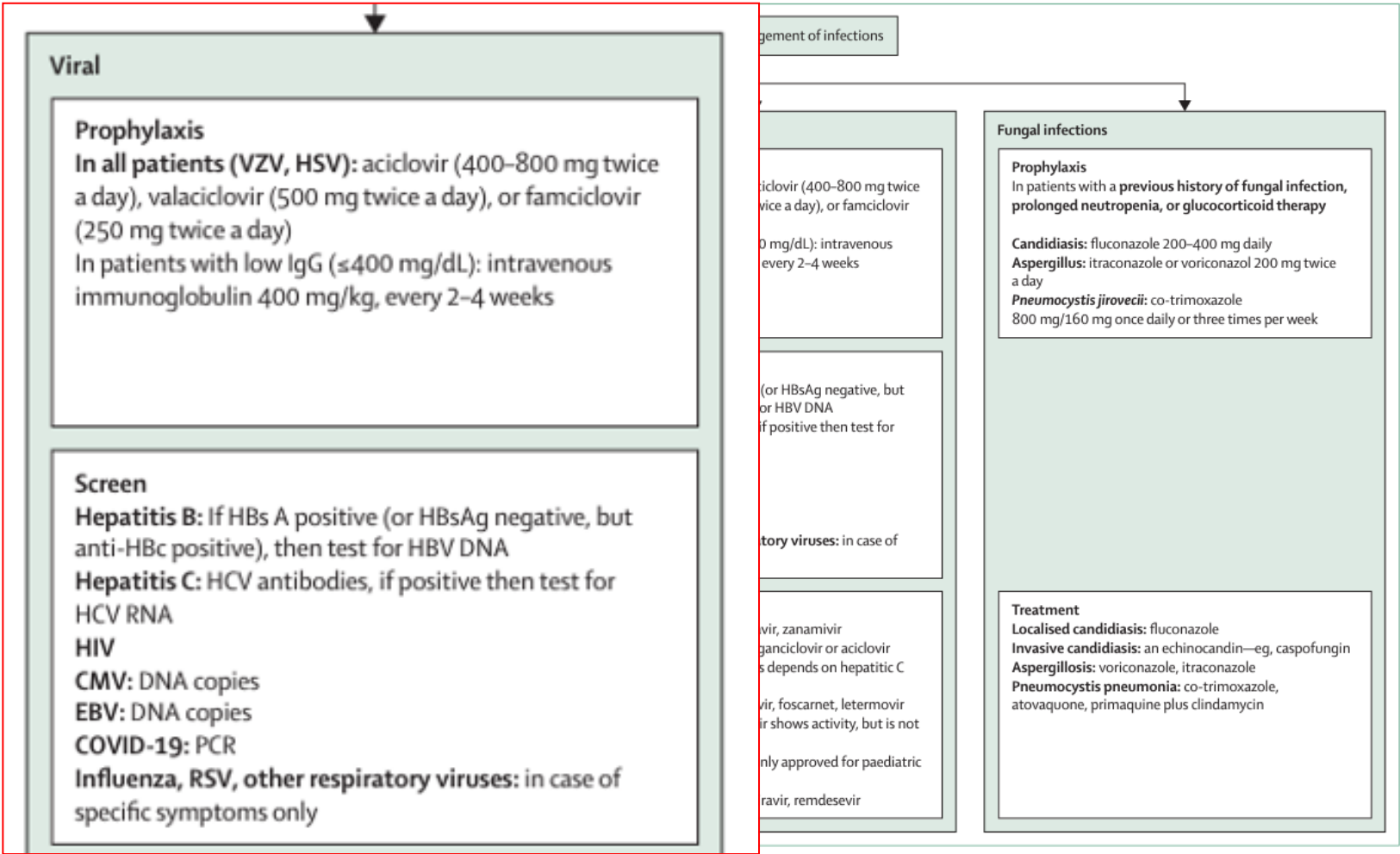


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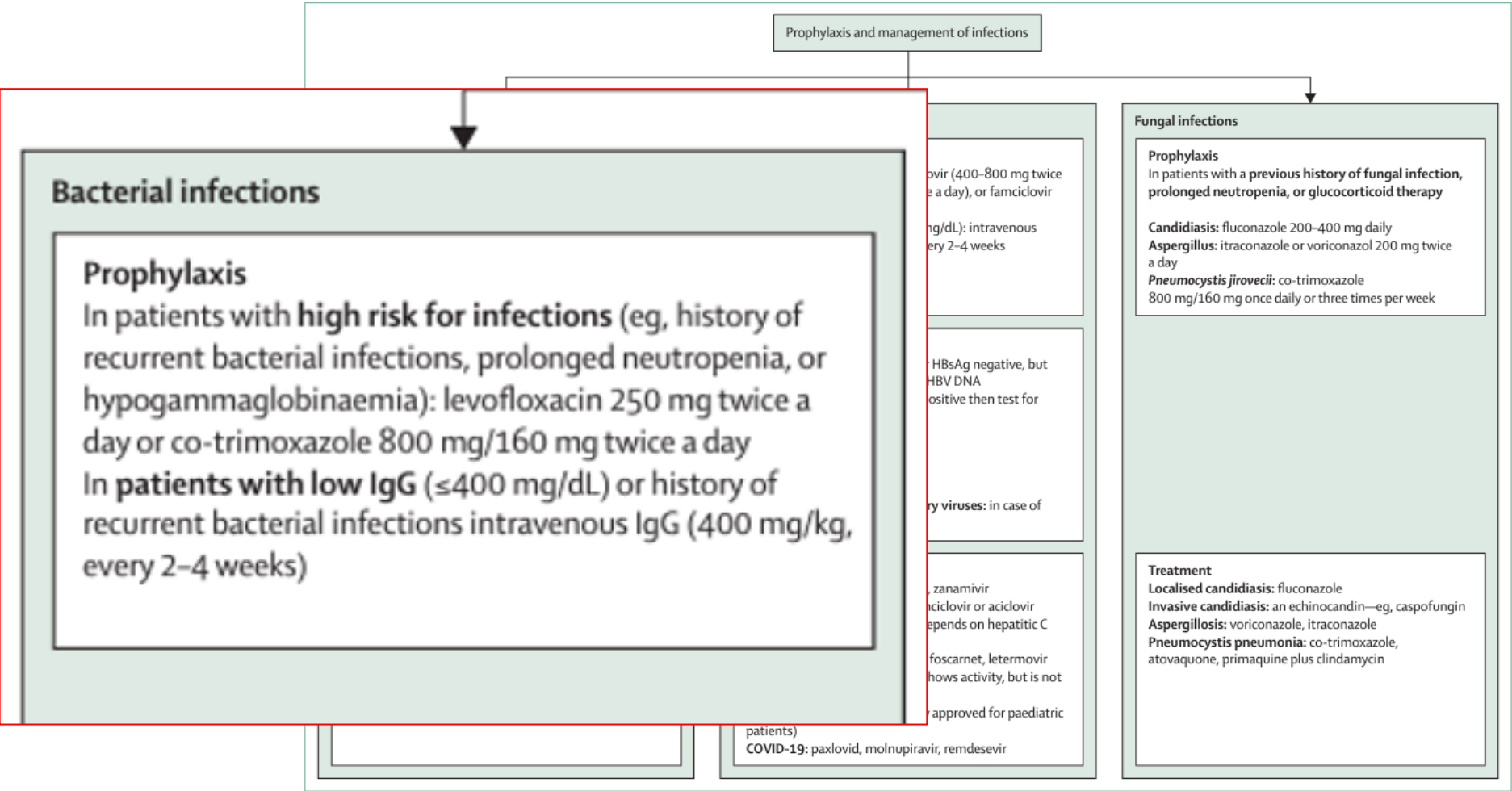


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- Follow general guidelines on use of live attenuated vaccines, however it should be noted that live vaccines are contraindicated in MM patients (level IIC)
- Ensure post-stem cell transplant vaccinations have been carried out (level III)
- COVID-19 vaccination recommended as per CDC guidelines, in patients without history of transplant (level III)
- Yearly influenza vaccination, pneumococcal vaccination and varicella zoster vaccination recommended in patients without history of transplant (level III)
- Close contacts should receive seasonal vaccines (level III)
- Health-care providers caring for MM patients should be fully immunized and should receive seasonal vaccines (level III)
- Prior to traveling to endemic areas of infection, patients should receive travel vaccinations and undergo consultation with a disease specialist (level III)

## REVIEW ARTICLE OPEN

 Check for updates

# Monitoring, prophylaxis, and treatment of infections in patients with MM receiving bispecific antibody therapy: consensus recommendations from an expert panel

Noopur Raje <sup>1,✉</sup>, Kenneth Anderson <sup>2</sup>, Hermann Einsele <sup>3</sup>, Yvonne Efebera<sup>4</sup>, Francesca Gay<sup>5</sup>, Sarah P. Hammond<sup>1,2,6</sup>, Alexander M. Lesokhin<sup>7,8</sup>, Sagar Lonial <sup>9</sup>, Heinz Ludwig <sup>10</sup>, Philippe Moreau <sup>11</sup>, Krina Patel<sup>12</sup>, Karthik Ramasamy <sup>13,14</sup> and Maria-Victoria Mateos <sup>15</sup>

## Vaccinations

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Flu; COVID, Pn conjugada, Hib (PNI - CRIEs/UBS)  
Zoster recombinante; RSV (novas e fora do PNI)

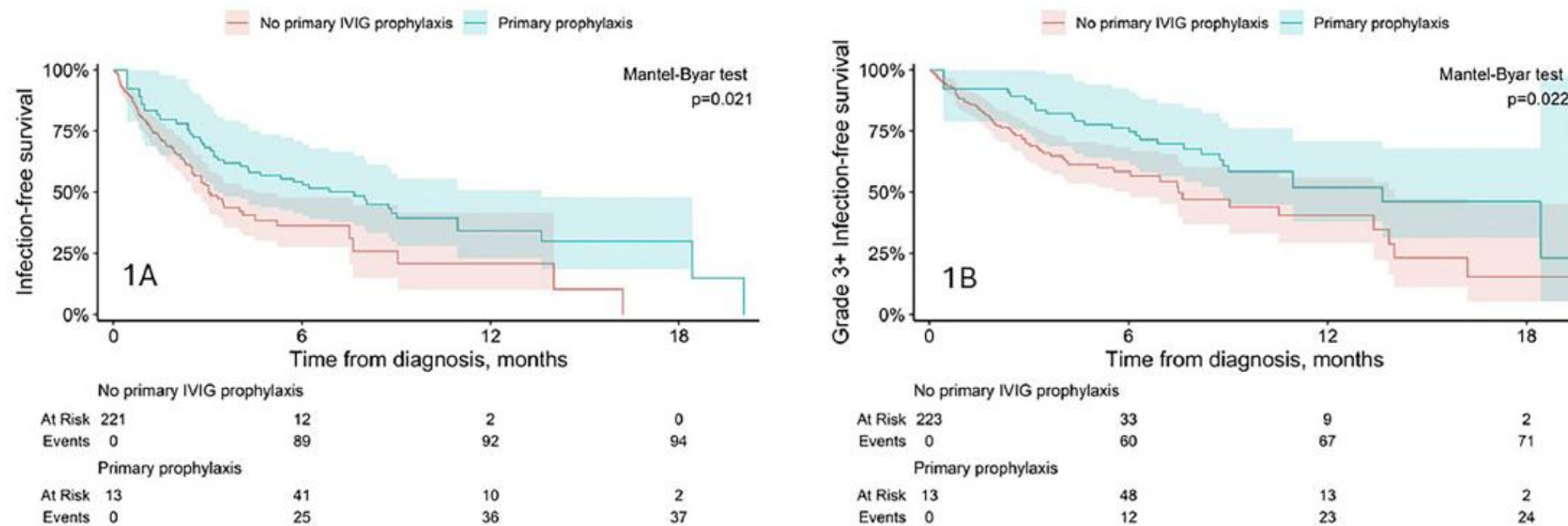
**ARTICLE** **OPEN**



# Effect of Intravenous Immunoglobulin (IVIg) Supplementation on infection-free survival in recipients of BCMA-directed bispecific antibody therapy for multiple myeloma

Meera Mohan <sup>1</sup>✉, Aniko Szabo <sup>2</sup>, Heloise Cheruvalath<sup>3</sup>, Anna Clennon<sup>4</sup>, Vineel Bhatlapenumarthi<sup>1</sup>, Anannya Patwari<sup>1</sup>, Metodi Balev<sup>5</sup>, Divaya Bhutani<sup>5</sup>, Asis Shrestha<sup>6</sup>, Sharmilan Thanendrarajan<sup>6</sup>, Binod Dhakal <sup>1</sup>, Maurizio Zangari<sup>6</sup>, Anup Trikannad<sup>6</sup>, Sruthi Vellanki<sup>6</sup>, Samer Al-Hadidi <sup>6</sup>, Suzanne Lentzsch<sup>5</sup>, Frits van Rhee <sup>6</sup>, Aishee Bag <sup>7</sup>, Anita D'Souza <sup>1</sup>, Nishi Shah <sup>8</sup>, Rajshekhar Chakraborty <sup>5</sup>, Mansi R. Shah<sup>7</sup> and Carolina Schinke <sup>6</sup>





**Fig. 1 Infection-free-survival.** Infection-free-survival for all-grade infection (**A**) and  $\geq$  grade 3 infection (**B**) in patients treated with and without primary IVIG.

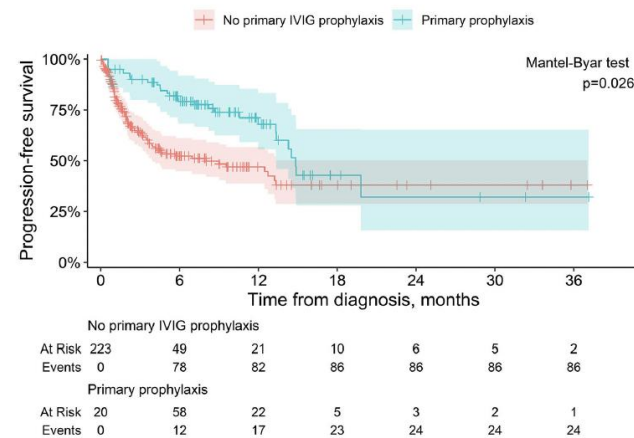


Fig. 2 Kaplan-Meier curve showing progression-free survival in patients with myeloma treated with BCMA-directed bispecific antibody therapy, stratified by IVIG status.

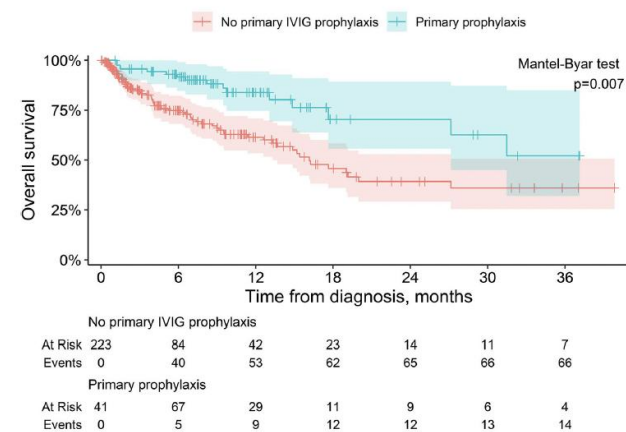


Fig. 3 Kaplan-Meier curve showing overall survival in patients with myeloma treated with BCMA-directed bispecific antibody therapy, stratified by IVIG status.

# Conclusion:

- BCMA and other targets offer great promise
- T-cell redirection with CAR T-cell therapies and bispecific antibodies is now moving into earlier lines of therapy
- Focus on supportive care will allow improved outcomes
- The future will explore alternate dosing schedules, combinations, and sequencing of all these approaches







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# Obrigado!

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