Primary Prophylaxis with Immunoglobulin Replacement Therapy Is Associated with Lower Cumulative Infection Burden and Healthcare Utilization in Patients with Multiple Myeloma Receiving BCMA-Directed BsAbs

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INTRODUCTION

- Patients with multiple myeloma (MM) receiving B-cell maturation antigen (BCMA)-directed bispecific antibodies (BsAbs) are at high risk for profound immunosuppression, hypogammaglobulinemia, and recurrent or severe infections, including pneumonia and sepsis/bacteremia[1-4]
- These infections contribute substantially to infection-related hospitalizations, healthcare utilization, treatment interruptions, and poor clinical outcomes[4,5]
- Although early immunoglobulin replacement therapy (IgRT) is increasingly considered for patients at highest risk of infection, real-world evidence evaluating this strategy remains limited[6]

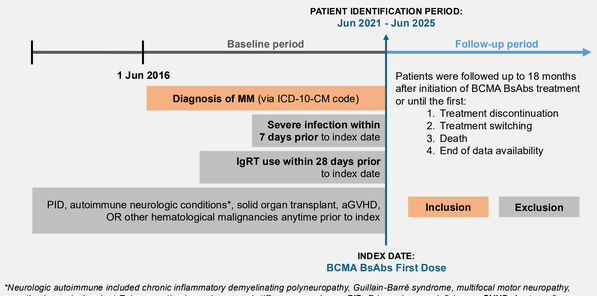
AIM

- To evaluate the association between early, primary prophylaxis with IgRT and cumulative infection burden among patients with MM receiving BCMA-directed BsAbs using the TriNetX U.S. electronic health record network

METHODS

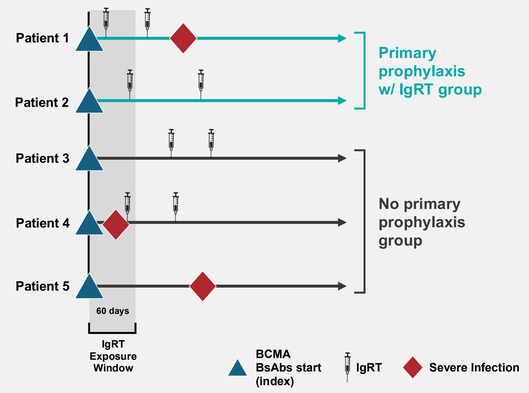
- Patients meeting the inclusion and exclusion criteria shown in Figure 1 were classified into the primary prophylaxis or no primary prophylaxis group (Figure 2)
- Endpoints of interest included severe and overall infection rates, infection-related inpatient hospital days, and IV antibiotic days, each expressed per patient-year

Fig 1. Cohort Definition and Study Timeline



*Neurologic autoimmune included chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome, multifocal motor neuropathy, myasthenia gravis, Lambert-Eaton myasthenic syndrome, and stiff person syndrome. **PID:** Primary immunodeficiency **aGVHD:** Acute graft-versus-host disease **ICD-10:** International classification of diseases, 10th revision

Fig 2. Primary Prophylaxis with IgRT Was Defined as IgRT within 60 days of BCMA BsAb Initiation and Prior to Severe Infection



CONCLUSIONS

Early IgRT was associated with substantially lower rates of severe bacterial and viral infections, as well as reduced infection-related healthcare utilization, among patients with MM receiving BCMA bispecific antibodies

These findings support early IgRT as an effective polyclonal immunoglobulin replacement strategy to reduce infectious morbidity during BCMA bispecific antibody therapy

RESULTS

Study population

- Among 965 patients initiating BCMA-directed bispecific therapy, 222 (23.0%) received IgRT as primary prophylaxis and 743 (77.0%) did not [Table 1]

Cumulative infection burden

- Primary prophylaxis was associated with a 57% lower rate of severe infections (1.11 vs 2.67 events/PPY; IRR 0.43, 95% CI 0.28–0.66) and a 25% lower overall infection rate (6.33 vs 8.14 events/PPY; IRR 0.75, 95% CI 0.60–0.94) [Figure 3A]

Healthcare utilization

- Primary prophylaxis was associated with 42% fewer infection-related inpatient hospital days and 37% fewer IV antibiotic days (6.56 vs 11.85 and 2.81 vs 4.24 days/PPY, respectively) [Figure 3B]

Clinically important infections

- Rates of severe bacterial and viral infections were 69% and 91% lower, respectively; rates of sepsis/bacteremia and pneumonia were 71% and 57% lower with primary prophylaxis [Figure 4]

Table 1: Baseline Characteristics

	Overall (n = 965)	Primary Prophylaxis (n = 222)	No Primary Prophylaxis (n = 743)	p-value*
Demographics				
Age at index, mean ± SD	69.6 ± 9.7	69.7 ± 9.8	69.6 ± 9.7	0.866
Sex, n (%)				0.659
Female	445 (46.1%)	99 (44.6%)	346 (46.6%)	
Male	520 (53.9%)	123 (55.4%)	397 (53.4%)	
Race, n (%)				0.349
White or Caucasian	602 (62.4%)	146 (65.8%)	456 (61.4%)	
Black or African American	233 (24.1%)	52 (23.4%)	181 (24.4%)	
Other/Unknown**	130 (13.5%)	24 (10.8%)	106 (14.3%)	
Clinical Characteristics				
Charlson Comorbidity Index, mean ± SD	1.9 ± 1.9	2.1 ± 2.0	1.8 ± 1.8	0.098
Time since MM diagnosis, months, mean ± SD	49.7 ± 31.4	49.1 ± 32.8	49.8 ± 31	0.763
Severe infection ≤12 months pre-index, n (%)***	276 (28.6%)	56 (25.2%)	220 (29.6%)	0.236
Treatment history before BCMA BsAb initiation, n (%)				
Anti-CD38 monoclonal antibodies	401 (41.6%)	114 (51.4%)	287 (38.6%)	0.001
Immunomodulatory drugs (IMiDs)	650 (67.4%)	162 (73.0%)	488 (65.7%)	0.051
Proteasome inhibitors	503 (52.1%)	141 (63.5%)	362 (48.7%)	<0.001
Systemic corticosteroids	834 (86.4%)	194 (87.4%)	640 (86.1%)	0.715
Hematopoeitic stem cell transplantation	381 (39.5%)	90 (40.5%)	291 (39.2%)	0.772

** P-values for categorical variables were calculated using chi-square tests; continuous variables were compared using two-sample z-tests. ** "Other" race includes American Indian or Alaska Native, Asian, Native Hawaiian, and Pacific Islander.*** History of severe infection was assessed within 12 months before index and on or after MM diagnosis.*

Figure 3A: Cumulative Infection Burden

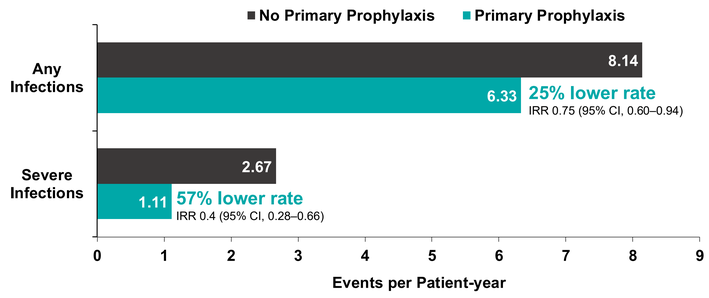


Figure 3B: Infection-related Healthcare Utilization

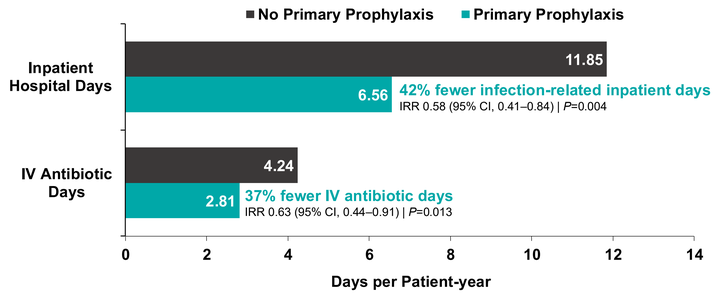
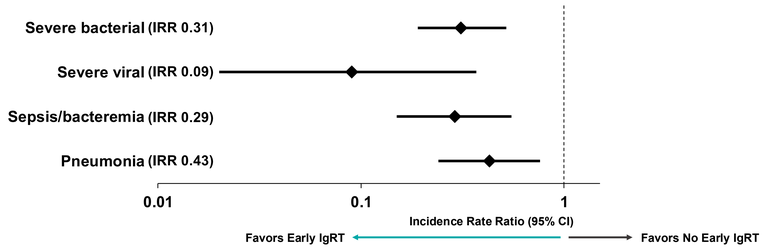


Figure 4. Incidence Rate Ratios for Selected Severe Infections: Primary Prophylaxis vs No Primary Prophylaxis



Note: Severe viral infections included viral meningitis and viral pneumonias. Severe bacterial infections included sepsis/bacteremia, bacterial pneumonia and meningitis, skin and soft-tissue infections, intra-abdominal infections, and osteomyelitis. Sepsis/bacteremia and pneumonia were evaluated as separate clinically defined infection categories and may overlap with the severe bacterial and severe viral infection categories

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