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POSTER ABSTRACTS

905.OUTCOMES RESEARCH-LYMPHOID MALIGNANCIES

Flat Dose Intravenous Immunoglobulin Primary Infection Prophylaxis in Multiple Myeloma Patients on Bispecific Antibody Therapy: Vanderbilt Experience

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BACKGROUND

Bispecific antibodies (BsAbs) are novel immunotherapeutic agents with prolific anti-multiple myeloma (MM) efficacy in highly relapsed/refractory disease (RRMM). They have been associated with profound and prolonged hypogammaglobinemia which represents a unique challenge regarding increased risk of serious (sometimes fatal) infections. Though IVIG has historically been dosed at 0.4g/kg for secondary prophylaxis, there is still uncertainty in optimal timing, schedule and frequency of supplementation in MM patients. At Vanderbilt University Medical Center, we have adopted a flat dose 10g IVIG prophylaxis schedule, which on average delivers ~36% of historical, weight-based dosing. At present, expert recommendations advise IVIG replacement every 4 weeks in recipients of BsAb starting the second month of therapy and continuing until the end of therapy or until serum IgG levels reach > 400 mg/dL, whichever is longer (*Mohan M et al. Br J Haematol.2023;00:1-11*). Considering that MM BsAbs are currently used with continued dosing schedule, adoption and anticipated new BsAb approvals are increasing, IVIG has previously been on national/global shortage (occasionally unavailable), IVIG replacement during hypogammaglobulinemia represents a crucial aspect of adequate infection prophylaxis in MM, we explored the impact of our institutional 10g IVIG prophylaxis on infection rates in RRMM patients receiving BsAbs. Prior studies with comparable BsAbs reported Grade (G) ≥3 infection rate of 32-45% and 18%, in anti-BCMA and anti-GPRC5D BsAbs, respectively. In these trials, overall, 14-53% of patients received IVIG prophylaxis.

METHODS

We performed a retrospective review using electronic medical record of RRMM patients receiving anti-BCMA or anti-GPRC5D BsAbs from Jan 2019 to Dec 2022, either on clinical trials or as a standard of care at our institution. The inclusion criteria were minimum of two months of BsAb therapy, and the use of at least one month of monthly IVIG prophylaxis for serum IgG < 400 mg/dL. All patients were also on baseline valacyclovir, trimethoprim-sulfamethoxazole and levofloxacin prophylaxis. Routine disease and treatment specifics as well as infection rates and grades were collected. Infections were defined as mild (infections treated outpatient), moderate (required hospital admission) or severe (hospital admission with intensive care unit level of care), next to also being graded by CTCAE v5 with the rest of hematologic and non-hematologic adverse events (AEs).

RESULTS

A total of 30 patients with RRMM were identified. Table 1 illustrates the demographic and disease specifics: 79% received a median (range) of 4 (2-7) lines of prior therapy, over half were penta-class exposed, 27% were triple and quad refractory, 67% received a prior autologous stem cell transplant and 17% underwent prior treatment with BCMA targeting CAR-T therapy. All except 2 patients received BsAb therapy on clinical trials. Anti-GPRC5D BsAb was used to treat 60% of patients, while the rest (40%) received anti-BCMA BsAb, all of which were given for a median of 27 (12-45) months (Table 1). Overall, 30% of patients had one infectious episode, while 43% had ≥2. Viral infections (57%) were twice as common as bacterial (30%)

(Table 2). Infections were mild in 60%, moderate in 23%, and severe in 6.6% of patients. We observed 27% rate of G ≥3 infectious complications. Patients had a median (range) IgG at diagnosis of 1284(196-5431), and 499(210-2246) at the time of onset of first infection (IgG values at the start of BsAb therapy, at first and at ≥2 infections are outlined in Table 2). The rate of G ≥3 neutropenia and lymphopenia was 6.6% and 30% respectively. There were 2 (6.6%) sepsis related deaths, one each with anti-BCMA and anti-GPRC5D BsAbs. Table 2 also describes severity and the rates of cytokine release syndrome and neurotoxicity.

CONCLUSIONS

We observed relatively lower rate of severe or ≥ G3 infectious events with 10g flat IVIG dosing schedule. While our results represent a small, single-institutional cohort of predominantly anti-GPRC5D treated RRMM patients and require prospective validation in a randomized (IVIG 10g vs 0.4g/kg body weight) fashion, they demonstrate feasibility of reduced level dosing of a critical resource such as IVIG, in the fast expanding, national/global BsAb-based MM armamentarium.

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Table 1: Demographics, disease, and treatment characteristics of study patients.

Demographics	N (%) or Median (min-max)
Age	71 (45-82)
Men	21 (70%)
Women	9 (30%)
Caucasian	20 (67%)
African American	10 (33%)
Year of Myeloma Diagnosis	
2000-2010	7 (23%)
2010-2020	23 (77%)
Extramedullary Disease	6 (21%)
>60% bone marrow plasmacytosis at diagnosis	13 (43%)
R-ISS Stage	
I	8 (27%)
II	12(40%)
III	10 (33%)
ECOG Performance Status	
1	25 (83%)
2	5(17%)
High Risk cytogenetics*	13 (43%)
Median Prior lines of therapy	4 (2-7)
Previous Treatment Exposure	
Triple Class	6 (20%)
Quad Class	9 (30%)
Penta Class	15 (50%)
Prior BCMA	9 (30%)
Refractory status to therapy	
Double Class	5 (17%)
Triple Class	8 (27%)
Quad Class	8 (27%)
Penta Class	2 (6%)
Previous ASCT	20 (67%)
Previous CAR-T (BCMA)	5 (17%)
Type of Bispecific Therapy	
Anti-BCMA BsAb**	12 (40%)
Anti-GPRC5D BsAb	18 (60%)
Duration of BsAb Therapy (months)	27 (12-45)

N: number; R-ISS: revised international staging system; ECOG: eastern cooperative oncology group; *defined by the presence of del17p, 1q21 gain or amplification, t(4;14), t(14;16), t(14;20); BCMA: B cell maturation antigen; ASCT: autologous stem cell transplantation; CAR-T: chimeric antigen receptor T cell; **of these, 2 patients were treated standard of care, and rest received therapy on various clinical trials; GPRC5D: G protein-coupled receptor, class C, group 5, member D; BsAb: bispecific antibody.

Table 2. Infection, cytokine release syndrome, neurotoxicity, and non-hematologic complications on therapy and primary intravenous immunoglobulin prophylaxis.

	N (%) or Median (min-max)	Grade 1 N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)	Grade 5 N (%)
Number of infections						
1	9 (30%)					
≥ 2	13 (43%)					
Type of infection						
Bacterial	9 (30%)					
Viral	17 (57%)					
Severity of Infections						
Mild	18 (60%)					
Moderate	7 (23%)					
Severe	2 (6.6%)					2 (6.6)
Upper Respiratory Infections			15 (50%)	4 (13%)	1 (3.3%)	
Infectious Diarrhea		4 (13%)				
Bacteremia				1 (3.3%)		
Sepsis						2 (6.6)
Urinary tract infection			1 (3.3%)			
IgG at start of BsAb Therapy	1284 (196-5431)					
IgG at First Infection	499 (210-2246)					
IgG at ≥ Second Infection	519 (110-1844)					
CRS	17 (57%)					
Grade 1	7 (23%)					
Grade 2	10 (33%)					
Time to onset of CRS (days)	3 (2-8)					
Duration of CRS (days)	2 (1-3)					
Neurotoxicity (NT)	3 (10%)					
Grade 1	3 (10%)					
Time to onset of NT (days)	9.5 (4-15)					
Duration of NT (days)	2 (1-3)					
Neutropenia at 1st infection		4 (13%)		2 (6.6%)		
Lymphopenia at 1st infection			6 (20%)	9 (30%)		
Non-Hematologic AEs						
Nail changes		4 (13%)	1 (3.3%)			
Skin rash		4 (13%)		2 (6.6%)		
Dysgeusia		9 (30%)				
Weight loss		5 (17%)	1 (3.3%)	3 (10%)		
Fatigue		3(10%)	1 (3.3%)			

N: number; BsAb: bispecific antibody; CRS: cytokine release syndrome; AEs: adverse events.

Figure 1

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