IVIG Replacement Therapy and Clinical Outcomes in Adults with Hematologic Malignancies and Secondary Hypogammaglobulinemia: A Propensity Score-Matched Analysis

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Introduction

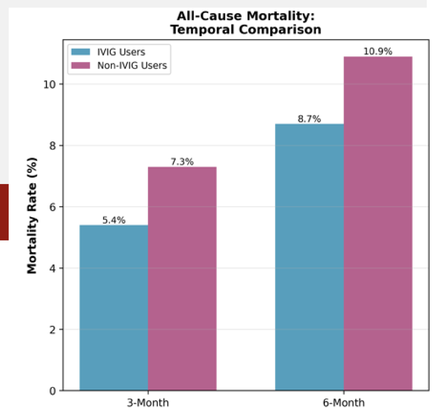
- Secondary hypogammaglobulinemia (SHG) is an increasingly recognized complication in patients with hematologic malignancies, including multiple myeloma (MM), chronic lymphocytic leukemia, and non-Hodgkin lymphoma, which predisposes them to severe infections.
- The treatment paradigm shifted with the advent of B-cell-directed therapies—Including anti-CD20 monoclonal antibodies, CAR-T cell therapy, and bispecific antibodies— particularly in MM; the incidence and severity of SHG have also dramatically increased
- Intravenous immunoglobulin (IVIG) replacement therapy is used to mitigate infectious complications, yet its mortality benefit remains unclear.

Aim

To compare survival impact, infection rates, and healthcare utilization between IVIG users and non-users among patients with hematologic malignancies and secondary hypogammaglobulinemia.

Results

- ✓ We identified total IVIG users (n=2,785) and non-IVIG users (n=31,095). After PSM, 2,730 patients remained in each cohort.
- ✓ At 3 months, IVIG users had lower all-cause mortality (95% CI: 0.600, 0.909; log-rank p=0.002).
- ✓ At 6 months, mortality remained lower (95% CI: 0.679, 0.940; log-rank p=0.004).
- ✓ Bacterial infection risk was lower at 3 months (log-rank p=0.004), though not sustained at 6 months (log-rank p=0.072).
- ✓ Hospitalization rates were lower at both 3 and 6 months. (log-rank p<0.001).
- ❖ No significant between-group differences were noted at either time point for MI, VTE, viral or fungal infection, and ER visits.



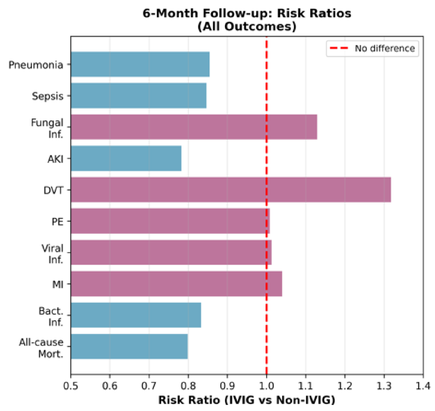


Table 1. Baseline Patients' Characteristics - After PSM

Characteristic	(IVIG users)	(Non-IVIG users)	Std diff.
Demographics			
Age at Index (Mean ± SD)	63.3 ± 18.1	63.9 ± 16.3	0.037
White	86.4%	86.5%	0.002
American Indian or Alaska Native	0.4%	0.4%	<0.001
Unknown Race	2.9%	2.3%	0.034
Female	45.5%	45.6%	0.002
Native Hawaiian or Other Pacific Islander	0.4%	0.4%	<0.001
Black or African American	5.0%	5.1%	0.002
Male	54.5%	54.4%	0.002
Other Race	3.6%	3.8%	0.010
Asian	1.6%	1.8%	0.014
Diagnosis			
Essential hypertension	55.2%	54.5%	0.015
Diabetes mellitus	21.8%	21.4%	0.009
Chronic kidney disease (CKD)	19.3%	19.4%	0.003
Tobacco use	3.4%	3.1%	0.017
Heart failure	14.6%	13.4%	0.033
Stem cells transplant status	23.0%	23.3%	0.005
Diseases of liver	17.3%	16.5%	0.022
Other chronic obstructive pulmonary disease	8.6%	8.6%	<0.001
Secondary and unspecified malignant neoplasm of lymph nodes	1.5%	1.4%	0.006
Secondary malignant neoplasm of other and unspecified sites	9.7%	9.3%	0.016
Multiple myeloma and malignant plasma cell neoplasms	30.0%	29.3%	0.015
Lymphoid leukemia	44.5%	46.5%	0.039
Follicular lymphoma	11.4%	11.5%	0.002
Non-follicular lymphoma	25.8%	24.2%	0.036
Mature T/NK-cell lymphomas	3.2%	3.0%	0.013
Other specified and unspecified types of non-Hodgkin lymphoma	32.0%	31.2%	0.016
Medication			
tisagenlecleucel	0.4%	0.4%	0.012
axicabtagene ciloleucel	2.0%	1.7%	0.022
brexucabtagene autoleucel	0.5%	0.5%	0.010
lisocabtagene maraleucel	0.8%	0.8%	0.004
idecabtagene vicleucel	0.5%	0.5%	<0.001
ciltacabtagene autoleucel	0.8%	0.8%	0.008
teclistamab	1.4%	0.9%	0.045
epcoritamab	0.4%	0.4%	<0.001
mosunetuzumab	0.4%	0.4%	<0.001
talquetamab	0.4%	0.4%	<0.001
elranatamab	0.4%	0.4%	<0.001
glofitamab	0.4%	0.4%	<0.001
blinatumomab	1.4%	1.0%	0.030
Laboratory			
IgG [Mass/volume] in Serum(Mean ± SD)	45.1 ± 150.6	28.6 ± 114.7	0.124
IgG [Mass/volume] in Serum (0 - 0 g/L)	74.0%	74.9%	0.023

Method

- We conducted a multicenter, retrospective, propensity score-matched (PSM) study using the TriNetX database. Adults (≥18 years) with hematologic malignancies and concurrent SHG were included.
- Outcomes were assessed at 3 and 6 months.
- **Primary outcomes**: all-cause mortality and bacterial infections.
- **Secondary outcomes**: viral and fungal infections, sepsis, acute kidney injury (AKI), venous thromboembolism (VTE), and acute myocardial infarction (MI). Risk ratios (RRs), confidence intervals (CIs), and Kaplan-Meier survival probabilities with log-rank p-values were calculated.

Conclusions

- Our study revealed that **IVIG was associated with a statistically significant reduction in all-cause mortality at 3 and 6 months, and lower bacterial infections at 3 months in patients with hematologic malignancies and secondary hypogammaglobulinemia**.
- These real-world findings underscore the potential early survival and anti-infective benefit of IVIG in this population—critical in immunocompromised patient management.
- Limitations include retrospective design, reliance on administrative data, and potential unmeasured confounding—warranting prospective validation.

References

1. Otani IM, et al. Practical guidance for the diagnosis and management of secondary hypogammaglobulinemia: a Work Group Report of the AAAAI Primary Immunodeficiency and Altered Immune Response Committees. J Allergy Clin Immunol. 2022;149(5):1525-1560.

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