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– ORIGINAL PAPERS –

Single Center Study Regarding Subucutaneous Immunoglobulins for Secondary Immunodeficiencies in Hematological Malignancies

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Abstract

Purpose: *We report a single center study experience with subcutaneous Immunoglobulin administrations in patients with secondary hematological defficiencies, aiming to explore the outcomes of the infectous complications in these patients.*

Materials and methods*: Evaluation of a lot of patients from the Hematology Department of Fundeni Clinical Institute that have been treated with subcutaneous Immunoglobulins since may 2022 untill september 2024; a retrospective, unicentric study, based on data from electronic records.*

Results*: We evaluated 32 patients for a period of over 2 years, diagnosed with multiple myeloma receiving specific therapy, that presented multiple infectious complications wtih at least 2 subcutaneous immunoglobulin (SCIg) administrations. The median age of the patients was 67 years old and 16 patients (50%) of the patients patients had hypogammaglobulinemia. We analzyed the number and severity of infections before and after multiple SCIg administrations – prior to SCIg administration 21 patients(65.63%) patients had severe grade 3 or 4 infections, with half of the patients (16) having hypogammaglobulinemia. Following multiple SCIg administrations, 24 patients (75%) did not present any infection following 3 consecutive administrations, and 12 out of 16 patients with hypogammaglobulinemia (75%) having IgG values elevated over 5 g/l.*

Conclusions: *The obtained results demonstrated a great reduction of the frequency and severity of infections in patients with SCIg administrations. Early administrations may decrease the risk of infection complications and mortality*

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Introduction

Multiple myeloma (MM) is a neoplasm of bone marrow plasma cells that causes severe immunodeficiency[1], [2]. The result is a high incidence of infectious complications, including life-threatening infections[3].

Immunoglobulin replacement therapy (IgRT) may be dispensed intravenously (IV) or subcutaneously (SC). In secondary immunodeficiency, the effectiveness and safety of SCIG have been reported in numerous subjects with lymphoproliferative diseases and hypogammaglobulinemia[4], [5], [6]. Infectious complications are a major cause for chemotherapy treatment delay and thus is associated with a poor prognosis, even more so in elderly patients who have a higher risk of infection[7], [8].

By decreasing the rate of infections, the prophylactic administration of SCIg improves both adherence to chemotherapy and health-related quality of life, and is cost-effective by reducing the need of hospitalization and the use of antibiotics[9].

Material and methods

A retrospective descriptive analysis was conducted and 39 patients were screeened for this study, and 32 patients that received at least 2 SCIg administrations in Fundeni Clinical Institute were included in the study. Clinical patient data were collected from Fundeni Clinical Institute database and patients' medical records. Microsoft Excel was used to build the database and statistical analysis was done through XLSTAT extension. Inclusion criteria were IgG values < 5 g/l and multiple infections or one severe (grade 3+) infection.

We analyzed the patient's variables, such as age, gender, diagnosis, previous treatment (including numbers of chemotherapy lines and previous autologous transplant), the severity of the infectious complications before and after SCIg and IgG values following multiple administrations.

Results

Patient characteristics: We included in this study 32 patients which received at least 2 SC Ig administration. The male to female ratio in the population study was 1.28 (n=18 to n=14). The median age was 67 years (range 40-80).(Figure 1)

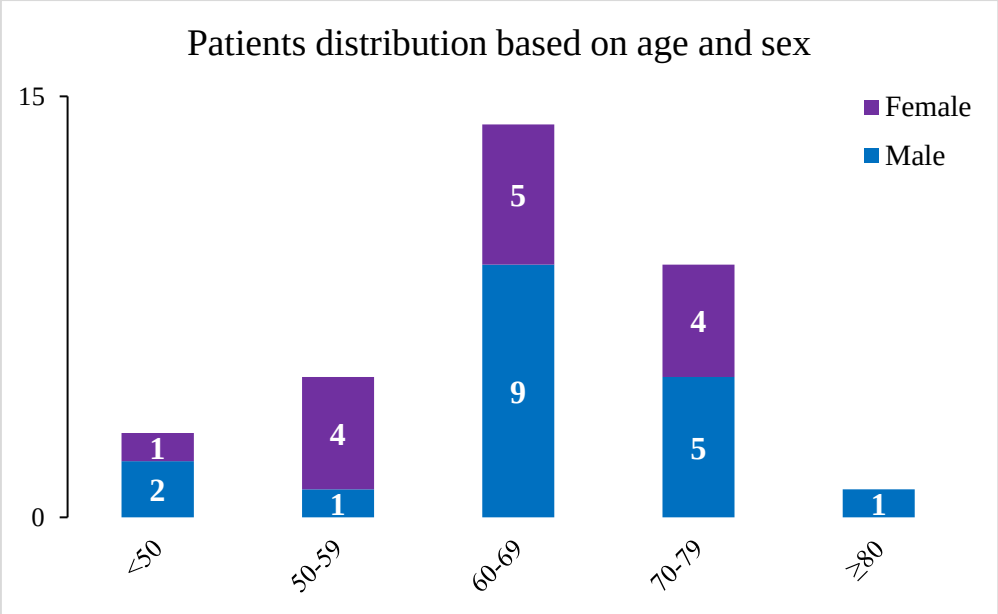

Figure 1. *Age and sex distribution within the study groug*

The study group consisted of 12 patients diagnosed with IgG multiple myeloma (37.5%), 10 with IgA MM (31.25%), 1 patient with IgM MM (3.13%), and 9 patients with micromolecular myeloma (28.13%), of which 2 patients also had a diagnosis of light chain amyloidosis (6.25%) (Fig. 2).

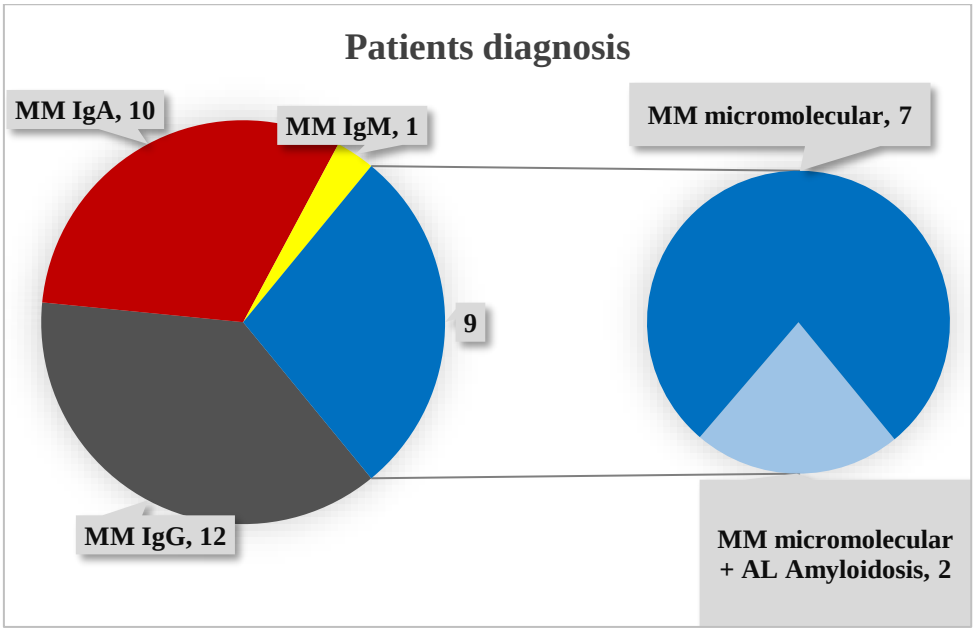

Figure 2. *Patient distribution based on diagnosis*

According to disease treatment, 12 patients (37.5%) had only received 1 line of treatment prior to immunoglobulin administration (range 1-10)(Fig. 3)

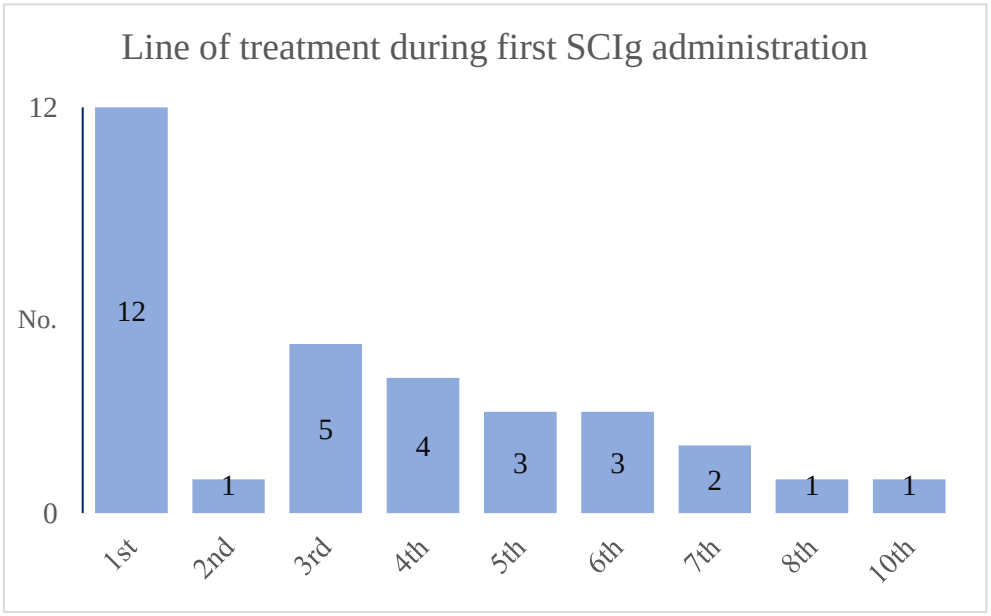

Figure 3. *Line of treatment during the first SCIg administration*

A. 28 patients received monoclonal anti CD38 antibodies (87.5%), with 20 patients following consolidation with autologous stem cell transplant (62.5 %), and 11 patients (34.38%) received either GPRC5D or BCMA bispecific antibodies (BsAbs) (Fig. 4)

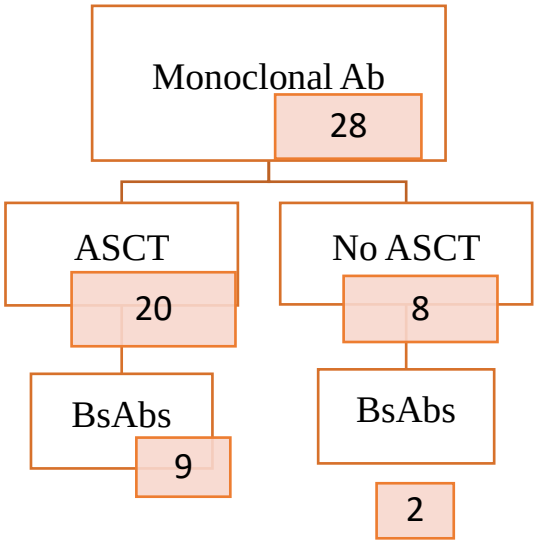

Figure 4. *Patients history of novel therapies that induce immunodeficiencys*

R Out of the 32 patients included in the study group, 21 patients (65.63%) had one grade 3 or 4 infection, 10 patients (31.25%) had multiple grade 2 infections and 1 patient (3.13%) had reccurent grade 1 infections (Fig. 5).

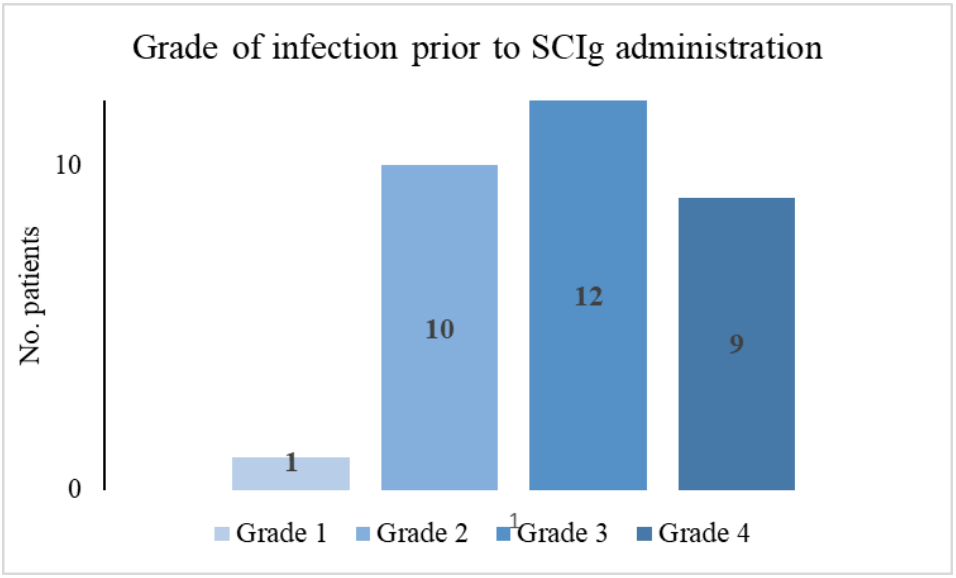

Figure 5 *Severity of infections in study patients prior to SC Ig administration.*

Half of the patients included in this study had hypogammaglobulinemia IgG<5 g/l prior to SCIg treatment.

14 patients (43.75%) received 6 or less administrations of SCIg, 15 patients (46.88%) received between 7 and 12 administrations and 3 patients received more than 12 SCIg administrations (9.38%) (Fig 6). SCIg was discontinued in patients following at least 6 consecutive administrations without an infection.

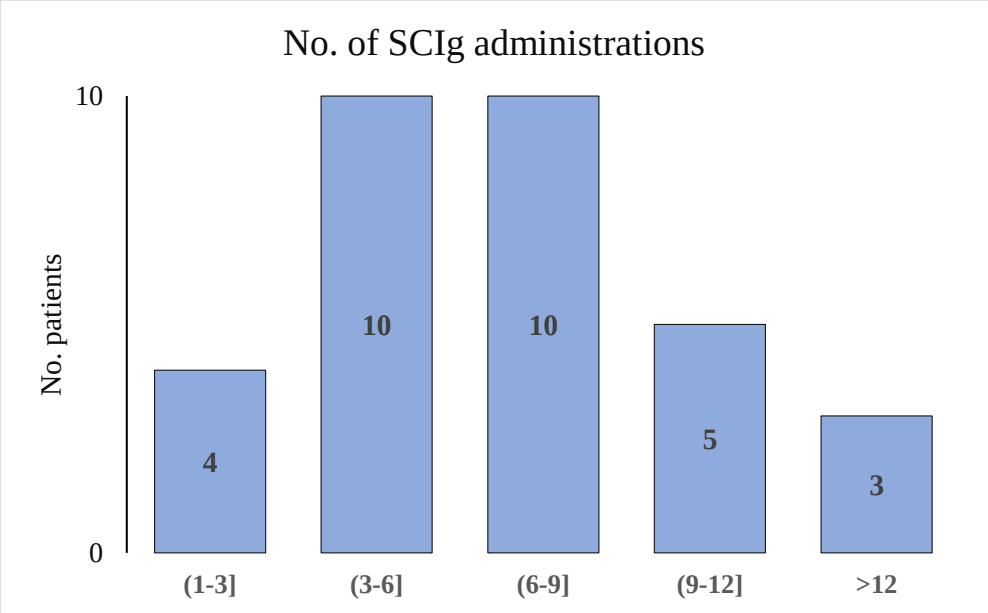

Figure 6. *Number of SCIg administrations in our study grou.*

We compared the frequency and severity of the infectious complications to the patients that received SCIg administrations (Fig. 7), alongside with polyclonal IgG values measured every 3 SCIg administratations in patients with hypogammaglobulinemia (Fig. 8).

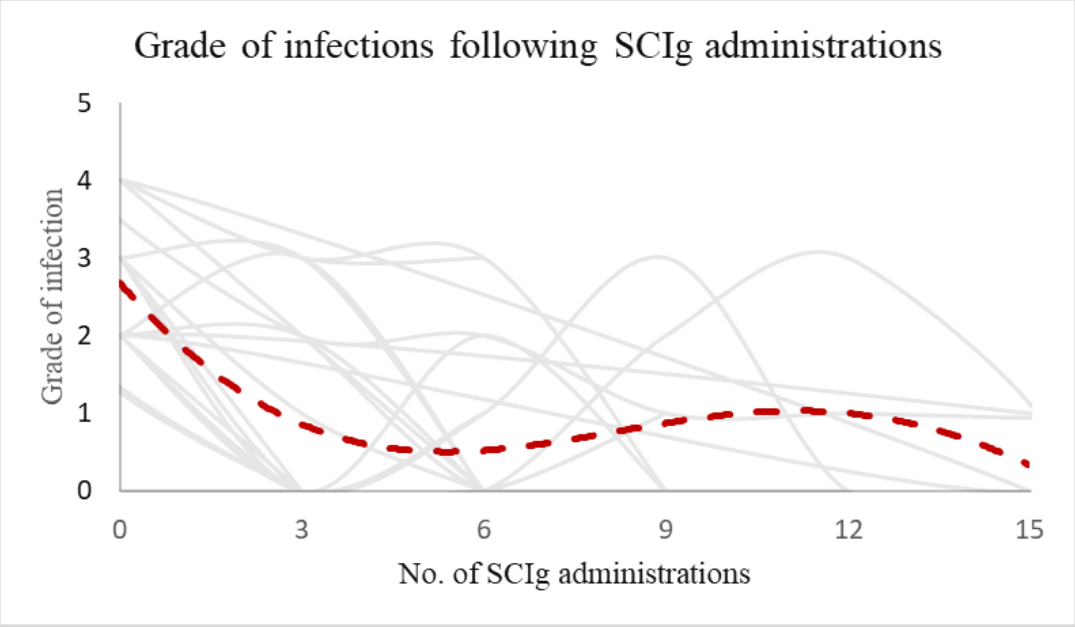

Figure 7. *Severity of infections following multiple SCIg administrations. We can observe by the trendline a decrease in the number and severity of the infections following 3 SCIg administrations.*

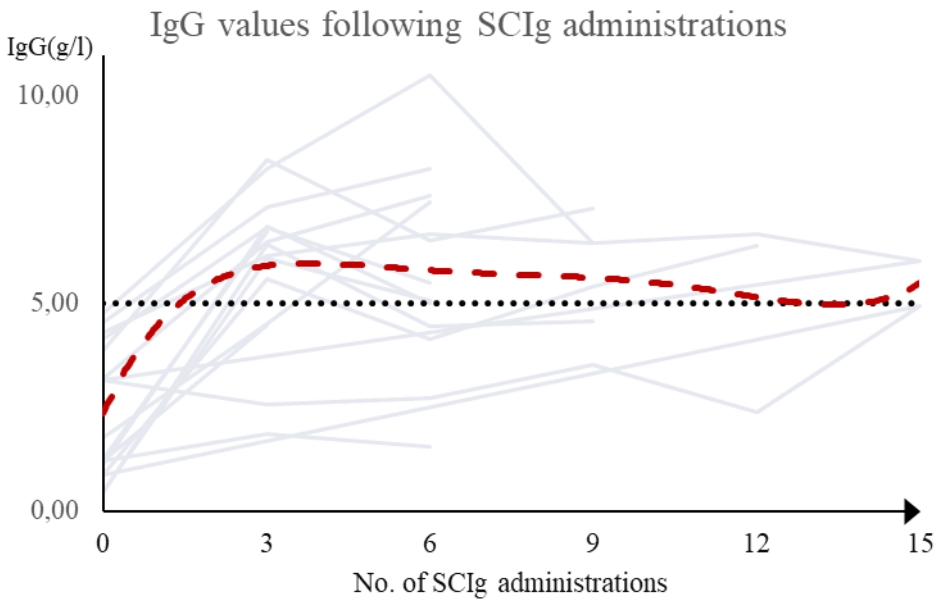

Figure 8. *Polyclonal IgG values evolution during multiple SCIg administrations. We can observe be the trendline an increase in IgG values, resulting in an IgG value mantained over 5g/l*

The infections decreased both in frequency and in severity, with 24 patients (75%) not having not having any more infections following at least 3 consecutive administrations, with 10 patients (31.25%) having SCIg discontinued after 6 SCIg adminsitrations without any infectious complication.

Discussions

Our study supports that multiple myeloma alongside it's treatment severely induce secondary immunodefficiency that results in frequent and severe infections, causing treatment delays, especially in front-line treatment.

These findings strongly support the prophylaxis with subcutaneous immunoglobulins in multiple myeloma patients, with a decrease of infections after multiple administrations. These results apply in all patients disregarding the number of treatment lines, history of ASCT, or use of monoclonal antibodies or bispecific antibodies. IgG values were also both elevated and mainted over 5g/l following multiple administrations.

2 patients (6.25%) with IgG values <5g/l suffered died from infections after 2 SCIg administrations, and 3 multiple myeloma patients that were screened but did not make the study had severe infection that resulted in death, following one single SCIg administration. These support our finding that immunoglobulin administration should be initiated as soon as possible in secondary immunodeficiency patients in order to decrease the risk of mortality.

The study's limitations, stemming from its retrospective design, a small number of patients registered, and the lack of follow-up in patients during and after the study, might have impacted the obtained results.

Conclusion

Subcutaneous Immunoglobulin replacement therapy greatly reduce infectious complications both in frequency and severity, with less0 delays in multiple myeloma treatment and thus better results. Patients have better quality of life, decreasing the number of hosptizatins and death related infections.

No funding for this study

Conflicts of interest

I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work. The authors declare no conflict of interest

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

1. K. R. A and R. S. Vincent, “Multiple Myeloma,” New England Journal of Medicine, vol. 351, no. 18, pp. 1860–1873, Aug. 2024, doi: 10.1056/NEJMra041875.

2. S. Srivastava and P. Wood, “Secondary antibody deficiency – causes and approach to diagnosis,” Clinical Medicine, vol. 16, no. 6, pp. 571–576, Dec. 2016, doi: 10.7861/clinmedicine.16-6-571.

3. B. M. Augustson et al., “Early Mortality After Diagnosis of Multiple Myeloma: Analysis of Patients Entered Onto the United Kingdom Medical Research Council Trials Between 1980 and 2002—Medical Research Council Adult Leukaemia Working Party,” Journal of Clinical Oncology, vol. 23, no. 36, pp. 9219–9226, Dec. 2005, doi: 10.1200/JCO.2005.03.2086.

4. N. Compagno, G. Malipiero, F. Cinetto, and C. Agostini, “Immunoglobulin Replacement Therapy in Secondary Hypogammaglobulinemia,” Front Immunol, vol. 5, Dec. 2014, doi: 10.3389/fimmu.2014.00626.

5. M. Reiser et al., “Management of patients with malignancies and secondary immunodeficiencies treated with immunoglobulins in clinical practice: Long-term data of the SIGNS study,” Eur J Haematol, vol. 99, no. 2, pp. 169–177, Aug. 2017, doi: 10.1111/ejh.12900.

6. C. Ye et al., “Secondary Immunodeficiency and Hypogammaglobulinemia with IgG Levels of <5 g/L in Patients with Multiple Myeloma: A Retrospective Study Between 2012 and 2020 at a University Hospital in China,” Medical Science Monitor, vol. 27, Mar. 2021, doi: 10.12659/MSM.930241.

7. B. Constantin, S. Barbu, L. Zidaru, L. Cirlan, M. Gaman, and S. Badelita, “Enhancing Multiple Myeloma Treatment Outcomes with Ixazomib: Insights and Perspectives,” Documenta Haematologica - Revista Romana de Hematologie, vol. 2, no. 2, pp. 75–79, Jul. 2024, doi: 10.59854/dhrrh.2024.2.2.75.

8. L. Cirlan, S. Badelita, and D. Coriu, “Multiple Myeloma and Solid Tumors – a Frequent Rarity –,” Documenta Haematologica - Revista Romana de Hematologie, vol. 2, no. 1, pp. 27–29, Mar. 2024, doi: 10.59854/dhrrh.2024.2.1.27.

9. A. Vacca, A. Melaccio, A. Sportelli, A. G. Solimando, F. Dammacco, and R. Ria, “Subcutaneous immunoglobulins in patients with multiple myeloma and secondary hypogammaglobulinemia: a randomized trial,” Clinical Immunology, vol. 191, pp. 110–115, Jun. 2018, doi: 10.1016/j.clim.2017.11.014.