

# Determination of Frequency and Risk Factors of Secondary Malignancy Development in Hematological Malignancies

Ennur RAMADAN<sup>1</sup>, Güven ÇETİN<sup>2</sup>, Özge PASİN<sup>3</sup>

<sup>1</sup>Bezmialem Vakif University, Faculty of Medicine, Istanbul, Türkiye

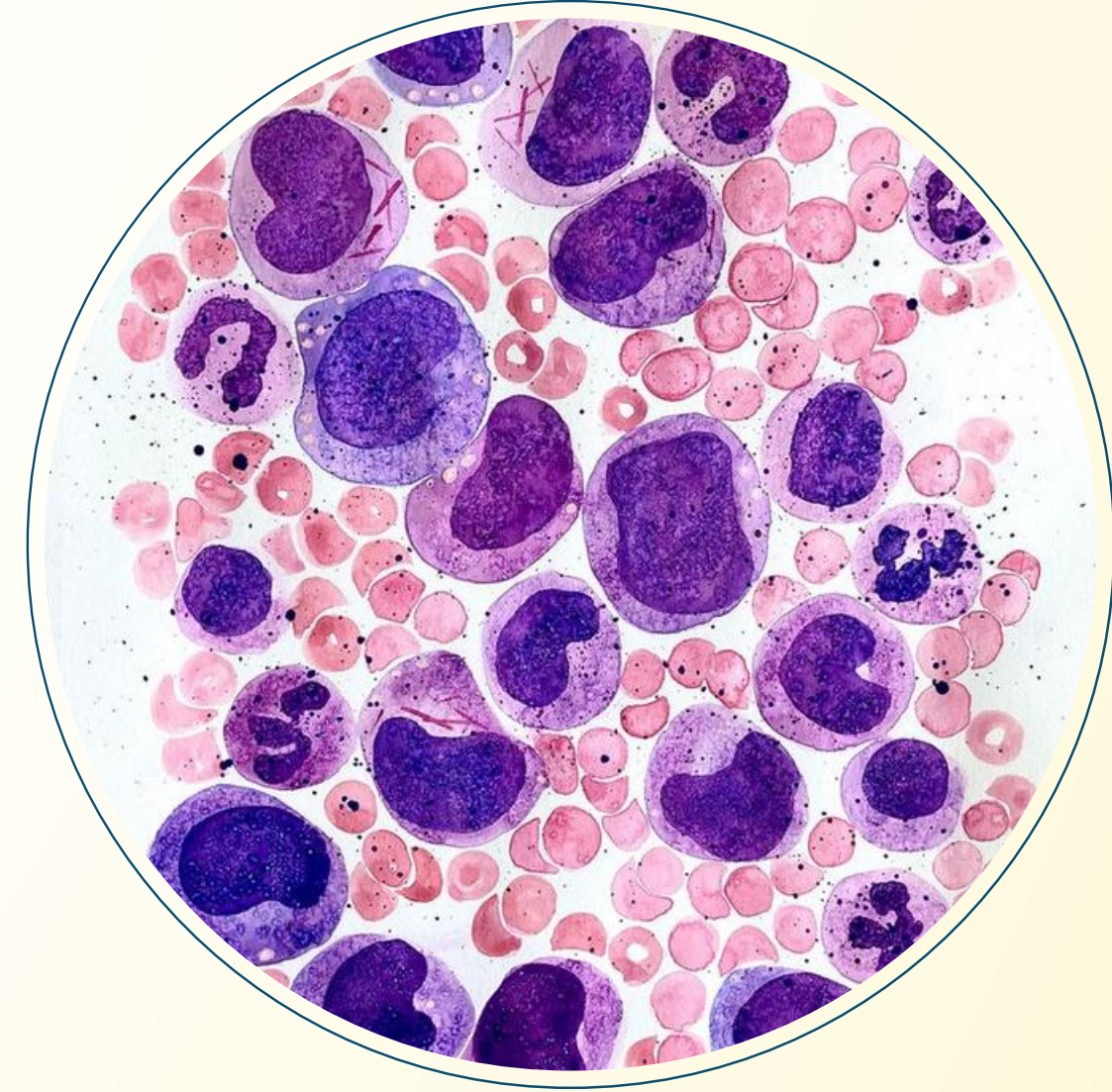
<sup>2</sup>Bezmialem Vakif University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Istanbul, Türkiye

<sup>3</sup>University of Health Sciences, Hamidiye Faculty of Medicine, Department of Biostatistics, Istanbul, Türkiye

9th Annual Medical Students' Research Day

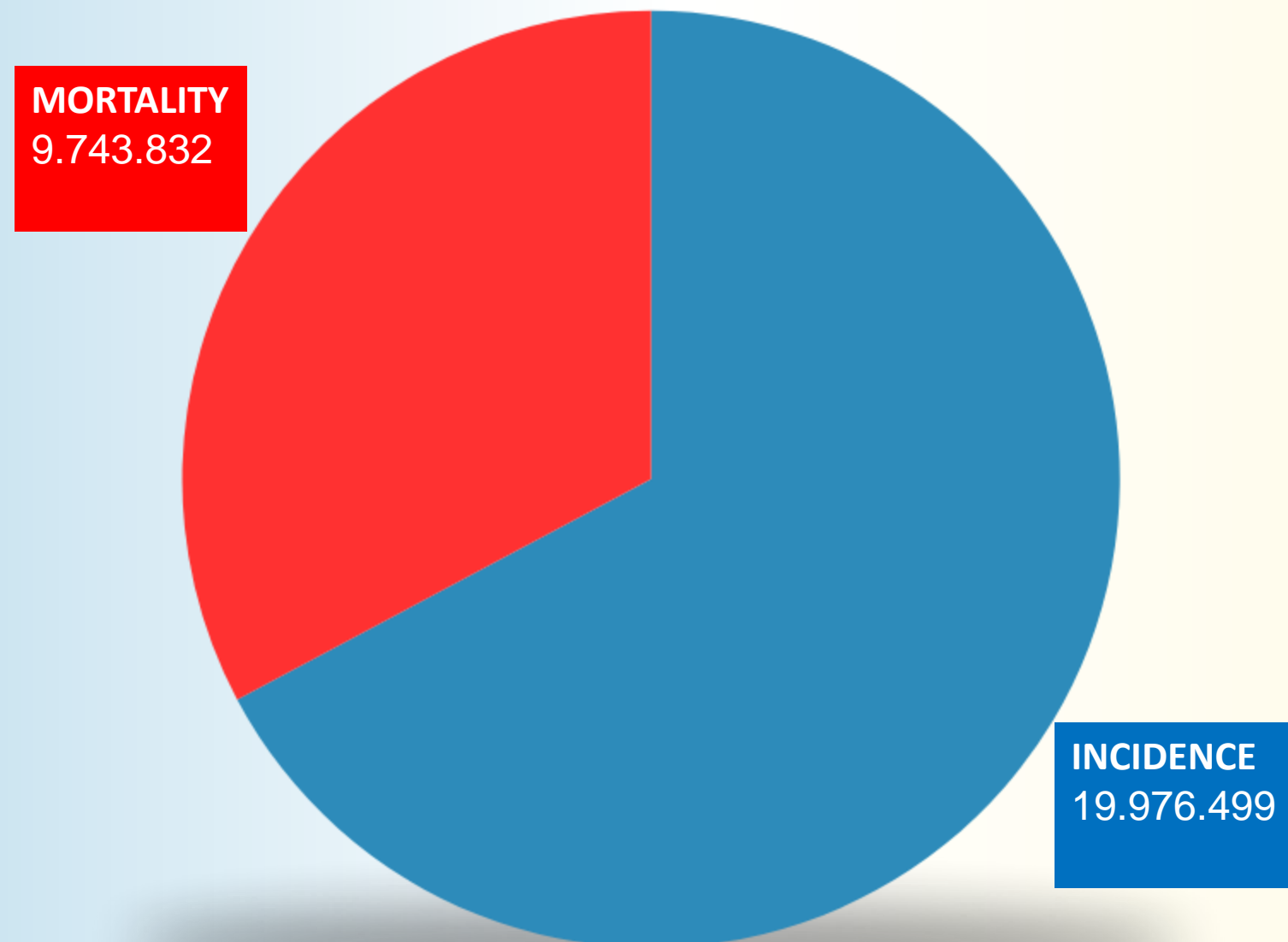
Bezmialem Vakıf University

14 March 2025





Cancer remains a significant challenge within the healthcare system.





# SECONDARY MALIGNANCY

A tumor that differs from the primary tumor in terms of **location, histopathology, and genetics.**

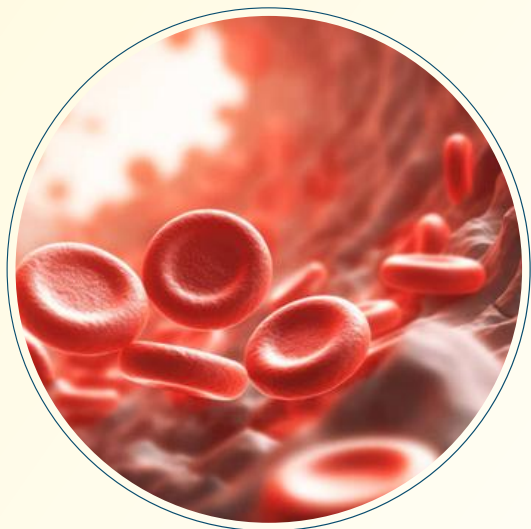


## Synchronous Tumor

A tumor diagnosed **within 6 months** of the primary cancer diagnosis.

## Metachronous Tumor

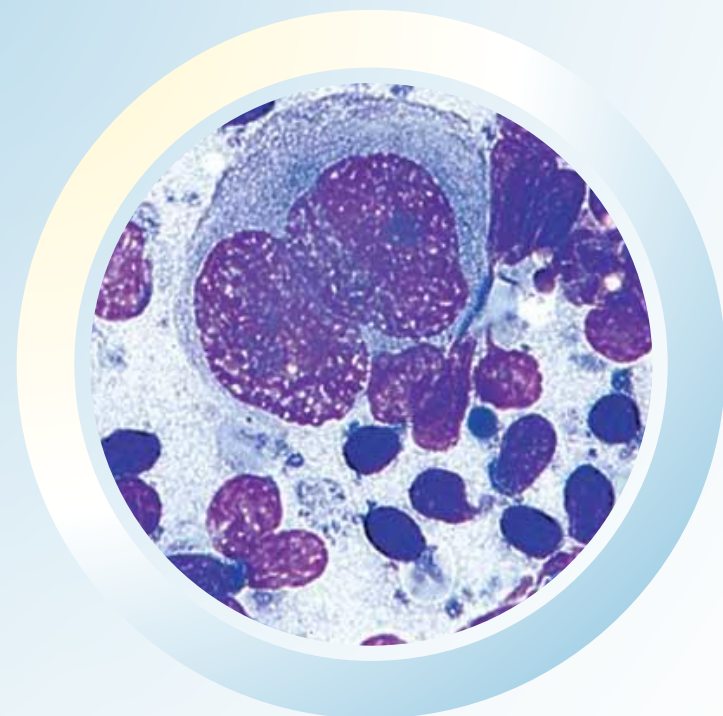
A tumor diagnosed **after 6 months** of the primary cancer diagnosis.



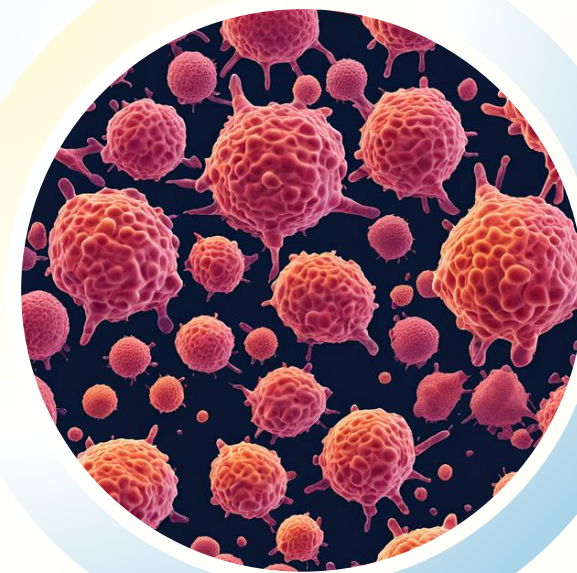




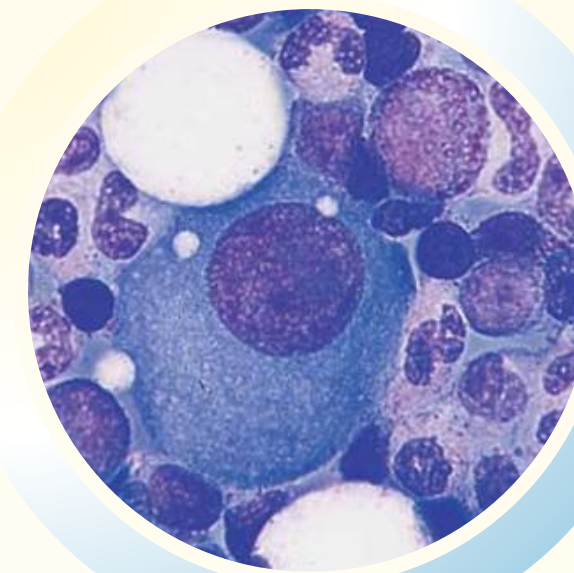
# Aim of the Study



To reveal the frequency of secondary malignancy development in hematological malignancies.



To analyze possible risk factors for the development of secondary malignancies.



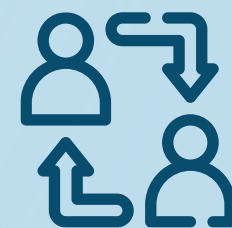
To contribute to the literature with our findings and emphasize the importance of secondary malignancy development.



# Method



- February 2012 - May 2024
- Bezmialem Vakif University Faculty of Medicine Hematology Clinic



## Study Group

Patients with secondary malignancies.



## Control Group

Patients who were matched with the study group in terms of diagnosis, age, and gender.



## Parameters

- Age, Gender
- Stage
- Presence of B symptoms
- Primary involvement
- Extranodal involvement
- Treatment (Chemo / Radiotherapy / HSCT)
- Relapse
- Family history of cancer
- Comorbidities



## Inclusion Criteria

- Patients aged 18 years and older diagnosed with hematological malignancy.
- Patients who have adequate medical records.



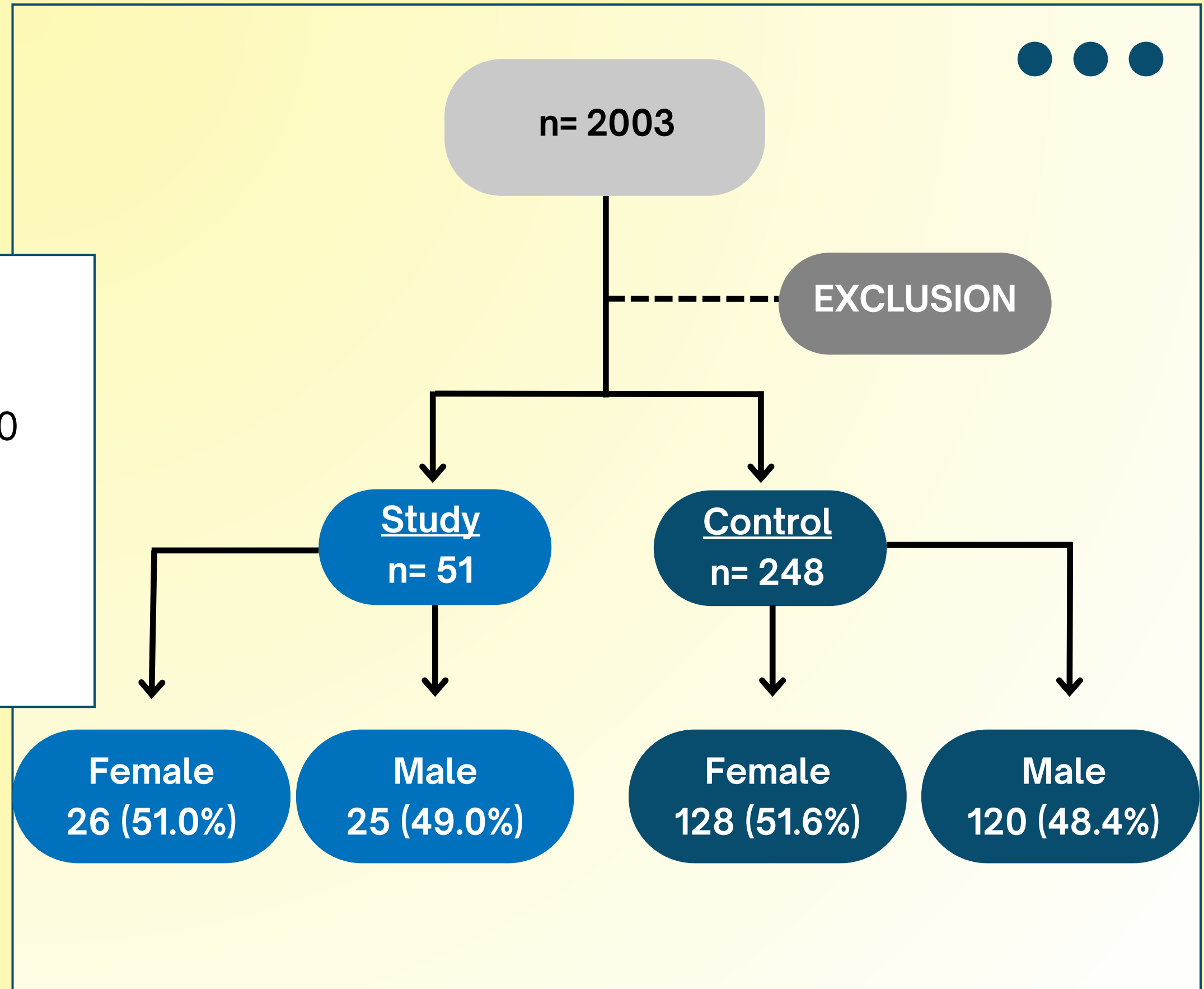
## Exclusion Criteria

- Patients with a prior cancer history.
- Patients with insufficient medical records.



## Results

- Follow-up: 70 months (5 years 10 months)
- Age: 64 (24-89)
- Female: 154 (51.0%)
- Male: 145 (48.5%)

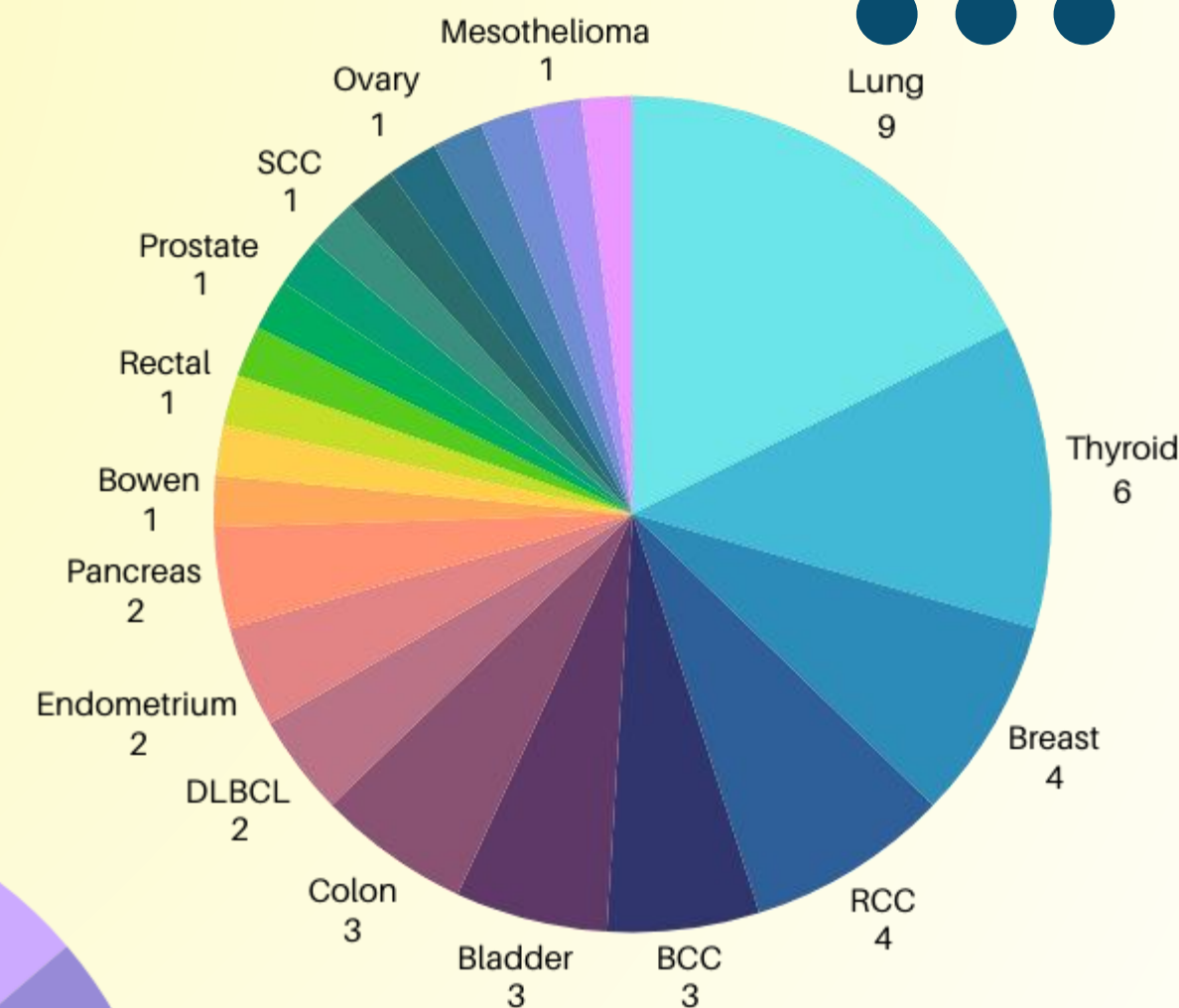
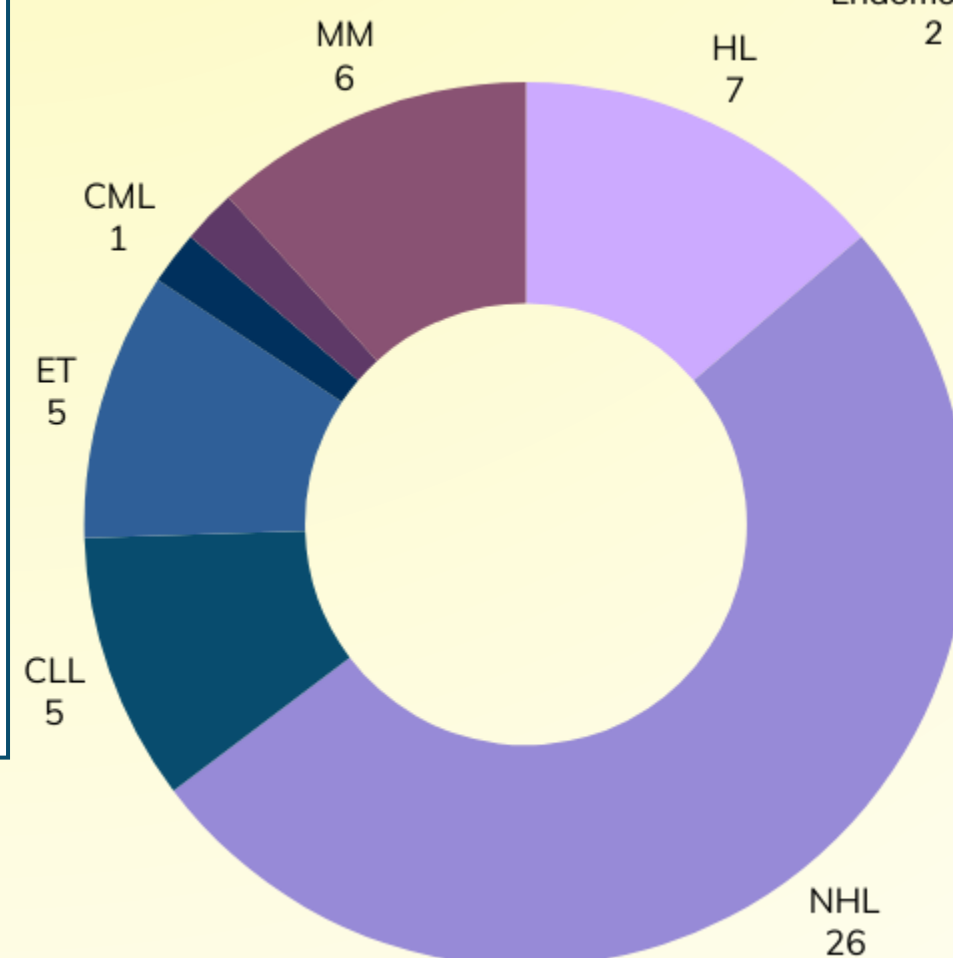






## Results

- The mean time to secondary malignancy development: 103.61 months
- 11 synchronous (21.6%) & 40 metachronous (78.4%)
- Hematological malignancy with the highest incidence of secondary malignancy: Non-Hodgkin Lymphoma (n= 26, 51.0%)
- Most common secondary malignancy: Lung Cancer (n= 9, 17.6%)
- Most common synchronous tumor: Thyroid Cancer (n= 3, 27.3%)







# Results

- Relapse and radiotherapy were significantly more common in the control group (p=0.023; p=0.038).
- A family history of cancer was statistically significant in the study group (p<0.001).

| Parameters                               | With SM (n= 51) Count (%) | Without SM (n= 248) Count (%) | p      |
|--|---------------------------|-------------------------------|--------|
| Relapse<br>No<br>Yes                     | 48 (%94.1)<br>3 (5.9%)    | 201 (%81.0)<br>47 (%19.0)     | 0.023  |
| Radiotherapy<br>No<br>Yes                | 36 (%76.0)<br>15 (%29.4)  | 136 (%54.8)<br>112 (%45.2)    | 0.038  |
| Family History<br>of Cancer<br>No<br>Yes | 36 (%70.6)<br>15 (%29.4)  | 242 (%97.6)<br>6 (%2.4)       | <0.001 |

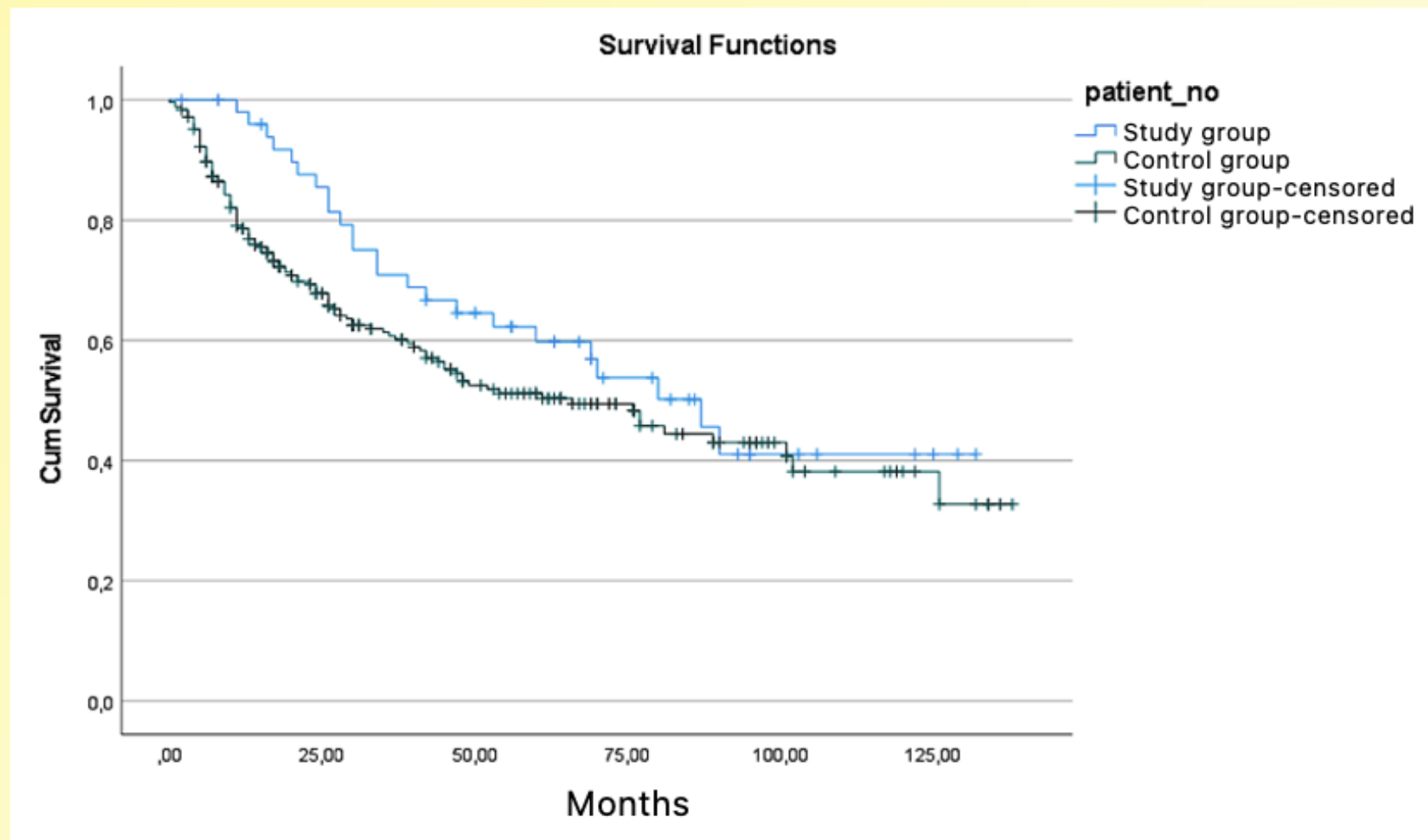


# Risk Factors for the Development of Secondary Malignancy

- No history of relapse
- No history of radiotherapy
- A family history of cancer

|                                       | Multivariate<br>OR (95% CI) | p      |
|---------------------------------------|-----------------------------|--------|
| Stage<br>Early<br>Advanced            | 1.47 (0.74-2.91)<br>1.00    | 0.248  |
| Relapse<br>No<br>Yes                  | 5.18 (1.27-21.16)<br>1.00   | 0.022  |
| Radiotherapy<br>No<br>Yes             | 2.44 (1.15-5.20)<br>1.00    | 0.020  |
| Comorbidities<br>No<br>Yes            | 1.00<br>1.86 (0.75- 4.64)   | 0.179  |
| Family History of Cancer<br>No<br>Yes | 1.00<br>21.90 (7.30-65.6)   | <0.001 |



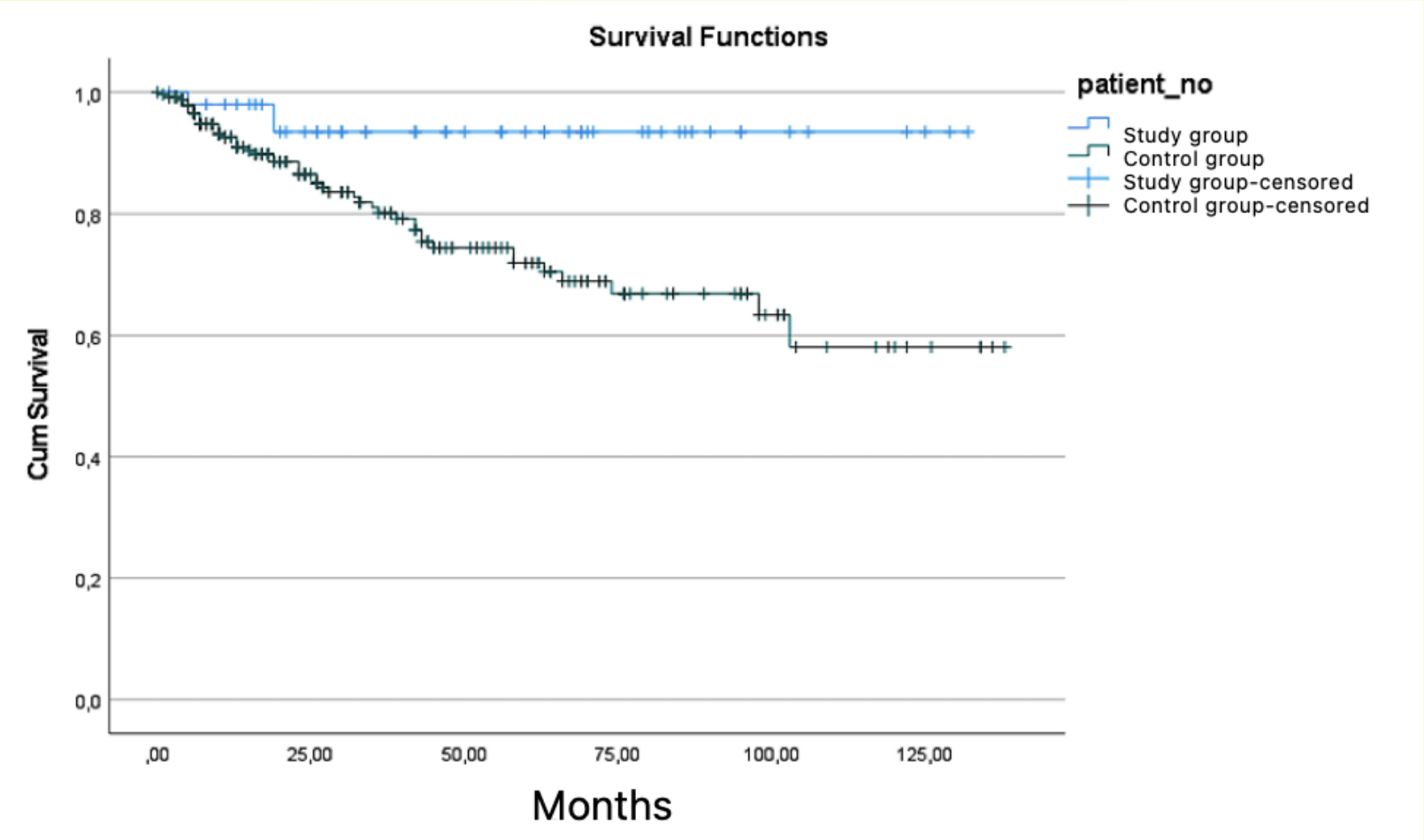


# Overall Survival (OS)

There was no statistically significant difference in OS between the groups (p=0.184).

|                                   | <sup>a</sup> Multivariate<br>OR (95% CI) | p      | <sup>b</sup> Multivariate<br>HR (95% CI) | p     |
|-----------------------------------|--|--------|--|-------|
| <b>Age</b><br>Young<br>Old        | 1.00<br>1.07 (1.04-1.10)                 | <0.001 | 1.00<br>1.07 (1.01-1.13)                 | 0.009 |
| <b>Gender</b><br>Female<br>Male   | 1.00<br>2.23 (1.33-3.74)                 | 0.002  | 1.00<br>3.60 (1.37--9.44)                | 0.009 |
| <b>Stage</b><br>Early<br>Advanced | 1.00<br>2.20 (1.24-3.91)                 | 0.007  | 1.13 (0.43-2.93)<br>1.00                 | 0.779 |
| <b>Relapse</b><br>No<br>Yes       | 1.00<br>3.14 (1.55-6.36)                 | 0.001  | 1.34 (0.03-58.09)<br>1.00                | 0.879 |

a= Logistic regression, b= Log-rank



# Relapse

The time to relapse was longer in those who developed secondary malignancies compared to those who did not (p=0.004).

|  | Multivariate<br>HR (95% CI) | p                |
|--|-----------------------------|------------------|
| <b>Patients</b><br>with secondary malignancy<br>without secondary malignancy | 1.00<br>5.16 (1.59-16.17)   | <b>0.006</b>     |
| <b>Stage</b><br>Early<br>Advanced  | 1.00<br>1.29 (0.68-2.45)    | 0.429            |
| <b>Extranodal Involvement</b><br>Absent<br>Present                           | 1.00<br>1.01 (0.48-2.12)    | 0.969            |
| <b>HSCT</b><br>No<br>Autologous  | 1.00<br>6.25 (3.40-11.51)   | <b>&lt;0.001</b> |
| <b>Chemotherapy</b><br>No<br>Yes   | 1.00<br>3.63 (0.49-26.44)   | 0.203            |





# Discussion



01

The fact that lung cancer is the most common secondary malignancy is consistent with other studies [4,6].

02

Interestingly, while the most common synchronous tumor in our patients was thyroid cancer, one of our patients developed peritoneal mesothelioma.

03

The risk factors indicated that the development of secondary malignancy could occur independently of relapse and treatment protocol.

04

Unlike previous studies, this study highlights that the mean time to the onset of secondary malignancy exceeded the follow-up duration (103.61 months) [6, 7, 9, 11-13].



# Limitations



- Single-center
- Retrospective study

# Powerful Sides



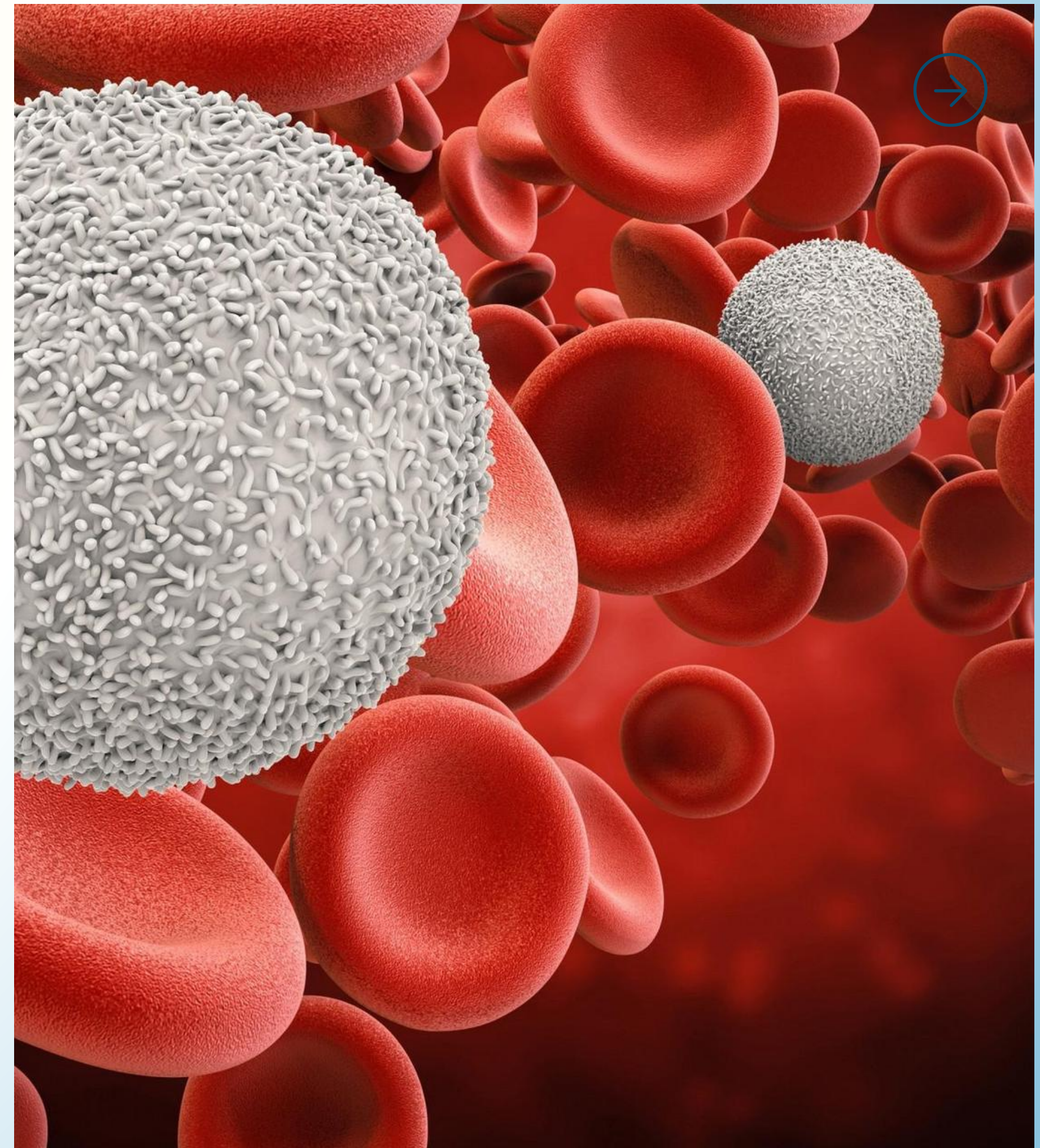
- The systematic recording of patient data
- The examination of patients with primary hematological malignancy





# Conclusion

- The presence of multiple malignancies in cancer patients is a significant health concern.
- Patients should be integrated into screening programs from the time of diagnosis of hematological malignancy.
- Further studies are needed to validate our findings and to gain a more comprehensive understanding of the risk factors and outcomes associated with secondary malignancies.





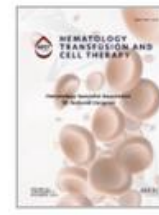


# ACKNOWLEDGMENTS



Hematology, Transfusion and Cell Therapy

Volume 46, Supplement 7, December 2024, Pages S35-S38



OP 18

## DETERMINATION OF FREQUENCY AND RISK FACTORS OF SECONDARY MALIGNANCY DEVELOPMENT IN HEMATOLOGICAL MALIGNANCIES

Ennur Ramadan<sup>1</sup>, Güven Çetin<sup>2</sup>, Özge Pasin<sup>3</sup>



Hematology, Transfusion and Cell Therapy

Volume 46, Supplement 7, December 2024, Pages S50-S51



PP 09

## PERITONEAL MESOTHELIOMA AS A CO-MALIGNANCY IN A PATIENT WITH CLL/SLL: CASE REPORT

Satı Betül Beydilli<sup>1</sup>, Ennur Ramadan<sup>2</sup>, Güven Çetin<sup>3</sup>, Mehmet Aydın<sup>4</sup>



Scan me!



HEMATOLOGY  
SPECIALIST ASSOCIATION



Scan me!





# References

1. Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R. L., Soerjomataram, I., & Jemal, A. (2024). Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 74(3), 229–263. <https://doi.org/10.3322/caac.21834>
2. Tanjak, P., Suktitipat, B., Vorasan, N., Juengwiwattanakitti, P., Thiengtrong, B., Songjang, C., Therasakvichya, S., Laiteerapong, S., & Chinswangwatanakul, V. (2021). Risks and cancer associations of metachronous and synchronous multiple primary cancers: a 25-year retrospective study. *BMC cancer*, 21(1), 1045. <https://doi.org/10.1186/s12885-021-08766-9>
3. Vogt, A., Schmid, S., Heinimann, K., Frick, H., Herrmann, C., Cerny, T., & Omlin, A. (2017). Multiple primary tumours: challenges and approaches, a review. *ESMO open*, 2(2), e000172. <https://doi.org/10.1136/esmoopen-2017-000172>
4. Deveci, B., Yildiz, A., Yilmaz, S., Ozcan, B., Kargi, A., Saba, R., Sahin, Z., Ozdogan, M. (2021). Evaluation of the Patients with Hematological Malignancies along with Synchronous or Metachronous Solid Tumors. *International Journal of Hematology and Oncology*, 31(4), 214–220. [doi.org/10.4999/uhod.215295](https://doi.org/10.4999/uhod.215295)
5. Nishiwaki, S., Okuno, S., Suzuki, K., Kurahashi, S., & Sugiura, I. (2017). Impact of Synchronous Multiple Primary Malignant Tumors on Newly Diagnosed Hematological Malignancies. *Clinical lymphoma, myeloma & leukemia*, 17(12), e79–e85. <https://doi.org/10.1016/j.clml.2017.09.006>
6. Zhang, Y., Han, Y., Teng, G., Du, C., Gao, S., Yuan, W., Zhang, L., & Bai, J. (2023). Incidence and risk factors for second malignancies among patients with myeloproliferative neoplasms. *Cancer medicine*, 12(8), 9236–9246. <https://doi.org/10.1002/cam4.5666>
7. Shbib Dabaja, B., Boyce-Fappiano, D., Dong, W., Damron, E., Fang, P., Gunther, J., Rodriguez M.A., Strati, P., Steiner, R., Nair, R., Lee, H., Abou Yehia, Z., Shihadeh, F., Pinnix, C., & Ng, A. K. (2022). Second malignancies in patients with Hodgkin's Lymphoma: Half a century of experience. *Clinical and translational radiation oncology*, 35, 64–69. <https://doi.org/10.1016/j.ctro.2022.04.011>
8. Joelsson, J., Wästerlid, T., Rosenquist, R., Jakobsen, L. H., El-Galaly, T. C., Smedby, K. E., & Eloranta, S. (2022). Incidence and time trends of second primary malignancies after non-Hodgkin lymphoma: a Swedish population-based study. *Blood advances*, 6(8), 2657–2666. <https://doi.org/10.1182/bloodadvances.2021006369>
9. Barbui, T., Ghirardi, A., Masciulli, A., Carobbio, A., Palandri, F., Vianelli, N., De Stefano, V., Betti, S., Di Veroli, A., Iurlo, A., Cattaneo, D., Delaini, F., Bonifacio, M., Scaffidi, L., Patriarca, A., Rumi, E., Casetti, I. C., Stephenson, C., Guglielmelli, P., Elli, E. M., ... Finazzi, G. (2019). Second cancer in Philadelphia negative myeloproliferative neoplasms (MPN-K). A nested case-control study. *Leukemia*, 33(8), 1996–2005. <https://doi.org/10.1038/s41375-019-0487-8>
10. Mathur, A., Edman, J., Liang, L., Scott, N. W., & Watson, H. G. (2022). Skin cancer in essential thrombocythaemia and polycythemia vera patients treated with hydroxycarbamide. *EJHaem*, 3(4), 1305–1309. <https://doi.org/10.1002/jha2.551>
11. Wang, F. (2022). Risk and outcome of second primary malignancy in patients with classical Hodgkin lymphoma. *Medicine*, 101(48), e31967. <https://doi.org/10.1097/MD.00000000000031967>
12. Fei, F., Reddy, V., & Rosenblum, F. (2021). Secondary primary malignancies in patients with multiple myeloma: A single institution experience. *Hematological oncology*, 39(5), 674–679. <https://doi.org/10.1002/hon.2923>
13. Halamkova, J., Kazda, T., Pehalova, L., Gonec, R., Kozakova, S., Bohovicova, L., Krakorova, D. A., Slaby, O., Demlova, R., Svoboda, M., & Kiss, I. (2021). Second primary malignancies in colorectal cancer patients. *Scientific Reports*, 11(1), 2759.
14. Turgutkaya, A., Yavaşoğlu, İ., Şahin, T., Sargın, G., & Bolaman, A. Z. (2021). Multiple myeloma and frequency of synchronous and second primary malignancies. *Journal of Hematopathology*, 14(3), 197–203. <https://doi.org/10.1007/s12308-021-00453-9>
15. Sud, A., Thomsen, H., Sundquist, K., Houlston, R. S., & Hemminki, K. (2017). Risk of Second Cancer in Hodgkin Lymphoma Survivors and Influence of Family History. *Journal of Clinical Oncology*, 35(14), 1584–1590.

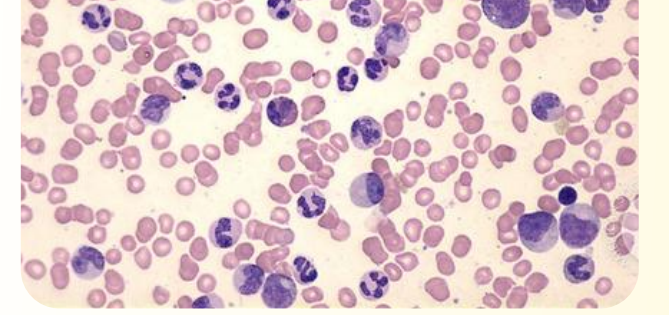
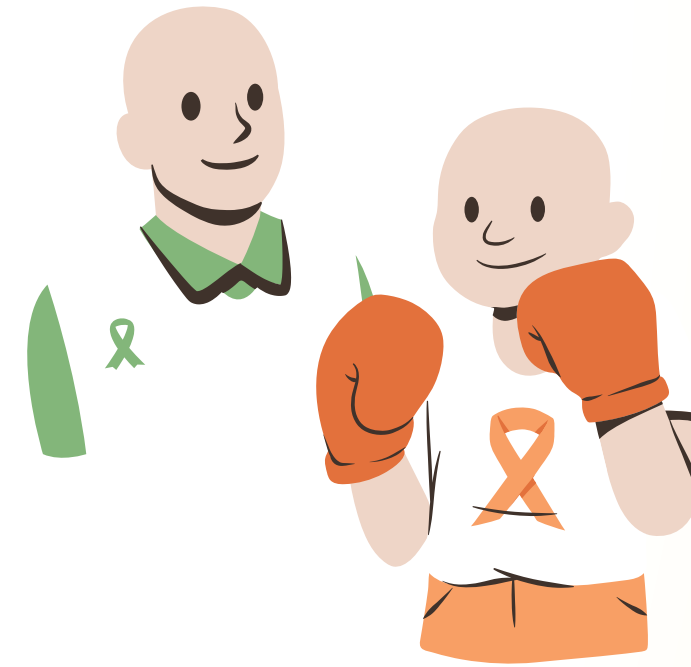


**Thank you for  
listening!**

I'd love to hear your thoughts—any  
questions or feedback?

Correspondence:

 [ramadanennur@gmail.com](mailto:ramadanennur@gmail.com)



**WARNING**  
MAY START TALKING ABOUT  
**HEMATOLOGY**

