Incidence of second primary malignancies in Chronic lymphocytic leukemia

Regina Zsigmond[1], Előd János Zsigmond [3], Zita Borbényi[1], Adrienn Sulák [1,2], Blanka Godza[2], Tímea Gurbity Pálfi[1]

Department of Internal Medicine, Centre of Hematology, University of Szeged, Szeged[1]; Department of Medical Genetics, University of Szeged, Szeged[2], Department of Cardiology, North-Pest Central Hospital-Honvéd Hospital, Budapest[3], Hungary

Introduction and Aims

Chronic lymphocytic leukemia (CLL) involves a broad spectrum of genetic mutations and is treated with multiple therapeutic approaches. This disorder may be associated with second primary malignancies (SPM), including solid tumors (ST) and other hematologic neoplasms (HN), potentially due to therapy side effect and genetic predisposition.
This study aimed to evaluate the incidence and and long-term prognostic value of SPM in CLL patients.

Method

We conducted a retrospective analysis at the Hematology Department of the University of Szeged, Hungary including consecutive CLL patients from January 2012 to January 2025. The study assessed the prevalence of SPM, the influence of therapy and genetic background on SPM development, and the long-term prognostic significance of SPM.

Results

CLL was confirmed in 515 patients and therapy was initiated in 268 cases. Among the treated 268 patients (164 male, 104 female; the average age at diagnosis was 66±10 years) SPM was diagnosed in 84 (31%) cases, from which 66 (25%) was ST and 19 (7%) was HN. The average age at diagnosis was 66.5±9 years of the 84 patients with SPM (55 male, 29 female). In the treated patient cohort, the following therapies were administered: Rituximab, Cyclophosphamide, Vincristine, Prednisolon (R-CVP) in 51 (19%) patients, Rituximab, Fludarabine, Cytoxan (R-FC) in 26 (10%), Rituximab, Bendamustine in 68 (25%), Rituximab, Chlorambucil in 90 (34%), Venetoclax in 41 (15%), Bruton tyrosine kinase-inhibitor (BTK-inhibitor) in 104 (39%), obinutuzumab in 49 (18%). None of these therapies had significant influence upon SPM development. Seventy-one (33%) of 211 patient treated with some of the above mentioned chemotherapeutical protocols developed SPM, while 13 (25 %) of 52 patients treated without chemotherapy developed SPM (Figure 1.).

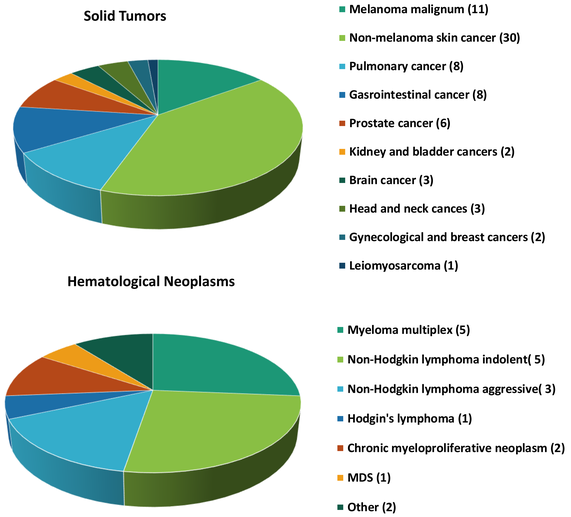


Figure 1.

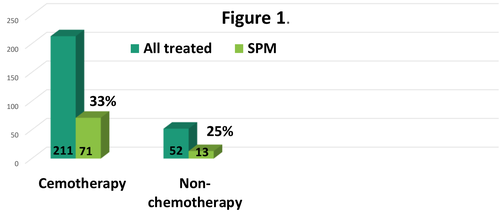
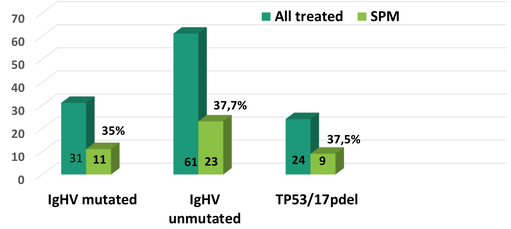
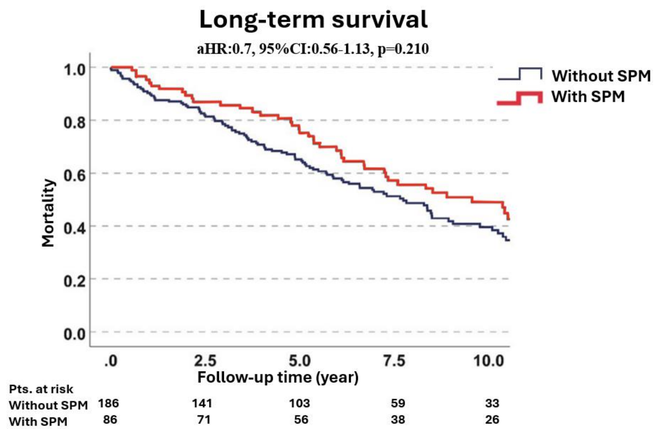


Figure 2.



A non-significant tendency toward higher SPM was noticed in case of R-CVP (OR 1.71, 95%CI:0.91-3.21, p=0.095) and R-FC (OR 2.02, 95%CI:0.89-4.59, p=0.092), while obinutuzumab exhibited a protective effect (OR 0.50, 95%CI:0.23-1.06, p=0.072, 15.1%). Among the treated patients IgHV status, TP53 mutation status and 17p deletion status was known in 33.9% (91 pts), 50.3% (135 pts) and 76% (204 pts) respectively. In 91 patients with known IGHV status (30 mutated, 61 unmutated), the presence of mutation did not influenced the SPM development (OR 0.95, 95%CI:0.38-2.36, p=0.923). Among the TP53/17pdel positive patients 37% (24/9) developed SPM, which is similar to patients with IgHV mutated or unmutated status (Figure 2.). The mean follow-up time was 6.5±4.8 years. The presence of SPM did not influenced the long-term survival in the treated CLL subgroup (aHR 0.7, 95%CI:0.56-1.13, p=0.210) (Figure 3.)

Figure 3.



Conclusion

In our cohort, 31% CLL patients were diagnosed with SPM similarly to other studies. The most common SPMs were skin cancer, emphasizing the importance of regular screening. The therapy and genetic status were not significant risk factors for SPM development. However a non-significant tendency toward higher SPM was noticed in case of R-CVP and R-FC treatments. Interestingly, SPM did not significantly worsen survival outcomes in the studied population.

References

1. Van der Straten L et al. Risk of second primary malignancies in patients with chronic lymphocytic leukemia: a population-based study in The Netherlands 1989–2019. Blood Cancer J. 2023 Jan 13;13(1):15. doi: 10.1038/s41408-023-00784-z.
2. Sikander Ailwadhi et al. Assessment of second primary malignancies among treated and untreated patients with chronic lymphocytic leukemia using real-world data from the USA. J Comp Eff Res. 2024 Feb;13(2):e230119. doi: 10.57264/cer-2023-0119.

Contact: Dr. Timea Gurbity Pálfi, Universitiy of Szeged, Department of Internal Medicine, Center of Hematology, Semmelweis street 6-8, 6725 Szeged, Hungary, phone: +3662545226, email: timea.gurbity@gmail.com