EPH248

Varying Latency Impact on Incidence of Second Primary Malignancy Among Patients With B-cell Malignancy

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Introduction

- Although cancer survival has improved over time since the introduction of innovative therapies, the occurrence of second primary malignancies (SPM) is an area of growing concern
- The occurrence of SPM is a leading cause of morbidity and mortality among cancer survivors
- Previous studies on SPM in patients with B-cell malignancies have been performed, but utilized registries dating back to the 1970s[1-4]
- Risk of SPM may be expected to vary over time as more innovative treatments and advanced cancer screening techniques (e.g., prostate-specific antigen, colonoscopy, mammography) become available for patients
- This study used a larger registry grouping, National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER), and more recent data to assess the incidence of SPM among patients with B-cell malignancies to complement previous studies

Objectives

Primary:

- Establish baseline rates of SPM occurring among the general population of patients with an index B-cell malignancy in the United States (US)

Secondary:

- Determine the impact of varying inclusion/exclusion criteria on the calculation of SPM rates by accounting for
  - different latency period lengths,
  - prior tumor histories, and
  - Richter's tumor transformation scenario
- Compare the rates of malignancies occurring as a SPM to the rates expected in the general US population

Methods

- The SPM incidence rate per 100 person-months and the multiple primary standardized incidence ratio (MP-SIR) of observed versus expected were calculated for patients with a B-cell malignancy.
  - Crude SPM incidence rate on single outcomes and 95% confidence intervals (95% CI) for SPM

$$\textit{Calculated as } SPM\ rate = \frac{\#\ patients\ with\ SPM}{total\ person\text{-}months\ in\ followup\ period^{*}}$$

* Patients were followed until occurrence of first SPM, death, loss to follow-up, resolution of cancer, or end of data collection, whichever came first

  - The MP-SIR overall and by latency months since diagnosis (e.g., 3-11 months, 12-23 months, etc.)

$$\textit{Calculated as } MP-SIR = \frac{observed\ numbers\ of\ SPM\ cases}{population\text{-}based\ expected\ counts^{*}}$$

- Data from the SEER 17 Registries database from 2000 to 2019 were analyzed.

Inclusion criteria:

- Index B-cell malignancies included chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), marginal zone lymphoma (MZL), Waldenström macroglobulinemia (WM), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, and hairy cell leukemia
- Patients were required to be at least 18 years old

Exclusion criteria:

- Patients with a previous malignancy
- Patients with a SPM within 3 months following B-cell malignancy were excluded from the incidence rate calculation
- Patients with a cancer diagnosis confirmed through death certification only or autopsy only were excluded
- Patients with missing data in age, sex, race, cancer summary stage, or surgery information were excluded

- Study outcomes included SPM combinations of all types of tumors and the individual tumors (**Figure 1**)

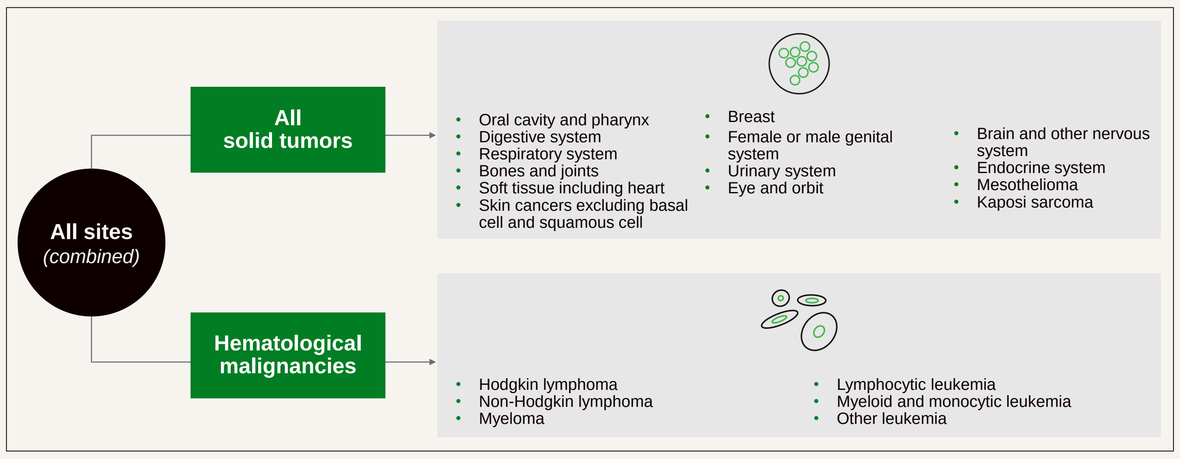
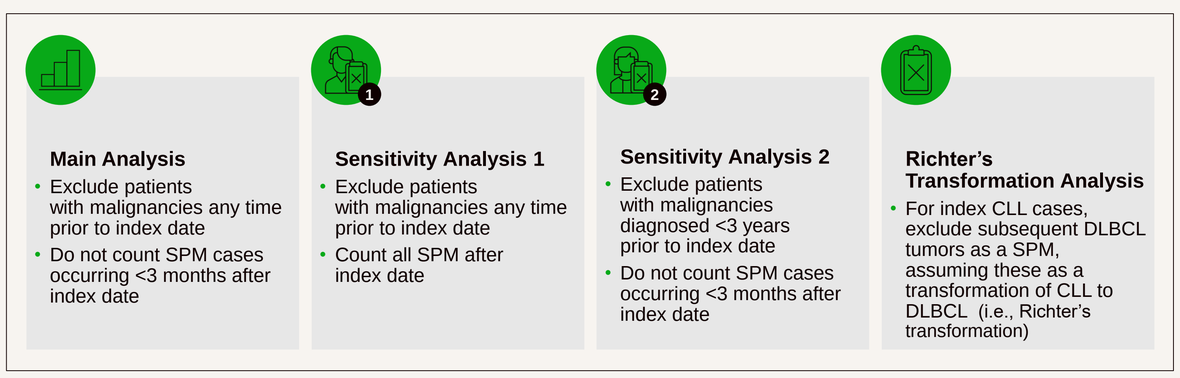


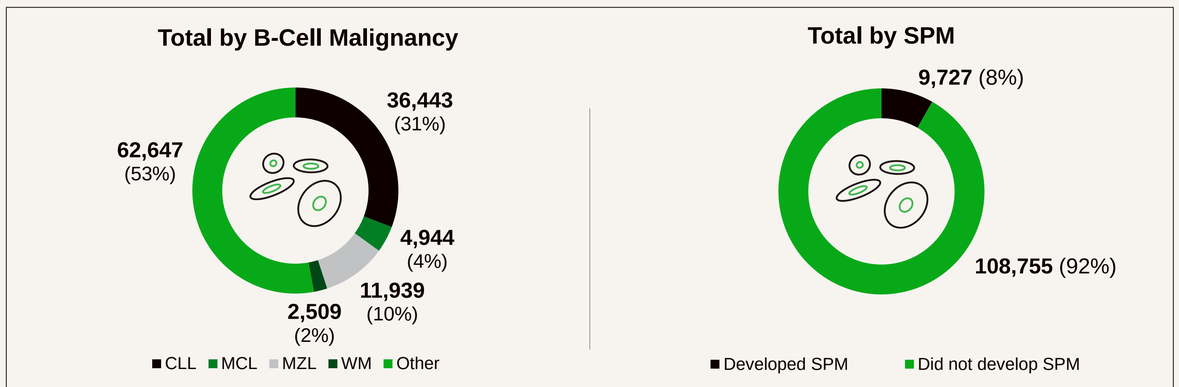
Figure 1. SPM Outcomes

- Varying latency, prior tumor histories, and the adoption of Richter's tumor transformation were applied as secondary analyses in order to further understand the timing of SPM occurrence relative to the B-cell diagnosis of interest



Results

- 118,482 patients with an index B-cell malignancy were identified and included in the analysis (**Figure 2**)
- A majority (53%) of index B-cell index malignancies were either DLBCL, follicular lymphoma, or hairy cell leukemia
- Most patients (92%) did not develop a SPM
- **Overall B-cell index population for primary analysis:** 118,482



Other B-cell malignancies included DLBCL, follicular lymphoma, and hairy cell leukemia

Figure 2. B-Cell Malignancies by Type and SPM Occurrence Sample Populations

SPM Incidence Rates

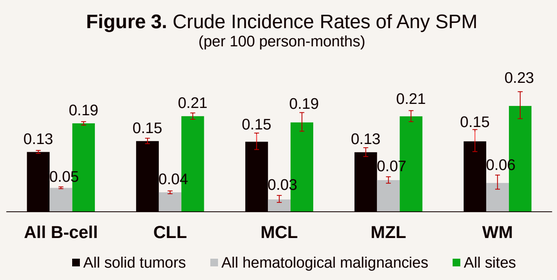
- The incidence rate of any SPM was 0.19 (95% CI: 0.187, 0.195), ranging from 0.19 (MCL) to 0.23 (WM) (**Figure 3**)
- **Most common solid tumors involved:** Respiratory system, Digestive system and Genital system
- **Most common hematological tumors:** Non-Hodgkin lymphoma
- Patients with an index CLL, MCL, MZL, or WM malignancy experienced a SPM at a higher rate than the combined group of patients with a B-cell malignancy– especially after 20 months

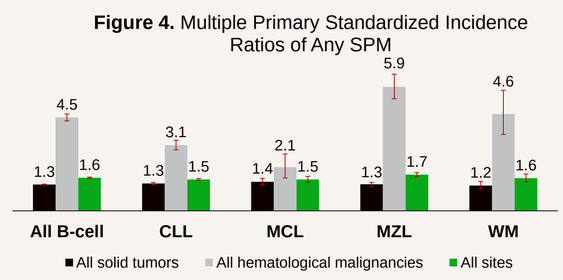
MP-SIR Rates

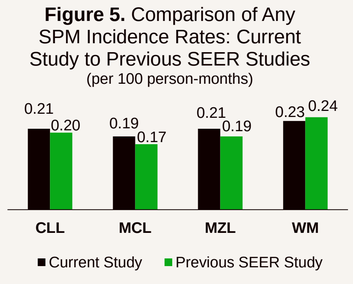
- The MP-SIR for any SPM was 1.58 (95% CI: 1.55, 1.61), ranging from 1.50 (CLL/MCL) to 1.73 (MZL) (**Figure 4**)
- The MP-SIR for any hematological SPM was 4.46 (95% CI: 4.30, 4.63), ranging from 2.09 (MCL) to 5.92 (MZL)
- The MP-SIR for any solid tumor SPM was 1.25 (95% CI: 1.23, 1.28), ranging from 1.21 (WM) to 1.39 (MCL)
- All MP-SIR values > 1.0 indicating higher than expected SPM event rates

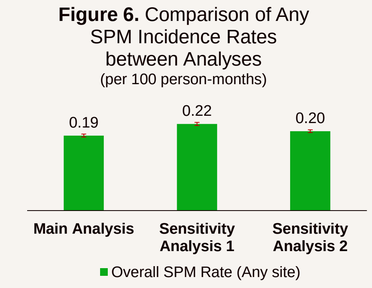
Comparisons

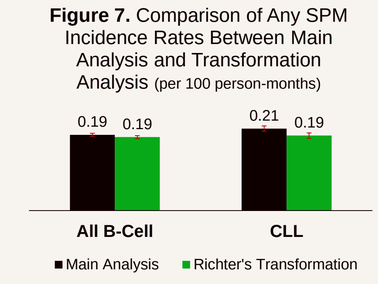
- There was little difference between this study and previous SEER studies in terms of SPM incidence rate (**Figure 5**)
- Including patients with SPM within 3 months increased incidence rate slightly (0.22, 95% CI: 0.216, 0.224, Sensitivity analysis 1) (**Figure 6**)
- Excluding patients with a prior malignancy within 3 years had little impact on incidence rate (0.20, 95% CI: 0.198, 0.206, Sensitivity analysis 2, **Figure 6**)
- Excluding Richter's transformation cases had a minor effect on incidence rate (All B-cell: 0.19, 95% CI: 0.181, 0.189; CLL: 0.19, 95% CI: 0.182, 0.196) (**Figure 7**)











Note: *Main analysis excluded patients with malignancies any time prior to index date, and did not count SPM cases occurring <3 months after index date. Sensitivity analysis 1 excluded patients with malignancies any time prior to index date, but counted all SPM after index date. Sensitivity analysis 2 excluded patients with malignancies diagnosed <3 years prior to index date and did not count SPM cases occurring <3 months after index date.*

Conclusions

- Patients with a B-cell malignancy had a 58% greater occurrence of any SPM and 446% greater occurrence of any hematological SPM than expected in the general population
- Varying latency and the occurrence of prior malignancy had only a slight influence on the incidence rates of SPM, suggesting that estimates may not be significantly affected to the methodology imposed

Abbreviations

CLL, chronic lymphocytic leukemia; DLBCL, diffuse large B-cell lymphoma; MCL, mantle cell lymphoma; MP-SIR, multiple primary standardized incidence ratio; MZL, marginal zone lymphoma; SEER, Surveillance, Epidemiology, and End Results; SPM, second primary malignancy; WM, Waldenström macroglobulinemia

References

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Data source: SEER 17 Registries: 2000 to 2019.

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