Is CLL the Second Cancer?

A Single Center Retrospective Analysis of Secondary Malignancies (SM) in Patients with Chronic Lymphocytic Leukemia (CLL)

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Background

- Patients with CLL have increased incidence of SM including genitourinary (GU) cancers [1,2].
- This has been attributed to immune dysregulation caused both by the disease and as a consequence of treatment, especially chemotherapy containing alkylating agents [2 - 4].
- There is very limited data on risk factors, timing and outcomes of SM in CLL including the impact of CLL cytogenetics on SM incidence.
- We describe the Roswell Park Comprehensive Cancer Center (RPCCC) experience of SM in CLL over a span of 27 years with a focus on GU cancers.

Methods

- The RPCCC translational lymphoma database was queried for all CLL patients treated between 1/1990 and 6/2017.
- Patient characteristics were summarized using simple descriptive statistics.
- Overall survival (OS) and progression free survival (PFS) were calculated from time of CLL diagnosis to last follow up/death and date of progression respectively.
- Patient characteristics were compared using Wilcoxon or Kruskal Wallis test, as appropriate, for continuous variables and Fisher's exact or chi-square test for categorical variables. Kaplan-Meier methods were used to estimate survival distributions.
- Univariate and multivariate proportional hazards modeling results were used to assess the effect of variables on overall survival. All analysis was conducted in SAS v9.4 (Cary, NC) at a significance level of 0.05.

Results

- Out of a total of 977 CLL patients, 165 (16.9%) patients had an additional diagnosis of SM. Forty five (4.6%) patients had ≥ 2 SM's.
- Most common SM was skin cancer (**Figure 1**).
- Median age of CLL patients with a SM was 65.6 (range 38.6-88.9) as compared to 60.0 (range 21.4-91.2) in the CLL only group ($p < 0.001$).
- No difference in Rai stage, white blood cell count, absolute lymphocyte count, hemoglobin and platelets were found between the two groups.
- There was no association between presence of del(13q), del(17p), trisomy 12 or del(11q) and incidence of SM.
- CLL patients with SM had lower OS but no statistically significant difference in PFS (**Figure 2**).

Figure 1: Incidence of SM in CLL

Figure 2: Overall Survival (OS) and PFS in CLL patients with and without second cancers

- Among GU cancers, presence of bladder cancer was associated with a shorter OS in CLL patients ($p = 0.049$) (**Figure 3**).
- Most GU cancers preceded the diagnosis of CLL (**Figure 4**).

Figure 3: Overall Survival in patients with and without GU cancers

Figure 4: Latency from CLL to GU tumor diagnosis

	Median Latency – m (range)	SD
Bladder Cancer	-54.54 (-193.93 - 12.58)	74.51
Prostate Cancer	-7.95 (-198.3 - 215.13)	92.95
RCC	-13.26 (-165.75 - 66.04)	89.19

Conclusion

- GU cancers are more frequent in patients with CLL, with majority preceding the diagnosis of CLL in our cohort.
- Our findings suggest that immune dysregulation might be present even at very early stages of CLL predisposing these patients to other malignancies. Hypothetically, these patients may benefit from early intervention.

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