1712: OTHER CANCERS IN PATIENTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA / SMALL LYMPHOCYTIC LYMPHOMA

Helen Ma,[1,2] Kari Rabe,[3] Edward Ratner,[4,5] Sam Kosydar,[3] Roberta Santos Azevedo,[6] Pankaj Gupta,[1] Susan O'Brien,[2] Paul Hampel,[3] Lindsey Roeker,[3] Yucai Wang,[3] Susan Slager,[3] Sameer A. Parikh,[3] Alessandra Ferrajoli[6]

1. Tibor Rubin VA Medical Center, Long Beach, CA, USA; 2. UCI Chao Family Comprehensive Cancer Center, University of California, Irvine, Orange, CA, USA; 3. Mayo Clinic, Rochester, MN, USA; 4. Minneapolis VA Medical Center, Minneapolis, MN, USA; 5. University of Minnesota, Minneapolis, MN, USA; 6. MD Anderson Cancer Center, University of Texas, Houston, TX, USA.

1. introduction

- Patients with CLL/SLL exhibit an elevated risk of developing **other cancers (OC)** relative to the general population.[1]
- 12.6% of patients on **chemoimmunotherapy (CIT)** clinical trials developed **OC**.[2]
- **Targeted therapies** (e.g., BTK and BCL2 inhibitors) are now the standard of care for the initial treatment of CLL/SLL.[3-4]
- **Risk of OC** in patients receiving **targeted therapies** is not known.

2. aim

Estimate the **risk of OC** in patients with newly diagnosed CLL/SLL in the current treatment era

3. methods

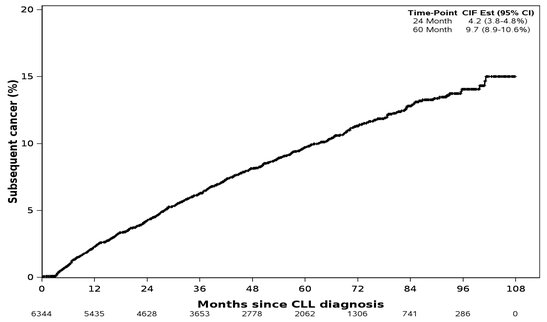
- Retrospective cohort analysis of patients diagnosed with CLL/SLL since 1/2016 from across the US Department of VA and Mayo Clinic in Rochester, MN
- Abstracted **OC**. Analysis exclusions:
  - Any **OC** prior to or concurrent (within 3 months) with CLL/SLL diagnosis
  - Non-melanoma skin cancers
- **Risk of OC** estimated using cumulative incidence methodology and analyzed using multivariable (MV) Cox regression; results reported as Hazard ratios (HR) and 95% confidence intervals (95% CI)
  - Any CLL-directed therapy as time-dependent covariate
  - MV subanalyses by type of CLL-directed treatment:
    - **CIT only**
    - **Targeted therapy only**
    - **CIT +/- Targeted therapy**

4. results

Patient Characteristics, n=6346	n (%)
Median Follow-up, years [IQR]	3.8 [2.1-5.9]
Age at diagnosis, median [range]	71 [23-102]
Male Sex	5811 (92)
Race and Ethnicity	
White	5148 (81)
Black	584 (9)
Other	308 (5)
Unknown	306 (5)
Prognostic factors	
IGHV mutated (n=1316)	673 (51)
CLL FISH panel (n=2517)	
del17	186 (7)
del11q	303 (12)
trisomy 12	502 (20)
del13q	883 (35)
Treatment	
Observation	4145
Targeted therapy only	1680
Monoclonal Ab	285
CIT only	141
CIT and Targeted therapy	95
Type of Targeted Therapy (+/- mAb)	
BTK inhibitor	
Ibrutinib	931 (52)
Acalabrutinib	357 (20)
Zanubrutinib	157 (9)
BCL2 inhibitor	
Venetoclax	258 (15)
BTK inhibitor + BCL2 inhibitor	28 (2)

Other Cancer, n=569	n (%)
Prostate	127 (22)
Lung	117 (21)
Hematologic malignancies	90 (16)
Melanoma	66 (12)
Gastrointestinal	64 (11)
Kidney and bladder	44 (8)
Head and neck	18 (3)
Other / Unknown	43 (8)

Cumulative Incidence of OC



MV Cox Regression Results

Factor	HR (95% CI)
Age (increase per year)	1.011 (1.003-1.018)
Male sex	1.671 (1.136-2.459)
Any CLL-directed therapy	1.448 (1.206-1.738)
Subanalyses by Type of CLL-Directed Therapy*	
CIT only	1.475 (1.050-2.070)
Targeted therapy only	1.264 (1.028-1.555)
CIT +/- Targeted therapy	1.651 (1.277-2.136)

* Age- and sex-adjusted

5. conclusions

- The most common types of **OC** were prostate, lung, and hematologic malignancies.
- In newly diagnosed patients with CLL/SLL, **risk of OC was 4.3% at 2 years and 9.7% at 5 years** after a diagnosis of CLL/SLL.
- Increasing age and male sex were significantly associated with risk of **OC** after CLL/SLL.
- Compared to patients managed with active surveillance, patients requiring therapy for CLL had a **45% increased risk of OC**.
  - Specifically, **risk of OC** is elevated in patients treated with **Targeted therapy only** (**26%**), but not as much as in those treated with **CIT only** (**48%**) nor with **CIT +/- Targeted therapy** (**65%**).

6. references

1. Greene MH, Hoover RN, Fraumeni JF Jr. Subsequent cancer in patients with chronic lymphocytic leukemia--a possible immunologic mechanism. J Natl Cancer Inst. 1978;61(2):337-340.
2. Csanádi M, Ágh T, Tordai A, Tapprich C, Vokó Z, Stamatopoulos K. Secondary primary malignancies after treatment with chemo-immunotherapy in treatment-naïve patients with CLL: a systematic literature review. Expert Rev Hematol. 2022;15(3):273-284.
3. Shanafelt TD, Wang XV, Kay NE, et al. Ibrutinib-Rituximab or Chemoimmunotherapy for Chronic Lymphocytic Leukemia. N Engl J Med. 2019;381(5):432-443.
4. Fischer K, Al-Sawaf O, Bahlo J, et al. Venetoclax and Obinutuzumab in Patients with CLL and Coexisting Conditions. N Engl J Med. 2019;380(23):2225-2236.

7. acknowledgments

The authors would like to thank patients, caregivers, and clinicians involved in this study.

Email: Helen.Ma@va.gov