



Clinical Characteristics and Outcomes of Patients with Chronic Lymphocytic Leukemia (CLL), 80 Years of Age or Older

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Abstract

Context: Nearly 20% patients are ≥80 years of age at CLL diagnosis. Increased comorbidities often accompany advanced age. However, clinical trials enroll a disproportionately low number of people this age, providing limited evidence for guidance.

Objective: To determine clinical characteristics and outcomes of patients ≥80 years of age at the time of CLL diagnosis.

Design: Retrospective.

Setting: Academic.

Patients or Other Participants: Between 1/1995–3/2020, we identified previously untreated CLL patients from the Mayo Clinic CLL Database ≥80 years of age at the time of CLL diagnosis and seen within 3 years of diagnosis.

Main Outcomes Measures: Baseline characteristics, treatments, and time-to-first-treatment (TFT) were analyzed for all patients. Overall survival (OS) was measured from diagnosis date in all patients and separately from treatment date for treated patients. Time-to-next-treatment (TTNT) was measured in treated patients from the first treatment date to the date of second treatment or last known treatment. TFT and TTNT were analyzed accounting for competing risk of death. Cox multivariable regression models were used to determine which factors were associated with OS and TTNT.

Results: Among 213 patients identified, the median age was 83 years (range 80–97). The median number of medical comorbidities among all patients was 4 (range 0–8). Fifty-six patients received treatment; median TFT 6.7 years. Treatment approaches included monoclonal antibody alone (n=17), chemotherapy alone (n=17), chemoimmunotherapy (n=14), novel agents (n=3), and multi-agent Richter's transformation regimens (n=5). Twenty-two of 56 treated patients received second-line therapy (median TTNT 2.8 years). Median OS among all 213 patients was 4.6 years. Standardized mortality ratio was 1.2 (p=0.008), excluding patients with Richter's transformation. In univariable analyses, receipt of therapy (HR 3.92, 95%CI 2.11–7.28; p<0.001), age (per 5-year increase; HR 1.84, 95%CI 1.43–2.38; p<0.001) and unmutated IGHV (HR 2.03, 95%CI 1.12–3.67; p=0.02) predicted shorter OS. The OS among treated patients was similar when compared across grouped periods of treatment start year (1995–2001, 2002–2013, 2014–2020).

Conclusions: Survival was similar across the 25-year span of this study; however, patients treated with novel agents were underrepresented and warrant additional evaluation. The 20% higher risk of death compared to an age- and sex-matched population emphasize the need for ongoing efforts to improve clinical outcomes for CLL patients in this growing demographic.

Background

- Nearly 20% of patients are ≥ 80 years of age at the time of CLL diagnosis.
- Increased medical comorbidities, declining functional status, and organ dysfunction may accompany advanced age.
- Limited prospective data that is generalizable to this population of 80+ individuals.

Objective

- Describe clinical characteristics and evaluate outcomes of patients ≥ 80 years of age at the time of CLL diagnosis

Methods

- Patients in Mayo Clinic CLL Database seen within 3 years of diagnosis.
- Time to first treatment and time to next treatment (in treated subgroup) were analyzed with competing risk of death.
- Overall survival was measured from diagnosis and treatment date (in treated subgroup).

Medical Comorbidities

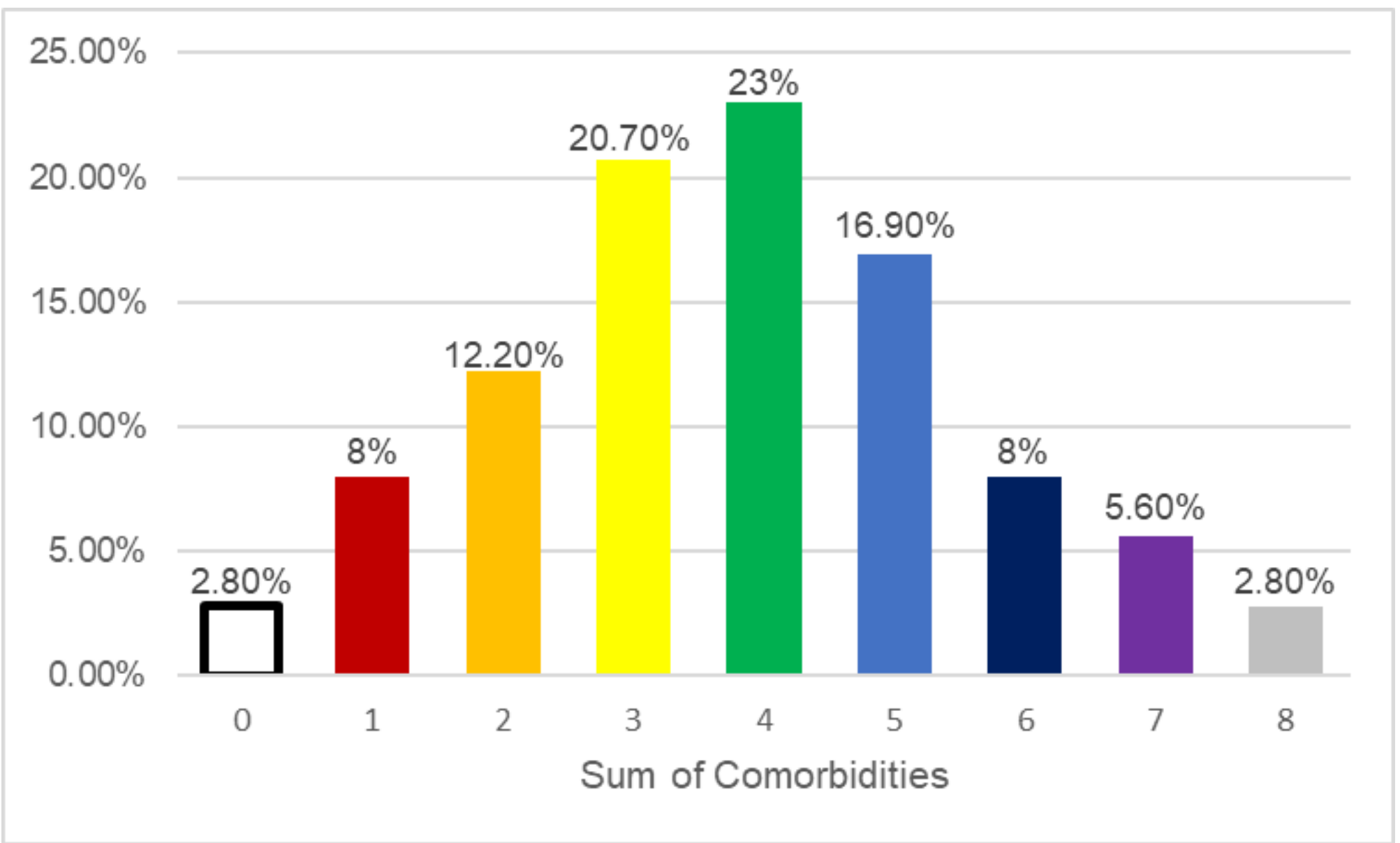
- Median sum of comorbidities: 4 (range 0-8)
- Most common: hypertension (57%), genitourinary (48%), rheumatological (46%), dyslipidemia (43%)
- Comorbidities of special interest: gastrointestinal (41%), atrial fibrillation (13%), PE/DVT (5%)

Baseline Characteristics at CLL Diagnosis

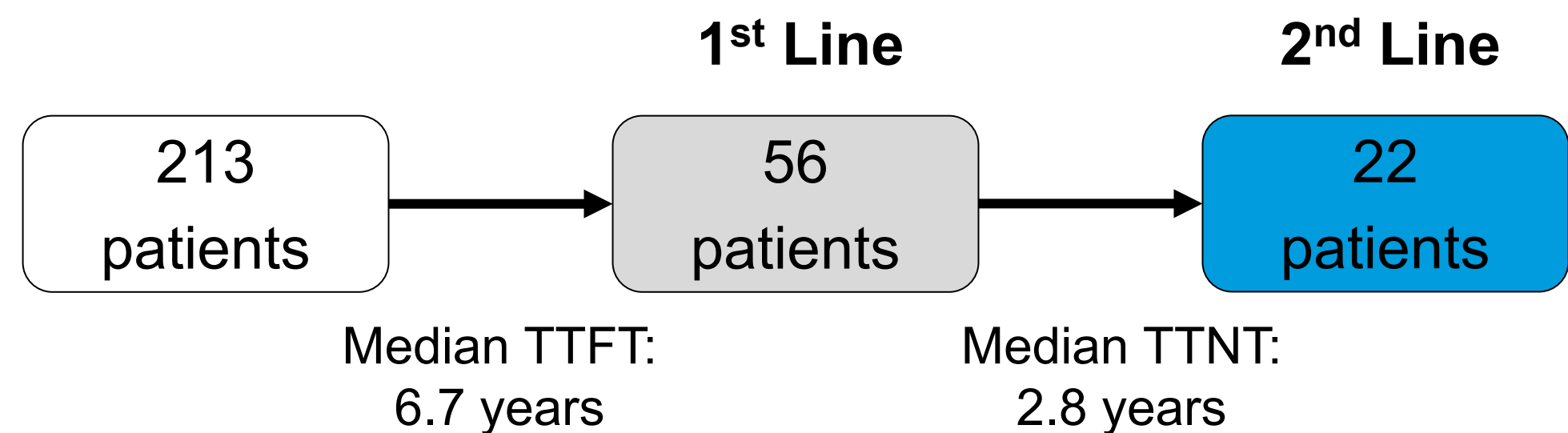
Characteristic		Number (%) or Median [range]
Total number of patients		213
Age, years		83 [80-97]
Males		134 (63)
Sum of medical comorbidities (Maximum=15)		4 (0-8)
Absolute lymphocyte count (x10 ⁹ /L)*		9.4 [0.5-172.6]
Rai stage*	0	89 (42)
	I-II	88 (42)
	III-IV	35 (17)
CD49d*	Negative (<30%)	52 (59)
	Positive (≥30%)	36 (41)
CD38*	Negative (<30%)	106 (65)
	Positive (≥30%)	56 (35)
ZAP70*	Negative (<20%)	52 (60)
	Positive (≥20%)	34 (40)
IGHV mutation status*	Mutated	38 (51)
	Unmutated	37 (49)
FISH*	Normal	31 (24)
	13q-	40 (31)
	Trisomy 12	30 (23)
	11q-	18 (14)
	17p-	8 (6)
	Other	2 (2)

*Patients with missing data not shown

Comorbidities: Distribution of Frequency



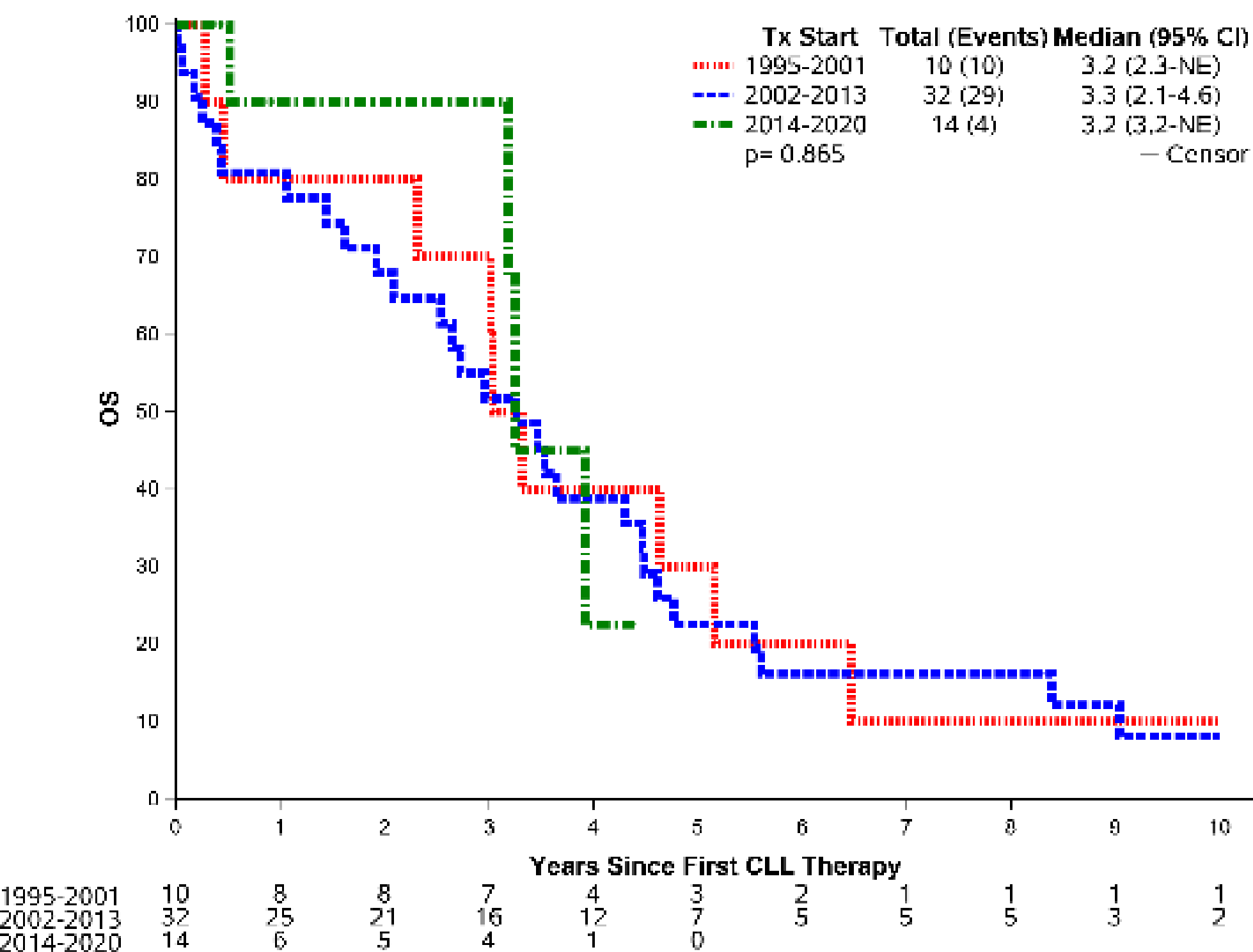
Treatment Disposition



First Therapy Across Time Periods

Treatment Category	1995-2001	2002-2013	2014-2020
Chemotherapy	8	9	0
Chemoimmunotherapy	0	11	3
Monoclonal antibody	0	12	5
Novel agents	0	0	3
Other	2	0	3

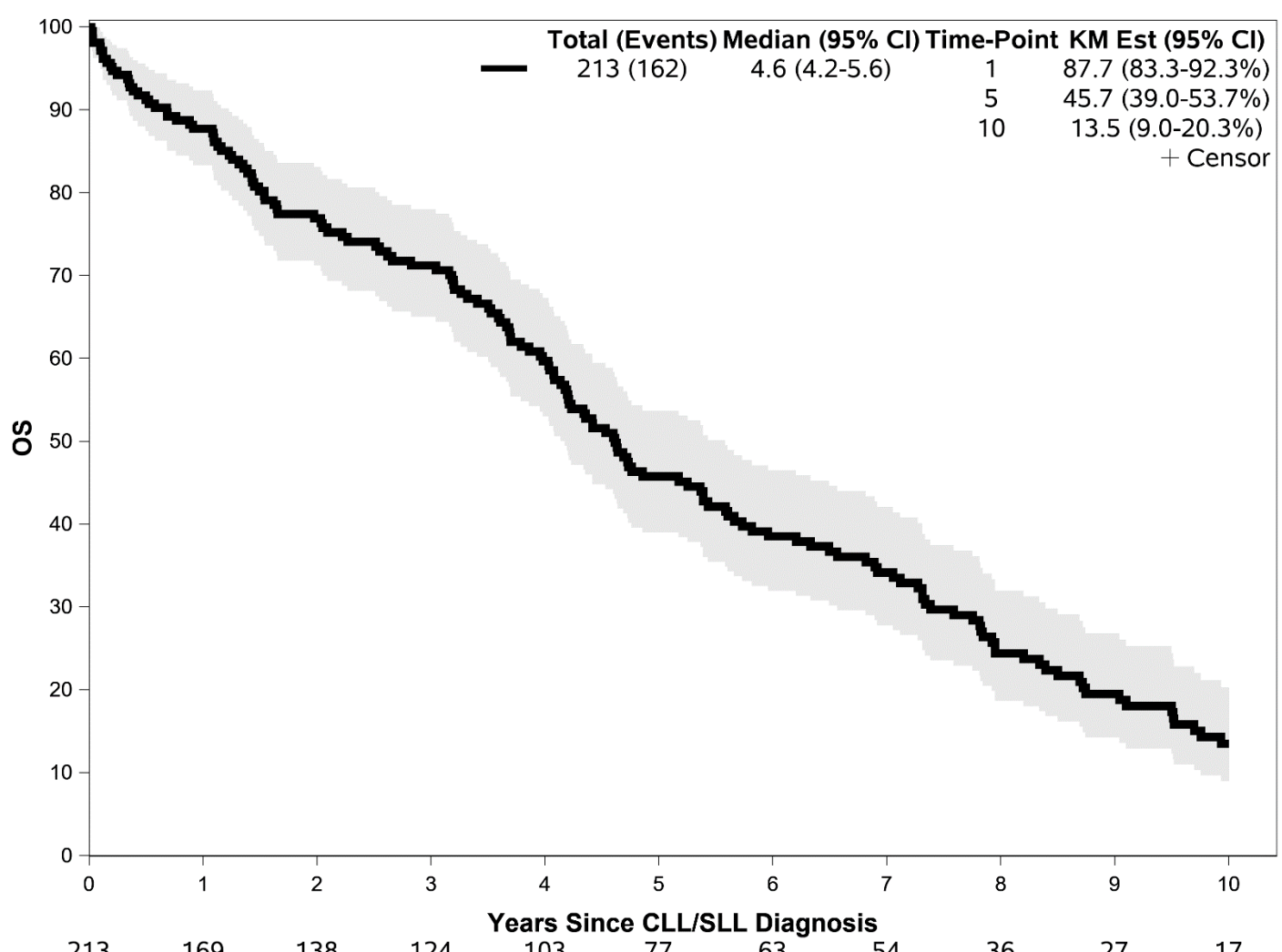
Overall Survival by Year of First Treatment



Treatment Regimens

- 1st Line most common: chlorambucil-based (n=20)
- 2nd Line most common: chlorambucil-based (n=6)
- Multi-agent chemotherapy was administered to 5 patients with Richter transformation

Overall Survival



- SMR compared to MN population: 1.3 (p=0.002); 1.2 (p=0.008) excluding Richter transformation
- Significant on univariable analyses:
 - Receipt of therapy: HR 3.92 (p<0.001)
 - Age(/5yr increase): HR 1.84 (p<0.001)
 - Unmutated IGHV: HR 2.03 (p=0.002)

Conclusions

- These findings emphasize the need for ongoing efforts to improve clinical outcomes for this patient population, hopefully through the incorporation of novel agents.