Chronic Myeloid Leukemia Reduces Survival in Elderly Patients (age ≥ 75 years old): An International Multicenter Study

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Introduction

- Tyrosine kinase inhibitors (TKIs) have significantly improved the life expectancy of individuals with chronic myeloid leukemia (CML), bringing it closer to that of the age-matched general population.
- However, epidemiological data indicates that only 3.8% of CML patients aged 75 or above participate in trials, despite this age group representing about 30% of CML patients.

Objective

•This study aims to assess the outcomes of elderly patients aged 75 years or older diagnosed with CML.

Methods

- A retrospective study of consecutive CML patients aged ≥ 75 years, diagnosed between January 2002 and December 2022 at four hematological centers in Israel and the Moffitt Cancer Center in Florida, United States (MCC).
- 1 year and 5 year overall survival (OS) rates were calculated.
- In addition, to assess if CML diagnosis affected life expectancy, we estimated the expected OS of the Israeli cohort based on life expectancy data from the Israeli Cental Bureau of Statistics (CBS).
- Kaplan-Meier curves were used to compare expected and observed median OS with the Log-rank analysis.
- Local Institutional Review Boards approved the study.

Results

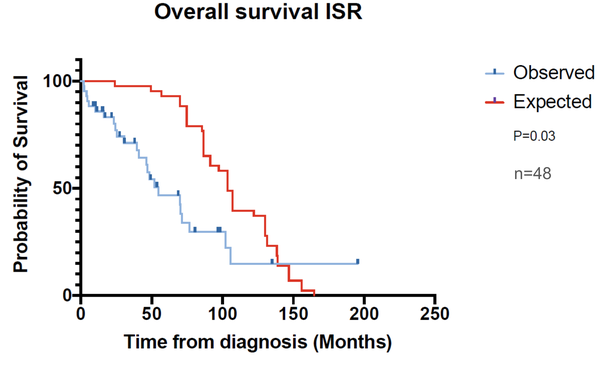
Table 1: Patient characteristics

Data	All	Israeli cohort	Moffitt cancer center cohort
Age at diagnosis, median, years (range)	79.1 (75-100)	81.3 (75-100)	78 (75-90)
≥ 80yrs, N (%)	55 (45%)	27 (60%)	28 (36%)
Sex, N (%)			
Female	49 (40%)	25 (55%)	24 (31%)
Male	74 (60%)	20 (45%)	54 (69%)
CML Phase, N (%)			
CP CML	115 (93%)	43 (96%)	72 (92.5%)
AP CML	6 (5%)	2 (4%)	4 (5%)
BP CML	2 (2%)	0 (0%)	2 (2.5%)
ELTS, N (%)			
Low	4 (3%)	3 (7%)	1 (1%)
Intermediate	65 (53%)	19 (42%)	46 (60%)
High	27 (22%)	12 (27%)	15 (19%)
Unknown	27 (22%)	11 (24%)	16 (20%)
Charlson Comorbidity Index Median (range)	5 (3-8)	5 (3-8)	5 (3-8)
Previous CVDs, N (%)			
No	73(59%)	20 (45%)	53 (68%)
Yes	50 (41%)	25 (55%)	25 (32%)
1st line treatment 2000-2009			
Imatinib N, (%)	13 (100%)	6 (100%)	7 (100%)
2010-2022			
Imatinib N, (%)	72 (66%)	38 (98%)	34 (48%)
2nd Generation TKIs N. (%)	38 (34%)	1 (2%)	37 (52%)
2nd line treatment			
Imatinib N, (%)	10 (15%)	3 (14%)	7 (16%)
Dasatinib N, (%)	26 (39%)	13 (59%)	13 (30%)
Nilotinib N, (%)	19 (29%)	3 (14%)	16 (36%)
Bosutinib N, (%)	8 (12%)	1 (4%)	7 (16%)
Ponatinib N, (%)	1 (2%)	0 (0%)	1 (2%)
Other N, (%)	2 (3%)	2 (9%)	0 (0%)
3rd line treatment			
Imatinib N, (%)	5 (17%)	0 (0%)	5 (22%)
Dasatinib N, (%)	3 (11%)	0 (0%)	3 (13%)
Nilotinib N, (%)	5 (17%)	1 (16.6%)	4 (17%)
Bosutinib N, (%)	12 (41%)	3 (50%)	9 (40%)
Ponatinib N, (%)	2 (7%)	1 (16.6%)	1 (4%)
Other N, (%)	2 (7%)	1 (16.6%)	1 (4%)

CP- chronic phase, AP- accelerated phase, BP- blast phase, ELTS- EUTOS long term survival, CVD- Cardiovascular disease, 2nd generation TKIs include- Dasatinib, Nilotinib and Bosutinib, Other treatments in 2nd and 3rd line included Hydroxyurea and Asciminb

- A total of 123 patients aged ≥ 75 years were diagnosed with CML (78 treated in MCC and 45 in Israel).
- Demographic and clinical data are presented in table 1.
- A large proportion of our cohort (45%), were octogenarians.
- Most patients were diagnosed in chronic phase CML
- Most patients had a high ELTS and Charlson comorbidity index (CCI) scores.
- Of note, in the era of 2nd generation TKIs, most patients in the Israeli cohort were treated with Imatinib as first line, while treatment of patients from the MCC cohort was divided between 1st and 2nd generation TKIs.
- The median OS for the whole cohort was 72.4 (53.1-91.7) months.
- Improved OS was documented in:
  - CCI< 5 (vs. ≥5, p=0.007), patients that achieved a DMR (vs. no DMR, p=0.001) and patients who received 2nd generation TKIs in 1st line treatment, 91.1 (81.5-131) vs. 57.7 (35.4-79.9) months in those who received imatinib, (p=0.023).
  - In the Israeli cohort, while the median expected OS was 103.7 (24-164.7) months, the median observed OS was only 54.77 (2.1-195) months (p=0.03) (Figure 1).

Figure 1: Overall vs. expected survival in the Israeli cohort



Median Observed OS 54.77 (2.1 - 195)
Median Expected OS 103.7 (24.1 - 164.7)

Conclusions

- Elderly CML patients were often diagnosed in chronic phase with high/intermediate risk scores.
- The majority received imatinib as 1st line treatment especially in the Israeli cohort.
- Clinical and demographic differences between the Israeli centers and MCC included the higher usage of 2nd generation TKIs in 1st line in MCC and a higher proportion of octogenarians in the Israeli cohort.
- These differences might reflect different populations referred to each center, insurance and socioeconomic issues.
- The Israeli cohort analysis supports reduced life expectancy in elderly patients with CML. This is in contrast to the prognosis of younger patients which is not affected by the disease.
- This discrepancy might be due to a higher prevalence of comorbities in the elderly population, thus complicating treatment.
- Other findings such as a better OS with 2nd generation treatment as 1st line and the importance of achieving a DMR- raises questions regrading treatment in this population.