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First-Line Ibrutinib in Patients With Chronic Lymphocytic Leukemia Demonstrates Overall Survival Comparable to an Age-Matched European Population

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Key Takeaway

Together with previous findings of significant OS benefit in patients with CLL treated with ibrutinib versus CT/CIT, this pooled analysis demonstrates that the OS benefit with 1L ibrutinib provides patients with a life expectancy comparable to that of an age-matched general European population

Conclusions

The OS estimate for patients with CLL treated with 1L ibrutinib was comparable to an age-matched general European population

For the subgroup of overall ibrutinib-treated patients aged ≥ 65 years, the OS estimate was also similar when compared with their respective age-matched general European population

The OS estimate with ibrutinib was comparable to an age-matched general European population when ibrutinib was administered as single agent or in combination with an anti-CD20 mAb

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Poster

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Introduction

- Chronic lymphocytic leukemia (CLL) mainly affects the older population, with a median age at diagnosis between 67 and 72 years; most have indolent course[1]
- The primary objective of cancer treatment is to extend survival, with overall survival (OS) considered the "gold standard" end point for evaluating clinical benefit of oncology therapies[2]
  - Assessing OS in patients with CLL has unique challenges due to the indolent nature and long-term control of the disease with subsequent lines of therapy[2,3]
- Ibrutinib has proven OS benefit across multiple phase 3 clinical trials[4,5]
- A pooled analysis of 3 phase 3 randomized trials (RESONATE-2, NCT01722487; ECOG1912, NCT02048813; iLLUMINATE, NCT02264574) showed that patients with CLL treated with first-line (1L) ibrutinib achieved similar OS estimates compared with an age-matched general US population[6]

Aims

- We compared OS estimates in patients with CLL treated with 1L ibrutinib versus an age-matched general European population, who may have lower standardized mortality rates than the US population
- 4 assessments were made to compare OS of patients with CLL treated with 1L ibrutinib versus the respective age-matched general European population:
  - Pooled ibrutinib-treated patients across all 3 trials
  - Subpopulation of patients aged ≥ 65 years
  - Patients treated with single-agent ibrutinib
  - Patients treated with ibrutinib + anti-CD20 monoclonal antibody (mAb; obinutuzumab, rituximab)

Methods

- Ibrutinib data were pooled from 3 phase 3 randomized trials in patients with previously untreated CLL/small lymphocytic lymphoma
  - Study designs for the 3 randomized trials were reported previously[5,7,8]
- Median follow-up time for each of the active trial arms (ibrutinib ± anti-CD20 mAb) under consideration[9]:
  - RESONATE-2 (single-agent ibrutinib): 88.5 months
  - ECOG1912 (ibrutinib + rituximab): 49.7 months
  - iLLUMINATE (ibrutinib + obinutuzumab): 40.6 months
- For each comparison, OS for ibrutinib-treated patients was compared with expected survival of a simulated age-matched general European population using survival probability by age group from 2019 life tables published by the World Health Organization[10]
  - Age at randomization of trial was used for age matching of patients
  - Available probabilities for 5-year age intervals were converted to a daily scale to avoid immortal time bias within each interval
- OS was analyzed using Kaplan-Meier methodology; hazard ratios (HRs) were derived from a Cox proportional hazards model using trial and simulated data

Results

Patients

- A total of 600 patients were treated with 1L ibrutinib across the 3 pooled studies (**Table 1**)
  - 45% of patients were aged ≥ 65 years
  - 56 patients had either del17p or *TP53* mutations
- Median follow-up time was 49.7 months

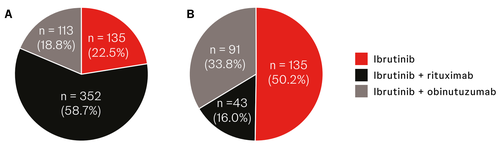
Table 1: Baseline Characteristics of Pooled Ibrutinib-Treated Patients

Characteristic	All treated patients (N = 600)
Median age at initial diagnosis (range), years	60 (30-87)
Median age at randomization (range), years	63 (31-89)
Age at randomization, n (%)	
< 65 years	331 (55.2)
65-75 years	190 (31.7)
≥ 75 years	79 (13.2)
Sex, n (%)	
Male	390 (65.0)
Female	210 (35.0)
ECOG PS, n (%)	
0	343 (57.2)
1	232 (38.7)
2	25 (4.2)
CIRS, n (%)	
≤ 6	479 (79.8)
> 6	93 (15.5)
Missing	28 (4.7)
Rai stage, n (%)	
0-II	317 (52.8)
III/IV	283 (47.2)
del11q, n (%)	
No	471 (78.5)
Yes	121 (20.2)
Missing	8 (1.3)
IGHV, n (%)	
Mutated	150 (25.0)
Unmutated	332 (55.3)
Missing	118 (19.7)
del17p or *TP53*, n (%)	
No	479 (79.8)
Yes	56 (9.3)
Missing	65 (10.8)

Percentages were rounded and may not total 100%.
CIRS, Cumulative Illness Rating Scale; ECOG PS, Eastern Cooperative Oncology Group performance status.

- For all pooled patients and those aged ≥ 65 years, the most common treatment regimens were ibrutinib + rituximab (n = 352, 58.7%) and single-agent ibrutinib (n = 135, 50.2%), respectively (**Figure 1**)

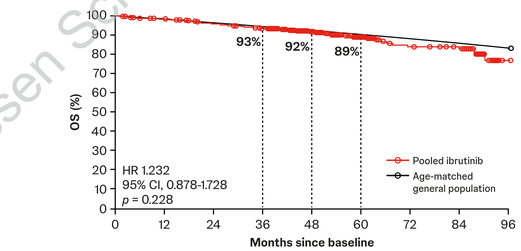
Figure 1: Treatment Regimen for Overall Pooled Ibrutinib-Treated Patients (A) and Pooled Ibrutinib-Treated Patients Aged ≥ 65 Years (B)



Overall survival

- The OS estimate was comparable (HR 1.232, $p = 0.228$) between ibrutinib-treated patients and the age-matched general European population (**Figure 2**)
  - The estimated OS rates for the ibrutinib-treated population were 93%, 92%, and 89% at 36, 48, and 60 months, respectively

Figure 2: Similar OS Estimate for Pooled Ibrutinib-Treated Patients Versus Age-Matched General European Population



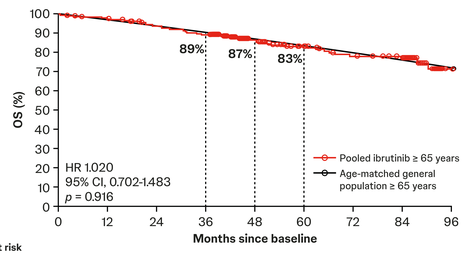
Patients at risk

Pooled ibrutinib	600	582	558	535	299	137	91	86	1
Age-matched general population	600	589	578	566	554	541	528	514	499

CI, confidence interval.
HR < 1 favors ibrutinib.

- Estimated OS was comparable (HR 1.020, $p = 0.916$) for the subgroup of ibrutinib-treated patients aged ≥ 65 years and the age-matched general European population (**Figure 3**)
  - The estimated OS rates for the ibrutinib-treated population aged ≥ 65 years were 89%, 87%, and 83% at 36, 48, and 60 months, respectively

Figure 3: Similar OS Estimate for Pooled Ibrutinib-Treated Patients Aged ≥ 65 Years Versus Age-Matched General European Population



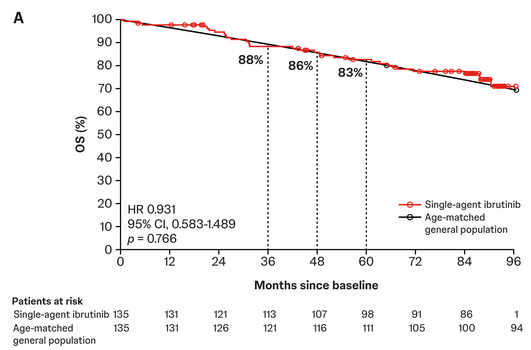
Patients at risk

Pooled ibrutinib ≥ 65 years	269	260	243	230	128	102	91	86	1
Age-matched general population ≥ 65 years	269	261	252	243	234	225	215	205	194

HR < 1 favors ibrutinib.

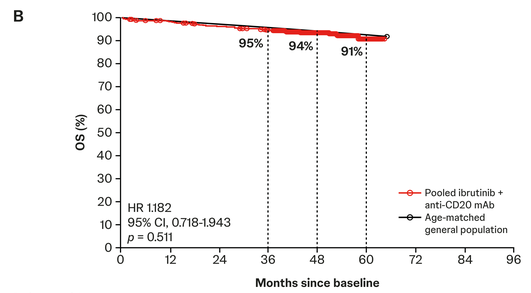
- Estimated OS was similar to the age-matched general European population regardless of receiving single-agent ibrutinib or in combination with an anti-CD20 mAb (**Figure 4**)
  - HR 0.931, $p = 0.766$ for single-agent ibrutinib (**Figure 4A**)
  - HR 1.182, $p = 0.511$ for ibrutinib in combination with an anti-CD20 mAb (**Figure 4B**)

Figure 4: Similar OS Estimate for Patients Treated With Single-Agent Ibrutinib Versus Age-Matched General European Population (A) and Combination of Ibrutinib and Anti-CD20 mAb Versus Age-Matched General European Population (B)



Patients at risk

Single-agent ibrutinib	135	131	121	113	107	98	91	86	1
Age-matched general population	135	131	126	121	116	111	105	100	94



Patients at risk

Pooled ibrutinib + anti-CD20 mAb	465	451	437	422	192	39	0		
Age-matched general population	465	459	452	445	438	430	0		

HR < 1 favors ibrutinib.

Limitations

- The age-matched general European population may include patients who received other treatments for CLL or those who may have other diseases that could impact survival rates; patients with severe cardiac comorbidities were excluded from the clinical trials

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B-cell Malignancies

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