Abstract: P664

Title: FIRST LINE (1L) IBRUTINIB (IBR) IN PATIENTS (PTS) WITH CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) DEMONSTRATES OVERALL SURVIVAL (OS) COMPARABLE TO AN AGE-MATCHED EUROPEAN POPULATION

Abstract Type: Poster Presentation

Topic: Chronic lymphocytic leukemia and related disorders - Clinical

Background:

The primary objective of cancer treatment is to extend survival, with OS considered the "gold standard" endpoint for evaluating clinical benefit of oncology therapies. However, assessing OS in pts with CLL has unique challenges due to the indolent nature and long-term control of the disease with subsequent lines of therapy. Ibr is the first targeted therapy to demonstrate significant OS benefit in pts with previously untreated CLL vs chemotherapy/chemoimmunotherapy. A pooled analysis of 3 phase 3 randomized trials (RESONATE-2, ECOG1912. iLLUMINATE) showed that pts with CLL treated with 1L Ibr achieved similar OS estimates compared with an age-matched general US population. Herein, we compare OS estimates in pts with CLL treated with 1L Ibr vs an age-matched European population, who may have distinct mortality rates when compared with the US population.

Aims:

Four assessments were made to compare OS of pts with untreated CLL given 1L Ibr vs the respective age-matched general European population: 1) pooled Ibr-treated pts across all 3 trials; 2) subpopulation of pts aged ≥65 years; 3) pts treated with single-agent Ibr; 4) pts treated with Ibr+anti-CD20 monoclonal antibody (mAb).

Methods:

Ibr** data were pooled from 3 phase 3 randomized trials in pts with previously untreated CLL/SLL: RESONATE-2 (NCT01722487, Ibr single-agent; median follow-up [FU], 88.5 mo; 32 OS events), ECOG1912 (NCT02048813, Ibr+rituximab [R]; median FU, 49.7 mo; 11 OS events), and iLLUMINATE (NCT02264574, Ibr+obinutuzumab [O]; median FU, 40.6 mo; 20 OS events). Study design for the trials were previously reported.

OS for Ibr-treated pts was compared with expected survival of the respective age-matched European population using survival probability by age group from 2019 life tables published by the World Health Organization. Age at randomization of trial was used for age matching of pts. Available probabilities for 5-year age intervals were converted to a daily scale to avoid immortal time bias. OS was analyzed using Kaplan-Meier methodology; HRs were derived from a Cox proportional hazard model using trial and simulated data.

Results:

Pts (N=600) were treated with Ibr in the 1L setting across pooled studies; 135 (22.5%) received single-agent Ibr, 352 (58.7%) and 113 (18.8%) received Ibr+R and Ibr+O, respectively. Median (range) age at randomization was 63 years (31-89); among all pts, 55 pts had del(17p) and/or *TP53* mutations; median FU was 49.7 mo. 269 pts were aged ≥65 years. Among them, 135 (50.2%) pts received single-agent Ibr; 91 (33.8%) and 43 (16.0%) pts received Ibr+O or Ibr+R, respectively.

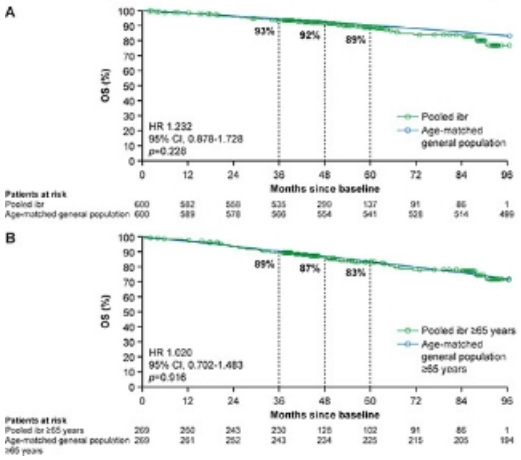
In the pooled population of 600 pts, OS was comparable between Ibr-treated pts and the age-matched general population (HR 1.232; 95% CI, 0.878-1.728; p=0.228; **Figure A**). Estimated OS was also comparable for the subgroup of Ibr-treated pts aged ≥65 years (HR 1.020; 95% CI, 0.702-1.483; p=0.916; **Figure B**).

Estimated OS was also similar to the age-matched European population when stratified by pts who received either single-agent Ibr (HR 0.931; 95% CI, 0.583-1.489; p=0.766) or the combination of Ibr+anti-CD20 mAb (HR 1.182; 95% CI, 0.718-1.943; p=0.511).

Summary/Conclusion:

This pooled analysis suggests that OS for pts with CLL treated with Ibr in the 1L setting was comparable to an age-matched general European population, including for older pts aged ≥65 years treated with Ibr. Single-agent Ibr or the combination of Ibr+anti-CD20 mAb also demonstrated estimated OS that were similar to their respective age-matched European population.

Figure. OS in the (A) pooled analysis of ibr-treated pts and (B) in the subgroup of ibr-treated pts aged ≥65 years. Hazard ratio <1 favors ibr. Dashed lines represent OS rates at 36 mo, 48 mo, and 60 mo for ibr-treated pts.



Keywords: ibrutinib, Chronic lymphocytic leukemia, Real world data, Survival