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Comparative Analysis of Patient Characteristics, Treatment Modalities, and Survival Outcomes in Chronic Lymphocytic Leukemia from China and the US

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Background Chronic lymphocytic leukaemia (CLL) is much more common in Americans compared with Asians. In addition to the observed differences in incidence rate and onset age, our previous research has also documented significant differences in the IGHV mutation status, VDJ rearrangement, and gene mutation spectrum among patients with CLL between China and Western countries. The bases for these differences and implications for therapy outcomes are controversial and mostly unknown.

Methods We compared baseline co-variates, therapies and outcomes of US and Chinese with CLL in the Flatiron Health (FH) (N = 15,786) and Tianjin CAMS databases (N = 2,996).

Results Age at diagnosis was younger in the CAMS database where people had higher ECOG scores, more frequent lymph node enlargement and hepato-spleno-megaly, thrombocytopenia, higher Rai stage, a higher β2-microglobulin concentration and fewer unmutated IGHV, del(17p), and other cytogenetic abnormalities. Several of these differences persisted after adjusting for age, Rai stage and IGHV mutation state.

There were also differences in therapies. We defined patients who received only traditional chemotherapy drugs as the traditional chemotherapy group, those treated with CD20 monoclonal antibodies as the immunotherapy group, and those receiving BTK inhibitors or BCL2 inhibitors as the targeted therapy group. This follows an upward classification principle where targeted therapy is considered superior to immunotherapy and traditional chemotherapy. Overall, CLL treatment patterns in China were lagged behind Western countries, with fewer patients receiving Rituximab and delayed adoption of targeted therapies. However, from 2019 onward, the proportions of patients receiving targeted therapy in both databases were approximately the same.

Median survival in the CAMS dataset was 9.7 years versus 7.5 years in the FH database ($P < 0.001$). In sub-group analyses Chinese with CLL had better 5-year survivals with chemotherapy (69% [95% Confidence Interval (CI), 66, 72%] versus 49% [47, 52%]; P <0.001), immune therapies (67% [63, 72%] versus 65% [64, 66%]; P = 0.04) and targeted therapies (85% [81, 88%] versus65% [64, 67%]; P < 0.001).

Considering the pivotal influence of IGHV mutation status, patient age, Rai staging, and TP53 status on CLL survival, these factors also constituted significant disparities in baseline characteristics between Eastern and Western CLL populations. Therefore, we conducted a survival subgroup analysis focusing on these four factors. Interestingly, within the IGHV mutation group, patients in the Tianjin CAMS database exhibited better survival than those in the FH database (median survival 13.2 vs. 10.7 years, P=0.008). Conversely, in the IGHV unmutated group, patients in the Tianjin CAMS database had significantly poorer survival than those in the FH database (median survival 6.7 vs. 9.0 years, P=0.008). The OS for younger CLL patients was similar between two databases (median OS 10.8 vs. 11.4 years, P=0.288). However, among older CLL patients, those in the Tianjin CAMS database had significantly better survival compared to those in the FH database (median OS 6.9 vs. 5.2 years, P<0.001). For patients with TP53 deletions, the prognosis was poor in both databases with no significant difference, whereas patients without TP53 deletions in the Tianjin CAMS database had better survival than those in the FH database (median OS 9.6 vs. 9.0 years, P=0.007).

Conclusion We highlight differences between Americans and Chinese with CLL and offer some explanations.

Disclosures Wang: *AbbVie:* Membership on an entity's Board of Directors or advisory committees. **Kipps:** *Abbvie/Janssen/Pharmacyclics/Genentech:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Lymphoma and Leukemia Society:* Research Funding; *Oncternal Therapeutics:* Current equity holder in private company.

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