



中山大学肿瘤防治中心

SUN YAT-SEN UNIVERSITY CANCER CENTER

附属肿瘤医院 肿瘤研究所



华南肿瘤学国家重点实验室
State Key Laboratory of Oncology in South China



世界卫生组织癌症合作中心
WHO Collaborating Center for Research on Cancer



国际抗癌联盟会员
Union for International Cancer Control (UICC)

Dear WHO Expert Committee,

6 APRIL,2023

It is my pleasure to write this letter to advocate the inclusion of A52 Zanubrutinib on the WHO Essential Medicine List for the treatment of Chronic lymphocytic leukemia/small lymphocytic lymphoma.

I am Dr. Huiqiang Huang, deputy director of the Department of Medical Oncology, SUN YAT-SEN University Cancer Center.

Zanubrutinib is a widely used BTK inhibitor to treat chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). It was approved by China NMPA in Jun. 2020 based on *205 study*, a phase II registrational clinical study for CLL/SLL patients. Soon after it's approval, Zanubrutinib was included in the National reimbursement Drug List (NRDL) to reduce economic burden and benefit more CLL/SLL patients in China.

In 2023, Zanubrutinib CLL/SLL indication was approved by EU and the U.S. market based on two global head-to-head phase III clinical studies, ALPINE and SEQUOIA studies. ALPINE study illustrates that Zanubrutinib shows superiority on progression free survival versus Ibrutinib on patients with R/R CLL/SLL. In addition to efficacy, Zanubrutinib also shows overall better safety profile compared with Ibrutinib, especially the cardiac profile, Zanubrutinib has lower rate of atrial fibrillation, serious cardiac events as well as fatal cardiac events. ALPINE result was recently reported on 2022 American Society of Hematology as "Late-breaker Abstract" oral and published on the *New England Journal of Medicine* at the same time. SEQUOIA study shows Zanubrutinib is a better regimen comparing to bendamustine-rituximab on frontline CLL/SLL treatment.

As a next-generation BTK inhibitors, Zanubrutinib also shows reliable safety profile through multiple global clinical studies and over 4000+ subjects enrolled around the world, including patients from United States, China, EU, etc. Zanubrutinib is also the first BTK inhibitor that are recommended by both U.S. NCCN CLL/SLL guideline and China CSCO lymphoma guideline as preferred/Class I regimen for CLL/SLL patients.

Until now, Zanubrutinib has been approved to list on over 65 countries and regions, and it shown significant therapeutic effects in clinical use, and improve patients' quality of life of patients. Zanubrutinib is also a more economical option comparing with Ibrutinib.



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Based on the evidence above, It is my great honored to recommend the inclusion of Zanubrutinib into the WHO Model list of Essential Medicines since Ibrutinib were already listed in the EML.

Thank you for your time and kind consideration.

Yours sincerely,

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