

Dear WHO representatives,

I, Prof. Yaling Han MD, PhD, chairman of Chinese Society of Cardiology, would like to declare my support for AstraZeneca's submission of ticagrelor for inclusion in the 2023 World Health Organization (WHO) List of Essential Medicines update. The key reasons behind my decision are as follows:

- 1. The number of patients with cardiovascular disease in China is about 330 million, and the incidence rate and mortality of patients with acute coronary syndrome (ACS) in China are still rising<sup>1</sup>. In 2021, the total number of coronary intervention treatment in mainland China was more than 1,16 million<sup>2</sup>.
- 2. The proportion of resistance or low response to clopidogrel caused by CYP2C19 gene polymorphism in the eastern population is significantly higher than that in the western population (3%-5% in the Caucasus population, 12%-23% in the eastern population, and 4%-8% in the African population)<sup>3</sup>. For these patients, ticagrelor can effectively reduce the cardiovascular events of ACS patients, and avoid the lack of efficacy caused by genetic differences<sup>4</sup>.
- 3. Study evidence:
  - a. PLATO<sup>5</sup>: In patients who have an ACS with or without ST-segment elevation, treatment with ticagrelor as compared with clopidogrel significantly reduced the rate of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall major bleeding.
  - b. Dayu Study<sup>6</sup>: Ticagrelor plus aspirin for up to 1 year was associated with a low rate of major bleeding events and a low incidence of major CV events in Chinese patients with ACS.
  - c. HOUYI Study<sup>7</sup>: Ticagrelor could achieve more rapid and efficient platelet inhibition than a high loading-dose of clopidogrel at the beginning of treatment in Chinese patients with ACS.
  - d. TWILIGHT-CHINA<sup>8</sup>: Ticagrelor monotherapy significantly reduced clinically relevant bleeding without increasing ischemic events as compared with ticagrelor plus aspirin in Chinese patients undergoing high-risk percutaneous coronary intervention.
- 4. Several Chinese guidelines recommend the use of ticagrelor over clopidogrel in ACS in numerous clinical scenarios<sup>9-14</sup>.
- Ticagrelor has been widely used in the clinical frontline in China since 2012, with its good effectiveness and safety. It was included in the National Essential Medicines List of China in 2018 and has benefited more than a million ACS patients every year.
- 6. Cost-effectiveness assessments in LMICs have found ticagrelor to be as, or more, cost-effective than clopidogrel in ACS.

I hope this information supports the decision to include ticagrelor in the 2023 WHO List of Essential Medicines update, and I remain at your disposal for any questions you may have.

Signed

Date

Prof. Yaling Han

Chairman of Chinese Society of Cardiology

Valing Han March. 28.2023