

## 2019 international clinical practice guidelines for the treatment of venous thromboembolism

### Authors' reply

We thank Kyaw Zin Thien and Thein Hlaing Oo for their comments on the 2019 international clinical practice guidelines for prevention and treatment of cancer-associated thrombosis.<sup>1</sup>

We acknowledge that patients with cancer receiving medical treatment are heterogeneous, both in terms of thrombosis and bleeding risks. However, our grade 1B recommendation for primary prophylaxis in patients with advanced or metastatic pancreatic cancer or with other tumour types at moderate-to-high thrombosis risk is based on the following: low-molecular-weight-heparin as primary prophylaxis in patients with pancreatic cancer is supported by evidence from two randomised controlled trials, and three meta-analyses,<sup>1,2</sup> including a study showing a significant 11% absolute risk reduction, without significant increase in major bleeding;<sup>1</sup> the use of direct oral anticoagulants as primary prophylaxis in pancreatic cancer was based on the high proportion (25%) of these specific patients in the AVERT and CASSINI trials,<sup>3,4</sup> and further supported by a subgroup analysis which showed significant reduction in the primary efficacy VTE composite endpoint, without an associated increase in major bleeding;<sup>5</sup> although CASSINI did not meet the primary efficacy endpoint at 180-day follow-up, a significant reduction in this VTE composite endpoint was reported while on treatment in the same intent-to-treat population in a pre-specified analysis; although we acknowledge the CASSINI and AVERT trial limitations, the totality of evidence in terms of net clinical benefit supports a

grade 1B recommendation favouring primary prophylaxis with direct oral anticoagulants in appropriately selected medical patients with cancer at moderate-to-high thrombosis risk and low bleeding risk. Implicit in the assignment of a B-level of evidence to this recommendation is the need for further research in this clinical domain, especially in patients with specific tumour types.

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