Study compares heparin to warfarin for treatment of blood clots in patients with cancer

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Among patients with active cancer and acute symptomatic venous thromboembolism (VTE; blood clots in the deep veins), the use of the low molecular-weight heparin tinzaparin daily for 6 months compared with warfarin did not significantly reduce recurrent VTE and was not associated with reductions in overall death or major bleeding, but was associated with a lower rate of clinically relevant nonmajor bleeding, according to a study in the August 18 issue of *JAMA*.

Venous thromboembolism is a major cause of illness and death in patients with cancer. Treatment with low-molecular-weight heparin is effective and is recommended over warfarin by clinical practice guidelines. These recommendations are largely based on results from a single, large randomized trial with supportive evidence from additional smaller studies that were conducted over a decade ago in academic centers primarily in North America and Western Europe, according to background information in the article.

Agnes Y. Y. Lee, M.D., M.Sc., of the University of British Columbia, Vancouver, and colleagues randomly assigned 900 adult patients with active cancer and documented deep vein thrombosis or pulmonary embolism to tinzaparin once daily for 6 months vs conventional therapy with tinzaparin once daily for 5 to 10 days followed by warfarin at a dose adjusted to maintain the international normalized ratio (INR) within the therapeutic range for 6 months. The patients, enrolled in 164

centers in Asia, Africa, Europe, and North, Central, and South America between August 2010 and November 2013, were followed up for 180 days and for 30 days after the last study medication dose for collection of safety data.

Recurrent VTE occurred in 31 of 449 patients treated with tinzaparin and 45 of 451 patients treated with warfarin (6-month cumulative incidence, 7.2 percent for tinzaparin vs 10.5 percent for warfarin). There were no differences in major bleeding (12 patients for tinzaparin vs 11 patients for warfarin) or overall mortality (150 patients for tinzaparin vs 138 patients for warfarin).

Tinzaparin significantly reduced the risk of clinically relevant nonmajor bleeding (included bleeding that required any medical or surgical intervention but was not fatal; did not occur in a critical area or organ; or did not cause a fall in hemoglobin of greater than 2 g/dL or lead to a transfusion of 2 or more units of whole blood or red cells) compared with warfarin (49 of 449 patients for tinzaparin vs 69 of 451 patients for warfarin). "Together with the adverse events data, [this trial] demonstrated that tinzaparin, even when given at a full therapeutic dose for up to 6 months, is safe in a broad oncology population," the authors write.

"Further studies are needed to assess whether the efficacy outcomes would be different in patients at higher risk of recurrent VTE."

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