Tinzaparin Reduces the Risk of Recurrent Thromboembolic Events in Patients With Cancer

Written by Lynne Lederman

Various strategies have been tested to prevent recurrent venous thromboembolism (VTE) in patients with cancer, including warfarin and low-molecular-weight heparins (LMWH), such as enoxaparin, dalteparin, and tinzaparin. Agnes Y. Y. Lee, MD, MSc, University of British Columbia, Vancouver, British Columbia, Canada, presented the safety and efficacy results of the Long-term Tinzaparin Treatment Versus a Vitamin K Antagonist (Warfarin) for the Treatment of Venous Thromboembolism (VTE) in Cancer study [NCT01130025].

The primary objective was to study the efficacy of tinzaparin in preventing recurrent VTE in patients with active cancer. Although Prof Lee did not report the secondary objectives, they included the safety of tinzaparin for long-term use, the incidence and severity of postthrombotic syndrome, the assessment of quality of life, and an estimate of health care resource utilization.

In this prospective open-label trial, patients were randomly assigned to tinzaparin, 175 IU/kg, once daily (n = 449) or to warfarin (target international normalized ratio, 2 to 3) plus initial tinzaparin, 175 IU/kg, for 5 to 10 days (n = 451).

Structured interviews by clinic visits and telephone were used to determine if outcome events occurred. The primary composite efficacy end point included symptomatic deep vein thrombosis (DVT), symptomatic pulmonary embolism (PE), fatal PE, incidental proximal DVT, and incidental proximal PE. Key safety end points included major bleeding, clinically relevant nonmajor bleeding, and overall mortality. Patients were well matched for previous VTE, type of cancer, metastatic disease (a little over half of patients in each group), active cancer treatment (a little over half of patients in each group), and symptomatic PE or DVT (Table 1). The most frequent types of cancer were gynecologic, gastrointestinal, lung, hematologic, and genitourinary.

Recurrent VTE occurred in 7.2% of patients on tinzaparin and 10.5% of patients on warfarin (time within therapeutic range, 47%) for a 35% risk reduction (HR, 0.65; 95% CI, 0.41 to 1.03; $P = .007$). In prespecified efficacy analyses, tinzaparin significantly reduced symptomatic DVT by 52% (HR, 0.48; 95% CI, 0.24 to 0.96; $P = 0.04$). Symptomatic PE and incidental VTE were low in both groups. Fatal PEs were similar in both groups, with 17 patients in each group. According to the per-protocol analysis, recurrent VTE was reduced 38% (HR, 0.62; 95% CI, 0.38 to 1.00).

Table 1. Selected Patient Characteristics

	Tinzaparin (n = 449)	Warfarin (n = 451)
Mean age, y (range)	60 (19 to 89)	59 (18 to 86)
Ethnicity, %		
Asian	44	43
European	38	38
American	19	19
History, No. (%)		
Previous VTE	27 (6)	30 (7)
Symptomatic PE, no DVT	107 (24)	87 (19)
Symptomatic DVT	334 (74)	349 (77)

DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism.

There were no differences in major bleeding or overall mortality between groups. Tinzaparin significantly reduced clinically relevant nonmajor bleeding by 31% (HR, 0.69; 95% CI, 0.49 to 0.96; $P = .03$). Overall mortality at day 180 was 34.2% in the tinzaparin group and 32.2% in warfarin group.

This is the largest randomized controlled trial studying the treatment of cancer-associated thrombosis, and it provides confirmatory data for the improved efficacy of LMWH over warfarin. Full-dose tinzaparin did not increase major bleeding and reduced clinically relevant nonmajor bleeding. This is also the first trial to document the prevalence and incidence of incidental thrombosis in cancer. Although quality-of-life results were not reported here, Prof Lee observed that patients on LMWH have less anxiety about being in the therapeutic range, are easier to manage, and have no drug interactions with diet or chemotherapy. Finally, global participation in the study led to the enrollment of Asian patients, a population not included in previous trials.