

# Oral apixaban as good as dalteparin for treating cancer-associated clots

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For people with cancer, the oral blood thinner apixaban is at least as effective as dalteparin, a low molecular weight heparin given by injection, in preventing a repeat venous thromboembolism (VTE), or

blood clot, with no excess in major bleeding events, according to Phase 3 trial results presented at the American College of Cardiology's Annual Scientific Session Together with World Congress of Cardiology (ACC.20/WCC).

It is estimated that one in five [blood clots](#) occur in people with cancer. This population has a much higher risk of developing dangerous VTEs, including [deep vein thrombosis](#) (DVT), a blood clot that forms deep inside a vein (usually in a leg) and, more worrisome, pulmonary embolism, which happens when a clot travels and gets lodged in a lung, which can be fatal. Experts say there are many reasons why people with cancer are more susceptible to clotting; for example, the cancer itself can thicken the blood, making it stickier and many cancer therapies and surgeries can inflame blood vessels and limit patients' movement so clots can form more easily.

The aim of the Caravaggio study—the largest study to evaluate the treatment of VTE in cancer—was to assess whether the direct oral anticoagulant apixaban is non-inferior to subcutaneous dalteparin for preventing a recurrent VTE in people with cancer and to evaluate the risk of bleeding. The data revealed that recurrent VTE, the study's primary endpoint, occurred in 32 of 576 patients (5.6%) in the apixaban group and 46 of the 579 patients (7.9%) in the dalteparin group over six months of follow-up, a difference that was not statistically significant. Moreover, major bleeding events, defined by the ISTH guidelines, were similar in the apixaban and dalteparin groups, occurring in 22 patients (3.8%) compared with 23 patients (4.0%), respectively. The proportion of patients who were free of a recurrent VTE, major bleeding events and death during the study period was 73.3% in the apixaban group and 68.6% in the dalteparin group.

"VTE is a major cause of complications and death in these patients, and the high risk of recurrent blood clots and bleeding in patients with cancer

make anticoagulant treatment challenging and, therefore, specific studies in these patients are necessary," said Giancarlo Agnelli, MD, professor of internal medicine at the University of Perugia, Italy, and lead author of this investigator-initiated, open-label trial. "Our data show that apixaban is at least as effective as dalteparin—the current gold standard treatment—without any excess in major bleeding, which is a common concern when giving blood thinners. These results should expand the proportion of patients with cancer-associated VTE who can be treated with oral apixaban, which is less cumbersome for patients because it's a pill, not a daily injection."

The Caravaggio trial enrolled 1,170 patients with a cancer-associated VTE at the time of diagnosis at 119 sites in nine European countries, Israel and the U.S. Participants were consecutively randomized to receive oral factor-Xa inhibitor apixaban at a dose of 10 mg twice daily for seven days followed by 5 mg twice daily, or subcutaneous dalteparin 200 units per kg once daily for one month followed by 150 units per kg once daily thereafter for a total of six months. The primary study outcome of recurrent VTE was confirmed by an independent adjudication committee unaware of the treatment patients received.

Patients were 68 years old on average. Pulmonary embolism, a blood clot in the lung, with or without DVT was present in 55% of patients, while 45% had an isolated DVT. Most patients (80.3%) had symptoms suggestive of a blood clot, while 20% had unsuspected VTE that was found through imaging tests performed for reasons other than clinical suspicion of VTE. Most patients (97%) in both the apixaban and dalteparin arms had an active cancer at the time of enrollment; 94.3% of patients in the apixaban arm and 91% in the dalteparin arm had a solid tumor of which 32.6% and 32.3% were located in the gastrointestinal tract, including the pancreatic and hepatobiliary cancer, which was of interest given that major bleeding events from [blood](#) thinners often occur in the gastrointestinal tract (GI) system.

Agnelli said that while previous studies have shown other direct oral anticoagulants (edoxaban and rivaroxaban) to be as effective as low molecular weight heparin, there is a trade-off given the observed increase in bleeding, particularly in people with gastrointestinal cancers. He said, for this reason, the most recent guidelines, which have long recommended low-molecular-weight heparin for cancer-associated VTEs, added the use of these agents with the exception of patients with GI cancers.

Agnelli said of note in this study, apixaban was not associated with an increase in GI bleeding compared to dalteparin; major GI bleeding occurred in 1.9% of apixaban and 1.7% of dalteparin-treated patients.

"This is the only trial in [cancer](#)-associated thrombosis where a DOAC (direct-acting oral anticoagulant) is not associated with increased GI bleeding, in spite of the inclusion of a substantial proportion of GI cancers," he said.

Interestingly, Agnelli reported that [apixaban](#) was more effective than dalteparin at preventing recurrent VTE in patients younger than age 65. Agnelli and team will be conducting several subgroup analyses to determine if certain patients benefit more from one approach.

The results of this study cannot be extrapolated to people with brain tumors, known cerebral metastases or acute leukemia, as they were not enrolled for safety reasons. Researchers added that, as with a large majority of studies on the treatment of VTE, the sample size of the study was powered for recurrent VTE, the primary outcome, and was not powered to make definitive conclusions about bleeding.

This study was simultaneously published online in the *New England Journal of Medicine* at the time of presentation. The trial was an investigator-initiated study supported by the BMS-Pfizer Alliance.

**More information:** Giancarlo Agnelli et al. Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer, *New England Journal of Medicine* (2020). [DOI: 10.1056/NEJMoa1915103](https://doi.org/10.1056/NEJMoa1915103)

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