Extended Evidence Update

API-CAT Trial

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Question

> *Is extended treatment with a reduced-dose regimen of apixaban in patients with active cancer associated deep-vein thrombosis (DVT) or pulmonary embolism (PE) who have completed at least 6 months of anticoagulation therapy non-inferior to continuation of full-dose apixaban for prevention of recurrent venous thromboembolism (VTE) while reducing clinically significant bleeding?*

Background

Patients with cancer are at higher risk for thromboembolism than the general population, and those with cancer-associated VTE are at a greater risk for recurrent events despite anticoagulation therapy.[1] According to current guidelines, anticoagulation with a direct oral anticoagulant (DOAC) or low-molecular-weight heparin (LMWH) is recommended for at least 3-6 months post VTE in patients with active cancer or receiving active cancer treatment.[2] However, a balance must be maintained between the benefits of anticoagulation and preventing recurrence and the risk of bleeding complications. Currently, standard dosing of apixaban for acute management of DVT/PE in cancer patients is 10 mg twice daily for 1 week, followed by 5 mg twice daily for 3-6 months.[2] Evidence for appropriate management beyond this initial period is limited. Continued anticoagulation beyond 3-6 months is recommended if the patient is receiving systemic chemotherapy, has metastatic disease, has progressive or relapsed disease, or risk factors for recurrent VTE.[2]

Evidence

One randomized, double blind, non-inferiority trial in patients with active cancer and proximal DVT or PE who had completed at least 6 months of anticoagulant treatment.[1]

- 1766 patients were randomly assigned in a 1:1 ratio to receive oral apixaban at a reduced dose (2.5 mg twice daily) or full dose (5 mg twice daily) for a duration of 12 months, stratified by trial center, index event (PE with or without DVT vs. isolated proximal DVT), and site of cancer
- Primary Outcome: fatal or non-fatal recurrent VTE during 12 months of follow-up
- Key Secondary Outcome: clinically relevant bleeding during 12 months of follow-up

Results

- Median population age of 69 years (43.4% male)
- Median treatment duration of 11.8 months
- Index event was a lower-limb proximal DVT without PE in 24.5% of patients and PE in 75.5% of patients

continued on page 2

Results continued

- Extended anticoagulation with reduced dose apixaban was noninferior to full dose apixaban for the prevention of recurrent VTE at 12 months of follow-up. (Adjusted sub-hazard ratio (HR), 0.76;95% confidence interval [CI], 0.41 to 1.41; P=0.001 for noninferiority)
- Clinically relevant bleeding occurred less frequently with reduced dose apixaban (cumulative incidence, 12.1%) than with full dose apixaban (cumulative incidence, 15.6%) over the 12-month follow-up period. (HR, 0.75;95% CI, 0.58-0.97, p=0.03 for superiority)

Safety

Major bleeding occurred in 24 patients (cumulative incidence, 2.9%) in the reduced-dose group and in 37 patients (cumulative incidence, 4.3%) in the full-dose group (HR, 0.66; 95% CI, 0.40 to 1.10).

- Major gastrointestinal (GI) bleeding occurred in 37 patients (upper GI bleeding in 6 patients in the reduced-dose group and 13 in the full-dose group; lower GI bleeding in 7 and 13 patients, respectively; 2 patients [1 in each group] had both upper and lower gastrointestinal bleeding)
- Most deaths were related to cancer (82.4% of patients in the reduced-dose group and 84.5% of patients in the full-dose group)

Limitations/Considerations

- No data collected on race or ethnic group of trial participants, therefore no data on treatment effects according to ethnicity.
- Data was collected over a 12-month period, potential efficacy and safety of longer duration of treatment remains uncertain.
- The incidence of recurrent VTE in this high-risk population receiving anticancer treatment was lower than anticipated. This could be related to inclusion of patients with various primary sites of cancer. Brain, stomach and pancreatic cancer are among the highest risk for recurrent VTE.[3] The most common primary cancer sites in trial participants were breast and colorectal, leading to potential lower representation of higher risk cancers.

Conclusion

> *Extended anticoagulation with reduced-dose apixaban was non-inferior to full-dose apixaban for the prevention of recurrent VTE in patients with active cancer who had completed at least 6 months of anticoagulant treatment for VTE. A reduced dose of apixaban led to a lower incidence of clinically relevant bleeding complications compared to continuation of the full dose regimen.*

References

1. Agnelli G, Ay C, Bamias A, et al. Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism. N Engl J Med. 2025;392(14):1363-1373. doi: 10.1056/NEJMoa2416112.
2. Cancer and Thrombosis Clinical Practice Guidelines Thrombosis Canada. Updated February 20, 2023. Accessed March 11, 2026. https://thrombosiscanada.ca/clinical_guides/pdfs/CANCERANDTHROMBOSIS_44.pdf
3. Abou-Nassar K, Carrier M, El-Maraghi R, et al. Supplementary Appendix: Apixaban to Prevent Venous Thromboembolism in Patients with Cancer. N Engl J Med. 2019;380(8):711-719. doi: 10.1056/NEJMoa1814468.