Direct Oral Anticoagulants in Cancer-Associated Thrombosis: Redefining Extended Therapy

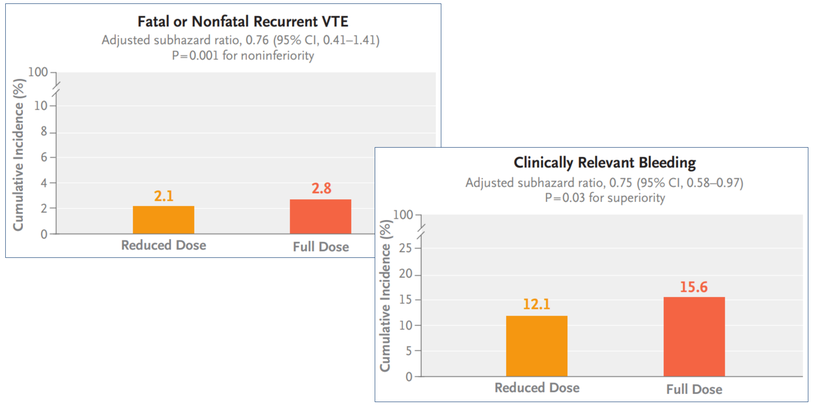
Ofek Raviv, MD
Department of Internal Medicine, Cleveland Clinic Florida, Weston, FL

Learning Objectives

- Describe the shift from LMWH to DOACs for cancer-associated thrombosis.
- Evaluate recent clinical trial evidence supporting reduced-dose apixaban for extended secondary prevention.
- Apply Khorana score stratification to identify ambulatory cancer patients who may benefit from prophylactic DOACs.

Background

Venous thromboembolism (VTE) is a leading cause of morbidity and mortality in cancer, accounting for 15–25% of all VTE cases. Cancer patients have a 4- to 7-fold higher risk of VTE than the general population. Historically, low-molecular weight heparin (LMWH) was the standard for prophylaxis and treatment. Since 2018, randomized trials and meta-analyses evaluated direct oral anticoagulants (DOACs), leading to updated recommendations from the National Comprehensive Cancer Network and the American Society of Hematology for their use in cancer-associated VTE.[1–3]



Key Developments

Recent studies, including the API-CAT trial (2025), have shown that apixaban 2.5 mg twice daily is non-inferior to 5 mg twice daily for extended secondary prevention of VTE in cancer patients who have completed at least 6 months of anticoagulation. In API-CAT, recurrent VTE occurred in 2.1% of patients on 2.5 mg BID and 2.8% on 5 mg BID (adjusted subhazard ratio 0.76; 95% CI, 0.41–1.41; P=0.001 for noninferiority). Clinically relevant bleeding was lower with the reduced dose (12.1% vs 15.6%; adjusted subhazard ratio 0.75; 95% CI, 0.58–0.97; P=0.03).[4] For primary prophylaxis, low-dose apixaban (2.5 mg BID) and rivaroxaban (10 mg daily) reduce VTE incidence in ambulatory cancer patients at intermediate or high risk, with a modest increase in major bleeding.[1 5–7] The number needed to treat (NNT) to prevent one VTE event is 25 for intermediate-to-high risk and 17 for high-risk patients.[8] Major bleeding risk is not significantly increased in these groups.[8]

Implementation

DOACs are now recommended as first-line agents for most cancer patients with VTE, except those with high bleeding risk, severe renal impairment, or significant drug-drug interactions.[1–3] The oral route improves adherence and quality of life compared to daily LMWH injections. Extended anticoagulation with apixaban 2.5 mg BID is recommended for patients with ongoing cancer or persistent risk factors. This strategy balances efficacy and bleeding risk.[1–4]

Significance

These recommendations, updated through 2025, have shifted the standard of care. DOACs at 2.5 mg BID for apixaban offer effective VTE prevention with lower bleeding risk for extended therapy. Individualized risk assessment is essential, especially for patients with GI or GU cancers. The Khorana score is a validated tool to identify high-risk patients (score ≥2 for intermediate risk, ≥3 for high risk), incorporating cancer type, platelet count, hemoglobin, leukocyte count, and BMI.[9–11] High-risk patients (Khorana ≥3) have an 11% 6-month VTE incidence and derive the greatest benefit from prophylaxis.[10,11] These evidence-based strategies are expected to improve outcomes and healthcare efficiency.[1–11]

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