Unlocking the potential of statins for VTE prophylaxis in cancer: why conduct the STAT-CAT trial?

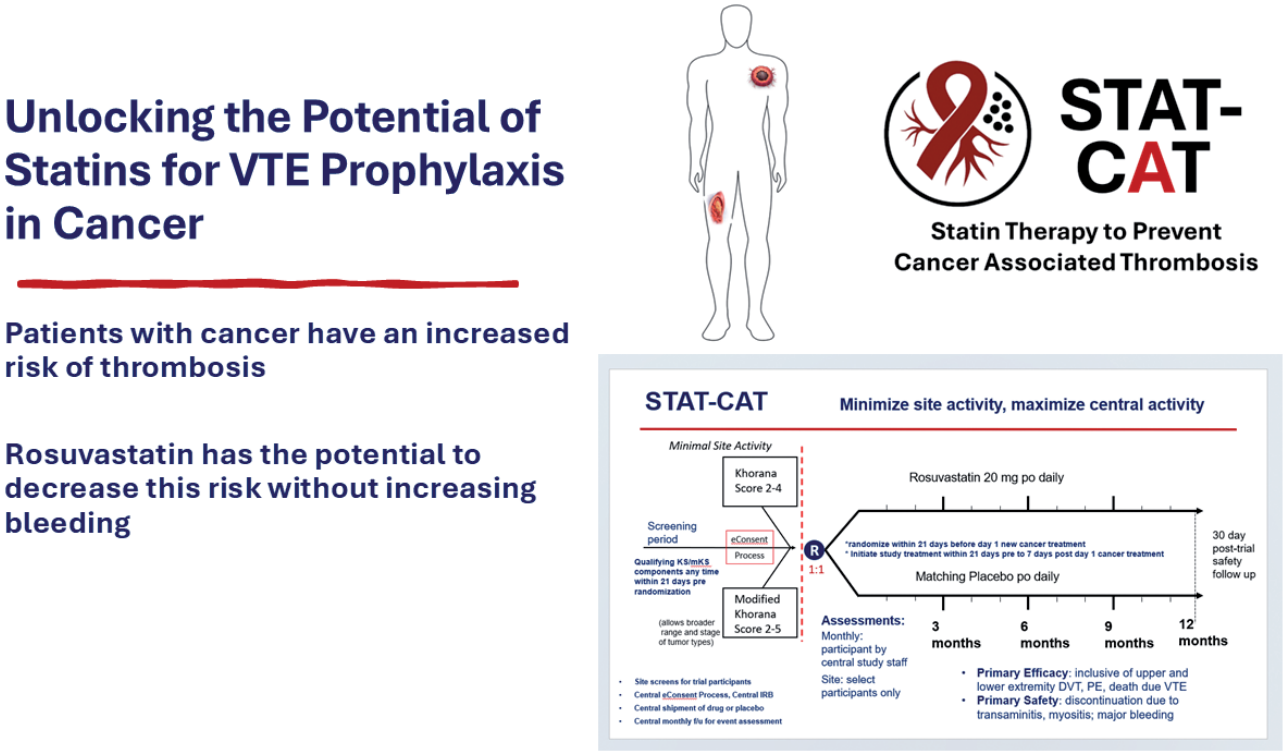
Jean M. Connors[1], Robert J. Glynn[2], Alok A. Khorana[3], Paul M. Ridker[4]

[1]Hematology Division, Dana Farber Cancer Institute, and Harvard Medical School, Boston, MA; [2]Harvard Medical School, Boston, MA; Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA; [3]Cleveland Clinic Cancer Center and Department of Hematology/Oncology, Case Comprehensive Cancer Center, Cleveland, OH; [4]Divisions of Preventive Medicine and Cardiovascular Diseases, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA

ABSTRACT

Patients with cancer have increased risk of venous thromboembolism (VTE), contributing to excess morbidity, mortality, treatment delays, and healthcare utilization. The incidence of cancer associated VTE has increased over the past two decades. Patients with malignancy now comprise approximately 20% of the global VTE burden. VTE risk is highest during the first 3–6 months after a new or recurrent cancer diagnosis. A new diagnosis of VTE can herald the presence of cancer. Although the risk declines over time it does not return to baseline for up to two years after completing cancer treatment in those with no evidence of disease. Randomized trials of prophylactic-dose anticoagulation for primary VTE prevention in ambulatory patients with cancer, including the direct oral anticoagulants, demonstrate a 35–60% reduction in VTE events, however, routine use of primary prophylaxis remains quite limited among patients with cancer due to excessive bleeding risks which are doubled with most anticoagulants. These competing risks are reflected in conditional guideline recommendations from major societies which suggest consideration of prophylaxis only in selected high-risk patients with concomitantly low bleeding risks. By contrast, in the general population, statin therapy has been shown to reduce VTE rates by 30 to 40% with no increase in hemorrhage and thus might be a highly effective intervention to reduce the risk of cancer associated thrombosis. The Statin Therapy to Prevent Cancer Associated VTE (STAT-CAT) trial, funded by the NHLBI, has been designed to directly test this hypothesis among 4,000 patients initiating cancer therapy. This review summarizes emerging evidence supporting statins as a potential approach to primary VTE prevention in patients with cancer and reviews clinical trials addressing statins for VTE risk reduction.

GRAPHICAL ABSTRACT



Key words: cancer; thrombosis prophylaxis; rosuvastatin.

Introduction

Patients with a wide range of cancers are at increased risk for venous thromboembolism compared with the general population, with associated increases in mortality and morbidity, including delays in cancer treatment and added costs of care.[1-3] The incidence of VTE in patients with cancer has increased over the past twenty years. [4,5] Twenty percent of the global VTE burden is due to patients with cancer.[2] The risks of VTE are highest in the first 3 to 6 months after a new diagnosis of cancer or of recurrent cancer with risk augmented by initiation of cancer treatments.[6-9] These risks slowly diminish over the first few years after diagnosis. [6,7]

Trials using prophylactic doses of anticoagulants in ambulatory patients with cancer, including LMWH and DOAC, have shown efficacy in reducing these life-threatening events, with approximately 35% to 60% reduction depending on the population.[1-5,10-13] Despite this demonstrated efficacy, anticoagulation prophylaxis is rarely used in routine cancer care as major bleeding events are almost doubled with their use. In a formal meta-analysis of the AVERT and CASSINI direct oral anticoagulant trials for primary VTE prophylaxis in patients with cancer, major bleeding was twice as high when compared to placebo and clinically relevant non-major bleeding (CRNMB) increased 30%.[12-14] For most oncology patients, major bleeding and CRNMB are often associated with more severe consequences than in the general population.[12,13,15,16]

The clinical uncertainties around anticoagulation use are reflected in weak guideline statements for the use of pharmacologic VTE prophylaxis from major societies including the American Society of Hematology (ASH), the American Society of Clinical Oncology (ASCO), the European Society of Medical Oncology (ESMO), the International Initiative on Thrombosis and Cancer (ITAC), and the National Comprehensive Cancer Network (NCCN).[17-22] All have recommendations about the use of primary prophylaxis in patients with cancer, however they "suggest" or advise to "consider" the use of prophylaxis in selected patients with intermediate to high risk for VTE with concomitant low risk of bleeding, as a conditional recommendation with low or moderate certainty of evidence. Most suggest using the Khorana VTE risk prediction score, recognized as the score with the most external validation and therefore frequently used, however many are silent on how to identify those at intermediate or high risk for VTE.[23,24] Some guidelines include caveats that primary prophylaxis be used in those with a "low risk of bleeding", however guidance for how to determine this risk is not provided. Bleeding risk prediction scores, such as HAS-BLED, VTE-BLEED, and HEMORR2-HAGES, have been validated in patients without cancer yet perform poorly in cancer populations with AUC's ranging from 0.54 to 0.59. A recently developed score specifically for patients with cancer demonstrated improved prediction (overall C-statistic for significant bleeding was 0.70 (95% confidence interval: 0.65-0.75), and 0.76 (0.68-0.84) and 0.67 (0.61-0.73) for major bleeding and for CRNMB) but requires prospective validation.[25]

As a result of lack of strong support for use of primary prophylaxis and concerns for bleeding, there is low use of primary prophylaxis in the oncology setting. In one contemporary survey, less than 5% of very high-risk oncology patients received anticoagulant prophylaxis, and among the minority that did, 30 to 40 percent discontinued therapy within 6 months largely due to bleeding concerns.[26] In another recent survey, no high-risk oncology patients received prophylaxis and 90 percent of oncology respondents had never prescribed primary prophylaxis.[11] A recent review highlights the barriers to implementation, which are a complex mix of factors.[27]

Improved uptake of primary prophylaxis in ambulatory oncology patients requires a simple method to reduce VTE events without increasing bleeding. This review highlights the accumulated data demonstrating the efficacy of statins to significantly reduce VTE without any increase in bleeding and provides the context for STAT-CAT, an NHLBI-funded randomized double-blind placebo-controlled trial of rosuvastatin in the prevention of cancer associated thrombosis.

Corresponding author: Jean M. Connors, MD, Hematology Division, 450 Brookline Avenue, Boston, MA 02215 USA.
E-mail: jean_connors@dfci.harvard.edu

Contributions: all authors made a substantive intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: JMC has received fees for scientific advisory boards, consulting, and data monitoring committees from Abbott, Alexion, Anthos, Bayer, Bristol Myers Squibb, Cerus Corporation, Janssen, Novartis, Pfizer, Perosphere Technologies, and Regeneron. AAK has received consulting honoraria from Sanofi, Pfizer, Anthos, Novartis, BMS, Regeneron, Sirius and Alnylam. RJG has received research support (to Brigham and Women's Hospital) from Amarin, Kowa, Novartis, and Pfizer. PMR has received institutional research grant support from Kowa, Novartis, Amarin, Pfizer, Esperion, Novo Nordisk, and the NHLBI; during the past 3 years has served as a consultant to Novartis, Agepha, Arrowhead, AstraZeneca, CSL Behring, Civi Biopharm, Glaxo Smith Kline, SOCAR, Novo Nordisk, Eli Lilly, Pfizer, New Amsterdam, Boehringer-Ingelheim, Cardio Therapeutics, Caristo, Heartflow, and Tourmaline Bio; has minority shareholder equity positions in Uppton, Bitteroot Bio, and Angiowave; and receives compensation for service on the Peter Munk Advisory Board (University of Toronto), the Leducq Foundation, Paris FR, and the Baim Institute (Boston, MA, USA).

Funding: STAT-CAT is funded through NHLBI grant UG3HL176627. AAK acknowledges research support from the Sondra and Stephen Hardis Chair in Oncology Research.

Received: 11 January 2026.
Accepted: 9 March 2026.

Publisher's note: all claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Bleeding, Thrombosis and Vascular Biology 2026; 5(s1):450
doi:10.4081/btvb.2026.450

Statins reduce VTE risk in the general population

In a pre-specified analysis of the landmark JUPITER primary prevention atherosclerosis trial rosuvastatin 20mg daily as compared to placebo not only lowered risks of arterial thrombosis such as myocardial infarction and stroke, but also lowered the risk of incident VTE by 43% (HR 0.57, 95%CI 0.37-0.86, p=0.007) with no bleeding risk; JUPITER thus demonstrated for the first time the considerable efficacy statin therapy has against venous as well as arterial thrombosis.[28,29] This observation was replicated in the subsequent HOPE-3 trial of rosuvastatin 10 mg daily compared to placebo, which found a 55% reduction in VTE (HR 0.45, 95% CI 0.24-0.84), again with no bleeding risk.[30] In both the JUPITER and HOPE-3 trials, benefits of rosuvastatin on VTE were equally large in subgroups of those with a prior history of cancer with no evidence of any excess bleeding in these two trials which together followed 30,507 patients for up to 5 years.[31] Thus, in the general population, statin therapy is proven to reduce VTE risk in the absence of bleeding, the exact combination of desirable effects needed for VTE prophylaxis among patients with cancer. Of note, there is a suggestion that the effect is more pronounced with higher-potency statins, particularly rosuvastatin, as one meta-analysis indicates, although this finding is based on very limited observational data, with no data in the cancer population.[32]

Epidemiologic data for reduced VTE risk with statins in patients with cancer

In addition to these two major placebo-controlled trials of rosuvastatin demonstrating decreased VTE events with use, observational data provide further evidence that statin use is associated with lower risks of VTE, including among those with a history of cancer. In one study among 1434 patients with newly diagnosed primary or recurrent cancer, those taking statin therapy had substantially lower rates of VTE at 12-months (2.94% *vs* 7.12%) and at 24 months (3.54% *vs* 8.13%) (p=0.04).[33] In another representative observational study of 740 consecutive patients with solid organ tumors, the rate of VTE among those taking a statin was 8% as compared to 21% among those not taking statin therapy, a 66% reduction in risk of VTE (OR 0.33, 95%CI 0.19-0.57) without bleeding risk.[34] Only one small trial has randomized patients with cancer to statin treatment. This trial prospectively allocated 86 patients with cancer to rivaroxaban or atorvastatin 20 mg. No difference in VTE rates was reported at 90 days between groups (p=0.95), yet a 5-fold increase in major bleeding was seen among those randomly allocated rivaroxaban (12 of 44 participants, 27.3%) as compared to atorvastatin (2 of 42 participants, 4.8%) (p=0.007).[35] While these observational data suggest that statins will result in VTE risk reduction in patients with cancer, the limitations, including selective prescribing, unmeasured confounding, and healthy user bias, indicate the need for a randomized controlled trial of statins to prevent cancer associated VTE.

Effect of statins on hemostatic parameters

From a mechanistic perspective, statin therapy is both lipid lowering and anti-inflammatory, a relevant observation as innate immune activation is well known to activate adverse coagulation.[36,37] The anti-inflammatory effects are independent of the lipid lowering effects. Data from the JUPITER trial demonstrate that rosuvastatin treatment resulted in a 37% reduction in high-sensitivity CRP levels in apparently healthy individuals with elevated baseline CRP, demonstrating clinically meaningful anti-inflammatory effects.[28] In animal models, rosuvastatin downregulates levels of multiple potent inflammatory mediators, including MYD88, CCL4, CCL20, CCR2, TNF-α, IFN-β, multiple interleukins (IL-1β, IL-2, IL-4, IL-8, IL-10), and MCP-1.[38,39]

Statins have also been shown to have multiple effects on hemostatic parameters that decrease the prothrombotic milieu. Downregulation of tissue factor expression, reduced thrombin generation, and modulation of several coagulation factor levels have all been reported.[40] Rosuvastatin in particular has been shown to decrease levels of coagulation factors VII, VIII, XI, and von Willebrand factor, and results in a decrease in thrombin generation *in vivo*.[41,42] Only the decrease in FVII and FXI levels has been associated with a decrease in apolipoproteins, suggesting that mechanisms other than shared pathways of synthesis or common regulatory pathways result in reduction of the other measured coagulation factors.[44] Decreased inflammatory cytokines will result in decreased levels of those coagulation factors that are acute phase reactants, such as fibrinogen, but decreased activation of inflammation likely inhibits the crosstalk of activation of inflammatory signals activating coagulation. Antiplatelet effects, with inhibition of activation, adhesion, and aggregation, have also been demonstrated.[44-47] Other antithrombotic effects have been found including favorable effects on vascular endothelial cells, and decreased levels of other coagulation factors.[41-43,48] These pleiotropic biologic mechanisms caused by statins are thought to play a role in reducing VTE events. Given the lack of associated bleeding with statin use, statins are an attractive candidate for primary VTE prophylaxis in patients with cancer.

Safety of statins use in patients with cancer

In the general population, statins are not associated with risks of bleeding and have only minimal toxicity when used long-term. Rates of statin associated myositis, transaminitis, and glucose intolerance are exceptionally low in the general population and markedly outweighed by the beneficial effects of these agents on lowering risks of myocardial infarction, stroke, and cardiovascular death.[49-51] Although public perception in the past has been that statins cause significant side effects, large meta-analysis findings should provide significant reassurance for patients about the safety and side effect profile of statins. A published individual patient data meta-analysis of 19 RCT comparing 5 statins (atorvastatin, fluvastatin, pravastatin, rosuvastatin, simvastatin) with placebo in almost 124,000 participants found no causal relationships between statin therapy and the majority of the side effects listed in package labels.[52] An earlier analysis of this same dataset found that most (>90%) of the muscle symptoms reported by those assigned to statin therapy were

not due to the statin, with only a small excess of mild muscle pain observed[53] in patients with cancer, a data base analysis at DFCI found that roughly 27% of individuals over age 50 initiating cancer therapy were taking a statin for cardiovascular risk reduction (*unpublished data*).

With rare exceptions (such as the concomitant use of certain antiviral/retroviral medications, or rare hormonal or targeted cancer therapies), oncologists initiating standard chemotherapy regimens or experimental protocols continue statin treatment as no contraindications exist for the great majority of cancer treatments. In one systematic review of observational studies inclusive of 95 cohorts with over 1.1 million cancer patients, baseline statin use in oncology settings was associated with a reduction in all-cause mortality (HR 0.70, 95% CI 0.66-0.74).[54] In another study of 11 short term intervention trials that included 2165 patients with cancer, adverse events were similar among those assigned to statins as compared to placebo, with no increased rates of myositis or transaminitis.[55] Patients in these trials were treated with a wide range of chemotherapy agents including 5-flurouricil, cisplatin, carboplatin, dexamethasone, epirubicin, etoposide, irinotecan, gemcitabine, gefitinib, sorafenib, thalidomide, and capecitabine. The most recent extensive review and meta-analysis of the literature indicates that use of statins in patients with cancer is associated with a very low number of severe transaminitis or clinically relevant myopathy events.[55]

The prospective randomized trial landscape for statins in VTE

Prevention of recurrent VTE in the general population

The JUPITER and HOPE-3 trials described above demonstrate the ability of statin therapy to reduce risks of first VTE in the general population, but did not address recurrent VTE or risks of post-thrombotic syndrome (PTS), areas of ongoing uncertainty.[28,30,31] For example, while a meta-analysis that included 2 retrospective cohorts and 3 RCT found that exposure to statins was associated with decreased risks of post thrombotic syndrome (PTS),a differential effect was observed with a decrease in PTS on analysis of the retrospective cohorts only but with no significant reduction in PTS in analyses limited to the randomized trials.[57] A pilot feasibility RCT of rosuvastatin for prevention of post thrombotic syndrome was conducted and completed, with a subsequent larger clinical trial now enrolling.[58] The SAVER (Statins for Venous Event Reduction in Patients With Venous Thromboembolism) pilot trial randomized 312 patients receiving standard anticoagulation for a newly diagnosed VTE to adjuvant rosuvastatin 20 mg once daily or no rosuvastatin for 180 days. The biologic rationale for this pilot trial is that rosuvastatin may have additional benefits to prevent PTS in patients with VTE by decreasing inflammatory mediators in the affected vessel. Although there was no difference in the primary outcome of PTS symptoms as measured by the mean Villalta score, the duration of exposure to rosuvastatin was short. Following the pilot SAVER trial, a larger RCT is now enrolling in Canada and Europe to determine the ability of rosuvastatin compared with placebo for up to 60 months to prevent recurrent VTE events in those with VTE diagnosed within 30 days of enrollment and treated with anticoagulation per standard of care. The primary aim of this trial is to test whether adding the anti-inflammatory effects of rosuvastatin to standard of care anticoagulation can decrease recurrent VTE events compared to placebo. Secondary aims will assess differences in the development of PTS and arterial thrombotic events (Clinical Trial NCT04319627),

Primary VTE prophylaxis in patients with cancer

The JUPITER and HOPE trials demonstrated that rosuvastatin is effective in preventing VTE in the general population including in a small subset or participants with a history of cancer although active cancer was an exclusion. Limited observational data report efficacy of statins to reduce VTE in patients with cancer. Based on these data and the need for an agent to prevent VTE in patients with cancer without increasing bleeding, the NHLBI has funded a randomized double-blind placebo controlled trial to test the efficacy of rosuvastatin 20 mg a day compared with placebo over 12 months to prevent VTE in ambulatory patients with cancer who are initiating new cancer therapy. STAT-CAT, the "Statin therapy to prevent cancer associated VTE" clinical trial, will launch in late spring in 2026 in the United States. Participants will be selected for increased thrombotic risk using the traditional well validated Khorana score, requiring a qualifying score of 2-4, or the newly developed EHR-CAT score (incorporating a wider range of known VTE risk factors and validated through replication) of 2-5 with a concomitant KS of 0-1.[59,60] Use of the EHR-CAT score, or modified Khorana score (mKS) as designated in STAT-CAT, should allow for a broader range of eligible patients. Randomization will be stratified by the qualifying risk score. Patients initiating prophylactic anticoagulation and those at extremely high risk for VTE, those with KS of $\geq$5 or mKS of $\geq$6, will not be eligible as their level of risk warrants primary prophylaxis with traditional anticoagulants. The primary aim is to determine whether rosuvastatin 20 mg once daily as compared to placebo reduces incident VTE events, encompassing non-fatal lower-extremity DVT, non-fatal upper-extremity DVT including catheter-associated events, non-fatal pulmonary embolism, and death attributable to venous thromboembolic disease. The secondary aim seeks to determine if rosuvastatin reduces the composite rate of venous and arterial thrombosis, with arterial thrombosis defined as fatal and nonfatal myocardial infarction, thromboembolic stroke, and peripheral limb events. The tertiary aim is to determine the safety of rosuvastatin 20 mg once daily as compared to placebo with respect to myositis, transaminitis, and bleeding (Clinical Trial NCT07303816).

We believe that the likelihood is high that generic rosuvastatin can significantly reduce rates of VTE in patients with cancer and increased VTE risk with no increase in bleeding. If successful, STAT-CAT will markedly improve thrombotic outcomes for large numbers of oncology patients with a safe and inexpensive intervention that avoids the hemorrhagic complications of conventional anticoagulation.

References

1. Khorana AA, Mackman N, Falanga A, et al. Cancer-associated venous thromboembolism. Nat Rev Dis Primers 2022;8:11.

2. Ay C, Pabinger I, Cohen AT. Cancer-associated venous thromboembolism: Burden, mechanisms, and management. Thromb Haemost 2017;117:219-30.
3. Grilz E, Posch F, Nopp S, et al. Relative risk of arterial and venous thromboembolism in persons with cancer vs. personswithout cancer-a nationwide analysis. Eur Heart J 2021; 42:2299-307.
4. Mulder FI, Horváth-Puhó E, van Es N, et al. Venous thromboembolism in cancer patients: a population-based cohort study. Blood 2021;137:1959-69.
5. Bertoletti L, Madridano O, Jiménez D, et al. Cancer-associated thrombosis: trends in clinical features ,treatment, and outcomes from 2001 to 2020. JACC CardioOncol 2023;5: 758-72.
6. Li A, La J, May SB, et al. Derivation and validation of a clinical risk assessment model forcancer-associated thrombosis in two unique US health care systems. J Clin Oncol 2023;41:2926-38.
7. Li A, De Las Pozas G, Andersen CR, et al. External validation of a novel electronic risk score for cancer-associated thrombosis in a comprehensive cancer center. Am J Hematol 2023;98:1052-17.
8. Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. JAMA 2005;293:715-22.
9. Lyman GH. Venous thromboembolism in the patient with cancer: focus on burden of disease and benefits of thromboprophylaxis. Cancer 2011;117:1334-49.
10. Agnelli G, Gussoni G, Bianchini C, et al. Nadroparin for the prevention of thromboembolic events in ambulatory patients with metastatic or locally advanced solid cancer receiving chemotherapy: a randomised, placebo-controlled, double blind study. Lancet Oncol 2009;10:943-9.
11. Agnelli G, George DJ, Kakkar AK, et al. Semuloparin for thromboprophylaxis in patients receiving chemotherapy for cancer. N Engl J Med 2012;366:601-9.
12. Carrier M, Abou-Nassar K, Mallick R, et al. Apixaban to prevent venous thromboembolism in patients with cancer. N Engl J Med 2019;380:711-9.
13. Khorana AA, Soff GA, Kakkar AK, et al. Rivaroxaban for thromboprophylaxis in high-risk ambulatory patients with cancer. N Engl J Med 2019;380:720-8.
14. Li, A, Kuderer, NM, Garcia, DA, et al. Direct oral anticoagulant for the prevention of thrombosis in ambulatory patients with cancer: A systematic review and meta-analysis. J Thromb Haemost 2019;17: 2141-51.
15. Prandoni P, Lensing AW, Piccioli A, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood 2002;100:3484-8.
16. Angelini DE, Radivoyevitch T, McCrae KR, Khorana AA. Bleeding incidence and risk factors among cancer patients treated with anticoagulation. Am J Hematol 2019;94:780-5.
17. Lyman GH, Carrier M, Ay C, et al. American Society of Hematology 2021 guidelines for management of venous thromboembolism: prevention and treatment in patients with cancer. Blood Adv 2021;5:927-74. Erratum in: Blood Adv 2021;5:1953.
18. Key NS, Khorana AA, Kuderer NM, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: ASCO Guideline Update. J Clin Oncol 2023;41: 3063-71.
19. Farge D, Frere C, Connors JM, et al. 2022 international clinical practice guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer, including patients with COVID-19. Lancet Oncol 2022;23:e334-47.
20. Falanga A, Ay C, Di Nisio M, et al. Venous thromboembolism in cancer patients: ESMO Clinical Practice Guideline. Ann Oncol 2023;34:452-67.
21. Elshoury A, Schaefer JK, Lim MY, et al. Update on guidelines for the prevention of cancer-associated thrombosis. J Natl Compr Canc Netw 2022;20:7108.
22. Ades S, Holmes CE. Implementing guidelines to prevent cancer associated thrombosis: how can we do better? Res Pract Thromb Haemost 2023;7:100038.
23. Khorana AA, Kuderer NM, Culakova E, et al. Development and validation of a predictive model for chemotherapy-associated thrombosis. Blood 2008;111:4902-7.
24. Mulder FI, Candeloro M, Kamphuisen PW, et al. The Khorana score for prediction of venous thromboembolism in cancer patients: a systematic review and meta-analysis. Haematologica 2019;104:1277-87.
25. Cohen AT, Wallenhorst C, Choudhuri S, et al. A novel risk prediction score for clinically significant bleeding in patients anticoagulated for venous thromboembolism with active cancer. Thromb Haemost 2024;124:324-36.
26. Holmes CE, Ades S, Gilchrist S, et al. Successful model for guideline implementation to prevent cancer-associated thrombosis: venous thromboembolism prevention in the ambulatory cancer clinic. JCO Oncol Pract 2020;16:e868-74.
27. Butera E, Wang TF, Pola R, Carrier M. Implementation failure: thromboprophylaxis in ambulatory patients with cancer. Hematology Am Soc Hematol Educ Program 2025; 2025:72-9.
28. Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med 2008;359:2195-207.
29. Glynn RJ, Danielson E, Fonseca FA, et al. A randomized trial of rosuvastatin in the prevention of venous thromboembolism. N Engl J Med 2009;360:1851-61.
30. Yusuf S, Bosch J, Dagenais G, et al. Cholesterol lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med 2016;374:2021-31.
31. Joseph P, Glynn R, Lonn E, et al. Rosuvastatin for the prevention of venous thromboembolism: a pooled analysis of the HOPE-3 and JUPITER randomized controlled trials. Cardiovasc Res 2022;118:897-903.
32. Zhu H, Zheng H, Xu T, et al. Effects of statins in primary and secondary prevention for venous thromboembolism events: A meta analysis. Vascul Pharmacol 2022;142: 106931.
33. Lötsch F, Königsbrügge O, Posch F, et al. Statins are associated with low risk of venous thromboembolism in patients with cancer: a prospective and observational cohort study. Thromb Res 2014;134:1008-13.
34. Khemasuwan D, Divietro ML, Tangdhanakanond K, et al. Statins decrease the occurrence of venous thromboembolism in patients with cancer. Am J Med 2010;123:60-5.
35. Setiawan B, Budianto W, Sukarnowati TW, et al. The effectiveness of atorvastatin for the prevention of deep vein

thrombosis in cancer patients undergoing chemotherapy: A randomised controlled trial: open label. Thromb J 2023; 21:54.
36. Ridker PM, Rifai N, Pfeffer MA, et al. Inflammation, pravastatin, and the risk of coronary events after myocardial infarction in patients with average cholesterol levels. Circulation 1998;98:839-44.
37. Delvaeye M, Conway EM. Coagulation and innate immune responses: can we view them separately? Blood 2009;114: 2367-74.
38. Mylonas KS, Peroulis M, Schizas D, Kapelouzou A. MYD88 and proinflammatory chemokines in aortic atheromatosis: exploring novel statin effects. Int J Mol Sci 2023;24:9248.
39. Kleemann R, Princen HM, Emeis JJ, et al. Rosuvastatin reduces atherosclerosis development beyond and independent of its plasma cholesterol-lowering effect in APOE*3-Leiden transgenic mice: evidence for antiinflammatory effects of rosuvastatin. Circulation 2003;108:1368-74.
40. Siniscalchi C, Basaglia M, Riva M, et al. Statins effects on blood clotting: a review. Cells 2023;12:2719.
41. Biedermann JS, Kruip MJHA, van der Meer FJ, et al. Rosuvastatin use improves measures of coagulation in patients with venous thrombosis. Eur Heart J 2018;39:1740-7.
42. Orsi FA, Biedermann JS, Kruip MJHA, et al. Rosuvastatin use reduces thrombin generation potential in patients with venous thromboembolism: a randomized controlled trial. J Thromb Haemost 2019;17:319-28.
43. Camilleri E, van Rein N, van Vlijmen BJM, et al. Influence of rosuvastatin on apolipoproteins and coagulation factor levels: Results from the STAtin Reduce Thrombophilia trial. Res Pract Thromb Haemost 2023;7:100063.
44. Chou TC, Lin YF, Wu WC, Chu KM. Enhanced nitric oxide and cyclic GMP formation plays a role in the antiplatelet activity of simvastatin. Br J Pharmacol 2008;153:1281-7.
45. Pignatelli P, Carnevale R, Pastori D, et al. Immediate antioxidant and antiplatelet effect of atorvastatin via inhibition of Nox2. Circulation 2012;126:92-103.
46. Puccetti L, Santilli F, Pasqui AL, et al. Effects of atorvastatin and rosuvastatin on thromboxane-dependent platelet activation and oxidative stress in hypercholesterolemia. Atherosclerosis 2011;214:122-8.
47. Serebruany VL, Miller M, Pokov AN, et al. Effect of statins on platelet PAR-1 thrombin receptor in patients with the metabolic syndrome (from the PAR-1 inhibition by statins [PARIS] study). Am J Cardiol 2006;97:1332-6.
48. Vadivel K, Bajaj SP. Structural biology of factor VIIa/tissue factor initiated coagulation. Front Biosci (Landmark Ed) 2012;17:2476-94.
49. Newman CB, Preiss D, Tobert JA, et al. Statin safety and associated adverse events: a scientific statement from the American Heart Association. Arterioscler Thromb Vasc Biol 2019;39:e38-e81.
50. Villani R, Navarese EP, Cavallone F, et al. Risk of statin-induced hypertransaminasemia: a systematic review and meta-analysis of randomized controlled trials. Mayo Clin Proc Innov Qual Outcomes 2019;3:131-40.
51. Shepherd J, Vidt DG, Miller E, et al. Safety of rosuvastatin: update on 16,876 rosuvastatin-treated patients in a multinational clinical trial program. Cardiology 2007;107:433-43
52. Cholesterol Treatment Trialists' (CTT) Collaboration. Assessment of adverse effects attributed to statin therapy in product labels: a meta-analysis of double-blind randomised controlled trials. Lancet 2026;407:689-703.
53. Cholesterol Treatment Trialists' Collaboration. Effect of statin therapy on muscle symptoms: an individual participant data meta-analysis of large-scale, randomised, double-blind trials. Lancet 2022;400:832-45. Erratum in: Lancet 2022;400:1194.
54. Mei Z, Liang M, Li L, et al. Effects of statins on cancer mortality and progression: a systematic review and meta-analysis of 95 cohorts including 1,111,407 individuals. Int J Cancer 2017;140:1068–1081. doi: 10.1002/ijc.30526. PMID: 27859151.
55. Thomas JP, Loke YK, Alexandre L. Efficacy and safety profile of statins in patients with cancer: a systematic review of randomised controlled trials. Eur J Clin Pharmacol 2020;76: 1639-51.
56. Bikdeli B, Tajrishi FZ, Connors JM. Risk of myopathy and hepatotoxicity in patients with cancer receiving statin therapy: Systematic review of randomized controlled trials. Vasc Med 2024;29:556-8.
57. Caiano LM, Drury T, Zahrai A, et al. Role of statins in the prevention of post-thrombotic syndrome after a deep vein thrombosis event: a systematic review and meta-analysis. J Thromb Haemost 2023;21:944-52.
58. Delluc A, Ghanima W, Kovacs MJ, et al. Prevention of post-thrombotic syndrome with rosuvastatin: A multicenter randomized controlled pilot trial (SAVER). Thromb Res 2022; 213:119-24.
59. Li A, La J, May SB, et al. Derivation and validation of a clinical risk assessment model for cancer-associated thrombosis in two unique US health care systems. J Clin Oncol 2023;41:2926-38.
60. Li A, De Las Pozas G, Andersen CR, et al. External validation of a novel electronic risk score for cancer-associated thrombosis in a comprehensive cancer center Am J Hematol 2023;98:1052-7.