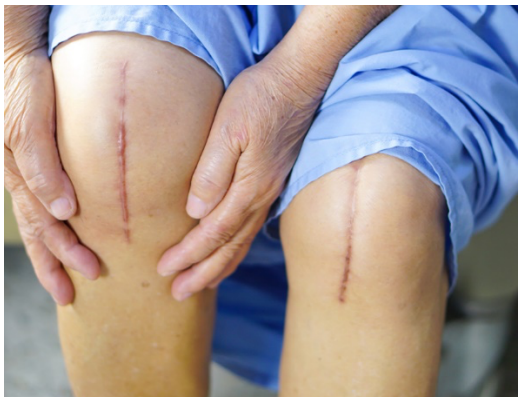
Abelacimab for Prevention of Venous Thromboembolism



Total knee arthroplasty is an extremely common procedure for the elderly population who have been active and put pressure on their knees and this procedure is associated with a high risk of postoperative venous thromboembolism. In order to prevent this complication, enoxaparin has been considered the standard postoperative prophylactic treatment for years because it is an inhibitor of factor Xa and thrombin. However, enoxaparin also carries the risk of bleeding. As a result, there has been a search for a safer and more effective anticoagulant.

One medication that is currently undergoing clinical trials has shown a lot of promise and has a unique mechanism of action is abelacimab. The main driver of postoperative venous thromboembolism through the extrinsic pathway is generally considered to be tissue factor exposed at the surgical site. However, the importance of the intrinsic pathway in this pathogenesis remains uncertain. New evidence suggests that targeting factor XI, which is a key component of the intrinsic pathway, would hinder thrombosis while not disrupting hemostasis. This has been shown in patients with congenital factor XI deficiency who are at lower risk for venous thromboembolism than those individuals with normal factor XI levels. These patients also rarely have spontaneous bleeding making this factor an attractive target.

Abelacimab (MAA868) is a fully human monoclonal antibody that binds to the catalytic domain of factor XI and locks it in the zymogen (inactive precursor) conformation, thereby preventing its activation by factor thrombin. The intravenous infusion of abelacimab almost immediately reduces the functional factor XI level in a dose-dependent manner. In a phase 2, prospective, parallel-group trial, 412 patients were randomly assigned to receive one of three regimens of abelacimab (30 mg, 75 mg, or 150 mg) administered postoperatively in a single intravenous dose or to receive 40 mg of enoxaparin administered subcutaneously once daily. Researchers found that the 30-mg abelacimab regimen was noninferior to enoxaparin in terms of VTE occurrence, and the 75-mg and 150-mg abelacimab regimens were superior to enoxaparin ($P<0.001$). Additionally, there was no significant differences in bleeding events through each of the groups.

While this was only a phase 2 trial, the results were extremely promising and display that there are other potential targets for postoperative VTE prophylaxis. Being a monoclonal antibody, the initial price of this medication would not be cheap, however, by learning more about the mechanisms in which there are safe interventions that can be made, there are more tools in the proverbial toolkit to use.

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