

Indraparinux for the treatment of thromboembolic disease

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The usual curative treatment for Thromboembolic disease (deep vein thrombosis, DVT and pulmonary thrombembolism, PTE) consists in administering heparins (either fractioned or unfractioned) followed by oral anticoagulation for 3 to 12 months. Profilaxis for recurrence consists of 6 to 12 months of oral anticoagulation. However, oral anticoagulation is associated with low compliance and the need for frequent laboratory monitoring. Thus, investigators are searching for new drugs that should become reliable alternatives to standard treatment for thromboembolic disease (TED). Two new studies evaluated the efficacy of indaparinux (a competitive inhibitor of factor Xa which is administered subcutaneously once weekly at a dose of 2.5mg and does not need laboratory monitoring) compared with standard treatment in TED, both as a curative treatment (the first study) and for secondary prophylaxis (the second study). The first study randomized 2904 patients with DVT and 2215 with PTE to receive in a 1:1 fashion either indaparinux or standard

treatment. The primary objective was the recurrence at 3 months of TED. For patients with DVT, indaparinux was non-inferior to standard treatment for the recurrence of TED (2.9% vs. 3.0%). However, in patients with PTE, indaparinux was inferior to standard treatment in the recurrence of TED (3.4% vs. 1.6%, 95% CI = 1.21 to 3.78). In the second study, 1215 patients were randomized to receive indaparinux or standard prophylactic treatment. The main objective was recurrence of TED after 6 months of secondary prophylaxis. Patients treated with indaparinux had a lower rate of recurrence of TED (1% vs. 3.7%, $p = 0.002$) but this benefit was counterbalanced by a significant increase in major hemorrhages (1.9 vs. 0%, $p < 0.001$). In conclusion, indaparinux is a valid alternative to standard treatment in DVT. For PTE, indaparinux is inferior to standard treatment. For secondary prophylaxis of TED, indaparinux is more efficient than standard treatment but at a cost or an increased risk of major hemorrhages. □

Comment on the paper:

The van Gogh Investigators – Indraparinux versus Standard Therapy for Venous Thromboembolic Disease. *N Engl J Med* 2007; 357:1094-1104

The van Gogh Investigators – Extended Prophylaxis of Venous Thromboembolism with Indraparinux. *N Engl J Med* 2007; 357:1105-1112