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211 Edoxaban For Long-Term Treatment Of Venous Thromboembolism In Cancer Patients

Program: Oral and Poster Abstracts
Type: Oral
Session: 332. Antithrombotic Therapy: Clinical Trials

Monday, December 9, 2013: 7:00 AM
278-282 (Ernest N. Morial Convention Center)

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Low-molecular-weight heparin (LMWH) is recommended for long-term anticoagulant therapy in cancer patients with venous thromboembolism (VTE).These patients have been mostly excluded from clinical trials comparing new oral anticoagulants with vitamin-K antagonists. Hokusai-VTE was a global randomized, double-blind, non-inferiority trial (margin 1.5) that compared edoxaban, an oral factor Xa inhibitor, with warfarin for long-term therapy in 8,292 patients with acute symptomatic proximal deep-vein thrombosis and/or pulmonary embolism; all patients received initial LMWH treatment for at least 5 days. Patients with active cancer in whom long-term treatment with LMWH was anticipated were excluded, but patients with a history of cancer or with active cancer were eligible if long-term LMWH treatment was not planned due to availability, physician judgment or patient preference; the analysis of outcomes in these patients was pre-specified before the trial. The edoxaban dose was 60 mg once daily (30 mg in patients with body weight less than 60 kg or creatinine clearance 30 to 50 ml/min). Warfarin was adjusted to maintain the INR between 2.0 and 3.0. The primary efficacy outcome was recurrent symptomatic VTE. The efficacy analysis included all patients who received at least one dose of study drug, and included all outcomes through 12 months follow-up or study closure, regardless of the duration of treatment. The principal safety outcome was major or clinically relevant non-major bleeding, occurring on treatment or within 3 days of stopping treatment. All outcomes were adjudicated by an independent committee blinded to treatment allocation. A total of 771 cancer patients (9.3%) were enrolled (208 with active cancer and 563 with a history of cancer).The baseline clinical characteristics of patients in the edoxaban and warfarin groups were similar. The median duration of treatment in the edoxaban group was 267 days and in the warfarin group was 266 days (interquartile range 180 to 360 days in both groups). Among patients with active cancer, recurrent VTE occurred in 4 of 109 patients (3.7%) who received edoxaban and in 7 of 99 patients (7.1%) who received warfarin (hazard ratio 0.55, 95% CI 0.16 to 1.85). Clinically relevant bleeding (major or non-major) occurred in 20 patients (18.3%) given edoxaban (5 patients with major, 4.6%) and 25 patients (25.3%) given warfarin (3 patients with major, 3.0%) (hazard ratio for clinically relevant bleeding 0.72, 95% CI 0.40 to 1.30). Among all 771 cancer patients at entry, recurrent VTE occurred in 14 of 378 patients (3.7%) given edoxaban and in 28 of 393 patients (7.1%) who received warfarin (hazard ratio 0.53, 95% CI 0.28 to 1.00). Clinically relevant bleeding (major or non-major) occurred in 47 patients (12.4%) given edoxaban (10 patients with major, 2.6%) and 74 patients (18.8%) given warfarin (13 patients with major, 3.3%) (hazard ratio for clinically relevant bleeding 0.64, 95% CI 0.45 to 0.92). Among patients without cancer, either at entry or occurring during follow-up, recurrent VTE occurred in 103 of 3,658 patients (2.8%) given edoxaban and in 99 of 3,629 (2.7%) who received warfarin (hazard ratio 1.03, 95% CI 0.78 to 1.36, p=0.004 for non-inferiority). Clinically relevant bleeding (major or non-major) occurred in 280 of 3658 patients (7.7%) who received edoxaban (39 patients with major, 1.1%) and in 330 of 3629 patients (9.1%) given warfarin (48 patients with major, 1.3%) (hazard ratio for clinically relevant bleeding 0.83, 95% CI 0.71 to 0.97, p=0.022). The results suggest edoxaban is as effective, and possibly more effective, than warfarin in cancer patients with VTE. In such patients, bleeding is appreciable during anticoagulant therapy, and may potentially be reduced by edoxaban therapy. Additional studies of edoxaban for initial and long-term therapy of VTE in cancer patients are indicated, with LMWH as the comparator, and including lower doses of edoxaban to determine if bleeding can be further reduced without loss of efficacy.

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