174 patients, 132 (75.9%) were enrolled in the extension study. Approximately half of the 174 patients were enrolled in Europe, 12.6% in the United States, 5.7% in Japan, and 32.2% from the rest of the world. The ethnic origins of the patients were white for 126 (72.4%), Asian for 31 (17.8%), black or African American for 14 (8.0%), and others for 3 (1.7%). Fourteen patients (8.0%) were adolescents.

The pharmacokinetic profile was further determined in 27 patients who received either rVIII-SingleChain 50 IU/kg or octocog alfa. Samples were collected at the following time points: before dosing; at 30 minutes, 1 hour, 4 hours, 8 hours, 10 hours, 24 hours, 32 hours, and 48 hours; and 72 hours after receiving the drug. Comparing rVIII-SingleChain with octocog alfa, the former had lower clearance, a greater area under the curve, and a longer half-life.

A total of 848 bleeds were treated during the study period. The treatment was rated as excellent or good in 93.8% of bleeds. A single injection controlled 81% of bleeds, and 94% of bleeds were controlled with 1 or 2 injections.

Eighty-six percent of patients were on prophylactic dosing with a 2- or 3-times-per-week regimen (median doses 30 and 36 IU/kg, respectively). The median annualized bleeding rate in the prophylaxis arm was 1.14, significantly less ($P<.0001$) than 19.64 in the on-demand arm. The annualized bleeding rates for the 2-times-weekly or 3-times-weekly groups were similar. Patients who received rVIII-SingleChain for prophylaxis before a total of 16 surgeries had a 100% success rate. A median dose of 89.4 IU/kg (range, 40.5 to 108.6) was used on the day of surgery.

Over 99% of injections were administered without reactions, and no inhibitors or anti-CHO antibodies were observed. The most frequent adverse events were nasopharyngitis, arthralgia, and headache. There were 10 serious adverse events, including 1 hypersensitivity reaction that was adequately managed with steroids and antihistamines. Overall, rVIII-SingleChain was considered well tolerated and effective in this study population.

PADIS-PE Identifies Risk Factors for Residual Perfusion Defects After Pulmonary Embolism

Written by Muriel Cunningham

Published reports suggest that 30% to 50% of patients experiencing a pulmonary embolism (PE) have perfusion defects 6 to 12 months later [Cosmi B et al. *Intern Emerg Med.* 2011; Sanchez O et al. *J Thromb Haemost.* 2010; Nijkeuter M et al. *Chest.* 2006]. An increased risk of dyspnea and greater pulmonary artery pressure can accompany these residual perfusion defects [Sanchez O et al. *J Thromb Haemost.* 2010]. The PADIS-PE study [NCT00740883] was a randomized, double-blind, multicenter study conducted to determine the rate of residual perfusion defects and associated risk factors in patients who had experienced a single episode of unprovoked PE. The study results were presented by Olivier Sanchez, MD, PhD, Georges Pompidou European Hospital, Paris, France.

The study was conducted from 2007 to 2012 at multiple centers in France. Patients having their first unprovoked PE received 6 months of anticoagulation therapy, then underwent a lung ventilation/perfusion (V/Q) scan, echocardiography, and a leg ultrasound. Patients with a normal or near-normal V/Q lung scan at baseline were classified as having no perfusion defect, and those with a pulmonary vascular obstruction ≥10% were classified as having a perfusion defect. Patients were randomized to 18 months of warfarin treatment (n=184) or placebo (n=187), evaluated at 18 months, and followed for another 24 months. Risk factors associated with the presence of residual perfusion defects were identified using univariate and multivariate analyses of the patients' baseline data.

PE was initially diagnosed via positive spiral computed tomography in 285 patients (77%) and via high-probability V/Q lung scan in 86 patients (23%). Proximal deep vein thrombosis and right ventricular dysfunction were diagnosed in 112 (30%) and 123 (33%) patients, respectively. A total of 234 patients received low-molecular-weight heparin (LMWH), 370 patients received vitamin K antagonists, 6 had fibrinolysis, and 1 patient was treated with rivaroxaban.

In this study, 124 patients (33%) had residual perfusion defects, 61 patients (16%) had residual deep vein thrombosis, and 95 (27%) had thrombophilia. The mean±SD D-dimer level was 352±459 µg/L. Univariate analysis indicated that patients with a perfusion defect were significantly older (66 vs 53 years; OR, 1.05; 95% CI, 1.03 to 1.06; $P<.0001$), and that significantly higher proportions of patients with a perfusion defect had chronic respiratory disease (39 vs 34%; OR, 2.77; 95% CI, 1.64 to 4.67; $P<.001$) and chronic cardiac disease (9 vs 4%; OR, 4.60; 95% CI, 1.39 to 15.2; $P=.013$). Independent risk factors for residual perfusion defects identified in the multivariate analysis included age >65 years (OR, 3.28; 95% CI, 1.91 to 5.63; $P<.0001$), chronic respiratory disease (OR, 2.10; 95% CI, 1.12 to 3.93; $P=.021$), and right ventricular dysfunction at diagnosis (OR 1.96; 95% CI, 1.14 to 3.37; $P=.014$). Initial treatment with LMWH vs unfractionated heparin or pentasaccharide was associated with a decreased risk of residual perfusion defects (OR, 0.50; 95% CI, 0.29 to 0.86; $P=.013$).