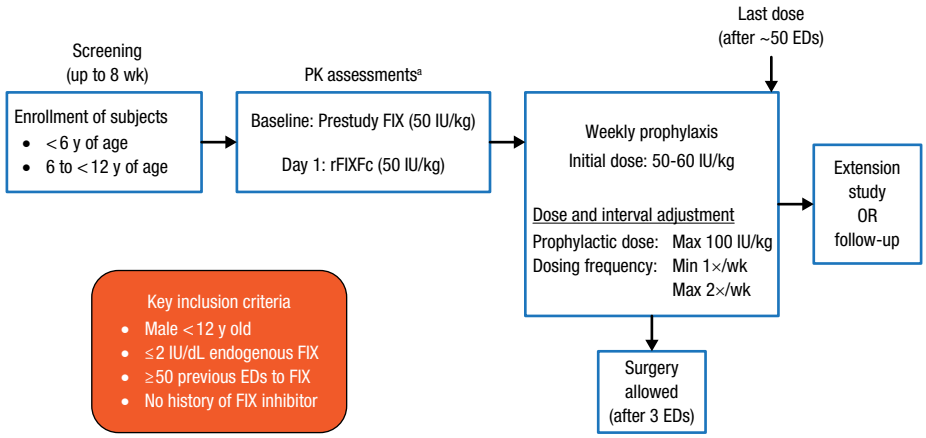
Figure 1. Kids B-LONG Study Design



ED, exposure day; FIX, factor IX; PK, pharmacokinetic; rFIXFc, recombinant factor IX Fc fusion protein.

[a]A 96-hour washout period with no FIX treatment was required prior to administration of prestudy FIX, 28±7 d prior to rFIXFc dosing at baseline, and prior to administration of rFIXFc on day 1; in younger children and subjects who required a second washout attempt, a 72-hour washout period was permitted.

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No inhibitors or anti-rFIXFc antibodies developed in study subjects. The majority of subjects (86.7%) had ≥1 adverse event, the most common being nasopharyngitis (23.3%) and fall (20.0%). One mild nonserious adverse event of decreased appetite was considered to be related to study treatment; all other adverse events were considered unrelated to rFIXFc. Eleven serious adverse events occurred in 4 subjects during the study; none was considered related to the study drug. There were no discontinuations from the study because of adverse events.

No changes were made to the dosing interval in 97% of subjects. The median prophylactic dose was 59.4 IU/kg/wk (interquartile range [IQR], 53.0 to 64.8) in subjects aged <6 years and 57.8 IU/kg/wk (IQR, 51.7 to 65.0) in subjects aged 6 to <12 years.

Thirty-three percent of subjects had no bleeding episodes, and there were no joint bleeds in 63% of subjects. The overall median annualized bleeding rate was 2.0 (IQR, 0.0 to 3.1). In acute bleeding episodes, 75.0% were controlled with 1 infusion, and 91.7% were controlled with 1 or 2 infusions (median dose per infusion, 63.5 IU/kg [IQR, 48.9 to 99.4]). After the first infusions, 88.7% had an excellent or good response. Although no major surgeries were performed with rFIXFc, 3 minor surgeries were performed in 2 subjects. Excellent hemostatic response was achieved in all surgical cases. Physical activity remained the same or increased in 77% of study subjects. In her concluding remarks, Dr Fischer said she believes these data support the potential for extended-interval dosing with low bleeding rates in this population.

SOME: No Benefit With Extensive Screening for Cancer in Unprovoked VTE

Written by Emma Hitt Nichols, PhD

An extensive screening strategy for occult cancers did not provide clinical benefit over a more limited screening in patients with first unprovoked venous thromboembolism (VTE). Marc Carrier, MD, MSc, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, presented data from the SOME trial [Carrier M et al. *N Engl J Med*. 2015].

Currently, there is little consensus regarding cancer screening strategies in patients with unprovoked VTE [Carrier M et al. *Ann Intern Med*. 2008]. Some strategies are extensive, including abdominal and pelvic computed tomography (CT) imaging, whereas others are more limited and include a physical examination, routine blood testing, and a chest radiograph. The purpose of the SOME trial was to determine the efficacy of occult cancer screening with a comprehensive abdominal/pelvic CT scan in patients with unprovoked VTE.

The multicenter, open-label SOME trial randomly assigned 862 patients who presented with first unprovoked VTE to undergo limited screening or limited screening plus comprehensive CT for occult cancer, with a follow-up period of 12 months. Limited occult cancer screening was defined as basic blood work, a chest radiograph, and breast/cervical/prostate cancer screening. The comprehensive CT scan included a virtual colonoscopy and

gastroscopy, a biphasic enhanced CT scan of the liver, a parenchymal pancreatogram, and a uniphasic enhanced CT scan of the distended bladder.

The primary end point was confirmed cancer detected within 1 year that was missed by screening. The secondary end points included total number of occult cancers diagnosed, total number of early cancer diagnoses, 1-year cancer-related mortality, 1-year overall mortality, time to cancer diagnosis, and recurrent VTE. The intention-to-treat analysis included 854 patients. At baseline, the mean age was 53.5 years, 67.5% were men, and the mean weight was 90.1 kg. In addition, 5.9% of patients had a prior cancer, 5.5% had a prior provoked VTE, 15.5% were current smokers, and 33.3% were former smokers. Deep vein thrombosis occurred in 67.5% of patients, pulmonary embolism in 32.5%, and both in 12.3%.

There was no significant difference in new cancer diagnoses among patients in either arm of the study, with 3.2% of patients in the limited-screening arm (95% CI, 1.9% to 5.4%) and 4.5% of patients in the limited screening with comprehensive CT arm (95% CI, 2.9% to 6.9%; $P=.28$). In addition, the time to cancer diagnosis was similar among both arms, with 4.2 months in the limited screening group and 4.0 months in the limited plus CT screening group ($P=0.88$). Furthermore, there was no significant difference in the detection rate of early cancers, overall mortality, cancer-related mortality, time to cancer diagnosis, and rate of recurrent VTE.

Dr Carrier stated that it is possible that an even more extensive screening strategy may have missed fewer occult cancers. He highlighted that there was an overall low rate of occult cancers in patients with unprovoked VTE, and the results of this study indicate that a comprehensive CT scan of the abdomen and pelvis does not provide a clinical benefit.

Risk Factors for Recurrent Venous Thromboembolism Revealed in PADIS-PE Trial

Written by Muriel Cunningham

Patients who have experienced an unprovoked pulmonary embolism (PE) may experience recurrence after stopping anticoagulant therapy, but the optimal duration of anticoagulation treatment is unclear. The primary objective of the double-blind multicenter PADIS-PE study [Couturaud F et al. *JAMA*. 2015] was to evaluate the efficacy and safety of an additional 18 months of oral anticoagulant treatment following an initial 6 months of therapy. The ability to classify patients according to risk of recurrence is also of benefit given the risks associated with anticoagulation therapy. Another objective of the study was to identify such risk factors. Findings from the study were presented by Francis Couturaud, MD, PhD, European Brittany University, Brest, France.

In the PADIS-PE study, 371 patients with their first unprovoked PE received 6 months of vitamin K antagonist treatment and were randomized to an additional 18 months of warfarin treatment (n=184) or placebo (n=187). At randomization, blood samples were taken, and patients underwent a ventilation/perfusion (V/Q) lung scan, echocardiography, and compression ultrasound of the legs. Patients were evaluated at the end of the 18-month treatment period and followed for an additional 2 years.

During 18 months of treatment, the primary outcome (composite of recurrent symptomatic venous thromboembolism [VTE] and major bleeding at 18 months) occurred in 3.3% of warfarin-treated patients vs 13.5% of placebo-treated patients (HR, 0.22; 95% CI, 0.09 to 0.55; $P=.001$). Recurrent symptomatic VTE occurred in 1.7% of warfarin-treated patients and 13.5% of those receiving placebo (HR, 0.11; 95% CI, 0.03 to 0.37; $P<.0001$). Major bleeds were not significantly different between the 2 groups (2.2% warfarin, 0.5% placebo; HR, 4.07; 95% CI, 0.45 to 36.38; $P=.18$). Over the entire study period, there were no statistically significant differences between the 2 treatment groups in composite events (20.8% warfarin vs 24.0% placebo; HR, 0.74; 95% CI, 0.47 to 1.17; $P=.19$), recurrent symptomatic VTE (17.9% warfarin vs 22.1% placebo; HR, 0.67; 95% CI, 0.41 to 1.08; $P=.10$), or major bleeds (3.5 warfarin vs 3.0 placebo; HR, 1.12; 95% CI, 0.38 to 4.10; $P=.71$).

One of the secondary objectives was to determine risk factors for recurrent symptomatic VTE during the 42-month follow-up period. Symptomatic recurrent VTEs were defined as follows: nonfatal recurrent PE (clinical suspicion of PE with positive V/Q lung scan, spiral computed tomography angiography, pulmonary angiography, or new noncompressibility of a proximal vein on ultrasound), fatal recurrent VTE (autopsy or unexplained sudden death), and symptomatic recurrent deep vein thrombosis (DVT; clinical suspicion of DVT and noncompressibility of a new segment of a proximal vein on ultrasound). Univariate analysis and a multivariate model were used to identify risk factors for recurrent VTE.

Age, residual perfusion defect at study inclusion, and residual DVT at study inclusion were identified as independent risk factors associated with recurrent VTE based on multivariate analysis (Table 1). On the basis of these findings, Dr Couturaud noted that it may be useful to perform a V/Q lung scan and lower limb ultrasound after 6 months of anticoagulation to help determine a patient's risk of recurrent VTE if treatment is discontinued.