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**Background:** Pediatric patients with ALL/LL are at increased risk of venous thromboembolism (VTE).

**Aims:** To assess efficacy and safety of prophylactic apixaban vs. standard-of-care (SOC) for VTE prevention during induction chemotherapy.

**Methods:** Following ethics committee approval and informed consent patients ≥1 to <18 years with (1) newly diagnosed ALL/LL, (2) central venous line, and (3) three or four drug induction chemotherapy with asparaginase, were randomized in an open label, randomized controlled trial conducted in collaboration with the Children's Oncology Group. Apixaban thromboprophylaxis was stopped at the end of induction (Figure). After induction, patients underwent VTE screening. The primary efficacy endpoint was a composite of symptomatic/asymptomatic VTE and VTE- related death. The primary safety endpoint was major bleeding.

**Results:** 512 patients (56.5% male, mean age 7.2 years) were randomized. VTE occurred in 12.1% ($n$ = 31) of apixaban patients and 17.6% ($n$ = 45) of SOC patients (Table). No differences were shown in the primary efficacy endpoint between study arms [RR: 0.69 (0.45–1.05), 1-sided $p$-value 0.04]. In obese patients ($n$ = 82), 1 VTE occurred in the apixaban arm vs. 10 in the SOC arm [RR: 0.11 (0.02–0.74), treatment-subgroup interaction $p$-value 0.036]. There were 2 major bleeding events in each arm (including 1 event before treatment with apixaban). A numerically higher incidence of clinically relevant non-major bleeding occurred in the apixaban arm (11 vs. 3 events) due to increased epistaxis.

**Conclusion(s):** PREVAPIX-ALL is the first trial to assess primary prophylaxis using a direct oral anticoagulant in pediatric ALL/LL. Apixaban was not shown to be efficacious in the primary analysis but decreased VTE risk in obese patients. Major and clinically relevant non-major bleeding was infrequent. No new safety signals were observed. Apixaban was found to be a safe pharmacologic prophylaxis agent in pediatric patients with ALL/LL receiving induction chemotherapy containing asparaginase.

## OC 15.5 | Validating direct oral anticoagulants (DOAC) for use in children by the Throm-PED DOAC registry of the International Pediatric Thrombosis Network

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**Background:** Dabigatran and rivaroxaban have recently been approved for treatment of venous thromboembolism in children. Based on the risk benefit profiles published so far, we expect DOACs to be widely used in children. The strict inclusion criteria for participation in the clinical trials limit their generalizability, particularly for those with serious medical conditions that account for a significant proportion of pediatric VTE patients in clinical practice.

**Aims:** To study efficacy and safety of DOACs in a large heterogeneous pediatric population. To expand our knowledge on treatment strategies and outcomes in children across different risk profiles and comorbidities including cancer and renal disease.

**Methods:** An international, multicentre, prospective observational cohort study of patients <18 years with thromboembolic disease treated with DOACs. Data collection includes thrombosis location, risk factors, medical conditions and concurrent medications. Outcomes (thrombus progression/recurrence and bleeding) are assessed every 3 months for 12 months. Additional variables include adherence, drug levels, renal function and dose adjustments.

**Results:** A total of 102 patients from 9 centers have been included in the registry to date, of which 81% of patients were >12 years old (Figure 1) and most 79% received rivaroxaban. Pulmonary embolism and thrombosis of the lower extremities were more common (30%) each, followed by cerebral thrombosis (16%). Risk factors included cancer (13%) and renal disease (5%). Of the 39 patients with follow-up at 3 months, bleeding was reported in 3 (8%) patients and thrombosis progression in 2 (6%) (Table 1).

**Conclusion(s):** Real world data collection is essential to assess the benefit risk profile of DOACs in children, to identify specific patient groups at risk of worse outcome and to understand drug interactions and the need for dose adjustments. Further data on younger age groups and children with comorbidities are required.