OBJECTIVES
Approximately 15-35% of patients with hemophilia A develop inhibitory antibodies to factor VIII. There are currently two bypassing agents to treat inhibitor patients in the case of bleeding episodes (BE) and preemptively before and during major surgeries. Both APCC and rFVIIa demonstrated similar efficacy and safety results [1]. Our aim was to compare the costs of bypass strategy based on APCC or rFVIIa, including acquisition costs, and the consequent costs of bleeding episodes and surgery costs in Hungary, Slovakia, Slovenia and Serbia.

RESULTS
In the scenario of bleeding episodes, the use of APCC instead of rFVIIa brings the potential savings of €4,596-8,704; €4,135-9,347; €6,738-10,807; €4,369-8,527 respectively in Hungary, Slovakia, Slovenia and Serbia (depending on the dosing scheme, see Figure 1). Lower savings are when dosing of 2x90μg/kg of rFVIIa is used, and higher when 1x270μg/kg of rFVIIa is used. While using APCC during major surgeries, the savings are equal to €157,159 (if compared to rFVIIa therapy) and €15,616 (if compared to the combination therapy of APCC and rFVIIa) in Hungary; €180,653 and €16,558 in Slovakia; €196,065 and €19,362 in Slovenia, and €145,979 and €15,422 in Serbia (see Figures 2 and 3).

The results of OWSA confirmed the results from the base-case setting. In case of BE with lower dosage of rFVIIa (see Table 1), the savings were well above zero indicating that even with price and dose changes of rFVIIa/APCC there is a certainty of cost-savings. When dosing rFVIIa with 1x270μg/kg per BE, the savings are substantially higher in both lower and higher case compared to situation of lower rFVIIa dosing scheme (Table 2). Finally, OWSA conducted in situation of surgery (Table 3) also confirmed the results from base-case setting. In this surgery situation, the lower case savings were around €100,000 and higher case savings were above €200,000.

For the purpose of cost comparison, we developed a model using cost-minimization approach including all relevant costs from the perspective of health care payer. The same approach was adopted in published literature [2-4]. We assessed the cost differences for two basic scenarios – patients with bleeding episodes and patients undergoing major surgeries. The doses used in model were: i) APCC 62.5 μg/kg per BE, ii) APCC 85 μg/kg per surgery, iii) rFVIIa 90 μg/kg per BE and surgery. The doses are based on the SmPCs (miscit of given dose intervals) and published literature (in the case of APCC used in surgery which is administered in higher doses in clinical practice compared to change in SmPC). The cost of APCC per unit (€) was in given countries equal to: 1) €0.77 in Hungary, 2) €0.90 in Slovakia, 3) €0.94 in Slovenia and 4) €0.84 in Serbia. The cost of rFVIIa per μg was then equal to: 1) €0.61, 2) €0.65, 3) €0.75 and 4) €0.62, respectively in these four countries.

Additionally, we performed one-way sensitivity (OWSA) analysis in which we changed the price and the dosage of APCC and rFVIIa.

OBSERVATIONS
APCC and rFVIIa are equal to PROTHROMBIN COMPLEX CONCENTRATE (APCC) COMPARISON TO RECOMBINANT FACTOR VIIa (RFVIIA) FOR HEMOPHILIA PATIENTS WITH INHIBITORS

CONCLUSIONS
The results confirmed that the use of APCC in hemophilia patients with inhibitors is the cost-saving therapy compared to intervention with rFVIIa, which confirm to previous analyses mentioned in published literature [2-4]. The potential savings by using APCC instead of rFVIIa are substantial from the health-care systems perspective in Hungary, Slovakia, Slovenia and Serbia. Moreover, these findings could also be interpreted that the APCC use thus indirectly enables more patients to be treated for the same health care costs consumption.