

ACCESS TO ULTRA-LONG HALF-LIFE FACTOR VIII AS THE DEFINITIVE MOTIVATION FOR ITI IN THE ERA OF NON-REPLACEMENT THERAPIES

B. Borsellino¹, T. Martini¹, I. Ricca², C. Linari³, B. Pollio¹

¹Paediatric Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy;

²Transfusion Medicine, Ivrea Hospital, Ivrea, Italy; ³Department of Laboratory Medicine, Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Turin, Italy

Background. Inhibitor development remains the most challenging complication of severe haemophilia A, especially in children with null F8 variants and early exposure to factor VIII. Although emicizumab has transformed bleed prevention, eradication of inhibitors is still clinically relevant because it restores access to factor VIII replacement. This case highlights the long-term value of repeated immune tolerance induction (ITI) in a child with severe haemophilia A and recurrent inhibitor relapse, ultimately enabling transition to efanesoctocog alfa prophylaxis with sustained trough FVIII levels.

Case Report. A boy born in 2012 with severe haemophilia A (FVIII:C <1%) due to a p.Trp979Stop mutation in F8 was diagnosed in 2013 after tongue bleeding. After fewer than ten exposures to octocog alfa, he developed a high-titre inhibitor (32 BU/mL). A first ITI course with octocog alfa (200 U/kg/day), started in 2015, achieved negativisation in 2016, but repeated relapses occurred during tapering. In 2018, rescue ITI with simoctocog alfa was required; despite a reactive inhibitor peak during a febrile illness, complete eradication was obtained by September 2018. In May 2021, prophylaxis was continued with emicizumab to improve quality of life, with excellent bleed control and preserved physical activity. In 2024, however, a post-traumatic fracture of the an-

terior superior iliac spine required several days of simoctocog alfa, followed by recurrence of a low-titre inhibitor. A third ITI course with simoctocog alfa was therefore started in September 2024. Emicizumab was suspended in January 2025 once the inhibitor became undetectable, and FVIII replacement was continued through June 2025 without further bleeds, confirming complete inhibitor eradication. Musculoskeletal assessment showed only mild ankle synovitis without significant functional impairment. In April 2026, after sustained negative inhibitor testing, the patient switched to weekly efanesoctocog alfa prophylaxis. Seven days after infusion, FVIII activity remained 15%, a particularly meaningful result in light of his previous inhibitor history.

Conclusions. This case shows that inhibitor eradication remains a key long-term objective even in the era of emicizumab. In a child with severe haemophilia A and multiple inhibitor relapses, three successive ITI courses ultimately restored the possibility of FVIII prophylaxis and enabled access to efanesoctocog alfa, an ultra-long half-life product capable of maintaining clinically meaningful trough levels on a weekly schedule. Beyond bleed prevention, this strategy offers a major practical and motivational advantage for patients and families. ITI, when feasible, may therefore still be justified to unlock the full therapeutic potential of modern FVIII replacement.