

CO-NCIZUMAB IN A YOUNG CHILD WITH SEVERE HEMOPHILIA B WITH INHIBITOR: EFFECTIVE BLEED CONTROL AND SAFE HOME MANAGEMENT

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Background. Inhibitors remain one of the major therapeutic hurdles in severe hemophilia B (HB). They develop in ~1-6% of patients—most often in those with severe genotypes—typically after 10-20 factor IX (FIX) exposure days and frequently within the first 75 infusions. By neutralizing FIX activity, they make replacement therapy ineffective and are associated with higher annualized bleeding rates (ABR), serious intracranial/visceral hemorrhage, progressive arthropathy, substantial healthcare costs, and increased mortality. Unlike hemophilia A, HB inhibitors can also be accompanied by IgE-mediated infusion reactions, including anaphylaxis, and by immune-complex-mediated nephrotic syndrome.

Case Report. A male child (born October 2022) with severe HB carrying a large F9 deletion (c.724-5_731del) was diagnosed at birth after a subgaleal hematoma. His mother is a carrier, and two cousins have HB with inhibitors. In the first 18 months of life, managed with on demand therapy, the child suffered a large cheek hematoma; prophylaxis with albutrepenonacog alfa (Idelvion®) 75 IU/Kg every 14 days was started in May 2024. In 9 months, 3 hemarthrosis happened. After the 24th infusion (February 2025), he developed a low-titer inhibitor (1 BU/mL) together with a diffuse urticarial eruption treated with IV corticosteroids and anti-

histamines. Given the risk of anaphylaxis and nephrotic syndrome, FIX was discontinued. During the following 5 months the child, treated with on demand bypassing agent (recombinant activated factor VII, rFVIIa), had 4 severe hemarthrosis (ankle, knee). Compassionate-use concizumab (anti-TFPI monoclonal antibody) was started on August 2025 with a loading dose of 1 mg/kg/day SC followed by a maintenance dose of 0.2 mg/kg/day. Breakthrough events were minimal: a labial laceration treated with tranexamic acid alone, and a right ankle mild traumatic hemarthrosis treated with rFVIIa. Based on therapeutic drug monitoring, the dose was increased in October 2025 to 0.25 mg/kg. At follow-up in March 2026, joint ultrasound showed only grade 1 tibiotarsal synovitis. Parents-reported patient quality-of-life improved markedly, and they quickly learned how to administer concizumab and felt confident performing the injections at home soon after treatment initiation.

Conclusions. By blocking TFPI, concizumab provides factor-independent hemostatic protection and isn't affected by FIX inhibitors. This case is consistent with phase 3 trial Explorer7 results about concizumab clinical value in pediatric HB with inhibitors, showing effective bleed prevention, reduced morbidity, and the practical benefit of safe, caregiver-led home administration.