

Emofilia

FROM PROPHYLAXIS TO ENDOGENOUS CONTROL: A SIX-MONTH REAL-WORLD EXPERIENCE WITH VALOCTOCOGENE ROXAPARVOVEC GENE THERAPY

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Background. Severe hemophilia A is an X-linked bleeding disorder characterized by factor VIII (FVIII) activity <1 IU/dL, leading to recurrent bleeding and long-term morbidity. Gene therapy with adeno-associated virus (AAV) vectors, such as valoctocogene roxaparvovec, enables sustained endogenous FVIII expression and reduces treatment burden. In the phase 3 GENEr8-1 trial, this approach significantly reduced bleeding and FVIII use, with alanine aminotransferase (ALT) elevations as the most frequent adverse event . We report a six-month follow-up of a 32-year-old man with severe hemophilia A due to intron 22 inversion.

Methods. The patient had no history of FVIII inhibitors and was on extended half-life FVIII prophylaxis. Baseline liver status was normal (Fibroscan 6.2 kPa). Gene therapy was administered as a single intravenous infusion according to the phase 3 protocol (N Engl J Med 2022;386:1013-25). FVIII prophylaxis was continued for four weeks and discontinued at week 5. Clinical outcomes and liver enzymes were prospectively monitored. ALT elevations were managed with corticosteroids.

Results. Treatment was well tolerated, with no infusion reactions or inhibitor development. FVIII prophylaxis was discontinued at week 5, with no bleeding events thereafter. At week 5, ALT increased (~230 IU/L) and was treated with prednisone 60 mg/day, tapered with normalization by week 16. A second, milder ALT rise at week 24 responded rapidly to prednisone 25 mg/day. This pattern is consistent with trial data, where ALT elevations were common and manageable . The patient reported a major improvement in quality of life, describing for the first time a “hemophilia-free mind.”.

Discussion and Conclusions. This case confirms the efficacy and manageable safety of valoctocogene roxaparvovec in clinical practice. The absence of inhibitors, sustained discontinuation of prophylaxis, and lack of bleeding align with trial results. ALT elevations remain the main safety issue but are controllable with timely corticosteroid therapy. Notably, gene therapy provided substantial psychological benefit, reducing disease burden perception. At six months, this treatment showed a favorable benefit–risk profile and highlights the transformative potential of gene therapy in hemophilia A.

