Benefits of valoctocogene roxaparvovec persist in hemophilia A

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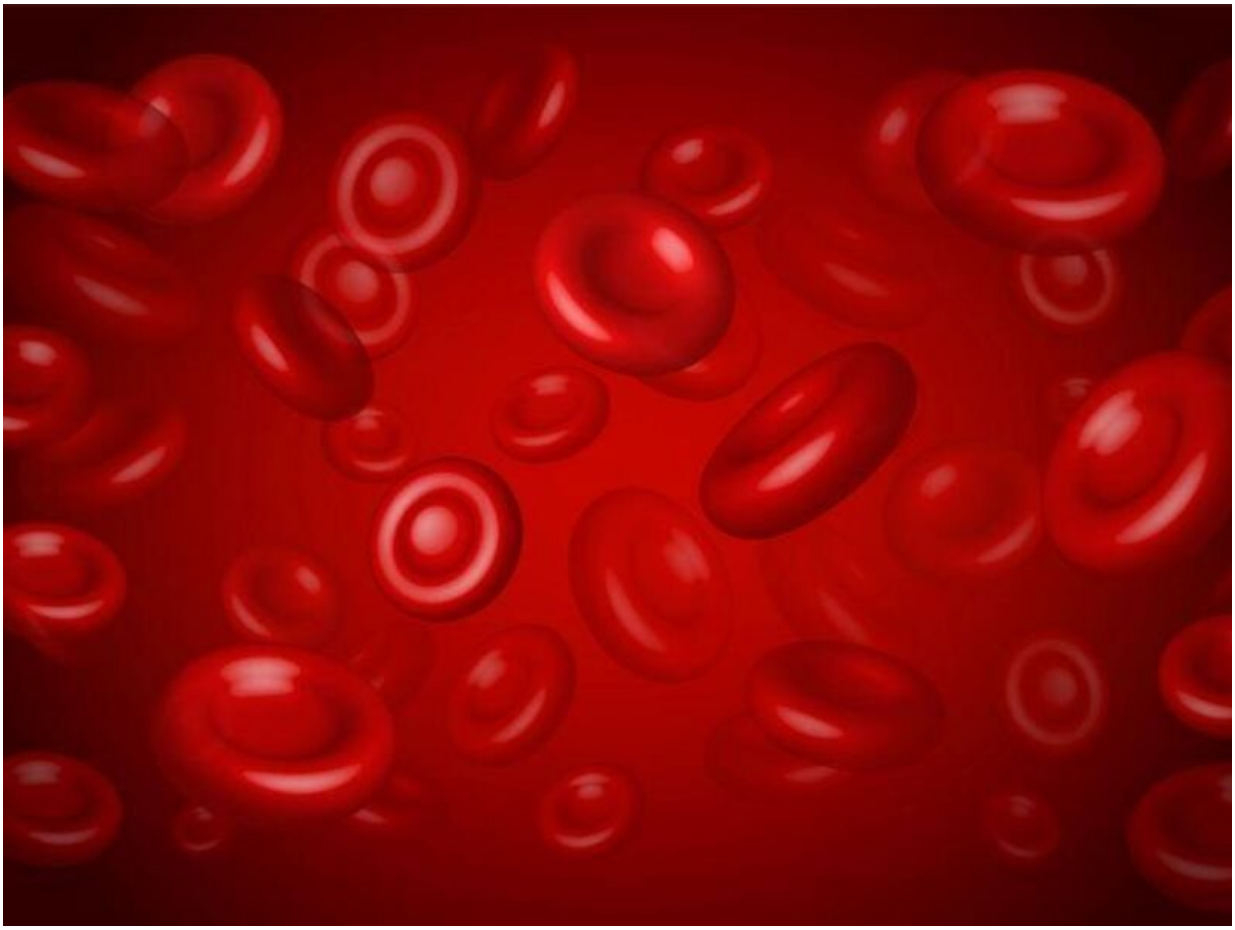

For patients with hemophilia A, factor VIII activity and bleeding

reduction persist at two years after gene transfer with valoctocogene roxaparvovec, which delivers a B-domain-deleted factor VIII coding sequence with an adeno-associated virus vector, according to a study published in the Feb. 23 issue of the *New England Journal of Medicine*.

Johnny Mahlangu, M.B., Ch.B., from the University of the Witwatersrand in South Africa, and colleagues conducted an open-label, single-group, multicenter, phase 3 trial involving 134 men with severe hemophilia A who were receiving factor VIII prophylaxis. Participants received a single infusion of $6x10^{13}$ vector genomes (vg) ofvaloctocogene roxaparvovec per kilogram body weight. The change from baseline in the annualized rate of treated bleeding events at week 104 after infusion receipt was examined as the primary end point. A total of 132 men remained in the study at week 104, including 112 with data that were prospectively collected at baseline.

The researchers found that among the participants, the mean annualized treated bleeding rate decreased by 84.5 percent from baseline. The trajectory of the transgene-derived factor VIII activity showed first-order elimination kinetics from week 76 onward; typical half-life of the transgene-derived factor VIII production system was 123 weeks as estimated by the model. The estimated joint bleeding risk was 1.0 episode per year at a transgene-derived factor VIII level of 5 IU/dL.

"Over a two-year period, valoctocogene roxaparvovec infused as a single dose of $6x10^{13}$ vg per kilogram provided control of bleeding that was superior to factor VIII prophylaxis in adult men with severe hemophilia A," the authors write.

Several authors disclosed financial ties to pharmaceutical companies, including BioMarin, which manufactures valoctocogene roxaparvovec and funded the study.

More information: Johnny Mahlangu et al, Two-Year Outcomes of Valoctocogene Roxaparvovec Therapy for Hemophilia A, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2211075

Lindsey A. George, Hemophilia A Gene Therapy—Some Answers, More Questions, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMe2212347