



BioMarin announced an additional serious adverse event in its gene therapy clinical trial for haemophilia A

September 13, 2022 – BioMarin reported today an update on the phase 3 clinical trial, which contained information on an additional serious adverse event (SAE) in a participant from the clinical trial with Roctavian™ (valoctocogene roxaparvovec).

A serious adverse event (SAE) is the term used to describe the occurrence of a serious health issue in a study, regardless of whether the treatment under investigation caused that health issue.

Roctavian™ (valoctocogene roxaparvovec) is a gene therapy for the treatment of severe haemophilia A in adult patients. It was granted Conditional Marketing Approval by the European Commission on August 24th. It is under review pending potential license by the US Food and Drug Administration (FDA).

In August 2022, BioMarin reported the discovery of B-Cell Acute Lymphoblastic Leukaemia (B-ALL) in one of the participants from its phase 3 trial infused with the gene therapy three years ago. BioMarin have reported that initial blood tests identify low levels of vector and other factors consistent with findings typically seen in patients who are diagnosed with B-ALL, leading the trials Data Monitoring Committee (DMC) to report the SAE to be unlikely related to the gene therapy. The patient is currently undergoing standard chemotherapy.

BioMarin will conduct whole genome sequencing analysis through an external company and have committed to reporting results publicly. BioMarin reported this case to regulators (EMA, FDA, etc). As yet, no change to the conduct of the study, or the conditional marketing licence have been requested.

Earlier this year, salivary gland cancer was reported in one of the participants from BioMarin's phase 1/2 study infused with the gene therapy over five years ago. The cancer was reported through the same external company by BioMarin as unrelated to the gene therapy by genomic analysis findings reported in April 2022. These reported that *"the results showed a comparable pattern of integration between healthy and tumour containing tissues, with no evidence emerging that vector integration contributed to the salivary gland mass."* See past statements on this below¹².

This is the fourth report of cancer (the other two being a liver cancer and a tonsil cancer) in participants of any haemophilia gene therapy trial and so far all are being reported as unrelated to the gene therapy at this time. See previous statements for further details²³.

The potential risk of cancer, in general, has been an element of focus for all gene therapies. The EHC, WFH, and NHF on behalf of its patient community remain vigilant and insistent on reviewing and examining any and all SAEs in these - like in all - therapies. This will help ensure the safety of these potentially life-changing treatments in the future.

Whilst staying vigilant, we must also remain aware of the general background risk of cancer, including in people with bleeding disorders. In addition to the general population risk for some form of cancer,



there is also an increased risk of liver cancer in those haemophilia patients who have had a history of HIV, hepatitis C and/or hepatitis B.

We shall continue to request investigators, clinicians, companies and regulators to make every effort to detangle a SAE from a general background risk in the most expedient manner possible so that patients can make decisions about future treatments with all available evidence.

Surveillance for safety issues for a new technology like gene therapy is critical for our community. Toward that end, the WFH [Gene Therapy Registry](#) is being developed to capture most or all of the patients who are treated with gene therapy as these products are licensed.

The three organisations will continue to monitor and report on all safety-related developments in all therapeutic areas relevant to our patient community.

¹ <https://www.ehc.eu/biomarin-follows-up-on-previously-reported-serious-adverse-event-in-its-phase-i-ii-gene-therapy-clinical-trial-for-haemophilia-a/>

² <https://www.ehc.eu/biomarin-reports-a-serious-adverse-event-for-its-phase-i-ii-gene-therapy-trial-for-haemophilia-a/>

³ <https://www.ehc.eu/8702/>