

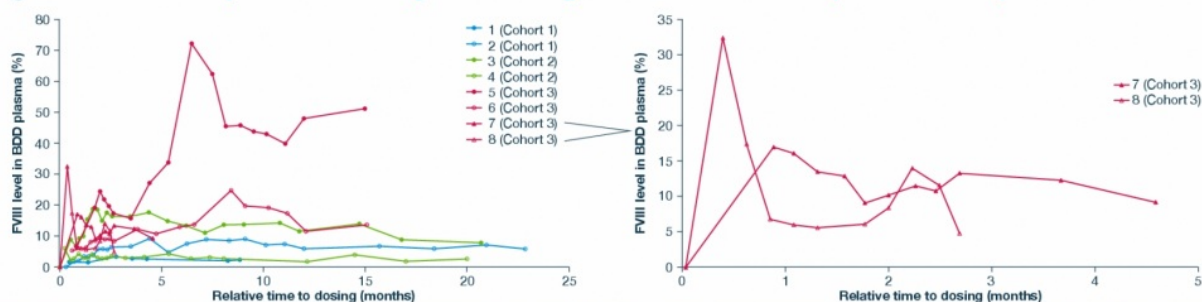
## ISTH 2021 - Bayer's haemophilia A gene therapy raises questions



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Bayer/Ultragenyx's haemophilia A gene therapy BAY 2599023 is supposed to be more durable than other contenders, but based on data presented on Saturday the jury is still out. True, the lower doses tested in the [phase 1/2 trial](#) did lead to consistent factor VIII levels, but these are unlikely to represent therapeutic doses. And the highest tested so far,  $2 \times 10^{13}$ vg/kg, has spurred liver enzyme elevations. Bayer tried to combat this by using prophylactic steroids, and it was data from two patients treated with this regimen, presented for the first time at the ISTH meeting, that could cause alarm bells. One of these patients experienced severe liver enzyme elevations; it appears that the subject was given famotidine to treat nausea related to steroid treatment, and then had a rise in liver enzymes. The enzymes returned to normal after stopping famotidine, the investigators said. FVIII levels from the two new patients were also not convincing, with one subject's levels declining rapidly. Bayer has already has the go-ahead to start the highest-dose cohort in the trial, testing  $4 \times 10^{13}$ vg/kg. Perhaps this will answer the question of whether BAY 2599023, already late to the party, could be a real contender.

Figure 2: FVIII LEVELS (CHROMOGENIC\* [BDD PLASMA]) BY PATIENT OVER TIME† IN COHORTS 1, 2 AND 3



\*Data obtained from one-stage assay not reported but the values obtained were consistently higher than those obtained using chromogenic assay, as observed in other gene therapy studies. †FVIII level measurements with sufficient wash out are displayed. ALT, alanine aminotransferase; FVIII, factor VIII; SAE, serious adverse events.

Source: Dr Steven Pipe and ISTH.

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