Supplemental Methods

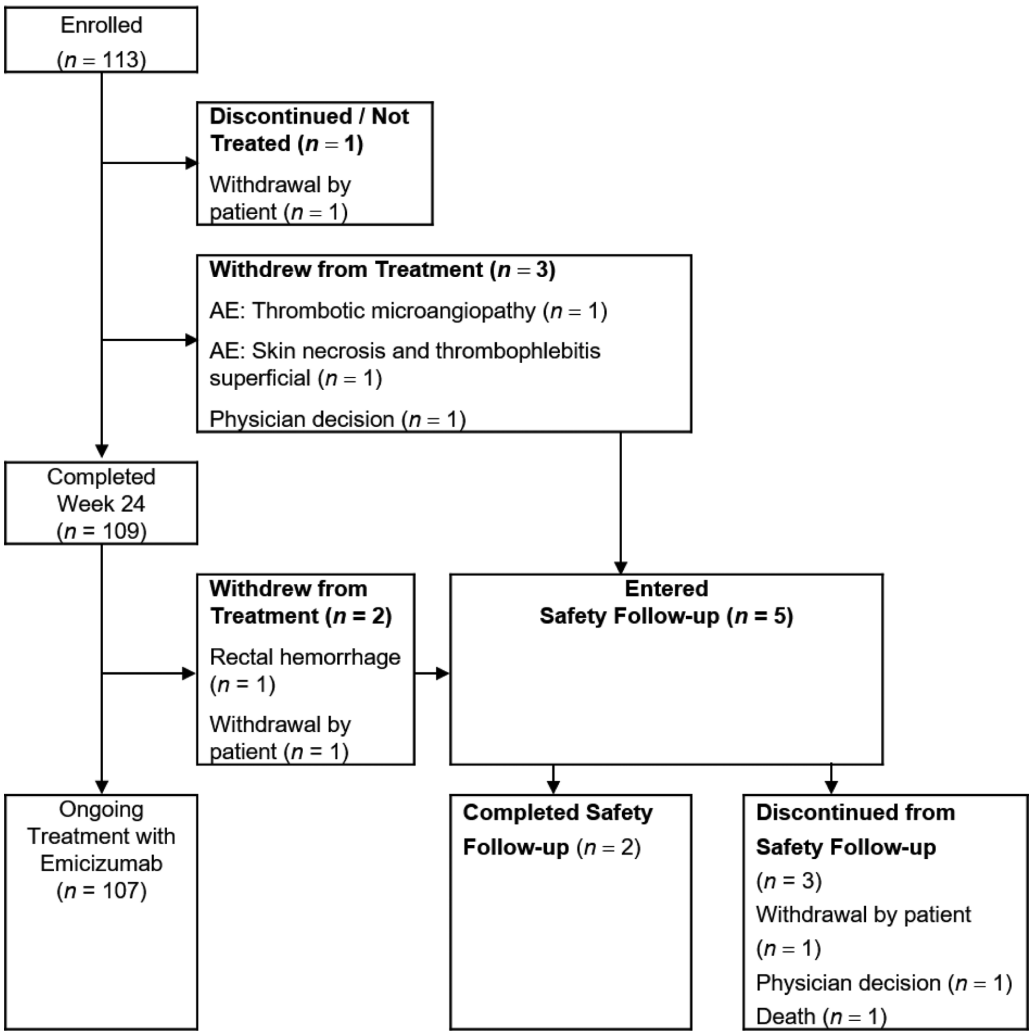
Manufacturers' Kit Insert Information

- aPTT: STA-PTT A; Diagnostica Stago, Cat. #00595
- PT: Neoplastine CI PLUS, Diagnostica Stago, Cat. #00595
- D-dimer: STA D-dimer kit, Diagnostica Stago, package insert REF 00505, dated August 2012
- PF1.2: Enzygnost F 1 + 2 ELISA, Siemens
- Fibrinogen: STA Fibrinogen kit, Diagnostica Stago, package insert REF 00674, dated July 2012
- VWF:Ag: STA von Willebrand Factor kit, Diagnostica Stago, package insert REF 00518, dated July 2011

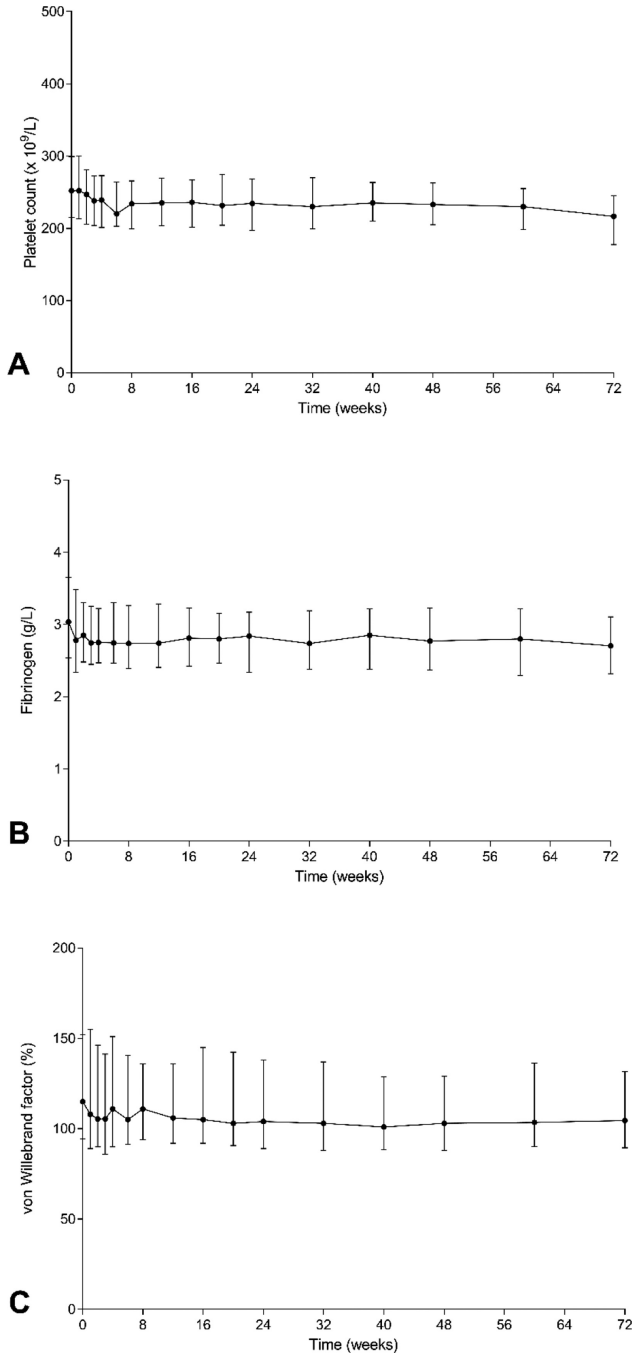
Supplementary Table S1 Pharmacokinetic/pharmacodynamic parameter estimates for aPTT

Parameters	Estimate	RSE (%)
E_0 (s)	83.8	0.55
IC_{50} (μg/mL)	1.13	11.0
I_{max} (s)	61.8	0.84

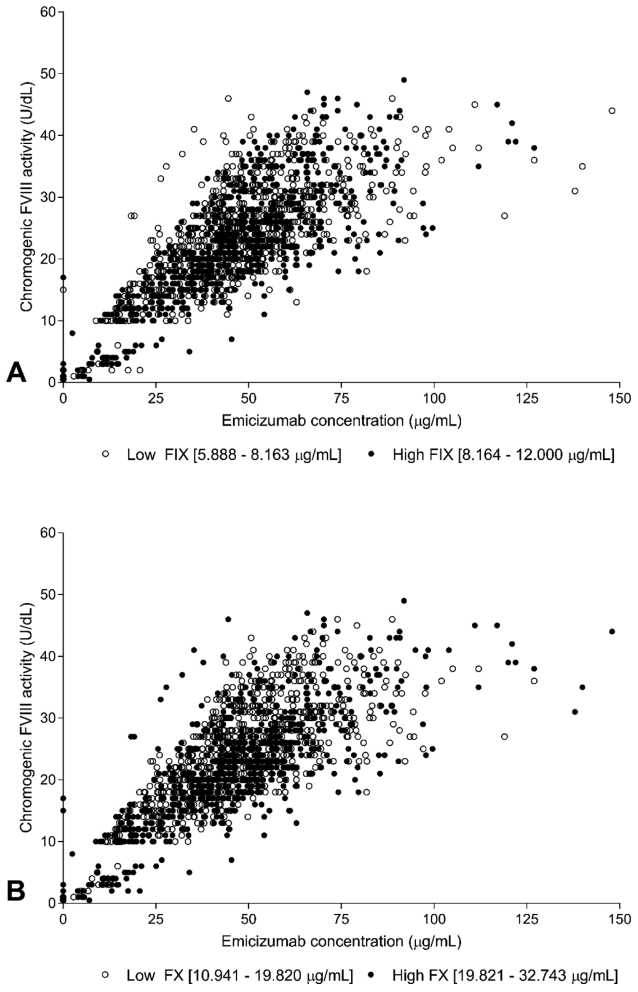
Abbreviations: aPTT, activated partial thromboplastin time; E_0, aPTT at baseline; IC_{50}, concentration causing half of the maximum effect; I_{max}, maximum inhibition; RSE, relative standard error.



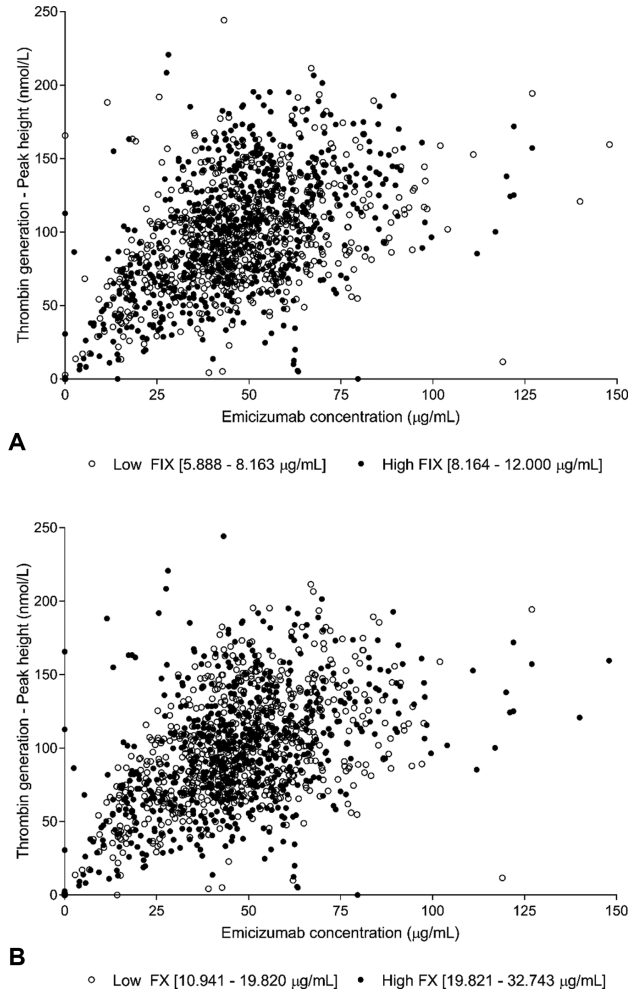
Supplementary Fig. S1 CONSORT diagram for participants in HAVEN 1. All patients treated with emicizumab were regrouped in one unique arm for the purpose of pharmacokinetic (PK)/pharmacodynamic (PD) analyses. AE, adverse event.



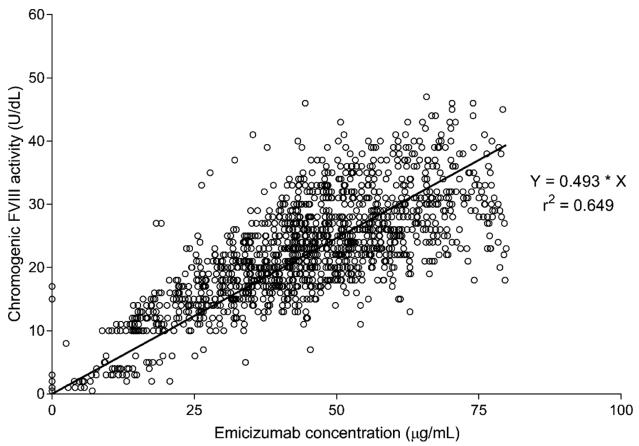
Supplementary Fig. S2 Safety biomarkers following once weekly dosing with emicizumab. Platelet count (**A**); fibrinogen (**B**); von Willebrand factor antigen (**C**). Median and interquartile ranges shown.



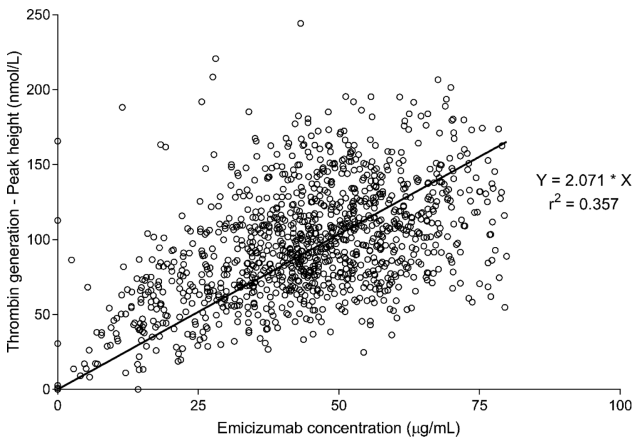
Supplementary Fig. S3 Pharmacokinetic/pharmacodynamic relationships. Correlation between emicizumab plasma concentrations and chromogenic FVIII-like activity by FIX (**A**) and FX exposure category (**B**).



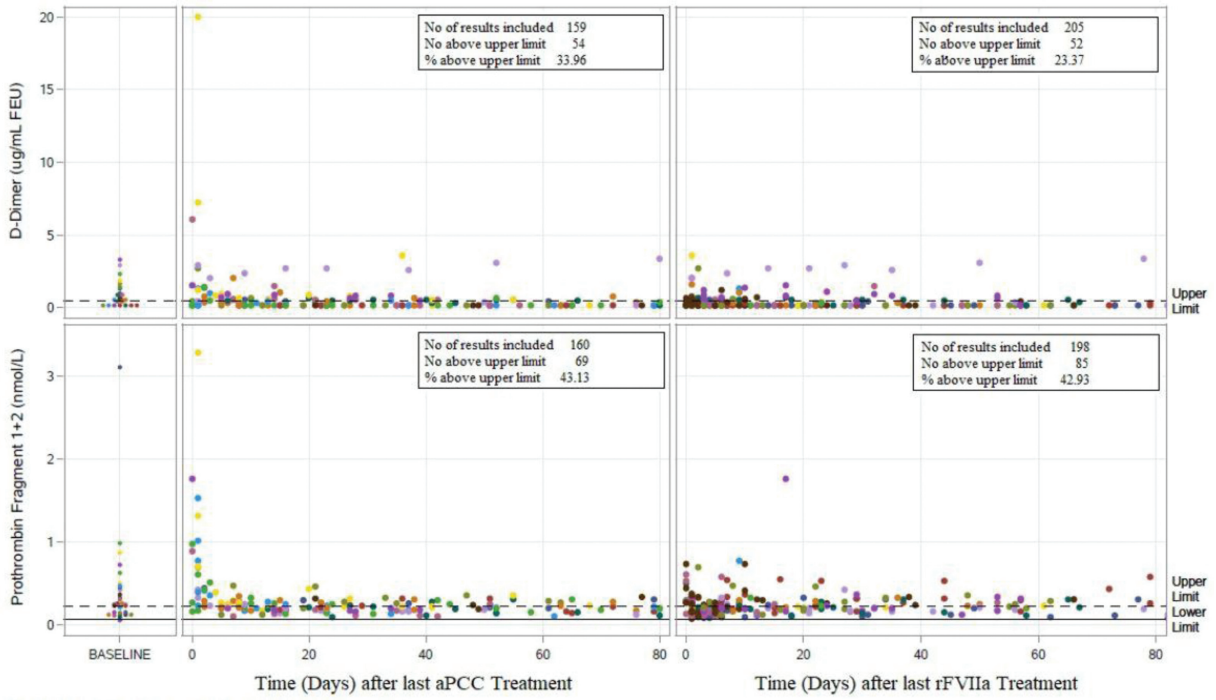
Supplementary Fig. S4 Pharmacokinetic/pharmacodynamic relationships. Correlation between emicizumab plasma concentrations and peak height of thrombin generation by FIX (**A**) and FX exposure category (**B**).



Supplementary Fig. S5 Pharmacokinetic/pharmacodynamic relationships. Linear regression between emicizumab plasma concentrations and chromogenic FVIII-like activity. Linear regression was performed on the "linear" portion of the E_{max} model, that is, based on an arbitrary selection on concentrations up to 80 μg/mL.



Supplementary Fig. S6 Pharmacokinetic/pharmacodynamic relationships. Linear regression between emicizumab plasma concentrations and thrombin generation (peak height). Linear regression was performed on the "linear" portion of the E_{max} model, that is, based on an arbitrary selection on concentrations up to 80 μg/mL.



Supplementary Fig. S7 D-dimer and prothrombin fragment 1 and 2 in function of time after treatment with recombinant activated human FVII (rFVIIa) or activated prothrombin complex concentrate (aPCC) in patients treated with emicizumab prophylaxis.[1] Baseline is the last available result before emicizumab treatment start. All other results are on emicizumab. Only participants with at least one laboratory test performed within 72 hours after rFVIIa or aPCC treatment are included. [1]Callaghan MU, Negrier C, Young G, et al. Use of bypassing agents prior to and post bypassing agent dosing guidance during emicizumab prophylaxis. ASH 2017; poster presentation 3668.