Supplemental Table 1. Description of all Breakthrough Bleeds that Occurred during Emicizumab Maintenance (≥ 4 weeks on Emicizumab), n=5.

Description of Bleed	Age	Trigger of Bleed	Severity[a]	Emicizumab Maintenance Regimen	Emicizumab Dosage Changes in Response to Bleed	IST Regimen	Rescue Hemostatic Agents Used	Procedures	Transfusions	Anticoagulants/ Antiplatelets
Gastrointestinal bleed	75	Spontaneous	Severe	3 mg/kg every 2 weeks	None	None	FVIII product, rFVIIa	Yes, Endoscopy and clips placed on gastric ulcer	Yes, 1 x pRBC	No
Gastrointestinal bleed	71	Spontaneous	Severe	1.5 mg/kg weekly	None	Rituximab, Glucocorticoid & Cyclophosphamide	rFVIIa, antifibrinolytic	Yes, Endoscopy	Yes, 7 x pRBC	No
Subcutaneous bleed in left arm	57	Trauma	Non-severe	1.5 mg/kg weekly	None	Rituximab, Glucocorticoid & Cyclophosphamide	rFVIIa	No	No	No
Left elbow hemarthrosis[b]	89	Trauma	Non-severe	1.5 mg/kg every 2 weeks	None	Rituximab & Mycophenolate mofetil	rFVIIa	No	No	No
Left knee hemarthrosis[b]	89	Trauma	Non-severe	1.5 mg/kg every 2 weeks	None	Rituximab & Mycophenolate mofetil	rFVIIa	No	No	No
Right knee hemarthrosis	69	Procedural	Non-severe	1.5 mg/kg every 2 weeks	Increased to 1.5 mg/kg weekly	Mycophenolate mofetil monotherapy	rpFVIII, rFVIIa	No	No	No

Recombinant activated factor VII (rFVIIa), Factor VIII (FVIII), Recombinant porcine factor VIII, Packed red blood cells (pRBC)

[a] A severe breakthrough bleed is defined as a drop in hemoglobin > 2g/dL, requiring >2 red blood cell transfusions, and/or organ-, limb- or life-threatening.

[b] These bleeds occurred separately in the same patient.

Supplement Table 2. Characteristics and Disease Course of AHA Patients With at least 12 Weeks of Follow-Up by Immunosuppression Therapy (IST) Regimen, n=55.

	None, n=4	Glucocorticoids Monotherapy, n=6	Glucocorticoids & Cyclophosphamide, n=3	Rituximab & Glucocorticoids, n=10	Rituximab Monotherapy, n=14	Rituximab & Other IST, n=17	MMF Monotherapy n=1	Total, n=55
IST Initiation Timing	NA							
Pre-emicizumab		3 (50%)	1 (33%)	5 (50%)	6 (43%)	12 (71%)	1 (100%)	28 (55%)
±1 week emicizumab		3 (50%)	2 (67%)	4 (40%)	5 (36%)	3 (18%)	0 (0%)	17 (33%)
Post-emicizumab		0 (0%)	0 (0%)	0 (0%)	1 (7%)	0 (0%)	0 (0%)	1 (2%)
Unknown		0 (0%)	0 (0%)	1 (10%)	2 (14%)	2 (12%)	0 (0%)	5 (10%)
Recent FVIII Activity Level,[a] median, (range)	232%, (48%-246%)	71%, (<1%-230%)	<4%, (<4%-<4%)	111%, (2.5%-255%)	115%, (<1%-320%)	113%, (<1%-515%)	8%	111%, (<1%-515%)
Recent FVIII Inhibitor Titer,[b] median, (range)	<0.6, (<0.3-2.3)	1, (<0.6-423)	53, (5.6-100)	<0.5, (<0.5-22.3)	<0.5, (<0.5-56)	<0.6, (<0.3-11)	0.4	<0.6, (<0.3-423)
Emicizumab Initiation Timing, median, (range)								
Time from diagnosis to emicizumab initiation (weeks)	6, (2-9)	2, (1-13)	4, (2-38)	7, (0-246)	1, (0-76)	7, (0-130)	8	3, (0-246)
Time on emicizumab (weeks)[c]	40, (12-52)	13, (1-20)	28, (28-28)	3, (1-15)	7, (4-52)	10, (1-46)	Ongoing	10, (0-48)
Relevant Medications								
Still on emicizumab at time of survey	1 (25%)	3 (50%)	2 (67%)	2 (20%)	2 (14%)	2 (12%)	1 (100%)	13 (24%)
Still on IST at time of survey	NA	1 (17%)	1 (33%)	0 (0%)	1 (7%)	2 (12%)	1 (100%)	6 (11%)
Hospitalizations (days) median, (range)								
Pre-emicizumab	31, (9-53)	10, (3-60)	2, (0-5)	11, (4-75)	11, (0-18)	17, (0-55)	29	11, (0-75)
Post-emicizumab	0, (0-28)	6, (0-24)	0, (0-1)	6, (0-12)	4, (0-26)	4, (0-30)	22	4, (0-30)
Pre-emicizumab Bleeding History								
Patients with acute bleeds	3 (75%)	6 (100%)	3 (100%)	9 (90%)	14 (100%)	16 (94%)	1 (100%)	52 (95%)
Patients with severe acute bleeds	1 (25%)	6 (100%)	2 (67%)	6 (60%)	13 (93%)	14 (82%)	1 (100%)	43 (78%)
Patients requiring hemostatic treatment	2 (50%)	6 (100%)	2 (67%)	8 (80%)	8 (57%)	16 (94%)	1 (100%)	43 (78%)
Post-emicizumab Breakthrough Bleeding								
Total no. of bleeds	2	0	0	0	2	5	1	10

No. of bleeds during emicizumab loading	1	0	0	0	2	1	0	4
No. of bleeds during emicizumab maintenance	1	0	0	0	0	4	1	6
No. of severe breakthrough bleeds	1	0	0	0	1	1	0	3
Pre-emicizumab AEs								
Patients with IST-related AEs	NA	2 (33%)[d]	0 (0%)	1 (10%)[f]	1 (7%)[e]	1 (6%)[f]	0 (0%)	5 (9%)
Patients with other AEs	1 (25%)	1 (17%)	0 (0%)	1 (10%)	1 (7%)	1 (6%)	0 (0%)	5 (9%)
Post-emicizumab AEs								
Patients with IST-related AEs	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Patients with other AEs	0 (0%)	1 (17%)	1 (33%)	1 (10%)	0 (0%)	1 (6%)	0 (0%)	4 (7%)

Factor VIII (FVIII), Adverse Events (AEs)

[a] FVIII activity level was measured with either a one-stage or chromogenic assay.

[b] FVIII inhibitor titer units are BU/mL

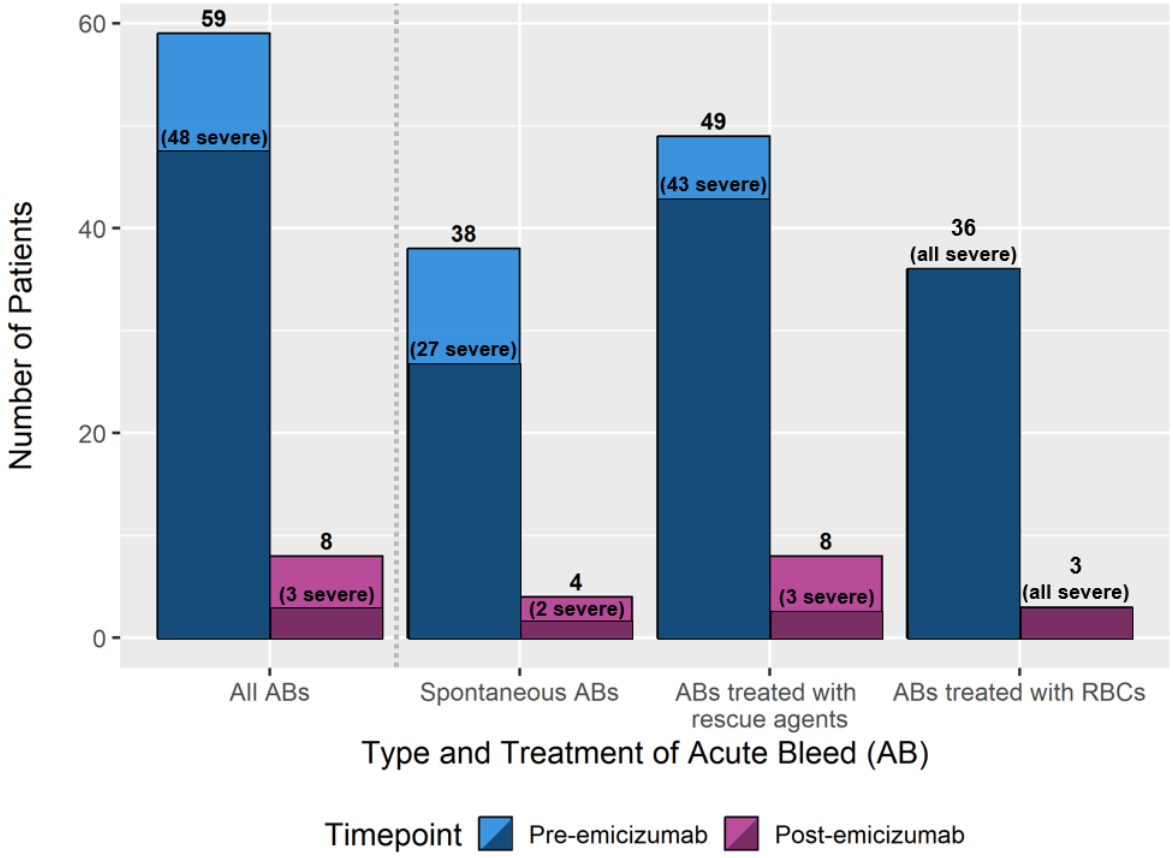
[c] Time on emicizumab was only calculated for patients who had discontinued emicizumab at time of survey (n=42)

[d] The two IST-related AEs were hyperglycemia and encephalopathy.

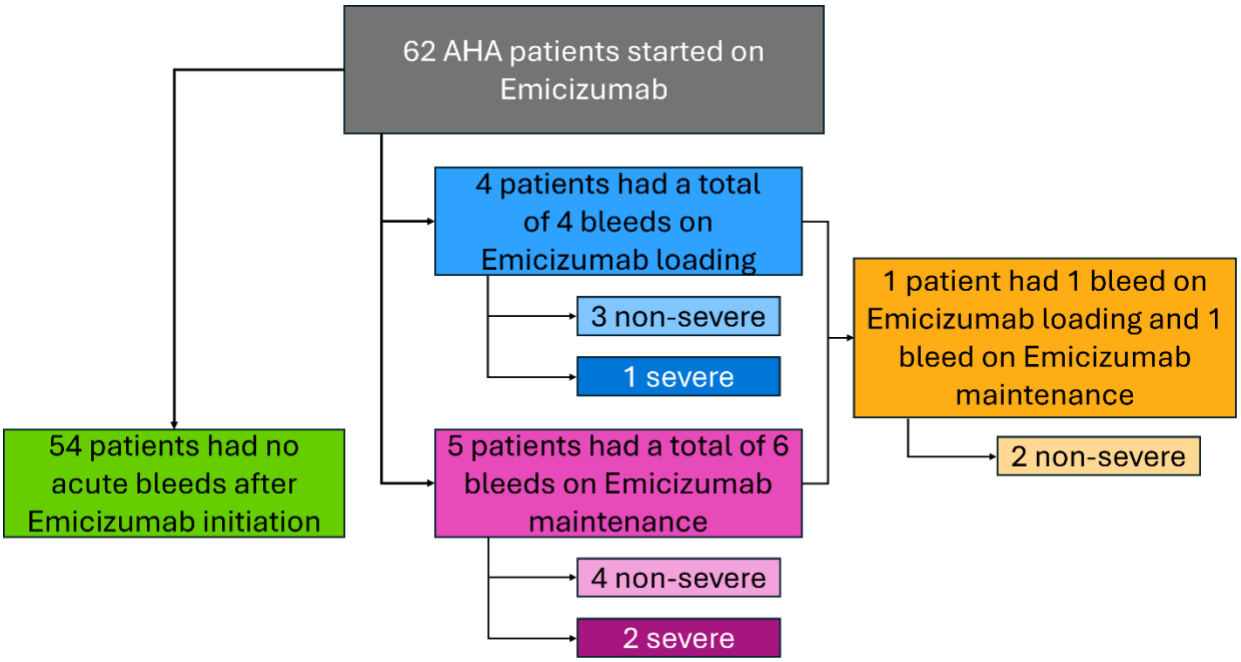
[e] The IST-related AE was a hypersensitivity reaction.

[f] The IST-related AE was an infusion reaction.

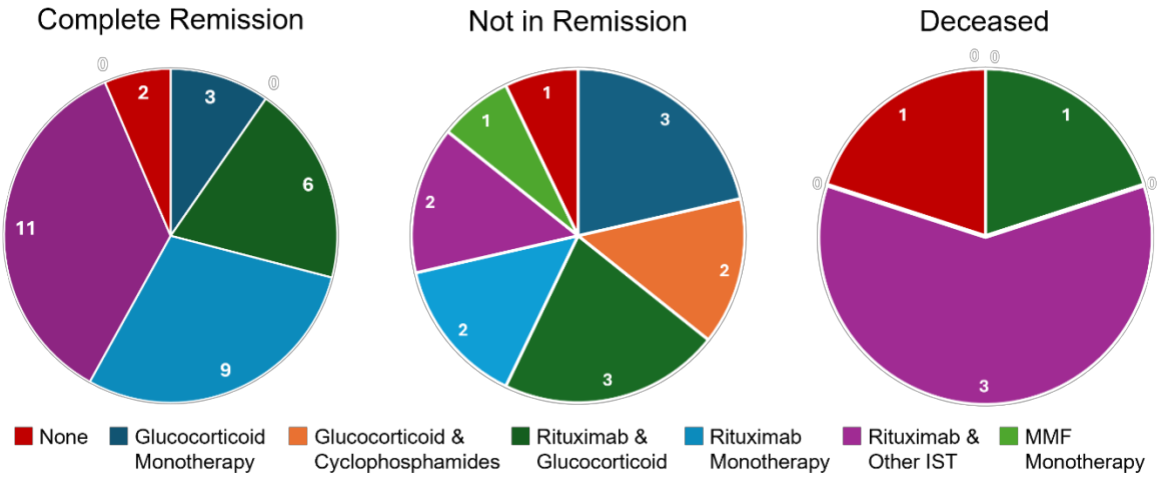
Supplemental Figure 1. Acute Bleeds and Rescue Treatments, Pre- and Post-Emicizumab Initiation for Total Cohort (n=62).



Supplemental Figure 2. Flowchart of Breakthrough Bleeds for Total Cohort, n=62



Supplement Figure 3. Comparison of Immunosuppression Therapy Regimens among AHA Patients with at least 12 Weeks of Follow-Up in Complete Remission, Not in Remission, or Deceased, n=50.



Supplemental Figure 4. Comparison of lowest FVIII activity level, maximum FVIII inhibitor titer, and current disease status by IST regimen for AHA patients with at least 12 weeks follow-up, (n=55).