

Terminal complement inhibition and control of hemolysis in patients with paroxysmal nocturnal hemoglobinuria who switched from high-dose eculizumab to ravulizumab: a phase IV, single-arm clinical trial

Authors

Morag Griffin,¹ Shreyans Gandhi,² Richard J. Kelly,¹ Talha Munir,¹ Roochi Trikha,² Eden Hicks,³ Deepak Jain,³ Masayo Ogawa,³ Ji Yu,³ Petra Muus¹ and Austin G. Kulasekararaj^{2,4}

¹St James's University Hospital, Leeds Teaching Hospitals NHS Trust, Leeds, UK; ²King's College Hospital, National Institute for Health and Care Research (NIHR) Wellcome Trust King's Clinical Research Facility, London, UK; ³Alexion, AstraZeneca Rare Disease, Boston, MA, USA and ⁴King's College London, London, UK

Correspondence:

M. GRIFFIN - m.griffin@nhs.net

<https://doi.org/10.3324/haematol.2024.285553>

Received: April 18, 2024.

Accepted: November 18, 2024.

Early view: November 28, 2024.

Published under a CC BY license 

Supplementary material**Table S1. Per-patient laboratory values throughout the study period (N=18).**

	Patients, N=18																	
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18
Patient sex	Male	Female	Male	Female	Female	Female	Male	Male	Female	Male	Male	Male	Male	Male	Female	Male	Male	Male
Age	50 years	64 years	62 years	65 years	22 years	51 years	57 years	46 years	45 years	64 years	60 years	65 years	58 years	59 years	73 years	58 years	57 years	46 years
Weight	108.0 kg	85.9 kg	80.4 kg	93.1 kg	49.5 kg	89.3 kg	70.1 kg	72.0 kg	71.5 kg	114.0 kg	82.3 kg	71.6 kg	78.1 kg	97.6 kg	56.6 kg	81.1 kg	90.1 kg	101.0 kg
LDH, U/L																		
Day –85*	240	344	245	294	191	255	233	206	203	252	223	211	248	151	245	216	233	–
Day –57*	246	327	215	278	174	255	233	227	276	213	240	191	239	166	170	–	242	251
Day –29*	202	358	226	291	213	235	265	251	249	224	223	188	–	163	160	234	251	227 ^a
Day 1 [#]	229	–	267	273	173	251	264	223	195	216	204	195	277	154	163	–	281	221
Baseline	229.25	343	238.25	284	187.75	249	248.75	226.75	230.75	226.25	222.5	196.25	254.67	158.5	184.5	225	251.75	232.5
Day 15 [#]	174	–	247	381	226	–	244	228	214	206	220	229	266	156	197	302	263	275
Day 71 [#]	179	314	271	317	212	246	208	238	198	284	229	190	378	181	272	233	300	262
Day 127 [#]	166	271	251	451	292	269	221	225	306	205	239	197	311	183	173	236	280	228
Day 183 [#]	171	394	208	284	231	266	197	277	256	211	226	181	338	186	167	198	257	253
Day 239 [#]	161	276	258	320	185	250	225	227	219	179	229	201	371	214	184	240	275	298
Day 295 [#]	143	–	248	305	218	–	171	236	273	187	236	243 ^b	410	202	–	243	260	303
Day 351 [#]	172	–	283	–	–	255	287	234	–	203	241	172	327	171	179	245	251	353
Hb, g/dL																		
Day –85*	12.4	12.8	–	9.9	–	12.1	11.2	10.9	12.9	12.0	–	9.1	–	12.6	8.7	9.0	11.2	–
Day –57*	10.3	12.4	10.1	–	11.3	11.0	10.9	10.3	13.3	12.5	–	9.1	14.1	13.0	9.0	8.7	11.9	–
Day –29*	11.0	11.1	8.9	9.2	11.2	–	10.0	9.4	12.9	12.5	11.1	9.4	–	13.3	9.3	8.2	11.6	–
Day 1 [#]	11.8	11.5	10.0	9.3	10.4	–	10.6	10.8	13.0	12.4	–	9.3	–	13.6	8.9	7.8	11.4	12.8
Day 15 [#]	10.6	11.4	9.6	–	10.2	10.9	10.6	10.5	12.7	12.0	–	8.7	–	13.5	8.6	10.2	10.7	13.2

	Patients, N=18																	
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18
Patient sex	Male	Female	Male	Female	Female	Female	Male	Male	Female	Male	Male	Male	Male	Male	Female	Male	Male	Male
Age	50 years	64 years	62 years	65 years	22 years	51 years	57 years	46 years	45 years	64 years	60 years	65 years	58 years	59 years	73 years	58 years	57 years	46 years
Weight	108.0 kg	85.9 kg	80.4 kg	93.1 kg	49.5 kg	89.3 kg	70.1 kg	72.0 kg	71.5 kg	114.0 kg	82.3 kg	71.6 kg	78.1 kg	97.6 kg	56.6 kg	81.1 kg	90.1 kg	101.0 kg
Day 71 [#]	11.9	11.9	–	9.2	10.4	10.7	10.6	10.0	12.9	11.5	11.2	9.8	–	14.3	8.3	9.0	11.3	12.5
Day 127 [#]	11.1	11.0	8.5	8.6	10.6	11.3	11.3	10.7	11.6	12.4	–	9.5	13.5	14.1	8.3	9.6	10.8	12.9
Day 183 [#]	10.9	11.3	10.1	9.6	10.6	11.8	11.0	10.4	12.8	12.3	10.9	9.5	12.5	13.4	8.0	11.4	11.5	12.8
Day 239 [#]	10.7	12.1	9.6	9.4	10.4	11.9	10.9	10.5	13.1	12.1	–	9.4	12.9	13.8	7.4	8.9	11.4	11.6
Day 295 [#]	11.3	12.3	8.9	9.5	–	12.6	12.5	10.5	12.8	12.1	11.0	9.4	11.9	13.8	8.7	9.0	10.6	12.0
Day 351 [#]	12.1	12.0	8.2	7.8	–	12.0	11.1	10.1	11.1	11.9	11.1	10.0	11.3	13.3	7.2	8.1	10.9	11.4
Free C5, µg/mL																		
Day –57*	0.0455	0.0244	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0224	<0.0183	<0.0183	<0.0183	<0.0183	0.0970	0.0329	<0.0183	0.0203	0.0185	0.0190
Day –29*	0.0510	0.0223	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0222	<0.0183	0.0190	<0.0183	<0.0183	<0.0183	0.0224	<0.0183	0.0194	<0.0183	0.0189
Day 1 [#]																		
Pre-dose	0.0483	0.0229	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0256	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0250	<0.0183	0.0251	<0.0183	0.0229
Post-dose	0.0238	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0204	<0.0183	<0.0183	<0.0183	<0.0183
Day 15 [#]																		
Pre-dose	0.1060	0.0492	0.0257	0.0321	<0.0183	0.0281	0.0280	0.0652	<0.0183	0.0295	0.0228	<0.0183	0.0290	0.0484	<0.0183	0.0591	0.0310	0.0469
Post-dose	0.0336	0.0233	<0.0183	<0.0183	<0.0183	<0.0183	<0.0183	0.0248	<0.0183	0.0192	<0.0183	<0.0183	<0.0183	0.0193	<0.0183	0.0218	0.0191	0.0191
Day 71 [#]																		
Pre-dose	0.1580	0.1430	0.0897	0.1130	0.0602	0.0888	0.1230	0.1490	0.0533	0.1050	0.0685	0.0506	0.1210	0.1070	0.0537	0.1320	0.1080	0.1070
Post-dose	0.0445	0.0405	0.0320	0.0318	0.0227	0.0263	0.0428	0.0311	0.0202	0.0369	0.0245	0.0198	0.0312	0.0310	0.0188	0.0355	0.0321	0.0267
Day 127 [#]																		
Pre-dose	0.1760	0.1580	0.0902	0.1330	0.0547	0.0942	0.1270	–	0.0715	0.0834	0.0765	0.0706	0.1300	0.1100	0.0676	0.1260	0.1120	0.1090
Post-dose	0.0413	0.0371	0.0284	0.0351	0.0195	0.0285	0.0411	0.0196	0.0278	0.0326	0.0269	0.0222	0.0237	0.0334	0.0218	0.0368	0.0319	0.0256
Day 183 [#]																		
Pre-dose	0.2390	0.1720	0.0909	0.108	0.0620	0.0833	0.0130	0.1620	0.0654	0.0972	0.0878	0.0777	0.1500	0.1090	0.0846	0.1310	0.1150	0.0873
Post-dose	0.0505	0.0352	0.0304	0.031	0.0211	0.0284	0.0382	0.0345	0.0231	0.0341	0.0304	0.0270 ^c	0.0296	0.0306	0.0206	0.0296	0.0343	0.0291
Day 351 [#]	0.1660	0.1630	0.0864	0.1090	0.0408	0.0706	0.1330	0.1220	0.0496	0.0886	0.0607	0.0746	0.1220	0.1020	0.0754	0.1250	0.0953	0.0868

	Patients, N=18																	
	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18
Patient sex	Male	Female	Male	Female	Female	Female	Male	Male	Female	Male	Male	Male	Male	Male	Female	Male	Male	Male
Age	50 years	64 years	62 years	65 years	22 years	51 years	57 years	46 years	45 years	64 years	60 years	65 years	58 years	59 years	73 years	58 years	57 years	46 years
Weight	108.0 kg	85.9 kg	80.4 kg	93.1 kg	49.5 kg	89.3 kg	70.1 kg	72.0 kg	71.5 kg	114.0 kg	82.3 kg	71.6 kg	78.1 kg	97.6 kg	56.6 kg	81.1 kg	90.1 kg	101.0 kg
<i>Reticulocyte count, $\times 10^9/L$</i>																		
Day –85*	91.4	354.8	–	278.6	–	120.6	195.6	269.6	92.7	260.8	–	321.1	–	131.2	230.5	234.5	326.0	–
Day 1 [#]	112.6	247.2	207.8	263.3	62.1	–	199.2	220.5	61.0	264.5	–	308.5	–	132.0	223.4	282.7	329.0	374.7
Day 351 [#]	131.6	264.5	244.5	299.4	–	128.3	225.6	225.0	50.6	227.1	–	274.6	476.5	118.7	220.2	321.1	335.2	453.2

Shaded cells represent study visits following a transfusion.

Patient numbers align with those in *Online Supplementary Figure S2*.

*Eculizumab infusion day.

[#]Ravulizumab infusion day.

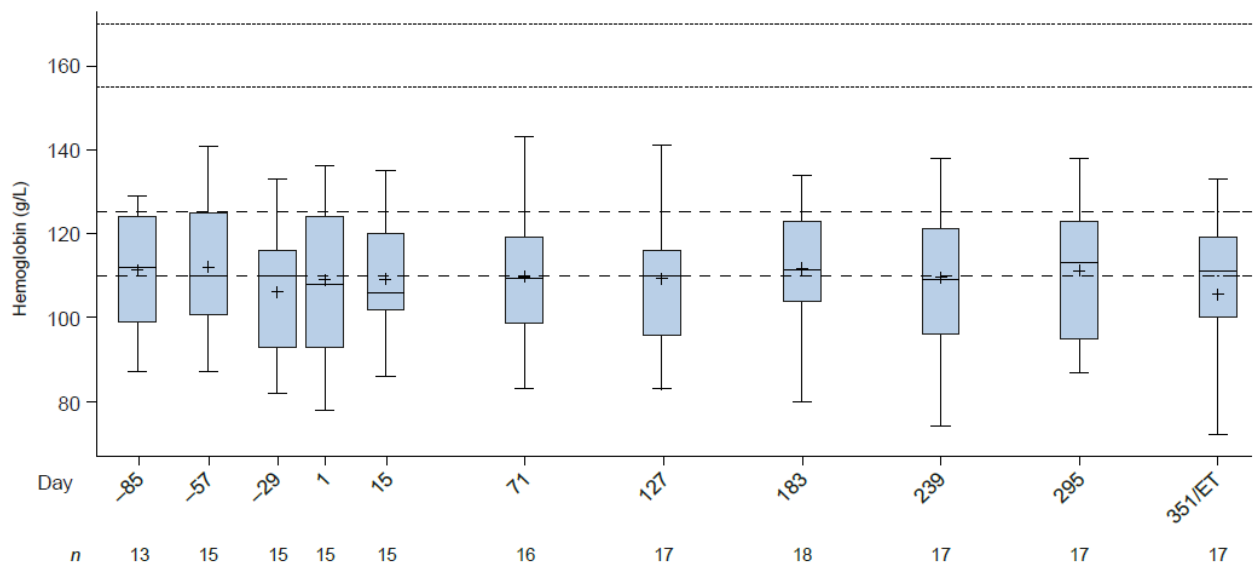
^aOne unscheduled visit was reported on day –1 (LDH recorded as 231 U/L).

^bOne unscheduled visit was reported on day 319 (LDH recorded as 202 U/L).

^cOne unscheduled visit was reported on day 319 (free C5 recorded as 0.0484 $\mu\text{g/dL}$).

C5: complement component 5; Hb: hemoglobin; LDH: lactate dehydrogenase.

Figure S1. Hemoglobin concentration over time, measured during pre-baseline and ravulizumab treatment period (N=18).

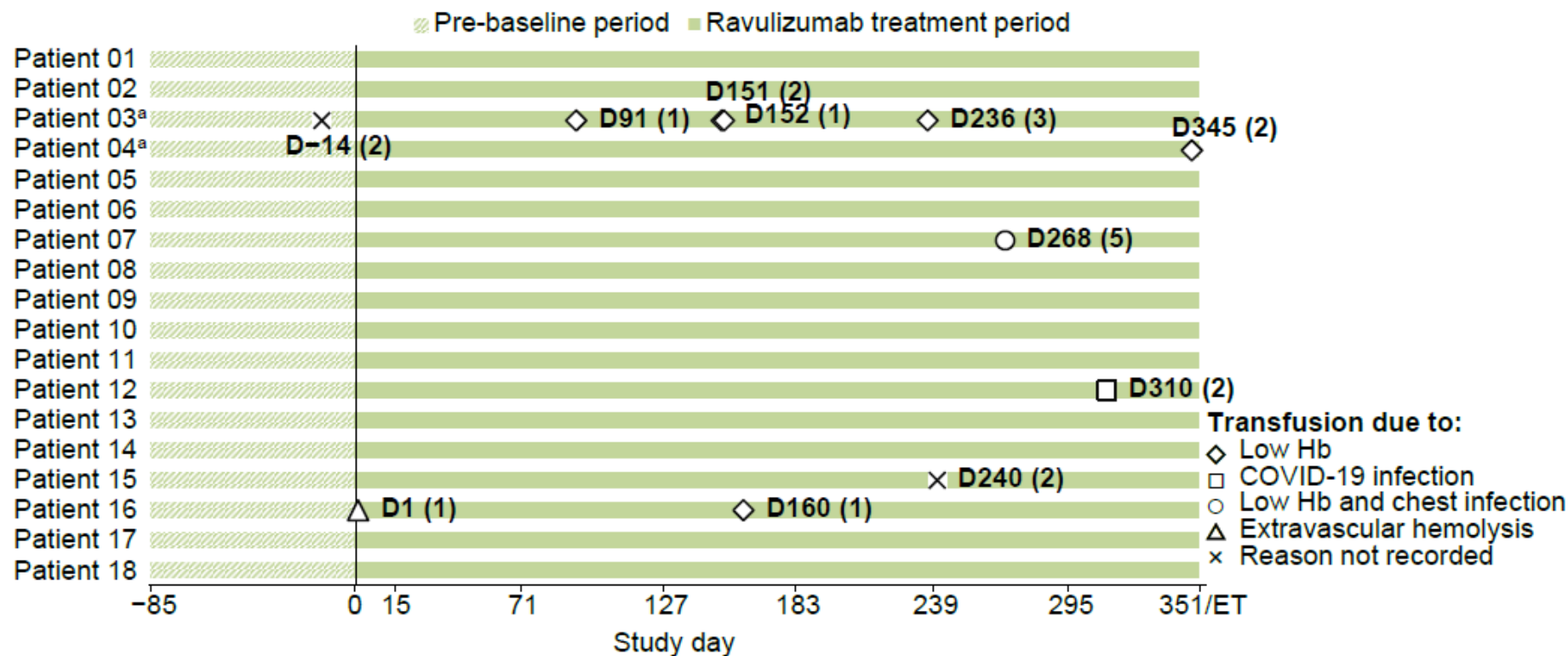


Data are irrespective of transfusions.

Box and whisker plots: cross (+), arithmetic mean; horizontal line, median; box, 1st and 3rd quartiles (25th and 75th percentile); whiskers, fences of $1.5 \times \text{IQR}$ or minimum/maximum range if $< 1.5 \times \text{IQR}$.

Dashed horizontal lines indicate lower normal value (110 g/L for women and 125 g/L for men). Dotted horizontal lines indicate upper normal value (155 g/L for women and 170 g/L for men).

ET: end of trial; IQR: interquartile range.

Figure S2. Transfusions during the 3 month pre-baseline period and ravulizumab treatment period (N=18).

The values in parentheses indicate the number of units of packed red blood cells transfused.

Patient numbers align with those in Table S1.

^aPatients with a history of transfusion in the 12 months prior to screening.

D: day; ET: end of trial; Hb: hemoglobin.