

SUPPLEMENTARY MATERIAL for “Phase 3 Study of Subcutaneous Versus Intravenous Ravulizumab in Eculizumab-Experienced Adult Patients with PNH: Primary Analysis and 1-Year Follow-Up”

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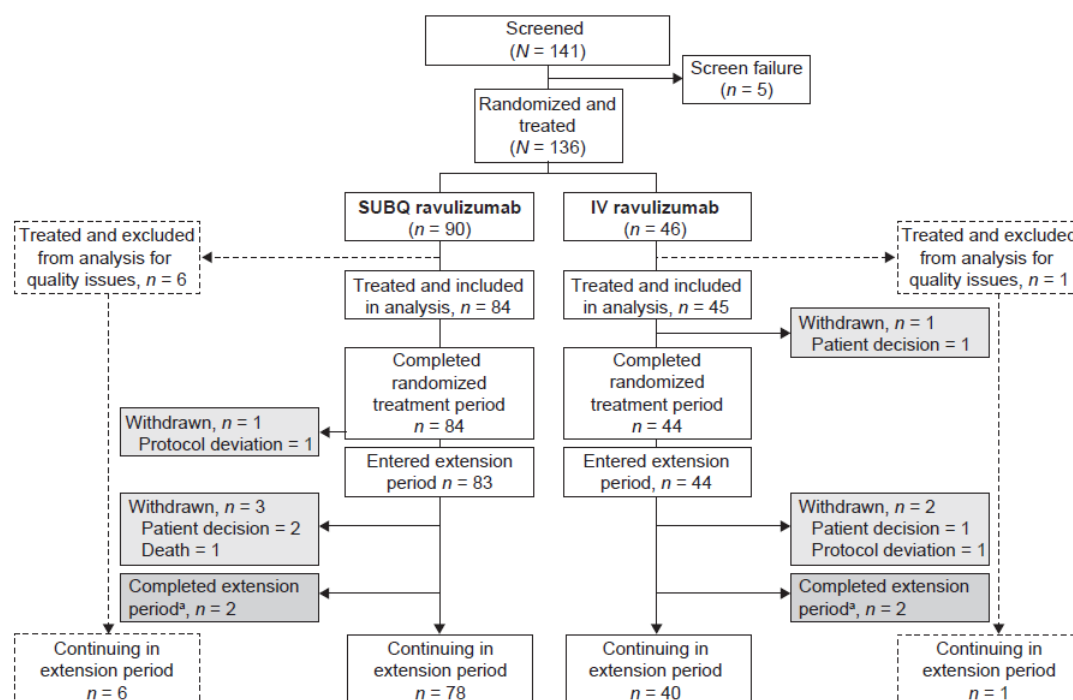
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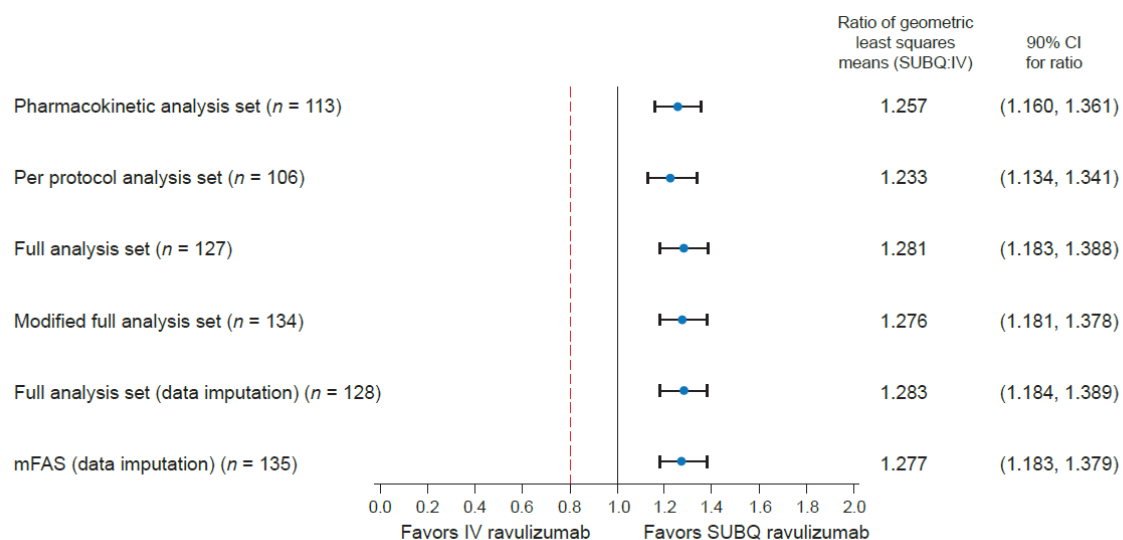


Supplementary Material Fig. S1 Disposition of patients (all screened patients)

Note: All patients ($n = 7$) from one site were excluded from the primary PK, PD, per protocol, FAS, SUBQ treated FAS, Safety, and SUBQ treated safety analysis sets due to important source documentation deviations and findings related to deficiencies in investigator oversight

^aFour patients completed the extension period and opted not to continue when the duration of the study was extended

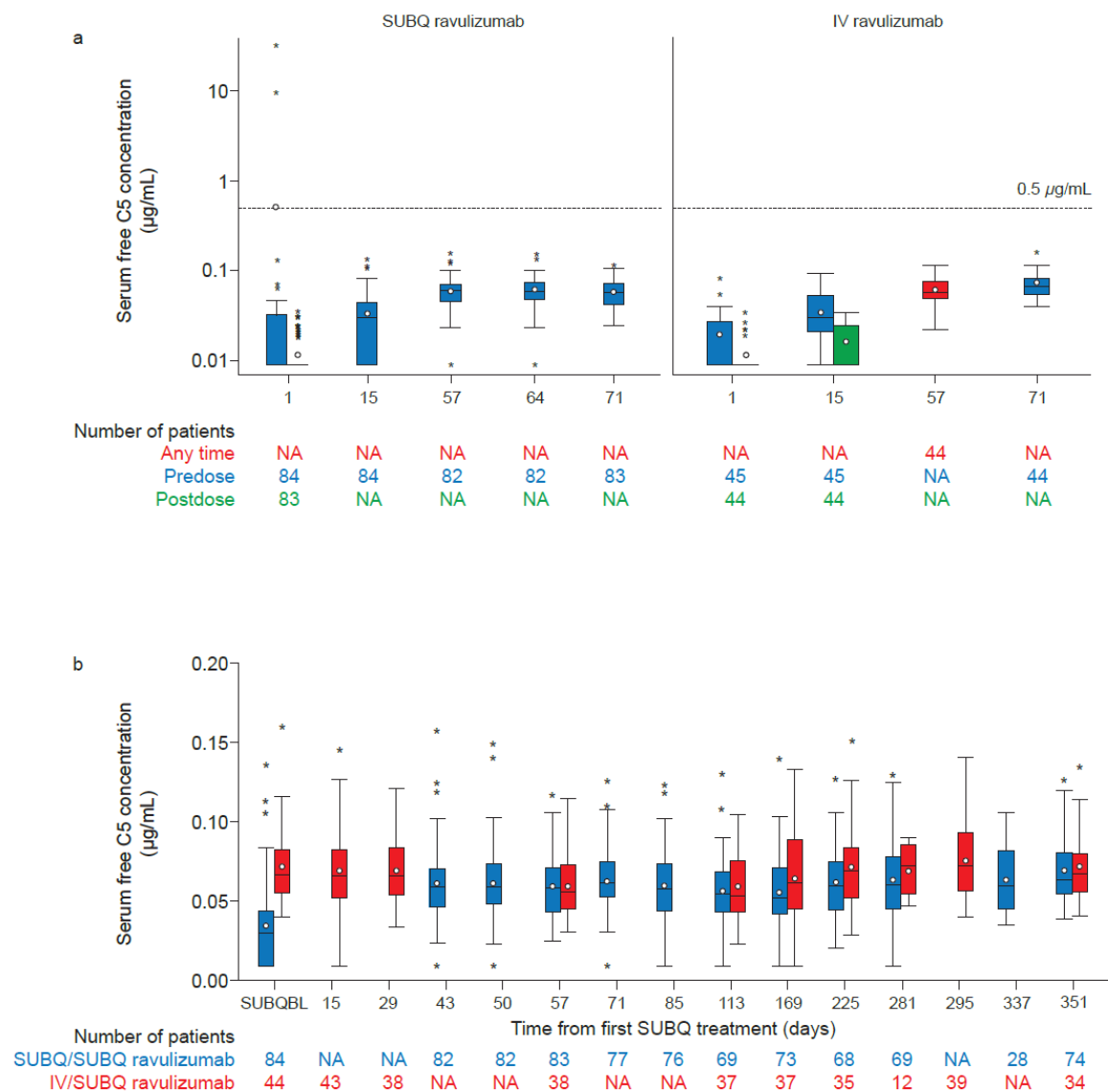
FAS full analysis set, IV intravenous, PD pharmacodynamic, PK pharmacokinetic, SUBQ subcutaneous



Supplementary Material Fig. S2 Forest plot of Day 71 serum ravulizumab concentration by population: non-inferiority by analysis set

Note: n is representative of the number of patients in each analysis set with available data. Each tail is representative of the 90% confidence interval for that analysis set. The null hypothesis that the ratio of geometric means of Day 71 ravulizumab C_{trough} between the SUBQ group and the IV group was less than or equal to the non-inferiority margin of 0.8 will fail to be rejected if the lower bound (left tail) crosses the non-inferiority margin represented by the red dashed line.

C_{trough} trough serum concentration, IV intravenous, mFAS modified full analysis set, SUBQ subcutaneous



Supplementary Material Fig. S3 Serum free C5 concentration over time during (a) the randomized treatment period (PD analysis set) and (b) the SUBQ treatment period by treatment group (SUBQ treated full analysis set)

Note: The SUBQ group had samples collected predose at days 1, 15, 57, 64, and 71, and postdose at day 1. The IV group had samples collected predose at days 1, 15, and 71, postdose at days 1 and 15, and any time at day 57. SUBQBL was defined as the last assessment from the central laboratory prior to first dose of SUBQ treatment. *IV* intravenous, *NA* not applicable, *PD* pharmacodynamic, *SUBQ* subcutaneous, *SUBQBL* subcutaneous baseline

Supplementary Material Table S1 List of ethics committees

Site No.	Investigator Name	Name / Address of Ethics Committee
AUSTRALIA		
0080	Dr. Danny Chih Tsai Hsu	South Western Sydney Local Health District Research and Ethics Office, Locked Bag 7103, Liverpool BC NSW 1871
0255	Prof Jeffrey Szer	South Western Sydney Local Health District, Research and Ethics Office, Locked Bag 7103, Liverpool BC NSW 1871
AUSTRIA		
0529	Univ. Prof. Dr. med. Wolfgang Füreder	Ethikkommission Medizinische Universität Wien Borschkegasse 8b/6 Vienna, Austria 1090
BELGIUM		
0126	Prof. Timothy Devos	UZ Leuven Campus Gasthuisberg Ethische Commissie onderzoek Herestraat 49 3000 Leuven Belgium
0535	Prof. Nicole Straetmans	Comite d'Ethique Promenade de l'Alma 51 1200 Bruxelles Belgium
0838	Prof. Koen Theunissen	Ethische Toetsingscommissie Jessa Ziekenhuis Stadsomvaart 11 3500 Hasselt Belgium
0996	Dr Ka Lung Wu	Commissie voor Medische Ethiek ZNA IRB-ZNA/OCMW Antwerpen ZNA Koningin Paola Kinderziekenhuis Lindendreef 1 2020 Antwerpen Belgium
BRAZIL		
0016	Lucas Oliveira Cantadori	Comissao Nacional de Etica em Pesquisa - CONEP SVTV 701, Via W5 Norte Edificio PO 700 - 3 Andar- Asa Norte Brasilia DF Brazil 70719-040
0020	Rodrigo do Tocantins Calado de Saloma Rodrigues	Comissao Nacional de Etica em Pesquisa - CONEP SVTV 701, Via W5 Norte Edificio PO 700 - 3 Andar- Asa Norte Brasilia DF Brasil 70719-040
0306	Sandra Fatima Menosi Gualandro	Comissao Nacional de Etica em Pesquisa - CONEP SVTV 701, Via W5 Norte Edificio PO 700 - 3 Andar- Asa Norte Brasilia DF Brasil 70719-040

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0657	Celso Arrais Rodrigues da Silva	Comissao Nacional de Etica em Pesquisa - CONEP SVTV 701, Via W5 Norte Edificio PO 700 - 3 Andar- Asa Norte Brasilia DF Brasil 70719-040
1143	Adriana Barretto	Comissao Nacional de Etica em Pesquisa - CONEP SRNTV 701, Via W5 Norte, Edificio PO 700 - 3 andar Asa Norte, Brasilia/DF, Brasil 70719-049
CANADA		
0158	Christopher Patriquin, MD	University Health Network Research Ethics Board 700 University Ave. 10th Floor, Room 1056 Toronto, Ontario M5G 1Z5 Canada
FINLAND		
0647	Anna-Elina Lehtinen	Helsingin ja Uudenmaan sairaanhoitopiiri Eettinen toimikunta II Biodemicum 2 C Tukholmankatu 2 C Helsinki Finland 000290
FRANCE		
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0125	Pr Jean-Francois Viallard	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0260	Pr Emmanuel Gyan	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
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0466	Dr Fiorenza Barraco	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0467	Dr Sophie De Guibert	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0544	Dr Jose Miguel Torregrosa Diaz	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0637	Dr Nicolas Blin	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0652	Dr. Jean-Richard Eveillard	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0688	Delphine Lebon, MD	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France
0689	Robert Navarro	Comite de Protection des Personnes OUEST 2 Maison de la Recherche Clinique - CHU d'Angers - 4 rue Larrey - 49933 Angers Cedex 9 - France

Site No.	Investigator Name	Name / Address of Ethics Committee
ITALY		
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0523	Dr. Wilma Barcellini	Comitato Etico Milano Area B Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Via F. Sforza, 28 - 20122 Milano, Italy
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0762	Prof. Francesco Di Raimondo	Comitato Etico di Catania 1 Azienda Ospedaliero - Universitaria "Policlinico - Vittorio Emanuele" via S. Sofia, 78 - 95123 Catania, Italy
NETHERLANDS		
0172	Marjolein W.M. van der Poel	METC azM/UM Maastricht University Medical Centre (MUMC) P. Debyelaan 25 Maastricht Limburg Netherlands 6229 HX
RUSSIA		
0427	Alexander D. Kulagin, MD	Local Ethics Committee of the Federal State Budgetary Educational Institution of Higher Education "First Saint Petersburg State Medical University name after Academician P. I. Pavlov" of Ministry of Healthcare of the Russian Federation 12, Rentgen street Saint Petersburg Russia 197022
0428	Elena Lukina, MD, Prof	Local Ethics Committee of the Federal State Budgetary Institution "National Medical Research Center of Hematology" of the Ministry of Healthcare of the Russian Federation 4, Novy Zykovsky pr. Moscow Russia 125167

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0905	Tatiana S. Konstantinova, MD, PhD	Local Ethics Committee of the State Budgetary Healthcare Institution of Sverdlovsk region "Sverdlovsk Regional Clinical Hospital #1" 185, Volgogradskaya Str. Ekaterinburg Russia 620102
SPAIN		
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0279	Ines Hernandez Rodriguez	CEIm Hospital Universitario Puerta de Hierro de Majadahonda Hospital Universitario Puerta de Hierro Majadahonda C\ Joaquin Rodrigo, 2 Majadahonda; Madrid Spain 28222
0282	Anna Gaya Valls	CEIm Hospital Universitario Puerta de Hierro de Majadahonda Hospital Universitario Puerta de Hierro Majadahonda C\ Joaquin Rodrigo, 2 Majadahonda; Madrid Spain 28222
0292	Ramiro Nunez Vazquez	CEIm Hospital Universitario Puerta de Hierro de Majadahonda Hospital Universitario Puerta de Hierro Majadahonda C\ Joaquin Rodrigo, 2 Majadahonda; Madrid Spain 28222
0429	Emilio Ojeda Gutierrez	CEIm Hospital Universitario Puerta de Hierro de Majadahonda Hospital Universitario Puerta de Hierro Majadahonda C\ Joaquin Rodrigo, 2 Majadahonda; Madrid Spain 28222

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1005	Maria Angelina Lemes Castellano	CEIm Hospital Universitario Puerta de Hierro de Majadahonda Hospital Universitario Puerta de Hierro Majadahonda C\ Joaquin Rodrigo, 2 Majadahonda; Madrid Spain 28222
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0556	Martin Hoeglund	Etikprovningsmyndigheten Box 2110 750 02 Uppsala Sweden
TURKEY		
0075	Mustafa Nuri Yenerel	Istanbul Medical Faculty Clinical Trials Ethics Committee Istanbul Tip Fakueltesi Klinik Arastirmalar Etik Kurulu, I.U. Istanbul Tip Fakueltesi Hulusi Behcet Kuetuephanesi Kat: 3 Istanbul Fatih Turkey 34093
0142	Professor Muhlis Cem Ar	Istanbul Medical Faculty Clinical Trials Ethics Committee Istanbul Tip Fakueltesi Klinik Arastirmalar Etik Kurulu I.U. Istanbul Tip Fakueltesi Hulusi Behcet Kuetuephanesi Kat:3 Istanbul Fatih Turkey 34093
0192	Professor Ayse Tuelin Tuglular	Istanbul Medical Faculty Clinical Trials Ethics Committee Istanbul Tip Fakueltesi Klinik Arastirmalar Etik Kurulu I.U. Istanbul Tip Fakueltesi Hulusi Behcet Kuetuephanesi Kat:3 Istanbul Fatih Turkey 34093

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USA		
0560	Caroline Piatek, MD	University of Southern California (USC) Institutional Review Board 1640 Marengo Street Suite 700 Los Angeles, CA USA 90033

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^bPrevious PI: Prof. Roberto Foa, MD

^cPrevious PI: Anunciacion Urquia Plazaola