Supplementary Appendix

Pegcetacoplan controls hemolysis in complement inhibitor-naive patients with paroxysmal nocturnal hemoglobinuria

Section 1. Investigator Listing

Site	Investigator	Role	# Patients Enrolled
Prince of Wales Hospital, 30-32 Ngan Shing Street, Sha Tin, Hong Kong	Raymond Siu Ming Wong	Principal Investigator	3
Queen Mary Hospital, 102 Pokfulam Road, Hong Kong, Hong Kong	Eric Tse	Principal Investigator	1
Hospital Ampang, Jalan Mewah Utara, Pandan Mewah, Selangor 68000, Malaysia	Veena Selvaratnam	Principal Investigator	4
University Malaya Medical Centre (UMMC), Jalan Universiti, Lembah Pantai, Kuala Lumpur 59100, Malaysia	Henning Cheng Kien Loo	Principal Investigator	3
Siriraj Hospital, 2 Wanglang Road, Bangkoknoi, Bangkok 10700, Thailand	Surapol Issaragrisil	Principal Investigator	2
Ramathibodi Hospital, 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand	Pimjai Niparuck	Principal Investigator	2
Hospital for Tropical Disease, 420/6 Ratchawithi Road, Ratchathewi, Bangkok 10400, Thailand	Supat Chamnanchanunt	Principal Investigator	1
Maharaj Nakorn Chiang Mai Hospital, 110 Intrawarorot Road Soi 2, Si Phum, Amphoe Mueang, Chiang Mai 50200, Thailand	Chatree Chai-Adisaksopha	Principal Investigator	2
Thammasat University Hospital, 95 Moo. 8, Khlongnueng sub-district, Khlongluang district, Pathumthani province, Pathum Thani 12120, Thailand	Nongluck Kanitsap	Principal Investigator	1
Songklanagarind Hospital, 15 Karnjanavanich Road, Hat Yai, Songkhla 90110, Thailand	Daolada Kongkabpan	Principal Investigator	3
Srinagarind Hospital, 123, Moo.16, Mittraphap Road, Nai Muang, Khon Kaen 40002, Thailand	Kanchana Chansung	Principal Investigator	2
St. Lukes Medical Centre, Rm. 222 Medical Arts Building, St. Luke's Medical Center, 279 E. Rodriguez Sr. Ave., Quezon City 1112, Philippines	Priscilla Caguioa	Principal Investigator	1

Site	Investigator	Role	# Patients Enrolled
Makati Medical Centre, 6th Floor Cellular Therapeutics Tower 2, Makati Medical Center, 2 Amorsolo St., Legazpi Village, Makati City 1229, Philippines	Teresita Dumagay	Principal Investigator	4
Perpetual Succour Hospital, Rm. 404 Cancer Institute Bldg., Gorordo Ave., Cebu City 6000, Philippines	Lynda Mae Lepatan	Principal Investigator	2
Mary Mediatrix Medical Centre, Research Center, 6th Floor Medical Arts Building 3, JP Laurel Highway, Lipa, Batangas 4217, Philippines	Narcisa Sonia Comia	Principal Investigator	3
The Medical City, Rm. 911, MATI Bldg., Ortigas Ave., Pasig, Manila 1604, Philippines	Catherine Rosales	Principal Investigator	2
Singapore General Hospital (SGH), Outram Road, Singapore 169608, Singapore	Yeow Tee Goh	Principal Investigator	3
Hospital Cayetano Heredia, Av. Honorio Delgado 262 San Martin de Porres, Lima 15102, Peru	Victor Ulloa	Principal Investigator	3
Hospital 2 de Mayo, Av. Miguel Grau 13, Cercado de Lima, Lima 15003, Peru	Oscar Ruiz	Principal Investigator	2
Edgardo Rebagliati Hospital, Av. Edgardo Rebagliati 490 piso 8 – B, Jesús María, Lima 15702, Peru	Juan Navarro	Principal Investigator	4
Julian Coronel Medical Center, Carrera 59 No. 1 E-21, Cali 760035, Colombia	Henry Idrobo	Principal Investigator	3
University Hospital "José Eleuterio González", UANL, Av. Madero y Gonzalitos S/N, Mitras Centro, Monterrey, Nuevo León 64460, Mexico	David Gómez Almaguer	Principal Investigator	2

Total Patients: 53

Section 2. Supplementary Methodology

2.1 Full list and details of inclusion and exclusion criteria for study enrollment

Inclusion criteria

Patients were required to have:

1. Aged ≥18 years
2. A paroxysmal nocturnal hemoglobinuria (PNH) diagnosis confirmed by high-sensitivity flow cytometry (granulocyte or monocyte clone >10%)
3. Hemoglobin levels below the lower limits of normal (LLN) (male: <13.6 g/dL; female: <12.0 g/dL)
4. Lactate dehydrogenase (LDH) levels ≥1.5 times the upper limit of normal (1.5x ULN; ≥339 U/L)
5. Vaccination against *Streptococcus pneumoniae*, *Neisseria meningitidis* (types A, C, W, Y, and B), and *Haemophilus influenzae* (type B) within 2 years prior to day 1 of pegcetacoplan dosing or agree to vaccination 14 days following initiation of pegcetacoplan treatment with prophylactic antibiotic therapy for ≥14 days before and after vaccination
6. Ferritin levels ≥LLN (≥13 ng/mL) or total iron binding capacity ≤ULN (≤155 μg/dL). If a patient was receiving iron supplements at screening, the investigator must have ensured that the patient's dosage was stable for 4 weeks prior to screening, and it must have been maintained throughout the study. Patients not receiving iron at screening must not have started iron supplementation during the course of the study
7. A body mass index ≤35 kg/m^2
8. A platelet count of >50,000/mm^3
9. An absolute neutrophil count >500/mm^3
10. Agreement to use protocol-defined contraception methods in women of childbearing potential (negative pregnancy test at screening required) and men, and to refrain from male seminal fluid donation for the duration of the study and for 90 days after their last dose of study drug
11. Be willing and able to give informed consent

Exclusion criteria

Patients were excluded if they had:

1. Received treatment with any complement inhibitor (ie, eculizumab, ravulizumab) within 3 months prior to screening
2. A hereditary complement deficiency
3. History of bone marrow transplantation
4. Concomitant use of any of the following medications if the patient was not on a stable regimen for the specified period prior to screening: erythropoietin, immunosuppressants (for ≥8 weeks), systemic corticosteroids, vitamin K antagonists (ie, warfarin) with a stable international normalized ratio, iron supplements, vitamin B12, folic acid, or low-molecular-weight heparin (for ≥4 weeks)
5. History or presence of hypersensitivity or idiosyncratic reaction to compounds related to the investigational product or subcutaneous (SC) administration
6. Participated in any other investigational drug trial or exposure to other investigational agent/device/procedure within 30 days or 5 half-lives
7. Plan to become pregnant or were currently a breastfeeding woman
8. History of meningococcal disease
9. Any comorbidity or condition (such as malignancy) that, in the opinion of the investigator, could put the patient at increased risk or potentially confound study data

In addition to the inclusion and exclusion criteria, each patient's hemoglobin level was evaluated by a local or central laboratory within 5 days prior to day 1 of the study, and participants meeting the protocol-specified transfusion threshold (hemoglobin levels <7 g/dL or ≥7 and <9 g/dL with signs and symptoms of sufficient severity to warrant a transfusion) received a red blood cell (RBC) transfusion. Patients remaining within the transfusion threshold following RBC transfusion were excluded from the study.

Patients eligible for study enrollment were required to meet all inclusion criteria and none of the exclusion criteria.

2.2 Normalization of units and normal ranges for data obtained at certified local laboratories

In the case of using a certified local laboratory instead of the central laboratory due to the COVID-19 pandemic or a medical emergency, local laboratory data units and normal ranges differing from the central laboratory were converted to SI units using the method developed by Chuang-Stein[1,2] to normalize laboratory data for the purpose of analyses. If, however, the normal ranges for all laboratories were close to each other, global normal ranges were created for each laboratory parameter to be used for the analyses.

2.3 Detailed pegcetacoplan dosing and administration information

Pegcetacoplan dosing

Each pegcetacoplan dose was administered twice weekly as an SC infusion from a single-dose vial containing 1080-mg pegcetacoplan in 20 mL of sterile acetate-buffered sorbitol solution (54-mg pegcetacoplan/mL). The preferred site for SC infusion was the abdomen, but if a patient did not tolerate abdomen administration, alternative sites were considered. Pegcetacoplan administration was performed using a commercially available infusion pump with a reservoir ≥20 mL, and administration typically took approximately 30 or 60 minutes when using 2 infusion sites or 1 infusion site, respectively. Treatment compliance was monitored by requiring participants to bring their empty or used pegcetacoplan product packaging to every clinic visit.

Pegcetacoplan dose adjustments (methods)

Following commencement of treatment with pegcetacoplan, LDH concentrations were monitored. After 4 weeks of pegcetacoplan treatment and reaching a steady state, any patient receiving pegcetacoplan with LDH concentrations >2 times the ULN on 1 occasion could be considered for dose adjustments to increase pegcetacoplan dosing to 1080 mg every third day rather than twice weekly.

2.4 Detailed description of statistical analyses

Additional details regarding the statistical analyses for coprimary endpoints

The number and percentage of patients with hemoglobin stabilization, the first primary endpoint, was computed and compared between treatment groups using a stratified Cochran-Mantel-Haenszel χ-square test, and the stratified Miettinen-Nurminen method was used to determine treatment difference in percentages and 95% CIs. The second coprimary endpoint of change from baseline (CFB) in LDH levels at week 26 was evaluated using an analysis of covariance (ANCOVA) model with a multiple imputation approach for handling missing data. The ANCOVA model included terms for treatment, stratification factor, and baseline LDH concentration and estimated the difference between treatment groups, 95% CI, and *P* value. All LDH concentrations obtained prior to transfusion, withdrawal from the study or treatment, and/or escape from the control arm to pegcetacoplan were included in the model.

Handling potential bias created by missing data for coprimary endpoints

Due to the potential bias that missing data can create in terms of the outcome of statistical analyses and the subsequent estimate for the magnitude of the treatment effect, evaluation for sensitivity and supportive analyses were performed to assess the robustness of the results from the primary analysis methods. This was applied to the coprimary endpoint of hemoglobin stabilization through utilization of a logistic regression with the effects of treatment group and stratification factor included and estimating the odds ratio of hemoglobin stabilization for the pegcetacoplan arm versus the control arm and associated 95% CI. Supportive analyses for the coprimary endpoint of CFB in LDH at week 26 used a mixed-effects model for repeated measures with the fixed effects of treatment, stratification factor, visit, visit by treatment interaction, and baseline LDH concentration using an unstructured covariance matrix. CFB in LDH at week 26 also was assessed using 2 separate ANCOVA model analyses for handling missing data: (1) an ANCOVA model with a last observation carried forward approach for handling missing data that included terms for treatment, stratification factor, and baseline LDH concentration; and (2) an ANCOVA model with a baseline best observation carried forward approach for handling missing data that included terms for treatment, stratification factor, and baseline LDH concentration.

Additional details regarding the statistical analyses for secondary endpoints

Median RBC units transfused between treatment arms were compared using a Wilcoxon rank-sum test, and an unadjusted post hoc χ-square analysis compared differences between treatment arms for clinically meaningful improvements in Functional Assessment of Chronic Illness-Fatigue (FACIT-Fatigue) scores ($\geq$3-point increase).[3]

Section 3. Supplementary Results

3.1 Prior and concomitant medications

Supplementary Table 1. Prior medications in ≥15% of patients

ATC level 2 term* (most common medications in each term)	**Pegcetacoplan** **(n=35)**	**Control** *supportive care only*† **(n=18)**
Any previous medications, n (%)	31 (88.6)	16 (88.9)
Antianemic preparations, n (%) (folic acid, iron supplements‡)	28 (80.0)	15 (83.3)
Corticosteroids for systemic use, n (%) (prednisolone, prednisone)	17 (48.6)	5 (27.8)
Vitamins, n (%) (vitamin B complex, vitamin D NOS)	10 (28.6)	6 (33.3)
Antithrombotic agents, n (%) (acetylsalicylic acid, warfarin)	6 (17.1)	5 (27.8)
Mineral supplements, n (%) (calcium carbonate, potassium chloride)	9 (25.7)	1 (5.6)
Antihistamines for systemic use, n (%) (chlorphenamine, chlorphenamine maleate)	5 (14.3)	4 (22.2)
Drugs for acid-related disorders, n (%) (omeprazole, famotidine)	5 (14.3)	4 (22.2)
Diuretics, n (%) (furosemide, hydrochlorothiazide)	4 (11.4)	3 (16.7)

Prior medications are those medications taken prior to the first dose of pegcetacoplan or randomization date to the control arm.

ATC, anatomical therapeutic chemical; DDE, Drug Dictionary Enhanced; NOS, National Osteoporosis Society; WHO, World Health Organization.

*Medications are coded to ATC class (ATC level 2) and preferred term using WHO DDE Version B3 WHO Drug Global – March 2021.

†Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).

‡Ferric hydroxide polymaltose complex, ferrous fumarate, and ferrous sulphate.

Supplementary Table 2. Concomitant medication during the randomized, controlled period

ATC level 2 term (most common medications in each term)	**Overall pegcetacoplan** *includes escape patients** **(n=46)**	**Control** *supportive care only*† **(n=18)**
Any concomitant medications, n (%)	46 (100)	15 (83.3)
Concomitant medication in ≥15% of patients, n (%)		
Antibacterials for systemic use (ciprofloxacin, phenoxymethylpenicillin)	45 (97.8)	14 (77.8)
Vaccines (pneumococcal, HIB, and meningococcal vaccines‡)	45 (97.8)	1 (5.6)
Analgesics (paracetamol, meloxicam; paracetamol)	12 (26.1)	4 (22.2)
Corticosteroids for systemic use (prednisolone, prednisone)	11 (23.9)	4 (22.2)
Antihistamines for systemic use (chlorphenamine, chlorphenamine maleate, cetirizine)	7 (15.2)	5 (27.8)
Drugs for acid-related disorders (omeprazole)	8 (17.4)	2 (11.1)
Mineral supplements (potassium chloride, sodium phosphate)	8 (17.4)	1 (5.6)
Diuretics (furosemide)	2 (4.3)	3 (16.7)
Concomitant antianemic preparations and antithrombotic agents, n (%)		
Antianemic preparations (folic acid, iron supplements§)	4 (8.7)	1 (5.6)
Antithrombotic agents (warfarin, enoxaparin)	3 (6.5)	0 (0)

Concomitant medication refers to medications taken on or after first dose of pegcetacoplan or randomization date to the control arm. Medications started before the date of first dose of pegcetacoplan or randomization date and continued after first dose of pegcetacoplan or randomization date are also considered as concomitant medications. Medications are coded to ATC class (ATC level 2) and preferred term using WHO DDE Version B3 WHO Drug Global – March 2021.

HIB, *Haemophilus influenzae* type B.

*This analysis used the safety analysis set, which includes all patients who received ≥1 dose of pegcetacoplan and patients who were randomized to the control arm.

[†]Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).
[‡]Pneumococcal vaccine polysacch 23V, HIB vaccine, meningococcal vaccine A/C/Y/W, meningococcal vaccine B, and meningococcal vaccine B recombinant factor H binding protein/neisserial adhesin A/neisserial heparin binding antigen outer membrane vesicles.
[§]Ferric hydroxide polymaltose complex, and ferrous sulfate.

3.2 Pegcetacoplan exposure and patients receiving dose adjustments

The mean duration of pegcetacoplan exposure for study participants who received ≥1 dose of pegcetacoplan (n=46) was 226.5 days, and 45 patients (97.8%) completed all prescribed pegcetacoplan infusions with a mean number of 65.8 pegcetacoplan infusions per patient. One study patient (2.2%) had 2 (0.07%) interruptions in pegcetacoplan treatment.

No dose adjustments were purposefully assigned to pegcetacoplan-treated patients during the randomized, controlled period. However, 2 patients (1 patient in the pegcetacoplan arm and 1 control arm patient who escaped to pegcetacoplan) were assigned in error the dosage of 1080-mg pegcetacoplan every 3 days instead of twice weekly without clinical justification and agreement by the sponsor's medical monitor. Dosing was changed to twice weekly after the error was found and the site was retrained.

3.3 Hematologic measurements over time

Supplementary Table 3. Mean and median observed hemoglobin levels by visit

Parameter	Mean (SD)		Median (minimum, maximum)	
	Pegcetacoplan	Control*	Pegcetacoplan	Control*
		Supportive care only†		*Supportive care only*†
Hemoglobin level (g/dL)	**(n=35)**	**(n=18)**	**(n=35)**	**(n=18)**
Baseline	n=35 9.4 (1.4)	n=18 8.7 (0.8)	n=35 9.2 (6.5, 13.1)	n=18 8.6 (6.5, 13.1)
Week 2	n=33 11.2 (1.6)	n=17 8.6 (1.7)	n=33 11.3 (7.8, 14.4)	n=17 8.6 (5.9, 11.9)
Week 4	n=33 11.7 (1.8)	n=17 8.1 (1.4)	n=33 11.9 (7.5, 16.0)	n=17 7.9 (6.5, 10.8)
Week 6	n=33 12.1 (1.8)	n=16 8.7 (1.7)	n=33 12.1 (7.8, 15.6)	n=16 8.1 (5.9, 11.4)
Week 8	n=33 12.1 (2.2)	n=13 7.7 (1.5)	n=33 12.4 (4.4, 15.6)	n=13 7.8 (5.4, 10.1)
Week 10	n=32 12.2 (2.3)	n=9 9.1 (1.8)	n=32 12.7 (5.1, 15.7)	n=9 8.7 (6.4, 11.8)
Week 12	n=34 12.0 (2.2)	n=8 9.4 (2.5)	n=34 12.4 (6.7, 15.1)	n=8 8.4 (6.6, 14.0)
Week 14	n=34 11.9 (2.3)	n=8 8.4 (1.2)	n=34 12.5 (5.4, 16.6)	n=8 8.2 (6.8, 10.8)
Week 16	n=34 12.1 (2.6)	n=8 8.1 (0.8)	n=34 12.7 (5.4, 16.1)	n=8 7.9 (7.0, 9.1)
Week 18	n=34 12.3 (2.3)	n=8 9.4 (1.7)	n=34 12.8 (4.4, 16.0)	n=8 9.5 (7.1, 11.5)
Week 20	n=33 12.5 (2.0)	n=7 8.8 (1.8)	n=33 12.8 (8.3, 16.2)	n=7 8.7 (5.8, 10.9)
Week 22	n=33 12.6 (2.1)	n=6 9.7 (1.3)	n=33 12.5 (8.6, 17.1)	n=6 9.6 (8.0, 11.4)
Week 24	n=34 12.6 (2.3)	n=7 9.3 (2.1)	n=34 13.0 (7.1, 16.5)	n=7 8.7 (7.4, 13.0)
Week 26	n=30 12.8 (2.1)	n=6 9.8 (2.4)	n=30 12.9 (8.0, 16.2)	n=6 9.1 (7.3, 14.4)

*All values after escape from control to pegcetacoplan were set to missing.

[†]Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).

Supplementary Table 4. Mean and median observed LDH levels by visit

Parameter	Mean (SD)		Median (minimum, maximum)	
	Pegcetacoplan	Control*	Pegcetacoplan	Control*
		Supportive care only†		*Supportive care only*†
LDH level (U/L)	**(n=35)**	**(n=18)**	**(n=35)**	**(n=18)**
Baseline	n=35 2150.9 (909.4)	n=18 1945.9 (1003.7)	n=35 2144.5 (538, 4946)	n=18 2007.8 (630, 4896)
Week 2	n=32 242.2 (109.6)	n=17 1887.4 (1041.8)	n=32 213.0 (129, 753)	n=17 1828.0 (438, 5008)
Week 4	n=33 150.4 (45.7)	n=17 1979.3 (1139.3)	n=33 148.0 (91, 337)	n=17 2012.0 (240, 4612)
Week 6	n=33 153.9 (45.8)	n=17 1930.8 (1337.5)	n=33 147.0 (102, 330)	n=17 1641.0 (606, 5582)
Week 8	n=33 165.1 (51.6)	n=13 1879.3 (1380.9)	n=33 158.0 (56, 351)	n=13 1895.0 (548, 5891)
Week 10	n=34 173.5 (43.7)	n=9 2088.0 (1253.1)	n=34 167.5 (58, 309)	n=9 1894.0 (664, 4899)
Week 12	n=34 185.1 (39.9)	n=8 2057.9 (1202.6)	n=34 171.5 (127, 311)	n=8 1898.0 (732, 4550)
Week 14	n=34 185.7 (45.5)	n=8 2114.9 (1433.0)	n=34 176.6 (123, 351)	n=8 1831.5 (592, 4964)
Week 16	n=34 190.8 (69.5)	n=8 2036.8 (1492.9)	n=34 183.0 (121, 540)	n=8 1670.0 (613, 5208)
Week 18	n=33 204.1 (103.2)	n=8 2243.9 (1547.5)	n=33 179.5 (122, 700)	n=8 1892.5 (719, 5544)
Week 20	n=34 181.7 (59.0)	n=7 2566.5 (2842.3)	n=34 165.0 (112, 441)	n=7 1408.0 (626, 8800)
Week 22	n=33 187.6 (51.0)	n=6 1629.2 (893.5)	n=33 172.0 (124, 343)	n=6 1470.0 (811, 3123)
Week 24	n=34 190.9 (62.5)	n=7 1466.8 (801.0)	n=34 183.7 (104, 473)	n=7 1747.0 (418, 2538)
Week 26	n=30 204.6 (90.0)	n=5 1535.0 (751.6)	n=30 181.0 (109, 612)	n=5 1895.0 (626, 2314)

*All values after escape from control to pegcetacoplan were set to missing.
†Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).

3.4 Additional transfusion-related endpoints

Improvement in transfusion burden with pegcetacoplan was further demonstrated by a significantly lower value for median transfusions among patients in the pegcetacoplan arm compared with the control arm (difference in median units, 3.0; 95% CI: 2.0, 4.0; *P* <0.0001) (Table S5). A composite analysis of transfusion requirements and reduced hemoglobin levels found that fewer patients in the pegcetacoplan arm received a transfusion and/or had a >2-g/dL decrease in hemoglobin from baseline (11.4%, n=4) versus the control arm (100.0%, n=18) (difference, –75.1%; 95% CI: –90.4%, –59.7%; *P* <0.0001) (Table S5).

Supplementary Table 5. Additional transfusion-related endpoints

Transfusion-related endpoint	**Pegcetacoplan (n=35)**	**Control** *supportive care only** **(n=18)**	***P*** **Difference (95% CI)**
Total number of transfusion units,[†] n (median units; range)	21 (0.0; 0-19[‡])	59 (3.0; 0-13)	*P* <0.0001 3.0 2.0, 4.0
Patients who received a transfusion and/or had a decrease in hemoglobin >2 g/dL from baseline (yes),[§] n (%)	4 (11.4)	18 (100.0)	*P* <0.0001 –75.1 –90.4, –59.7

*****Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).

[†]Transfusions were defined as any transfusion of RBCs, leukocyte-depleted packed RBCs, leukocyte-poor packed RBCs, leukocyte-poor blood, or whole blood.

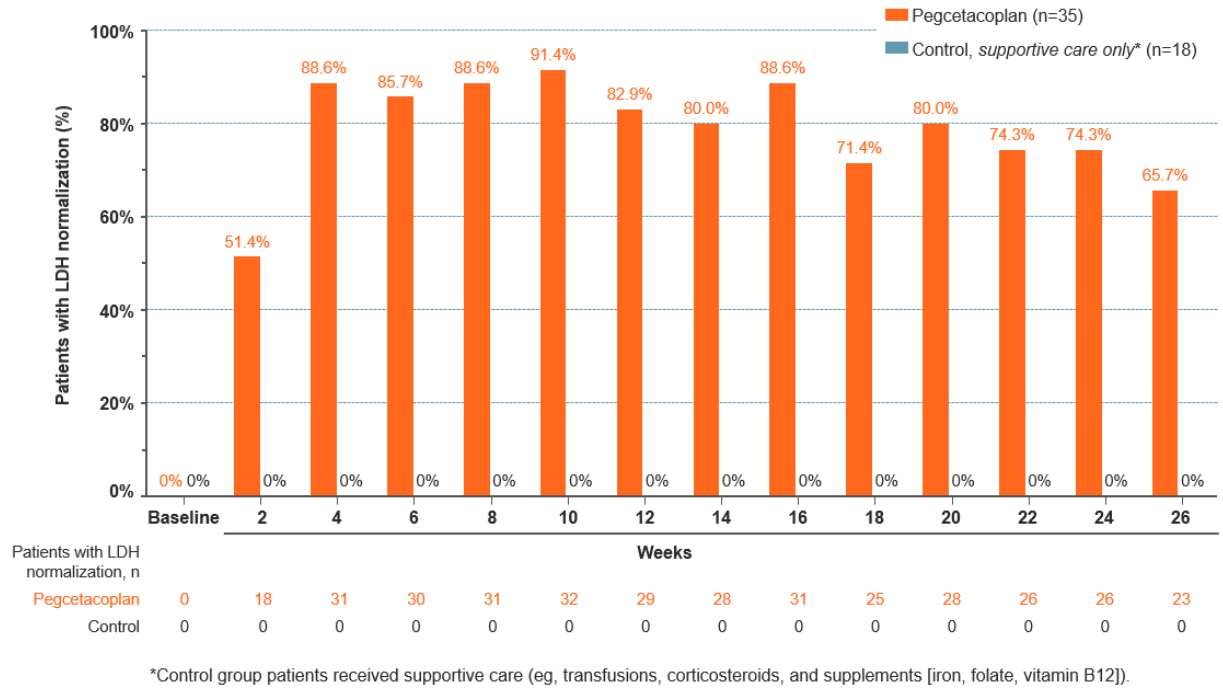
[‡]Patient who died due to septic shock in the context of bone marrow failure, which was unrelated to pegcetacoplan, received 19 units of transfusion.

[§]Patients who received a transfusion through week 26, had a decrease in hemoglobin levels >2 g/dL from baseline, escaped from the control arm to pegcetacoplan treatment, withdrew from the study, or were lost to follow-up were categorized as “Yes”.

3.5 LDH normalization

The percentage of patients with LDH normalization at each respective timepoint from baseline to week 26 among pegcetacoplan arm patients and control arm patients is shown in the supplementary figure. Patients who received a transfusion, escaped from the control arm to pegcetacoplan treatment, withdrew from the study before week 26, or were lost to follow-up were categorized as non-responders.

Supplementary Figure 1. LDH normalization from baseline to week 26



*Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).

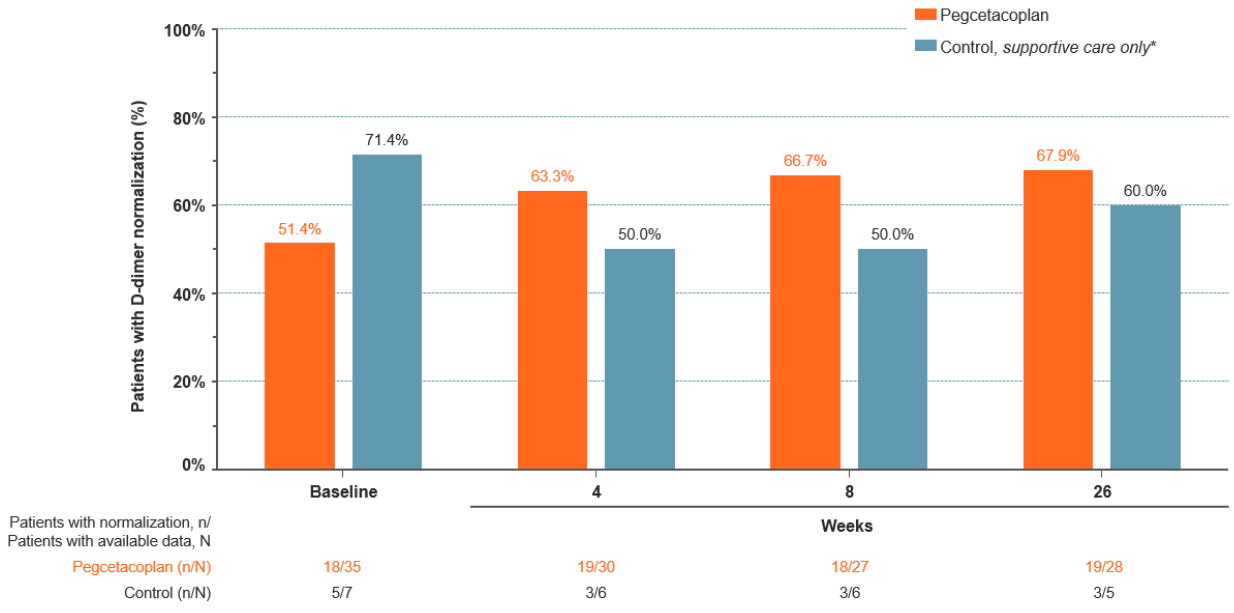
3.6 Post hoc analyses

Supplementary Table 6. Post hoc analyses: mean CFB to week 26 in hematologic parameters and FACIT-Fatigue and EORTC QLQ-C30 scale scores for patients randomized to pegcetacoplan group

Parameter	Mean (SD)			*P**
	Baseline	Week 26	CFB [95% CI]	
LDH, U/L, n=30	2261.7 (909.0)	204.6 (90.0)	–2057.0 (925.08) [–2402.53, –1711.67]	<0.001
Hemoglobin, g/dL, n=30	9.6 (1.4)	12.8 (2.1)	3.16 (1.93) [2.447, 3.876]	<0.001
ARC, cells x 10^9/L, n=26	249.9 (76.5)	101.2 (30.8)	–148.7 (75.27) [–179.12, –118.32]	<0.001
FACIT-Fatigue Scale score, n=28	35.8 (10.3)	45.3 (7.3)	9.5 (9.93) [5.65, 13.35]	<0.001
EORTC QLQ-C30 scale score, n=27	61.9 (19.5)	83.3 (14.7)	21.91 (21.58) [13.378, 30.449]	<0.001

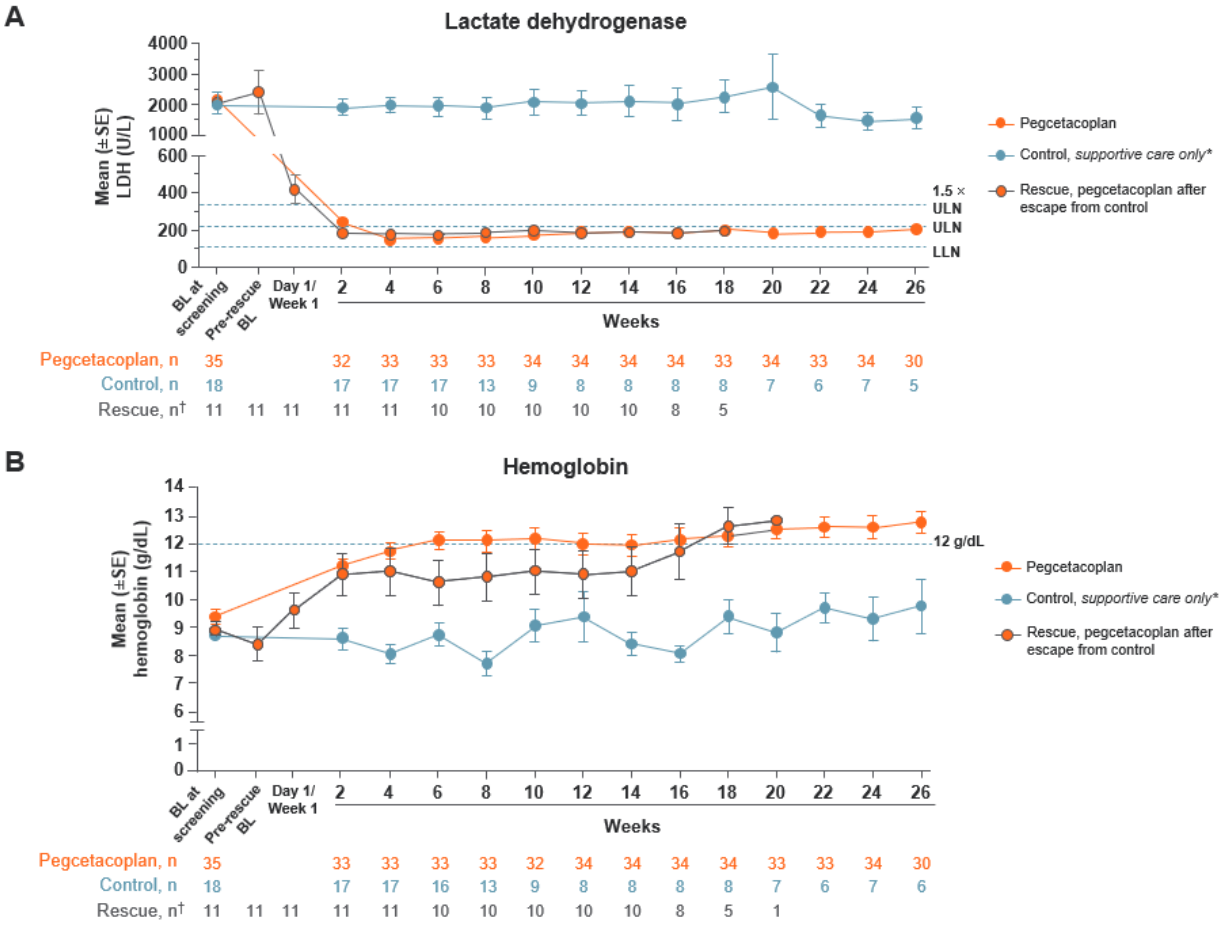
ARC, absolute reticulocyte count; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30.
*Calculated with student t-test.

Supplementary Figure 2. Post hoc analyses: D-dimer normalization from baseline to week 26 for patients randomized to pegcetacoplan or supportive care



*Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]). The control group did not include the patients who escaped to pegcetacoplan treatment (n=11) during the 26-week study period.

Supplementary Figure 3. Post hoc analyses: time-aligned mean LDH (A) and hemoglobin (B) levels from baseline to end of study for patients who switched from supportive care to pegcetacoplan



BL, baseline; LDH, lactate dehydrogenase; LLN, lower limit of normal; PEG, pegcetacoplan; SE, standard error; ULN, upper limit of normal.
*Control group patients received supportive care (eg, transfusions, corticosteroids, and supplements [iron, folate, vitamin B12]).
†Rescue n is the number of patients from the control arm that switched to pegcetacoplan when hemoglobin decreased by ≥2 g/dL from baseline. Baseline for the escape group was the time of the switch to pegcetacoplan. Due to the time alignment based on treatment with pegcetacoplan, this group does not have data out to week 26.

Supplementary Appendix References

1. Chuang-Stein C. Summarizing laboratory data with different reference ranges in multi-center clinical trials. *Drug Inf J.* 1992;26(1):77-84.
2. Chuang-Stein C. Some issues concerning the normalization of laboratory data based on reference ranges. *Drug Inf J.* 2001;35(1):153-156.
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