Supplementary Materials

Summary of Eligibility Criteria

The Period 1 major inclusion criteria were: Japanese men and women aged ≥20 years; hemodialysis or hemodiafiltration three times per week for at least 12 weeks prior to the start of the screening period (Scr Visit 1); erythropoietin-stimulating agent (ESA) therapy for at least 4 weeks prior to Scr Visit 1; mean hemoglobin (Hb) level at Scr Visit 1 and 2 weeks later (Scr Visit 2) of 9.5–12.0 g/dL with an absolute difference of ≤1.0 g/dL; and transferrin saturation (TSAT) >20% or ferritin >75 ng/mL at either Scr Visit 1.

The Period 1 major exclusion criteria were: concurrent presence of uncontrolled hypertension or severe hepatobiliary disease; onset of myocardial infarction, cerebral infarction, or venous thromboembolism within 24 weeks prior to Scr Visit 1; intact-parathyroid hormone (PTH) ≥500 pg/mL at Scr Visit 1; receipt of an erythrocyte transfusion or surgery involving massive blood loss in the 12 weeks prior to Scr Visit 1; receipt of intravenous iron therapy in the 4 weeks prior to Scr Visit 1, or initiation of or withdrawn from oral iron therapy or receipt of oral iron therapy at different doses in the 4 weeks prior to Scr Visit 1; receipt of protein anabolic hormones, testosterone enanthate, or mepitiostane in the 12 weeks prior to Scr Visit 1; severe infection, systemic blood disorder, hemolytic anemia, or obvious bleeding lesions such as gastrointestinal hemorrhage; and suspected anemia caused by noninfectious chronic inflammatory disease.

The Period 2 inclusion criteria were: participating in Period 1 and suitable for prolonged receipt of study treatment according to the judgment of the principal investigator or the subinvestigator; and Hb level ≥8.0 g/dL and <13.0 g/dL at Week 6.

Table S1. Iron-related parameters at Week 0.

Iron-related parameters at Week 0 Median (Q1, Q3)	Placebo (*n* = 22)	Enarodustat 2 mg (*n* = 21)	Enarodustat 4 mg (*n* = 20)	Enarodustat 6 mg (*n* = 22)
Serum iron (μg/dL)	62.5 (52.0, 76.0)	67.0 (54.0, 71.0)	70.5 (57.0, 83.5)	63.5 (52.0, 77.0)
Ferritin (μg/L)	81.0 (37.9, 115.0)	85.1 (36.5, 166.0)	53.5 (32.1, 80.6)	98.6 (36.7, 169.0)
Hepcidin (μg/L)	67.1 (24.6, 127.0)	130.0 (38.3, 199.0)	59.9 (26.1, 79.3)	64.9 (37.0, 156.0)
TIBC (μg/dL)	248.0 (216.0, 273.0)	248.0 (217.0, 262.0)	258.0 (222.5, 275.0)	231.5 (207.0, 250.0)
TSAT (%)	23.7 (22.1, 30.0)	26.7 (20.2, 33.5)	26.5 (23.1, 30.2)	27.5 (23.3, 35.4)

TIBC, total iron-binding capacity; TSAT, transferrin saturation

Table S2. Descriptive statistics of EPO and VEGF in Period 1.

			Placebo	Enarodustat 2 mg	Enarodustat 4 mg	Enarodustat 6 mg
EPO (IU/L)	Week 0	*n*	22	21	20	22
		Median	20.00	17.80	19.20	22.05
		Q1, Q3	14.60, 38.00	13.80, 26.90	14.90, 30.95	14.20, 46.70
	Week 2	*n*	21	18	20	21
		Median	13.30	17.95	27.30	33.40
		Q1, Q3	12.10, 16.20	12.70, 20.90	20.00, 91.35	24.40, 53.30
	Week 4	*n*	21	18	18	19
		Median	13.80	15.95	24.05	32.00
		Q1, Q3	12.40, 15.50	14.30, 19.70	16.50, 36.10	18.50, 63.80
	Week 6	*n*	17	17	19	15
		Median	14.50	18.40	22.50	23.70
		Q1, Q3	13.50, 15.70	13.60, 21.10	18.80, 33.30	16.80, 38.30
VEGF (ng/L)	Week 0	*n*	22	21	20	22
		Median	41.95	45.70	44.80	46.00
		Q1, Q3	35.00, 56.00	38.90, 70.10	32.40, 56.15	31.10, 55.40
	Week 2	*n*	21	18	20	21
		Median	43.70	43.80	45.85	51.10
		Q1, Q3	38.60, 54.90	34.70, 50.50	39.20, 68.90	43.90, 63.80
	Week 4	*n*	21	18	18	19
		Median	45.20	46.50	49.95	53.70
		Q1, Q3	42.40, 54.40	36.40, 52.70	32.40, 53.90	40.10, 60.00
	Week 6	*n*	17	17	19	15
		Median	46.10	44.20	46.00	47.10
		Q1, Q3	31.50, 55.00	37.10, 50.80	34.40, 63.60	41.70, 59.30