**Supplementary Materials**

**Summary of Eligibility Criteria**

Eligibility criteria for Period 1: Japanese, aged ≥20 years with chronic kidney disease (CKD) not on dialysis (estimated glomerular filtration rate <60 mL/min/1.73 m2) and unlikely to require dialysis or renal transplantation before completion.

Major inclusion criteria for Period 1: mean Hb at Screening (Scr) Visit 1 and Scr Visit 2 of 8.0–10.5 g/dL for the correction group and 9.5–12.0 g/dL for the conversion group; absolute difference in Hb between the two time points ≤1.0 g/dL in both groups; transferrin saturation >20% or ferritin >50 μg/L at Scr Visit 1; Erythropoiesis-stimulating agent not received for ≥12 weeks before Scr Visit 1 for the correction group; stable Erythropoiesis-stimulating agent treatment for ≥8 weeks before Scr Visit 1 at a dosing interval of 2 or 4 weeks, the last two doses before Scr Visit 1 being the same, for the conversion group.

Major exclusion criteria for Period 1 included poorly controlled hypertension; severe hepatobiliary disease; development of acute kidney injury within 12 weeks before Scr Visit 1; development of myocardial infarction, cerebral infarction, or venous thromboembolism within 24 weeks before Scr Visit 1; Intact parathyroid hormone of ≥500 ng/L at Scr Visit 1; having received an erythrocyte transfusion or undergone surgery involving massive blood loss within 12 weeks before Scr Visit 1; having received intravenous iron therapy within 4 weeks before Scr Visit 1, or having been started on or withdrawn from oral iron therapy or received oral iron therapy at different doses within 4 weeks before Scr Visit 1; having received protein anabolic hormones, testosterone enanthate, or mepitiostane within 12 weeks before Scr Visit 1; having severe infection, systemic blood disorder, hemolytic anemia, or obvious bleeding lesions, such as gastrointestinal hemorrhage; suspected to have anemia caused by noninfectious chronic inflammatory disease.

Major inclusion criteria for Period 2 were: participants in Period 1 who, in the judgment of the principal investigator or the sub-investigator, were fit to undergo extended study treatment; unlikely to require dialysis or renal transplantation during the period from Week 6 (6 weeks after the start of treatment) to the end of the study; Hb ≥8.0 g/dL and <13.0 g/dL at Week 6.

**Fig. S1. Subject disposition.**





(a) Correction group, (b) Conversion group.

**Table. S1: Iron-related Parameters at Week 0.**

Correction group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Iron-related parameters at Week 0Median (Q1, Q3) | Placebo(*n* = 23) | Enarodustat2 mg(*n* = 24) | Enarodustat4 mg(*n* = 24) | Enarodustat6 mg(*n* = 23) |
| Serum iron (µg/dL) | 78.0 (62.0, 87.0) | 76.5 (65.0, 81.0) | 75.5 (67.0, 92.0) | 77.0 (66.0, 91.0) |
| Ferritin (µg/L) | 159.0 (103.0, 244.0) | 94.9 (59.9, 194.5) | 130.5 (52.8, 181.5) | 131.0 (89.4, 269.0) |
| Hepcidin (µg/L) | 89.3 (33.5, 144.0) | 65.0 (35.5, 108.5) | 49.3 (34.8, 104.3) | 70.8 (46.0, 125.0) |
| TIBC (µg/dL) | 272.0 (245.0, 291.0) | 258.5 (240.5, 272.0) | 255.5 (242.0, 301.0) | 252.0 (241.0, 283.0) |
| TSAT (%) | 28.7 (23.7, 33.6) | 29.9 (25.4, 33.7) | 28.6 (22.5, 33.4) | 29.4 (24.4, 36.4) |

Conversion group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Iron-related parameters at Week 0Median (Q1, Q3) | Placebo(*n* = 26) | Enarodustat2 mg(*n* = 26) | Enarodustat4 mg(*n* = 27) | Enarodustat6 mg(*n* = 27) |
| Serum iron (µg/dL) | 90.5 (78.0, 103.0) | 77.5 (64.0, 97.0) | 87.5 (77.0, 103.0) | 85.0 (73.0, 99.0) |
| Ferritin (µg/L) | 150.0 (82.5, 193.0) | 165.0 (86.1, 226.0) | 145.0 (66.0, 179.0) | 114.0 (70.9, 215.0) |
| Hepcidin (µg/L) | 95.6 (61.0, 126.0) | 87.3 (52.5, 173.0) | 80.7 (54.5, 153.0) | 88.6 (44.3, 206.0) |
| TIBC (µg/dL) | 261.5 (236.0, 299.0) | 256.0 (234.0, 285.0) | 266.0 (248.0, 291.0) | 269.0 (247.0, 300.0) |
| TSAT (%) | 32.1 (27.6, 39.0) | 28.7 (22.4, 35.9) | 34.3 (24.9, 39.3) | 33.1 (25.6, 35.2) |

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