SUPPLEMENTARY MATERIAL

Switching from Epoetin Alfa (Epogen®) to Epoetin Alfa-epbx (Retacrit™) Using a Specified Dosing Algorithm: A Randomized, Non-Inferiority Study in Adults on Hemodialysis

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Protocol withdrawal criteria

Patients randomized into the trial who were determined to meet any of the following criteria were withdrawn from the study:

1. Patients who were determined to have a clinically serious intercurrent illness onset during the course of the study, as determined by the clinical judgment of the investigator. Serious intercurrent illnesses included, but were not limited to, blood transfusion, myocardial infarction, stroke, heart failure, blood clots, menorrhagia, peptic ulcer disease, gastrointestinal bleeding, blood dyscrasia, hemoglobinopathy, or blood loss of >475 mL by volume (including plasmapheresis).
2. Patients noted to have antibodies against erythropoietin by positive test results for anti-recombinant human erythropoietin antibodies.
3. Female patients who became pregnant.
4. Retacrit™-arm patients who had more than 12 missed doses of Retacrit™ during the study, more than 3 missed doses during Weeks 13–24 of the study, and/or who had more than 3 missed-plus-alternate doses.
5. Standard-of-care-arm patients who had more than 12 missed doses of Epogen® during the study or more than 3 missed doses during Weeks 13–24 of the study, and/or who had more than 3 missed-plus-alternate doses.
6. Any patients who received a prohibited concomitant therapy, including but not limited to a long-acting erythropoiesis-stimulating agent.
7. Use of anticoagulation therapy, including warfarin with a target international normalized ratio (INR) of 2 or greater. Anti-platelet therapy (e.g., aspirin or clopidogrel) was permitted, as was heparin given during hemodialysis. Low-dose warfarin was permitted and defined as the presence of at least two INR values less

than or equal to 1.5 during the 120 days prior to enrollment and no values exceeding 1.5 at any time after 120 days prior to enrollment.

Patients started on warfarin with a known INR goal of 2.0 or greater were to receive no further treatment with the study drugs, but follow-up visits could continue.

Patients on warfarin who met criteria to enter the study were terminated if an INR >2.0 was discovered or if no INR was available for 60 days.

Table S1. Mean change from baseline in weekly mean ESA dose (U/week) over the final 8 weeks of the study (full analysis set)

	Retacrit™ (N=212)	Standard-of-care (N=206)
n	180	174
Mean (SD)	−1728.2 (8785.9)	−937.9 (8669.7)
LS mean (SE)	−1861.8 (563.5)	−799.8 (573.1)
95% CI of LS mean	(−2970.0, −753.5)	(−1927.0, 327.5)
LS mean difference against standard-of-care (SE)	−1062.0 (804.0)	
95% CI of LS mean difference against standard-of-care	(−2643.2, 519.2)	
P-value against standard-of-care[a]	0.1874	

Standard-of-care is equivalent to Epogen®.

[a] *P*-value calculated using analysis of covariance model with treatment as factor and baseline ESA dose as covariate.

CI, confidence interval; ESA, erythropoiesis-stimulating agent; LS, least-squares; N, total number of patients; n, number of patients meeting specified criteria; SD, standard deviation; SE, standard error; U, unit.

Table S2. Percentage of patients with mean hemoglobin levels within specified ranges at baseline and over the final 8 weeks of study treatment (full analysis set)

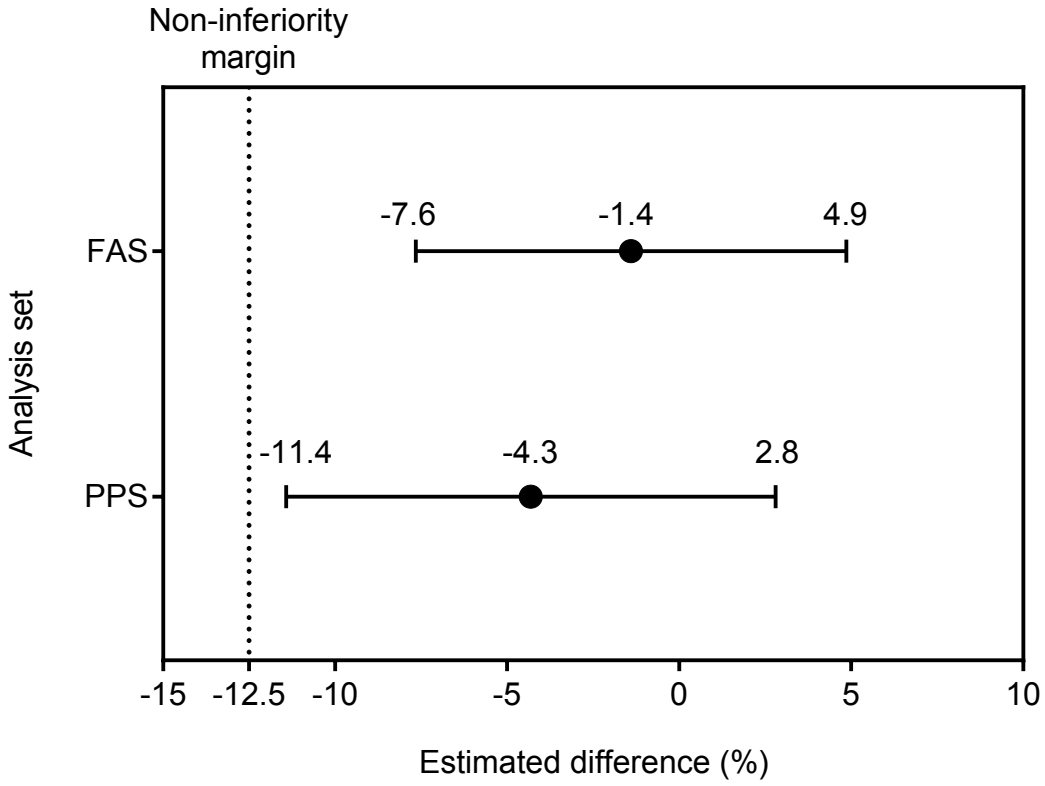
	Retacrit™		Standard-of-care	
Mean hemoglobin range	**Baseline (N=178) n (%)**	**Final 8 weeks (N=178) n (%)**	**Baseline (N=173) n (%)**	**Final 8 weeks (N=173) n (%)**
<8 g/dL	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)
≥8 to <9 g/dL	4 (2.2)	5 (2.8)	1 (0.6)	6 (3.5)
≥9 to <10 g/dL	23 (12.9)	20 (11.2)	21 (12.1)	22 (12.7)
≥10 to ≤11 g/dL	105 (59.0)	101 (56.7)	106 (61.3)	92 (53.2)
>11 to ≤12 g/dL	44 (24.7)	51 (28.7)	42 (24.3)	49 (28.3)
>12 g/dL	2 (1.1)	1 (0.6)	3 (1.7)	2 (1.2)

Baseline defined as the mean of the hemoglobin measurements during the 8 weeks before the first administration of study drug. Data for patients with at least one hemoglobin value available in the baseline period and at least one value at the end of the treatment period were used for the analysis of hemoglobin levels.

Standard-of-care is equivalent to Epogen®.

N, total number of patients; n, number of patients meeting specified criteria.

Fig. S1. Estimated difference in proportion of time (%) patients' hemoglobin levels were 9–11 g/dL over the final 8 weeks of the study and 95% CI (full analysis set and per protocol set)



A clustered binomial analysis using the logistic regression method was performed with centered version of baseline hemoglobin levels included as a covariate. The generalized estimating equation method was used to construct 95% two-sided CIs.

In the analysis in the FAS, data were included from 178 patients in the Retacrit™ arm and 173 patients in the standard-of-care arm. Corresponding patient numbers in the analysis in the per protocol set were 137 and 130, respectively.

An estimated difference <0 indicates a lower proportion in the Retacrit™ arm versus the standard-of-care arm.

CI, confidence interval; FAS, full analysis set.