

# ONCE MONTHLY C.E.R.A. PROVIDES STABLE Hb LEVELS WITHIN NARROW TARGET RANGES FOLLOWING DIRECT SWITCH FROM SHORTER ACTING ESA - THE MIRACEL STUDY

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## INTRODUCTION

- Current KDOQI guidelines<sup>1</sup> recommend that the haemoglobin (Hb) of patients with renal anaemia receiving dialysis should be maintained at a stable level, within a narrow range of 11.0-12.0 g/dL.
- Many patients with renal anaemia receiving erythropoiesis-stimulating agents (ESAs) experience fluctuations in Hb levels outside this range.<sup>2,3</sup> Hb variability is associated with increased mortality.<sup>4</sup>
- One potential strategy to preserve Hb stability is to employ longer-acting ESA therapy, since multiple dose changes are associated with Hb cycling.<sup>4</sup> Continuous erythropoietin receptor activator (C.E.R.A.) is a new, long-acting ESA that is approved for once-monthly (QM) administration in dialysis patients.
- MIRACEL is the first real-life study to investigate direct switching from shorter-acting ESAs to once-monthly C.E.R.A. administered using pre-filled syringes in chronic kidney disease (CKD) patients on haemodialysis.

## OBJECTIVE

- To evaluate the effect of a simple monthly C.E.R.A. regimen using pre-filled syringes on maintenance of stable Hb levels within a specified range in haemodialysis patients in a routine clinical setting.

## METHODS

### Study design

- MIRACEL was a Phase IIIb, multicentre, single-arm study.
- After a 2-month screening period, patients who had been previously treated with either epoetin alfa, beta, or delta, or darbepoetin alfa (intravenous [IV] or subcutaneous [SC]), administered tiw-q2w, were switched to once-monthly IV C.E.R.A. administered via pre-filled syringes.
- After a 5-month titration phase, Hb levels were analysed during a 3-month evaluation phase (Figure 1).
- The target range for Hb levels was 11.0-12.5 g/dL (MIRACEL was initiated before new KDOQI guidelines were introduced recommending an Hb target range of 11.0-12.0 g/dL<sup>1</sup>).

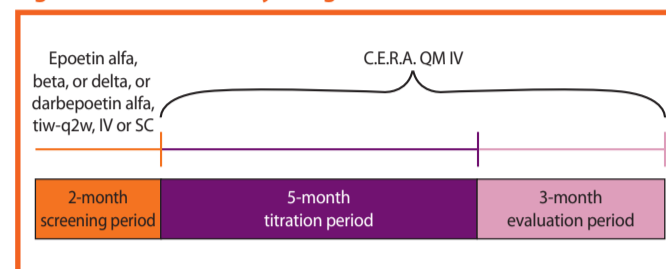
### Patients

- Major inclusion criteria:
  - Patients (aged  $\geq 18$  years) with chronic renal anaemia receiving regular haemodialysis for  $\geq 12$  weeks
  - Baseline Hb 10.0-13.0 g/dL
  - Stable IV or SC maintenance treatment with epoetin alfa, beta, or delta, or darbepoetin alfa, administered from three times weekly to once every 2 weeks (tiw-q2w) for 4 weeks before the screening period
  - Adequate iron status.
- Major exclusion criteria:
  - Blood transfusion or gastrointestinal bleeding within the last 8 weeks before the screening period
  - Severe diseases
  - Thrombocytes  $>500 \times 10^9/L$  or  $<100 \times 10^9/L$
  - Life expectancy  $<12$  months.

### Primary efficacy variables

- The number of patients with Hb values in the range 11-12.5 g/dL or 10-13 g/dL at all three visits during the evaluation phase ('responders').

Figure 1. MIRACEL study design



## RESULTS

### Patients and treatment

- 424 patients were enrolled and started C.E.R.A. therapy (safety population) (Table 1).
- 416 (98.1%) patients provided at least one Hb value during C.E.R.A. treatment (intent-to-treat [ITT] population).
- 72.2% of patients were receiving epoetin and 27.8% were receiving darbepoetin before study entry (Table 1).

Table 1. Patient characteristics at baseline (safety population, n=424)

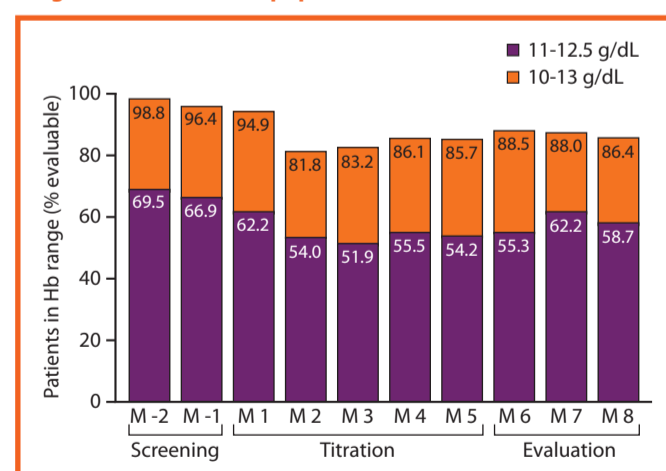
Male, n (%)	258 (60.8)
Median age, years (range)	66.0 (24-93)
Caucasian, n (%)	416 (98.1)
Previous ESA treatment, n (%)	
Epoetin alfa	113 (26.7)
Epoetin beta	188 (44.3)
Epoetin delta	5 (1.2)
Darbepoetin alfa	118 (27.8)
Previous route of ESA administration, n (%)	
IV	336 (79.2)
SC	88 (20.8)
Mean (SD) Hb, g/dL	11.7 (0.84)
Diabetes mellitus, n (%)	90 (21.2)
Mean (SD) time on dialysis, years	4.3 (4.3)

ESA, erythropoiesis-stimulating agent; Hb, haemoglobin

### Efficacy

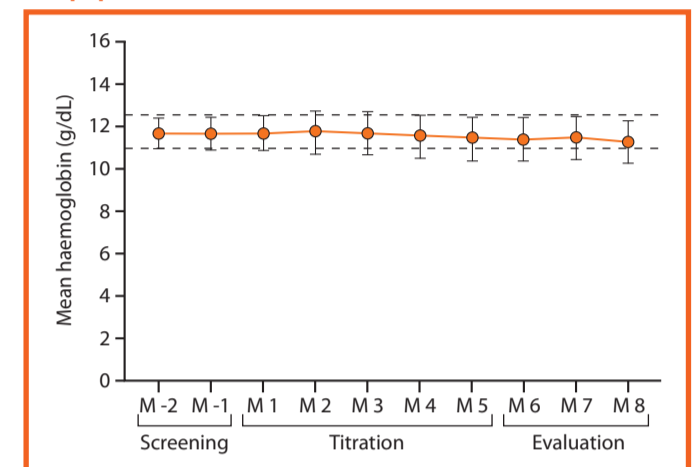
- For the primary efficacy variables, 30.8% and 74.9% of evaluable patients had an Hb value in the range 11-12.5 g/dL and 10-13 g/dL, respectively, at all visits during the evaluation phase ('responders') (Figure 2).

Figure 2. Percentage of evaluable patients achieving Hb target ranges at each visit (ITT population)



- Among patients who completed the study on C.E.R.A., 31.7% and 75.6% of patients were in the range 11-12.5 g/dL or 10-13 g/dL, respectively, at all visits during the evaluation phase.
- Hb levels remained stable during the titration and evaluation period (Figure 3). Mean (SD) Hb was 11.7 (0.7) mg/dL, 11.6 (0.9) mg/dL and 11.4 (1.0) mg/dL during the screening, titration and evaluation phases, respectively.
- The majority of patients showed only small fluctuations in Hb level. There was  $\leq 1$  g/dL change from phase-specific individual mean values in 70.4% of patients during the titration phase and 82.9% of patients during the evaluation phase.

Figure 3. Mean ( $\pm$ SD) Hb values during the course of the study (ITT population, n=416)



- The mean C.E.R.A. dose throughout the study was  $142 \pm 48 \mu\text{g}$  (titration period  $140 \pm 43 \mu\text{g}$ , evaluation period  $145 \pm 188 \mu\text{g}$ ).
- Patients required an average of two C.E.R.A. dose changes (Table 2).

Table 2. C.E.R.A. dose changes during titration and evaluation phases (ITT population, n=416)

Any change	
Mean (SD)	2.0 (1.4)
Median (range)	2.0 (0-5)

### Safety and tolerability

- C.E.R.A. was generally well tolerated, with a safety profile similar to that reported in Phase III studies.

## CONCLUSIONS

- Converting haemodialysis patients with renal anaemia from conventional ESA therapy to once-monthly IV C.E.R.A. using pre-filled syringes in a real-life setting is easily achieved, safe and tolerable. This regimen offers a high degree of Hb stability, accomplished within an average of two dose modifications per patient.

## REFERENCES

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2. Berns JS et al. Kidney Int 2003; 64: 1514-1521.
3. Fishbane S, Berns JS. Kidney Int 2005; 68: 1337-1343.
4. Yang W et al. J Am Soc Nephrol 2007; 18: 3164-3170.

### MIRACEL Study Investigators

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