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C.E.R.A. IN CKD

General Medicine

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ABSTRACT

Objective: To evaluate once-monthly continuous erythropoiesis receptor activator (C.E. R.A.) in patients with chronic kidney disease (CKD) for one year under standard conditions.
Methods: In a non-interventional study, C.E.R.A. was administered according to local practice in patients with dialysis dependent or non-dialysis dependent CKD.
Results: 20 patients were evaluable to month 12. In the dialysis dependent and non dialysis dependent patients who had received ESA therapy prior to study entry, Hb remained stable from baseline to the end of the study. The mean (SD) dose of C.E.R.A. was 114 (78) µg in dialysis dependent patients and 97 (71) µg in non-dialysis dependent patients at baseline, remaining virtually unchanged during the study (109 (76) µg and 99 (68) µg).
Conclusions: Once-monthly C.E.R.A. is effective and convenient in dialysis dependent and non-dialysis dependent patients with renal anemia under routine conditions for at least one year, and requires few dose changes. C.E.R. A. was well-tolerated with a good safety profile over the two-year study period.

KEYWORDS

INTRODUCTION :

- Hemoglobin (Hb) control in patients with CKD centers on erythropoiesis-stimulating agent (ESA) therapy , but the short half-lives of conventional ESAs, such as **epoetin alfa and epoetin delta**, necessitate relatively frequent dosing (one to three times a week). The impact on patients and for the healthcare system, and the fact that **frequent ESA administration may contribute to increased Hb fluctuation** , led to the investigation of agents with longer dosing intervals

- **Darbepoetin alfa** was developed, ith a half-life of approximately **25 hours** when administered intravenously, and more recently the continuous erythropoiesis receptor activator **(C.E.R.A.)** was introduced, which has a **half-life of more than 100 hours**. As a result, C.E.R.A. can be given once a month during the maintenance phase of management .

METHODS:

- **Study design:** This was a non-interventional, 12-month study undertaken during JANUARY 2020 to DECEMBER 2020. Patients provided written informed consent prior to study entry.
- **Recruitment and C.E.R.A. administration:** All patients with dialysis-dependent stage 5 CKD or non-dialysis dependent stage 4 CKD for whom the treating physician had decided to manage renal anemia with C.E.R.A. were eligible for inclusion in the study. All patients were required to be at least 18 years of age with a life expectancy of more than 12 months and pregnant females were excluded.

Data collection :

- At subsequent standard clinic visits, information was recorded on C.E.R.A. administration, requirement for dialysis , laboratory values, and adverse events and serious adverse events, including causal relationship to C.E.R.A. treatment.
- Serious adverse events were defined as adverse events considered fatal or life threatening, which necessitated hospitalization or extension of hospitalization, resulted in permanent or serious disability or invalidity, or which were regarded as clinically significant

DATA ANALYSIS:

- All analyses were descriptive in nature. Efficacy and C.E.R.A. dosing data are shown here from the month 12 efficacy population, defined as all patients with at least one Hb level recorded at the end of the full study period, defined as any Hb value within the period month 11 to month 12. Safety analyses are based on all patients who received at least one dose of C.E.R.A.

RESULTS :

• Study population:
Baseline characteristics (month 24 efficacy population) Total (n=20)
Age, years 63.8 (14.2)
Male gender, n (%) 11 (54.9)
Dialysis-dependent at study entry 16 (79.6)
Time since start of dialysis, years 4.5 (4.1)
ESA therapy in 16 weeks prior to study entry, n (%)
None 2 (9.7)
An 18 87.6
C.E.R.A. therapy (month 12 efficacy population):
• **C.E.R.A. dose at baseline**(µg) ,Mean (SD)
114 (78) for Dialysis dependent(n=16),
97 (71) for Non-dialysis dependent (n=4),
111 (76) for All patients(n=20)

• **C.E.R.A. dose during the 12-month study period, µg :**
Mean (SD) 109 (76) for Dialysis dependent(n=16),
99 (68) for Non-dialysis dependent (n=4),
107 (75) for All patients(n=20)

Hb level :

- Overall, mean (SD) Hb was 11.5 (1.1) g/dL at baseline and 11.4 (1.2) g/dL at month 12, a change of -0.1 (1.6) g/dL.
- In the patients who had received ESA therapy (including C.E.R.A.) prior to study entry, there was again only a minor change in Hb level from baseline to month 12 {mean -0.3 (1.5) g/dL in dialysis dependent patients and 0.3 (1.6) g/dL in non dialysis dependent patients
- The mean maximum intra-individual fluctuation in Hb levels from mean (defined as the maximum difference from individual mean Hb during the six-month period) ranged from 0.9 g/dL to 1.0 g/dL.
- Mean (SD) serum ferritin was similar at baseline {464 (377)ng/mL} and month 24 {484 (416) ng/mL}. There was a small rise in transferrin saturation (TSAT) {26.3 (9.9) % at baseline, 32.2 (10.5) % at month 12}.

DISCUSSION :

- Maintaining Hb levels within the desired target range is extremely challenging in patients with severe CKD. Episodic administration of ESA agents artificially stimulates an acute erythropoietic response. This provokes a peak in the Hb levels that can prompt the

clinician to reduce or miss the next ESA dose, often until Hb declines to below the minimum acceptable level leading to **marked oscillation in Hb levels**

- The oscillation between overly high Hb level and then a downwards effect due to ESA dose adjustment may be relatively infrequent using long-acting C.E.R.A.

CONCLUSION :

- Once-monthly C.E.R.A. maintained Hb stability in patients with dialysis dependent or non-dialysis dependent CKD over a 12-month period under standard conditions
- Few C.E.R.A. dose changes were required and the safety profile of C.E.R.A. was good over the one-year . Despite the limited final population size, once-monthly ESA therapy using C.E.R.A. appears to be effective and convenient.

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