MON-355

A prospective trial of hemoglobin outcomes with continuous erythropoietin receptor activator (C.E.R.A.) therapy under routine conditions according to dialysis requirement and diabetes status

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BACKGROUND

- Erythropoiesis-stimulating agent (ESA) therapy is the mainstay of anemia therapy but frequent administration is time-consuming and inconvenient for staff and patients.
- Continuous erythropoietin receptor activator (C.E.R.A.) can be dosed monthly during maintenance therapy[1]. Randomized studies have demonstrated the effectiveness of C.E.R.A. in patients with hemodialysis-dependent (HDD) or non-dialysis dependent (NDD) chronic kidney disease (CKD).
- However, results may not be replicated in routine practice. In particular, the use of C.E.R.A. in specific CKD patient subpopulations remains largely unexamined outside the confines of controlled trials.
- A prospective, observational study was undertaken to evaluate hemoglobin (Hb) outcomes in patients receiving C.E.R.A. therapy under routine conditions.

METHODS

- This was a 12-month, prospective, observational study of adult patients with HDD or NDD CKD undertaken at 33 specialist nephrology centers in Germany.
- C.E.R.A. initiation and dosing were at the discretion of the treating physician.
- Inclusion criteria included: no malignancy, no serious hematological or infectious disease, life expectancy ≥12 months, and no acute bleeding for ≥16 weeks prior to enrollment.
- Data obtained at routine clinic visits were captured and analyzed descriptively for patients with or without dialysis at study entry, and in specific subpopulations within the HDD and NDD groups.

RESULTS

Study population

- 1,510 patients were eligible for the efficacy analysis (1,184 HDD, 326 NDD).
- The study was discontinued prematurely by 469/1,510 patients (31.1%), with death (n=130) and discontinuation of treatment (n=114) the most common reasons.

Hb outcomes in HDD patients

- The majority of HDD patients (81.3%) were receiving ESA therapy prior to study entry, including 36.7% who received C.E.R.A. (Table 1).

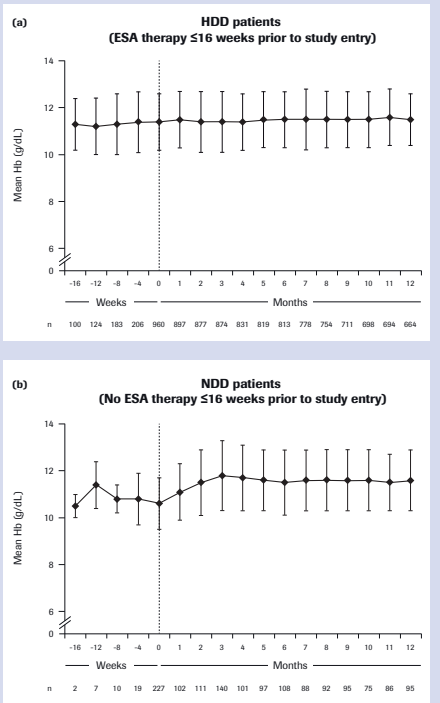
Table 1. Baseline characteristics

	HDD (N=1,184)	NDD (N=326)
Age, years	68.0 (13.8)	71.8 (13.3)
Male gender, %	59.5	51.5
Underlying disease, %		
Diabetic nephropathy	31.8	31.0
Hypertensive nephrosclerosis	20.6	39.3
Glomerulonephritis	15.0	6.4
Pyelonephritis/interstitial nephritis	5.7	7.4
Polycystic kidney disease	6.0	4.9
Other/missing	27.7	22.4
ESA therapy <16 weeks prior to study entry, %[a]		
Any	81.3	30.4
C.E.R.A.	36.7	14.4
Darbepoetin alfa	17.9	13.8
Epoetin beta	19.3	1.8
Epoetin alfa	11.1	0
Biosimilar	9.0	0.3
Frequency of previous ESA therapy, %[a]		
More than once a week	37.4	0
Once a week	29.0	4.3
Once every 2–3 weeks	6.2	12.9
Once every four weeks	49.7	15.0
Other/missing	1.9	0.9

Continuous variables are shown as mean (SD).
[a] More than one ESA was possible

- The HDD patients who had received ESA therapy before entering the study showed stable mean Hb values under C.E.R.A. during the 12-month study (range 11.4–11.6g/dL) (Table 2) (Figure 1a).

Figure 1. Mean (SD) Hb levels in (a) HDD patients who received ESA therapy ≤16 weeks prior to study entry (b) NDD patients without ESA prior to study entry



Hb outcomes in NDD patients

- Mean Hb increased in the NDD cohort from baseline to month 12 (Table 2).
- This was accounted for by the subpopulation of NDD patients who started C.E.R.A. after no prior ESA. In this group, mean (SD) Hb increased from 10.6 (1.1) g/dL at baseline to 11.8 (1.5) g/dL by month 3, remaining in the range 11.5–11.6g/dL during months 6–12 (Figure 1b).

Table 2. Hb outcomes

	N	Hb at baseline, g/dL	Hb at month 12 g/dL	Hb fluctuation g/dL
HDD	1,184	11.3 (1.3)	11.6 (1.1)	1.6 (0.8)
Prior ESA	962	11.4 (1.2)	11.5 (1.1)	1.6 (0.8)
Prior ESA, diabetes	301	11.5 (1.3)	11.5 (1.2)	1.6 (0.8)
Prior ESA, no diabetes	661	11.4 (1.2)	11.6 (1.1)	1.6 (0.8)
NDD	326	10.9 (1.3)	11.6 (1.2)	1.3 (0.8)
ESA-naïve	227	10.6 (1.1)	11.6 (1.3)	1.4 (0.8)
ESA-naïve, diabetes	71	10.5 (1.1)	11.8 (1.3)	1.2 (0.8)
ESA-naïve, no diabetes	156	10.7 (1.1)	11.6 (1.3)	1.5 (0.8)

Values are shown as mean (SD)

Influence of diabetes

- The presence or absence of diabetes in either the HDD or NDD groups did not appear to influence the effectiveness of C.E.R.A. therapy (Table 2).
- Patients with diabetes showed no consistent differences from non-diabetic patients in either the HDD or NDD groups in terms of C.E.R.A. dose or the number of C.E.R.A. dose changes (Table 3).

Table 3. C.E.R.A. dosing

	N	Total C.E.R.A. dose, µg	C.E.R.A. dose changes
HDD	1,184	127 (89)	2.9 (2.4)
Prior ESA	962	127 (89)	3.0 (2.4)
Prior ESA, diabetes	301	126 (85)	3.2 (2.5)
Prior ESA, no diabetes	661	127 (90)	2.9 (2.4)
NDD	326	76 (42)	1.0 (1.3)
ESA-naïve	227	76 (42)	1.0 (1.4)
ESA-naïve, diabetes	71	71 (35)	1.1 (1.4)
ESA-naïve, no diabetes	156	79 (44)	1.0 (1.4)

Values are shown as mean (SD)

Fluctuation in Hb level

- Mean intra-individual fluctuation in Hb was ≤1.6g/dL in all groups, with lower fluctuations observed in patients with NDD CKD compared to patients with HDD CKD (Table 2).

C.E.R.A. dosing

- The median number of C.E.R.A. doses per month was 1.0 (interquartile range 1.0, 1.0) throughout the study.
- The mean number of C.E.R.A. dose changes during months 0–12 was 3.2 or fewer in each HDD subpopulation and ≤1.1 in the NDD subpopulations (Table 3).

Tolerability and satisfaction

- C.E.R.A. was discontinued due to adverse events in 5/1510 patients (0.3%).
- At the final study visit, 85.3% of physicians and 86.5% of patients were very satisfied or satisfied with C.E.R.A. therapy.

SUMMARY

- Once-monthly treatment with C.E.R.A. maintained a mean Hb level of 11.4–11.6g/dL in CKD patients with or without hemodialysis.
- HDD patients who received ESA therapy prior to study entry showed stable Hb levels throughout the one-year study when given once-monthly C.E.R.A.
- In NDD patients who were ESA-naïve at baseline, mean Hb showed an initial rise after C.E.R.A. initiation then remained stable to month 12.
- Effectiveness was not influenced by the presence of diabetes in either HDD or NDD patients.
- Few changes to C.E.R.A. dose were required during the one-year study.
- Tolerability of C.E.R.A. was good, with only rare cases (0.3%) of drug discontinuation due to adverse events.

CONCLUSIONS

- **Switching HDD patients from more frequent ESA regimens to once-monthly C.E.R.A. therapy, or initiating once-monthly C.E.R.A. in ESA-naïve NDD patients, appears to be an effective therapeutic strategy for renal anemia.**

STUDY PARTICIPANTS

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FUNDING

This study was funded by Roche Pharma AG, Germany.

Presented at the World Congress of Nephrology 2015, Capetown, South Africa (13–17 March 2015)