Efficacy and Safety of AND017 for Treatment of Anemia in Dialysis-Dependent CKD

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KIND PHARMACEUTICAL

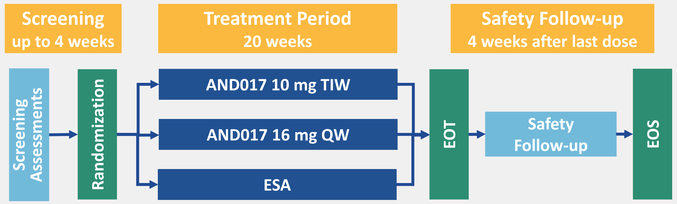
Background

- AND017 is a novel orally administered hypoxia-inducible factor-prolyl hydroxylase inhibitor (HIF-PHI) designed to treat anemia in patients with chronic kidney disease (CKD).
- This phase II clinical trial was conducted in the US and China to evaluate the efficacy and safety of AND017 in patients with end-stage kidney disease (ESKD). (NCT05265325)

Methods

Study Design

- Phase II, randomized, open-label, active-controlled study
- Eligible patients were randomized at a ratio of 1:1:1 to AND017 10 mg three times per week (TIW) group, 16 mg once per week (QW) group, or the active comparator ESA treatment group for a total of 20-week study treatment.
- The doses of AND017 were adjusted based on the study protocol during the entire treatment period; the use of ESA was based on local package insert or clinical practice.
- The target Hb ranges in the study were 10.0-11.0 g/dL for the US and 10.0-12.0 g/dL for China.



❖ TIW – Three times per week; QW – Once per week; ESA – Erythropoietin stimulating agents; EOT – End of treatment; EOS - End of study

Figure 1. Study Design

Eligibility

- Age ≥18 years
- On stable hemodialysis, home hemodialysis, or peritoneal dialysis for at least 16 weeks
- On stable ESA treatment for at least 6 weeks
- Baseline Hb 9.0-11.0 g/dL for the US and 9.0-12.0 g/dL for China

Primary Objective

- To evaluate the efficacy of AND017 for the treatment of anemia in ESA-treated ESKD patients compared with ESA treatment

Secondary Objectives

- To evaluate the safety and tolerability of AND017 following different AND017 oral dosing regimens in ESKD patients on dialysis with anemia
- To evaluate the effect of AND017 on other Hb related efficacy parameters in treatment of anemia in ESKD patients on dialysis with anemia compared with ESA treatment

Results

Disposition and Demographics

- A total of 175 patients were enrolled with 59 patients in the AND017 10 mg TIW, 57 patients in the AND017 16 mg QW, and 59 patients in the ESA group.
- All patients were included in the safety analysis set; 174 subjects were included in the full analysis set for primary analysis.
- Patients in all treatment groups were of relatively similar demographic and baseline characteristics (mean age 55.5 years, 45.7% female, 54.9% Asian, 30.9% White, 10.3% African American, baseline Hb 10.7 g/dL, baseline eGFR 5.2 mL/min/1.73m^2).

Efficacy Analysis

- The primary efficacy endpoint was the mean change in Hb levels from baseline, averaged over Weeks 17-21.
- The non-inferiority of AND017 10 mg TIW or 16 mg QW to the active comparator ESA treatment will be established if the lower bound of the one-sided 95% CI in Hb change from baseline is ≥-1 g/dL.
- In the primary efficacy analysis, both AND017 10 mg TIW and 16 mg QW groups showed non-inferiority to ESA in maintaining Hb levels within the targe range during the 20-week treatment (**Table 1**).

Table 1. Change from Baseline in Hb Levels Averaged from Week 17-21 by MMRM Model

Hb Levels (g/dL)	AND017 10 mg TIW N=59	AND017 16 mg QW N=56	ESA N=59
Hb at baseline, Mean (SD)	10.67 (0.84)	10.65 (0.64)	10.83 (0.74)
Hb at Week 17-21, Mean (SD)	10.86 (0.92)	10.11 (0.77)	10.56 (0.95)
Hb change from baseline, Mean (SD)	0.09 (1.02)	-0.49 (1.02)	-0.28 (1.01)
AND017 VS ESA, MMRM model			
LS mean Hb change from baseline (95% CI)	0.09 (-0.17, 0.35)	-0.54 (-0.79, -0.28)	-0.15 (-0.40, 0.10)
LS mean Diff. (95% CI)	0.24 (-0.09, 0.57)	-0.39 (-0.74, -0.04)	
P-value	0.15	0.03	

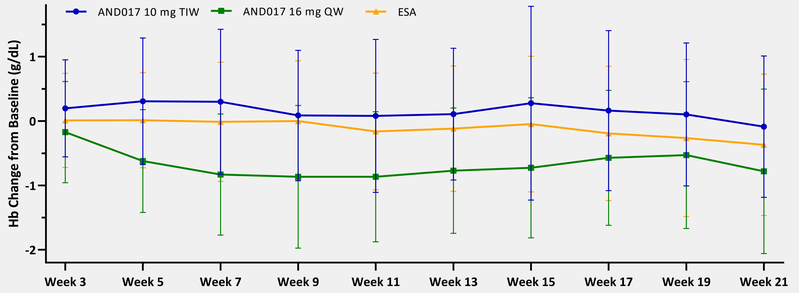


Figure 2. Mean Change from Baseline in Hb Levels at Each Visit

Safety Analysis

- Treatment emergent adverse events (TEAEs) occurred in 91 patients (78.4%) treated with AND017 and 39 patients (66.1%) treated with ESA (**Table 2**).
- The frequently reported TEAEs (>5%) in the pooled AND017 group were upper respiratory tract infection (12.1%), pneumonia (9.5%), AVF site complication (7.8%), hyperkalemia (6.9%), diarrhea (6.0%), hypotension (6.0%), and dialysis hypotension (5.2%) (**Table 2**). These events were commonly observed in studies of other HIF-PHIs and are typical among ESKD patients.
- A total of 12 patients experienced treatment-related TEAEs, with 10 patients (8.6%) treated with AND017 and 2 patients (3.4%) treated with ESA.
- Among the above frequently reported TEAEs, the only TEAE deemed treatment-related was hyperkalemia, reported in one patient (1.7%) from the AND017 10 mg TIW group. Other treatment-related TEAEs were all <5% and occurred in no more than 2 patients in the pooled AND017 or ESA groups.
- A total of 48 patients experienced SAEs, with 35 patients (30.2%) treated with AND017 and 13 patients (22.0%) treated with ESA; none were assessed as treatment related.

Table 2. Summary of TEAEs with Incidence >5% in Any Treatment Group

Adverse Events n (%)	AND017 10 mg TIW N=59	AND017 16 mg QW N=57	Pooled AND017 N=116	ESA N=59
Any TEAE	48 (81.4%)	43 (75.4%)	91 (78.4%)	39 (66.1%)
Upper respiratory tract infection	8 (13.6%)	6 (10.5%)	14 (12.1%)	5 (8.5%)
Pneumonia	6 (10.2%)	5 (8.8%)	11 (9.5%)	2 (3.4%)
AVF site complication	6 (10.2%)	3 (5.3%)	9 (7.8%)	1 (1.7%)
Hyperkalemia	6 (10.2%)	2 (3.5%)	8 (6.9%)	7 (11.9%)
Diarrhea	3 (5.1%)	4 (7.0%)	7 (6.0%)	2 (3.4%)
Hypotension	2 (3.4%)	5 (8.8%)	7 (6.0%)	1 (1.7%)
Dialysis hypotension	1 (1.7%)	5 (8.8%)	6 (5.2%)	4 (6.8%)
Hyperphosphatemia	3 (5.1%)	2 (3.5%)	5 (4.3%)	1 (1.7%)
Cough	1 (1.7%)	4 (7.0%)	5 (4.3%)	0
Headache	3 (5.1%)	1 (1.8%)	4 (3.4%)	0
Nausea	1 (1.7%)	3 (5.3%)	4 (3.4%)	0
Hyperlipidemia	3 (5.1%)	0	3 (2.6%)	2 (3.4%)
Vomiting	0	3 (5.3%)	3 (2.6%)	2 (3.4%)
Lymphocyte count decreased	3 (5.1%)	0	3 (2.6%)	0
Hyperparathyroidism secondary	0	1 (1.8%)	1 (0.9%)	3 (5.1%)

Conclusion

- At both TIW and QW dosing frequencies, AND017 effectively maintained Hb levels after 20 weeks of treatment in ESA-treated ESKD patients and demonstrated non-inferiority to ESA treatment with a favorable safety profile.

KIDNEY WEEK 2024

For more information, please contact by email yushazhu@kindpharmaceutical.com or visit www.kindpharmaceuticals.com

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