Effect of Ocedurenone (KBP-5074) in Patients with Uncontrolled Hypertension and Stage 3b/4 Chronic Kidney Disease - Subgroup Analysis of a Phase 2b Clinical Trial

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ABSTRACT

TITLE:

Effect of Ocedurenone in Patients with Uncontrolled Hypertension and Stage 3b/4 Chronic Kidney Disease - Subgroup Analysis of a Phase 2b Clinical Trial.

BACKGROUND:

Ocedurenone is a novel non-steroidal MRA being developed for the treatment of uncontrolled hypertension in patients with Stage 3b(eGFR ≥30 and ≤44 mL/min/1.73 m^2) or Stage 4 (eGFR ≥15 and <30 mL/min/1.73 m^2) CKD.

OBJECTIVE:

BLOCK-CKD is a Phase 2b, multicenter, randomized, double-blind, placebo-controlled study evaluating the safety, efficacy, and pharmacokinetics of the nonsteroidal MRA Ocedurenone in patients with stage 3b/4 CKD and uncontrolled hypertension while taking 2 or more antihypertensive medications. Although the study is not powered for subgroup analysis, it is of interest to examine the consistency of results across various subgroups.

METHOD:

Of 162 patients randomized, 138 (85.2%) completed the study. Effect of Ocedurenone on SBP reduction and serum potassium levels by baseline eGFR < 30 mL/min/1.73 m^2, eGFR ≥ 30 mL/min/1.73 m^2, and diabetic status was explored.

RESULT:

Consistent and clinically meaningful SBP reduction at Day 84 was observed in the subgroups analyzed. SBP mean (SE) change from baseline to day 84 in the eGFR < 30 mL/min/1.73 m^2 group were 0.2 (3.03) mmHg, -12.7 (5.45), and -15.4 (5.01) for placebo, 0.25mg, and 0.5mg doses respectively. In the ≥ 30 mL/min/1.73 m^2 group, the changes were -9.7 (3.38), -10.8 (3.29), and -16.1 (4.08), respectively. In the diabetic patient group, the changes were -4.2 (4.22), -11.8 (5.91), and -13.0 (6.5) respectively. In the non-diabetic patient group, the changes were -6.0 (2.93), -11.4 (3.34), and -17.1 (3.51) respectively. Similar small dose-dependent increases in serum potassium were observed in nearly all subpopulations.

CONCLUSION:

In this Phase 2 trial, the effect of Ocedurenone on SBP reduction and serum potassium levels was consistent among clinically important subgroups. Due to the relatively small number of patients these conclusions need to be confirmed in the larger ongoing Phase 3 trial.

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BACKGROUND

- Ocedurenone, a novel highly protein-bound and highly selective non-steroidal mineralocorticoid receptor antagonist (MRA), is currently under development, for the treatment of uncontrolled hypertension in patients with chronic kidney disease (CKD)(1).
- BLOCK-CKD in subjects with stage 3b/4 CKD (eGFR 15-44 mL/min/1.73 m^2) demonstrated significant blood pressure lowering with minimum risk of hyperkalemia (2,3).
- It is important to evaluate the consistency safety and efficacy of ocedurenone in patients with across difference CKD stages, with or w/o proteinuria and with or w/od diabetes

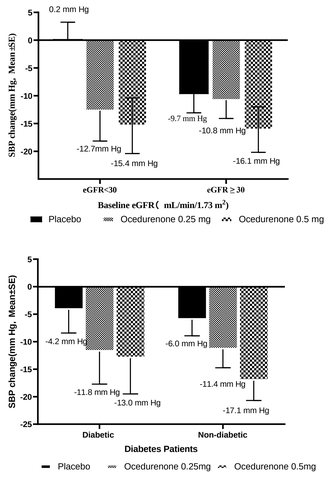
METHOD

- This was a randomized, double-blind, placebo-controlled, multi-center, Phase 2b study was to assess the efficacy, safety, and PK of KBP-5074 0.25 mg QD and KBP-5074 0.5 mg QD versus placebo in subjects with moderate to severe CKD and uncontrolled hypertension. Overall, a total of 162 subjects were randomized and 138 (85.2%) completed the study.
- Effect of Ocedurenone on efficacy (SBP reduction) and safety (eGFR change and serum potassium levels) are summarized by baseline eGFR < 30 mL/min/1.73 m^2, eGFR ≥ 30 mL/min/1.73 m^2, and diabetic status was explored.

RESULT

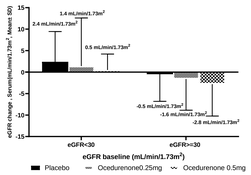
- Consistent and clinically meaningful SBP reduction at Day 84 was observed in the subgroups analyzed. SBP change from baseline showed in Figure 1. There were significant and consistent SBP reduction in subgroups.

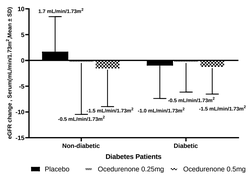
Figure 1 SBP Changes from baseline to day 84 in by baseline eGFR and diabetic status



- eGFR change from baseline to day 84 in by baseline eGFR and diabetic status was showed in below Figure 2. There were no obvious reduction from baseline in subgroups by baseline eGFR and diabetic status, and no significant differences between subgroups

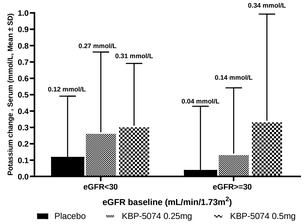
Figure 2 eGFR change baseline eGFR and diabetic status

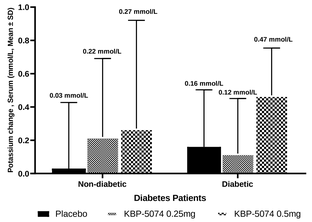




- Serum potassium change from baseline to day 84 in by baseline eGFR and diabetic status was showed in below Figure 3. Increases in potassium post-treatment were observed in all subgroups, with the largest increase in the 0.5 mg dose group (Figure 3), which were consistent with overall study data, but no obvious differences between subgroups.

Figure 3 potassium change baseline eGFR and diabetic status





CONCLUSION

In this Phase 2 trial, the effect of Ocedurenone on SBP reduction, eGFR levels and serum potassium levels was consistent among clinically important subgroups.

- The two dosing regimens of Ocedurenone evaluated in this study (0.25 mg QD and 0.5 mg QD) showed consistent SBP reduction across baseline eGFR < 30 mL/min/1.73 m^2 , eGFR ≥ 30mL/min/1.73 m^2 , and diabetic or non-diabetic in subjects with moderate to severe CKD.
- There were no significant eGFR reduction from Baseline to Day 84 across baseline eGFR < 30 mL/min/1.73 m^2 , eGFR ≥ 30mL/min/1.73 m^2 , and diabetic .and non-diabetic in subjects with moderate to severe CKD.
- Increases in potassium post-treatment were observed in all groups. There were no obvious difference in serum potassium elevation among patients with or without diabetes, baseline eGFR < 30 mL/min/1.73 m^2 , eGFR ≥ 30mL/min/1.73 m^2post-treatment.
- Due to the relatively small number of patients these conclusions need to be confirmed in the larger ongoing Phase 3 trial.

References

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