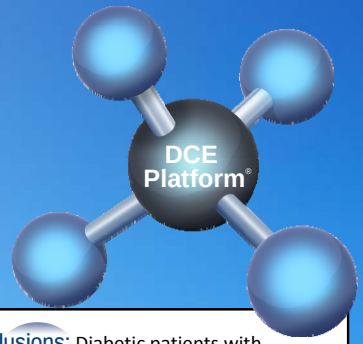
Baseline Characteristics of Diabetic Kidney Disease Patients Enrolled in a Phase 2 Trial of CTP-499

CoNCERT Pharmaceuticals Inc.

www.concertpharma.com
Lexington, MA 02421

LuAnn A. Sabounjian[1]*, Philip B. Graham[1], Lijun Wu[1], Ara Aslanian[1], Changfu Cheng[1], David J. Turnquist[1], James Shipley[1] and George L. Bakris[2]. [1]Concert Pharmaceuticals, Inc., Lexington, MA, United States and [2]The University of Chicago Pritzker School of Medicine, Chicago, IL, United States



Background:

Type 2 diabetes is the leading cause of chronic kidney disease and transition to dialysis[1] in the US and most developed countries.

CTP-499, a novel, deuterium-containing methylxanthine derivative which selectively inhibits several PDE isozymes that modulate cAMP and cGMP hydrolysis, is currently being developed as an additive treatment for delaying the progression of diabetic kidney disease. In preclinical studies, CTP-499 has been shown to suppress inflammatory, oxidative, and fibrotic processes associated with the pathophysiology of diabetic kidney disease.

The objective of this double-blind, placebo-controlled, multicenter study is to assess safety and efficacy up to 24 weeks of treatment with CTP-499 in patients with macroalbuminuric type 2 diabetic kidney disease who were maintained on a stable ACEi/ARB regimen. Patients have the option to continue to participate in the placebo-controlled study for an additional 24 weeks, and patients who complete 48 weeks of treatment are then eligible to enter the open-label portion of the study for a further 48 weeks.

For further information

LuAnn Sabounjian lsabounjian@concertpharma.com

Methods:

The primary endpoint is the change in urinary albumin-to-creatinine ratio (UACR) over a minimum 24 weeks of treatment. Secondary endpoints include 24 and 48 week changes in eGFR, serum creatinine, inflammatory and fibrotic biomarkers and hematology markers, as well as assessment of population PK. Across the 48 week placebo-controlled study period, UACR for each of the 3 pre-treatment and 5 post-treatment time points is determined as the geometric mean of 3 consecutive first morning voids. Serum creatinine (for determination of eGFR) is measured at 3 pre-treatment and 6 post-treatment time points. Patients are stratified by eGFR (≥45/<45 mL/min/1.73m²) and UACR (≥1500/<1500 mg/g). Other details of the study design have been previously described.[2] Males or females aged 18 or older with chronic kidney disease believed due to Type 2 diabetes and macroalbuminuria, who are on a stable anti-hypertensive medication regimen and diabetes management one month prior to and throughout screening period were eligible for enrollment. Patients are not expected to start dialysis in the next year. Stable ACEi/ARB therapy is required throughout the study. Patients with unstable renal impairment and those taking aliskiren are excluded. Other key inclusion criteria are:

eGFR	≥23 and ≤89 mL/min/1.73m²	HbA1c	<10.5%
UACR	≥200 mg/g (male), ≥300 mg/g (female), ≤5000 mg/g	Serum albumin	> 3.0 g/dL
Blood Pressure	≤ 145 mm Hg systolic and ≤ 90 mm Hg diastolic	Potassium	≥ 5.5 mEq/L

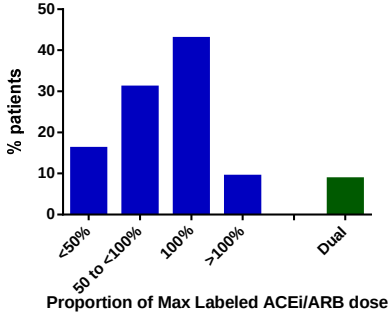
Results:

Patients entered screening from December 2011 to December 2012 and 182 patients were enrolled in the study at 39 centers across the United States. A higher proportion of males (78.0%, n=138) than females (22.0%, n=39) were enrolled. BMI (kg/m²) mean was 33.8 (median 33.4).

Age		Race, n (%)	
Mean	63.7 yrs	White	121 (68.4)
Media	65.0 yrs	Black	42 (23.7)
Range	29.0 – 86.0 yrs	Asian	9 (5.1)
Number (%) < 65 yrs	92 (52.0)	Native Hawaiian or Pacific Islander	2 (1.1)
Number (%) >65 yrs	85 (48.0)	Multiple Races	3 (1.7)

Baseline Parameters		
	Mean (± SD)	Median
eGFR (mL/min/1.73m²)	46.0 ± 15.4	44.7
UACR (mg/g)	1086.8 ± 791.2	852.1
Serum Creatinine (mg/dL)	1.67 ± 0.51	1.60
BP Systolic (mm Hg)	131.8 ± 10.4	134.0
BP Diastolic (mm Hg)	75.0 ± 9.2	76.0
HbA1c (%)	7.5 ± 1.4	7.4
Serum albumin (g/dL)	4.1 ± 0.38	4.1
Potassium (mEq/L)	4.4 ± 0.40	4.4
Phosphorus (mg/dL)	3.7 ± 0.53	3.7
Duration of diabetes (years)	16.3 ± 8.9	15.4
Duration of CKD diagnosis (years)	4.3± 4.4	3.1

*5 patients excluded due to major protocol violation



Stratification Groups	n (%)
UACR <1500 and eGFR <45	67 (37.9)
UACR <1500 and eGFR ≥45	67 (37.9)
UACR ≥1500 and eGFR <45	23 (13.0)
UACR ≥1500 and eGFR ≥45	20 (11.3)

Conclusions:

Diabetic patients with macroalbuminuria are at elevated risk for poor outcomes.[3] While renin-angiotensin system blocking drugs (ACEi/ARB) have been shown to lower the risk of disease progression[4,5] there remains a clear unmet need for additional therapies in this aging patient population with an increasing prevalence of risk factors.[6] CTP-499 is being studied as an add-on treatment to current standard-of-care therapy – the current study population has well-controlled blood pressure and diabetes; 84% of subjects are receiving at least 50% of the maximum labeled dose of ACEi/ARB. This study is intended to provide data on CTP-499's early and later effects on albuminuria, renal function and safety as adjunctive therapy to ACEi/ARB in patients with diabetic kidney disease and may provide additional insights into the compound's mechanism of action. The results of this study are expected to inform the next stage of clinical development.

Literature cited

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