CERTARA

Quantify Chronic Kidney Disease Clinical Outcomes Database

Summary Information

The current version of the database includes clinical safety and efficacy information on treatment options currently approved or in development for Chronic Kidney Disease (CKD) progression in patients with Type 2 Diabetes Mellitus (T2DM) and overt albuminuria/proteinuria, as well as patients with IGA nephropathy.

Table 1. Summary information

Parameter	Description
format	Excel or KEEP format
indications	iga nephropathy, diabetic nephropathy, nephropathy, proteinuria
references	99
trials	88
trial.arms	214
patients	17,364
data.rows	5,456
compounds	aliskiren, amlodipine, atenolol, atrasentan, avosentan, azathioprine, azelnidipine, bardoxolone methyl, benazepril, canagliflozin, candesartan cilexetil, captopril, chlorthalidone, cilazapril, clopidogrel, daglutril, diltiazem, doxazosin, enalapril, finerenone, hydrochlorothiazide, irbesartan, leflunomide, lisinopril, losartan, methylprednisolone, metoprolol, mizoribine, mycophenolate mofetil, nefidipine, nisoldipine, nitrendipine, no treatment, olmesartan, pentoxifylline, perindopril, placebo, prednisolone, prednisone, pyridorin, ramipril, sirolimus, spironolactone, telmisartan, temocapril, temocapril or trandolapril, trandolapril, trichlormethiazide, valsartan, verapamil
key.efficacy.endpoints	composite event, cv event, dbp, death, double serum cr, egfr, esrd, fbg, gfr, hba1c, map, sbp, serum cr, uacr, uae24, upcr, upe24
key.safety.endpoints	dropout ae, dropout other, dropout total, edema, hyperkalemia, hypotension

Features and Benefits

Key Features

- **Comprehensive:** includes information for marketed drugs; data sources include journal publications, conference posters, regulatory reviews, etc
- **Ease of tracking:** all clinical trial publications are listed in a separate source database and linked to unique clinical trial names
- **Flexibility:** the database design allows for quick updates as well as expansions to include additional indications/drugs/endpoints/trials
- **Model-friendliness:** designed and reviewed by experienced modelers to ensure highest quality and usability for modeling and simulation to support drug development strategies
- **Customizability:** can be augmented with clinical trial data proprietary to the client (this information goes into a separate proprietary database and will be owned by the client)

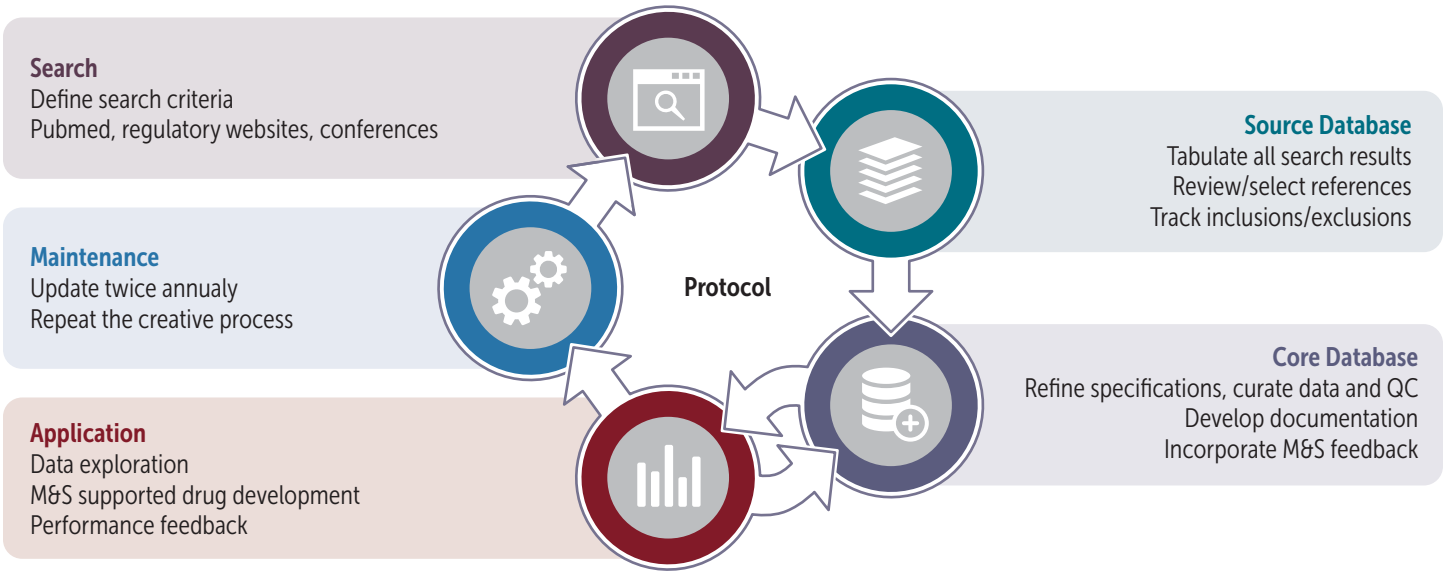
Why Use Our Databases

- Designed and managed by experienced modelers
- Provides most relevant data to support clients' needs for quantitative decision making
- Contains up-to-date and high quality data so that it is always readily available to provide timely analysis required to support critical clinical trial decisions
- Supported by additional services such as modeling and simulation consulting services and custom curation services (by our partner, GVK Bio)

Organization and Structure

This product consists of two databases, the source database and the clinical outcomes database (core database), developed for chronic kidney disease. The source database is a database that maintains the sources of information identified by searches and reviewed for inclusion or exclusion from the database. The clinical outcomes database contains the information on trial, treatment and patients characteristics and safety and efficacy results of the trials identified for inclusion in the database. In addition, a detailed documentation is provided with these databases.

The following is a flowchart showing the process with which databases are created, optimized and updated.



Overview of the Chronic Kidney Disease Source Database

The primary data sources were controlled clinical trials published in the medical literature or available through the FIA from the FDA. A secondary source of information was published abstracts or presentations of clinical trial data from conferences and corporate websites.

609 references were identified and documented in the source database, of which a total of 99 references were selected for inclusion in the database after careful review of the abstracts. The detailed reference information as well as reasons for exclusion is recorded to facilitate potential future expansion of the database. The 99 references selected for inclusion in the database provide information on 88 unique trials and 214 unique treatment arms.

Overview of the Chronic Kidney Disease Clinical Outcomes Database

The clinical outcomes database contains information from 88 trials, representing 214 unique treatment arms and 17,364 patients. There are a total of 5,456 rows in the database. Each row contains the information for an endpoint in one arm of a trial at a specific point in time. The table below provides an overview of the available data for randomized treatments.

Table 2. Number of trials, treatment arms and patients for each drug class

randomized.drug	trials	arms	patients
aliskiren	2	2	78
aliskiren+losartan	1	1	301
amlodipine	5	5	627
atenolol	5	5	68
atenolol+furosemide	1	1	10
atrasentan	2	5	227
avosentan	2	6	1162
azathioprine	3	3	133
azelnidipine	1	1	75
bardoxolone methyl	1	3	170
benazepril+amlodipine	1	1	166
benazepril+hydrochlorothiazide	1	1	166
canagliflozin	1	2	703
candesartan cilexetil	6	12	496
captopril	5	6	85
captopril+pentoxifylline	1	1	37
chlorthalidone	1	1	12
cilazapril	1	1	23
clopidogrel	1	1	42
clopidogrel+leflunomide	1	1	42
daglutril	1	1	45
diltiazem	1	1	10
doxazosin	1	1	10
enalapril	15	16	422
enalapril+hydrochlorothiazide	1	1	52
enalapril+losartan	2	2	23
finerenone	1	7	729
hydrochlorothiazide	1	1	90
irbesartan	4	4	636
leflunomide	1	1	42
lisinopril	5	5	810
lisinopril+irbesartan	1	1	70
losartan	12	13	1541
losartan+aliskiren	1	1	58
losartan+hydrochlorothiazide	1	1	30
losartan+n-acetyl cysteine	1	1	35
losartan+pioglitazone	1	1	30
methylprednisolone	1	1	26
methylprednisolone+cyclosporin	1	1	25
methylprednisolone+prednisone	1	1	43
metoprolol	1	1	18
mizoribine	1	1	35
mizoribine +losartan	1	1	34
mycophenolate mofetil	3	3	58
nefidipine	1	1	11
nisoldipine	1	1	25
nitrendipine	2	2	73
no treatment	9	9	380
olmesartan	1	1	288
pentoxifylline	5	5	179
perindopril	1	1	20
perindopril+irbesartan	1	1	20
placebo	36	36	4276
placebo+losartan	1	1	298
prednisolone	2	2	67
prednisolone+losartan	1	1	22
prednisone	1	1	48
pyridorin	1	2	211
ramipril	2	2	74
sirolimus	1	1	14
spironolactone	5	5	177
telmisartan	2	2	862
telmisartan+enalapril	1	1	40
temocapril	2	2	19
temocapril or trandolapril	1	1	26
temocapril+losartan	1	1	11
trandolapril	2	2	44
trandolapril+verapamil	3	3	97
trichlormethiazide	1	1	77
valsartan	2	2	496
verapamil	1	1	14
TOTAL	**88**	**214**	**17364**

ACE: angiotensin converting enzyme inhibitor ARB: angiotensin receptor blockers; ERA: endothelin A receptor antagonists; AA: aldosterone antagonists.

Table 3. Summary of studies with CKD related endpoints

Category	Efficacy Endpoints	# of Studies	# of Subjects
GFR	eGFR	26	11,183
GFR	GFR	23	993
Protein	UACR	14	7,925
Protein	UAE24	28	3,307
Protein	UPCR	13	2,633
Protein	UPE24	42	5,615
ESRD	ESRD	13	8,324
ESRD	ESRD or Death	1	1513
Death	Death	19	11,848

Outcome fields

Efficacy Endpoints

- CKD-related endpoints
  - Urine Albumin to Urine Creatinine Ratio
  - Urine Protein to Urine Creatinine Ratio
  - Urine Albumin Excretion Rate Urine Protein Excretion Rate
  - Creatinine Concentration in Serum
  - Doubling of serum creatinine
  - Estimated GFR
  - Measured GFR
  - Half of eGFR
  - End Stage Renal Disease
  - End Stage Renal Disease or death
  - Death
  - Composite of doubling of serum creatinine, ESRD, or death
- T2DM related endpoints
  - HbA1C
  - Fasting blood/plasma glucose
  - T2DM responders
- CV related endpoints
  - Cardiovasuclar event
  - Heart failure resulting in hosptalization
  - Mean Arterial Pressure
  - Systolic Blood Pressure
  - Diastolic Blood Pressure

Safety/Tolerability endpoints

- Dropout
  - Dropout Adverse Event
  - Dropout Lack of Efficacy
  - Dropout Other
  - Dropout Total
- AE
  - Hypotension
  - Hyperkalemia
  - Cramping
  - Edema

About Certara

Certara is a leading provider of decision support technology and consulting services for optimizing drug development and improving health outcomes. Certara's solutions, which span the drug development and patient care lifecycle, help increase the probability of regulatory and commercial success by using the most scientifically advanced modeling and simulation technologies and regulatory strategies. Its clients include hundreds of global biopharmaceutical companies, leading academic institutions and key regulatory agencies.

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