CERTARA

Quantify Glaucoma Clinical Outcomes Database

Summary Information

The Quantify Glaucoma Clinical Outcomes Database is developed to document clinical safety and efficacy information from all randomized placebo and active controlled trials in patients with ocular hypertension or (open angle) glaucoma treated with latanoprost, bimatoprost, travoprost, tafluprost, dorzolamide, brinzolamide or timolol (timolol is included as control only). Trials in the database also include washout designs and add on designs.

Table 1. Summary information

Parameter	Description
format	Excel or KEEP format
indications	glaucoma
references	125
trials	141
trial.arms	345
patients	30,020
data.rows	4,343
compounds	ar-13324, betaxolol, bimatoprost, brimonidine, brinzolamide, dorzolamide, latanoprost, tafluprost, timolol, travoprost
key efficacy endpoints	iop
key safety endpoints	dropout ae, dropout le, dropout total, hyperemia, hyperemia increase mild or more

Features and Benefits

General Features of the Database:

- **Comprehensive:** includes information for marketed drugs as well as drugs in development; data source includes journal publications, conference posters, regulatory reviews, etc
- **Ease of tracking:** all clinical trial publications are listed in a separated 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)

Sample Application of the Database – Model-based Meta-analysis of the IOP

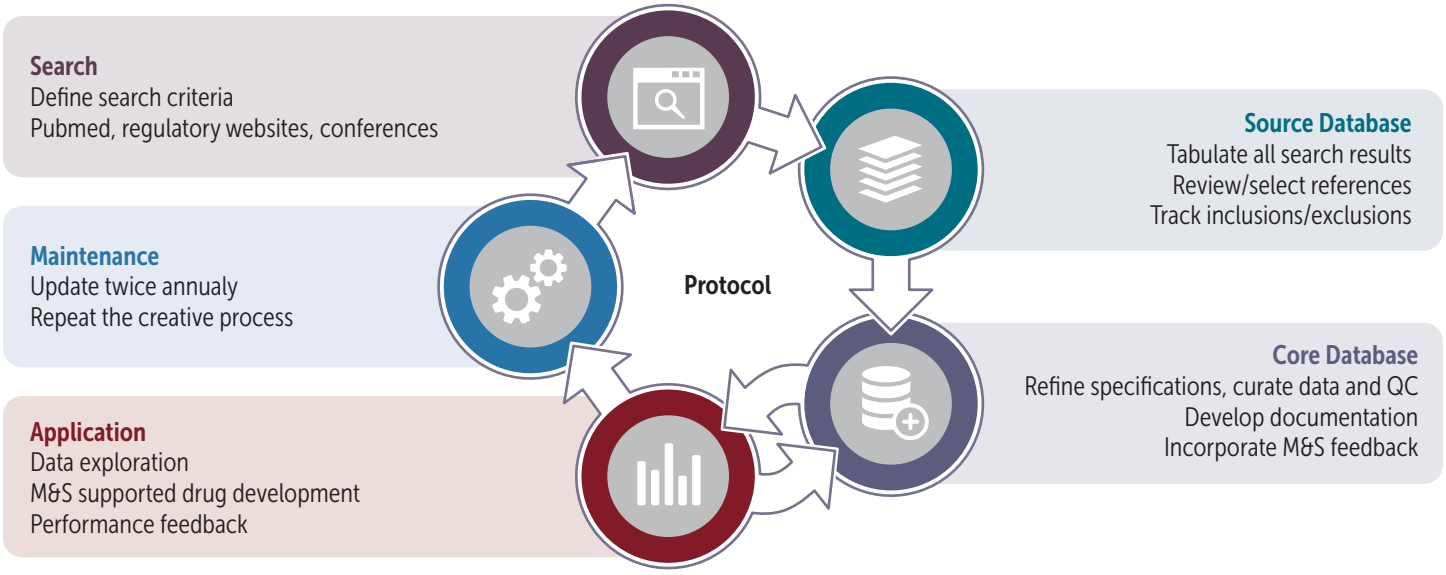
- Model of 24-hour time course of IOP lowering of mono and combination therapy of prostaglandins, timolol, and carbonic anhydrase inhibitors (CAIs). The model can account for the following variables:
  - Impact of treatment and dose
  - Impact of baseline IOP
  - Impact of time of day
  - Impact of regimen (time and frequency of administration)
  - Impact of time after dose
  - Impact of combinations vs. mono therapy vs. add-on therapy

Organization and Structure

This product consists of two databases, the source database and the clinical outcomes database (core database), developed for Glaucoma. 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.

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



Overview of the Glaucoma Source Database

Medline search on 7/27/15 yielded 562 references, the total number of references including data from FDA, EMEA and clinicltrials.gov is 573 references, of which 125 were selected for inclusion. The source database documents all search results and reasons for exclusion (mostly because control treatment was not relevant, patients not relevant, only mean diurnal IOP, etc).

Overview of the Glaucoma Clinical Outcomes Database

The clinical outcomes database contains information from 141 trials, representing data for about 30,020 patients. The table below provides an overview of the available data for IOP in the database. It shows the number of data points and the number of patients for each study drug on this endpoint.

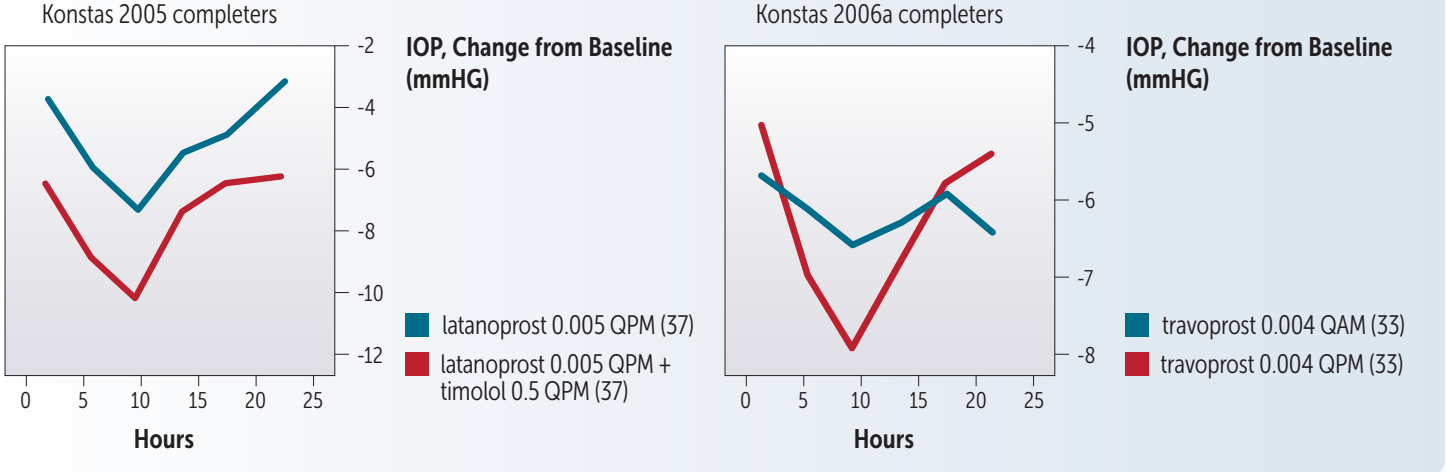
Table 2. Number of trials, treatment arms and patients by drug

randomized.drug	trials	arms	patients
ar-13324	1	2	147
betaxolol	1	1	107
bimatoprost	29	44	3752
bimatoprost+brimonidine	1	1	24
bimatoprost+brinzolamide	1	1	23
bimatoprost+dorzolamide	1	1	24
bimatoprost+timolol	5	7	1585
brimonidine	5	5	676

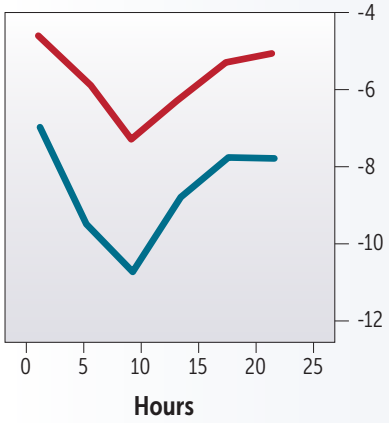
brimonidine+brinzolamide	3	3	630
brinzolamide	8	16	1753
dorzolamide	13	20	1550
dorzolamide+timolol	1	1	32
latanoprost	48	63	3937
latanoprost+brimonidine	1	1	12
latanoprost+brinzolamide	2	2	27
latanoprost+dorzolamide	3	4	78
latanoprost+timolol	21	24	1633
latanoprost+timolol+dorzolamide	2	2	74
tafluprost	2	2	360
tafluprost+timolol	1	2	400
timolol	38	38	3571
timolol+brimonidine	2	2	193
timolol+brinzolamide	6	7	734
timolol+dorzolamide	33	37	3107
timolol+dorzolamide+brimonidine	2	2	114
travoprost	23	32	2681
travoprost+brimonidine	2	2	21
travoprost+brinzolamide	5	5	240
travoprost+dorzolamide	1	1	4
travoprost+timolol	12	21	2368
travoprost+timolol+brinzolamide	1	2	163
TOTAL	**141**	**345**	**30020**

Example Plots of Actual Trial Data

The following graphs show an example of the 24-hour IOP time course in selected trials.



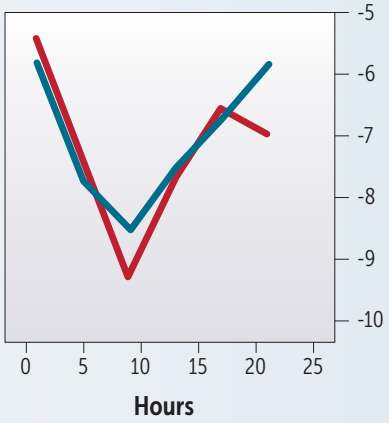
Konstas 2006b completers



IOP, Change from Baseline (mmHG)

- latanoprost 0.005 QPM + timolol 0.5 QPM (34)
- timolol 0.5 BID (34)

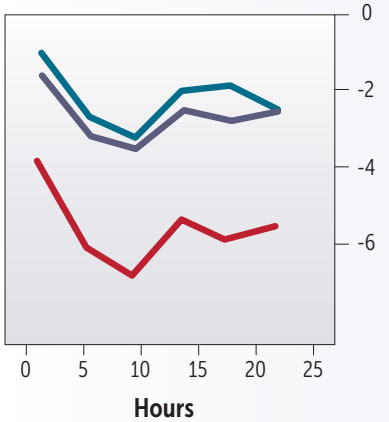
Konstas 2008a completers



IOP, Change from Baseline (mmHG)

- latanoprost 0.005 QPM (58)
- timolol 0.5 BID + dorzolamide 2 BID (58)

Konstas 2008b completers sitting



IOP, Change from Baseline (mmHG)

- latanoprost 0.005 QPM + timolol 0.5 BID + dorzolamide 2 BID (34)
- timolol 0.5 BID + dorzolamide 2 BID (34)
- timolol 0.5 QPM (34)

Konstas 2009a completers sitting

IOP, Change from Baseline (mmHG)

- travoprost 0.004 QAM + timolol 0.5 QAM (34)
- travoprost 0.004 QPM + timolol 0.5 QPM (34)

About Certara

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