

Quantify Paclitaxel Clinical Outcomes Database

Release 1.0 Jan 15, 2011

1. Summary Information

The current version of the database includes clinical PK and toxicity information on paclitaxel mono-therapy as well as efficacy outcomes of paclitaxel mono-therapy in the treatment of advanced or metastatic breast cancer.

Table 1. Summary information

Parameter	Description
Format	Excel
Indications	Advanced/metastatic breast cancer (efficacy outcomes) Solid cancer (PK and toxicity)
#Trials/References	49/63
# Patients	4,256
# Rows of Data	2,471
Last Updated	September 1, 2010
Compounds	Paclitaxel mono-therapy
Key efficacy end points	Tumor response, time to progression, overall survival
Key safety end points	Neutropenia, thrombocytopenia, leucocytopenia

2. Features and benefits

Key Features:

- **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 and will be owned by the client)

Potential Applications:

Characterize paclitaxel toxicity and efficacy profile by dose and regimen:

Example:

- Perform time-to event analysis of survival data, identifying key factors that impact the survival curve
- Understand the impact of dose and dosing regimen on key toxicity endpoints such as neutropenia and thrombocytopenia

Ultimately, these analysis help drug companies to understand the role of paclitaxel in potential combination therapies, optimize trial design, improve trial outcomes, and strengthen product differentiation.

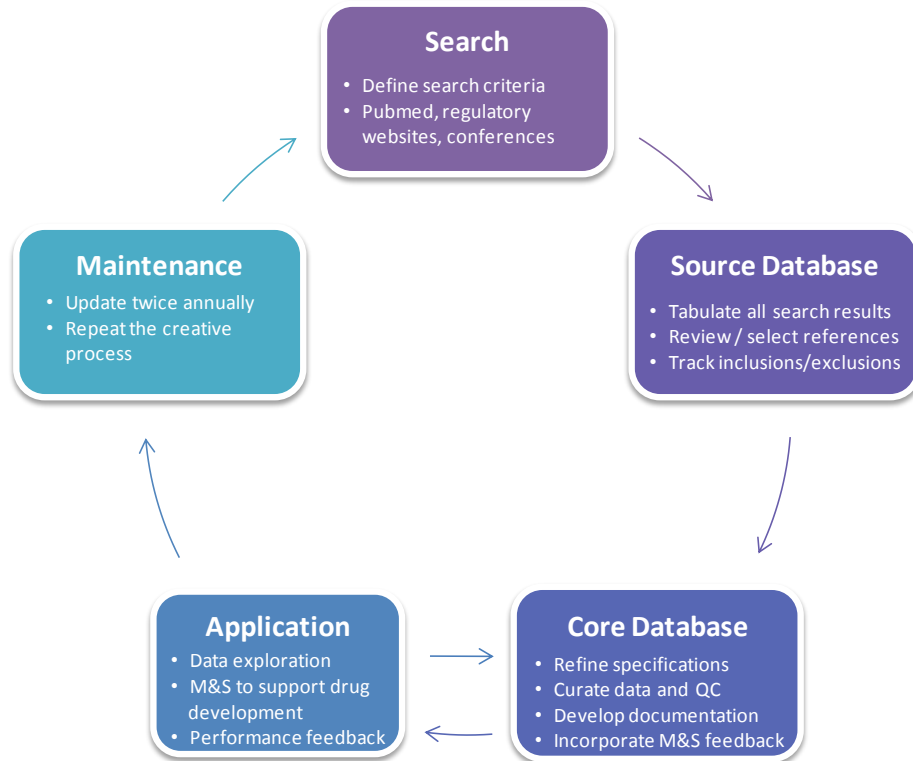
Why use our databases:

- Designed and managed by experienced modelers. There is a strong emphasis to making it easy to extract analysis datasets from the database
- Provide most relevant data to support clients' needs for quantitative decision making
- Contain 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 (by QS) and custom curation services (by GVK Bio)

3. Organization and Structure

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



4. Overview of the Paclitaxel Source Database

The primary data sources were 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.

1082 references were identified and documented in the source database, of which a total of 63 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.

5. Overview of the Paclitaxel Clinical Outcomes Database

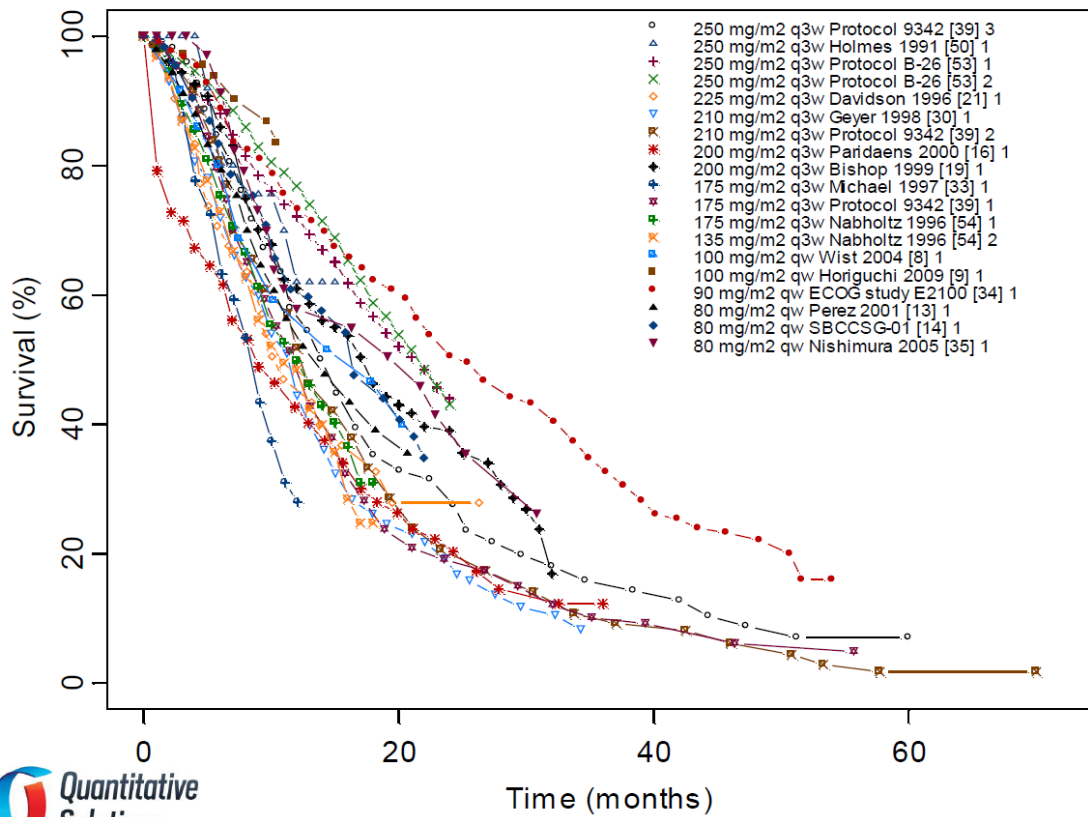
The paclitaxel Clinical Outcomes database includes 49 unique clinical trials, representing 95 arms and contains trial-level information for 4,256 patients. The following table summarizes total number of trials by infusion frequency, type of data reported (PK/TOX/Efficacy), as well as patients (breast cancer versus mixed or others).

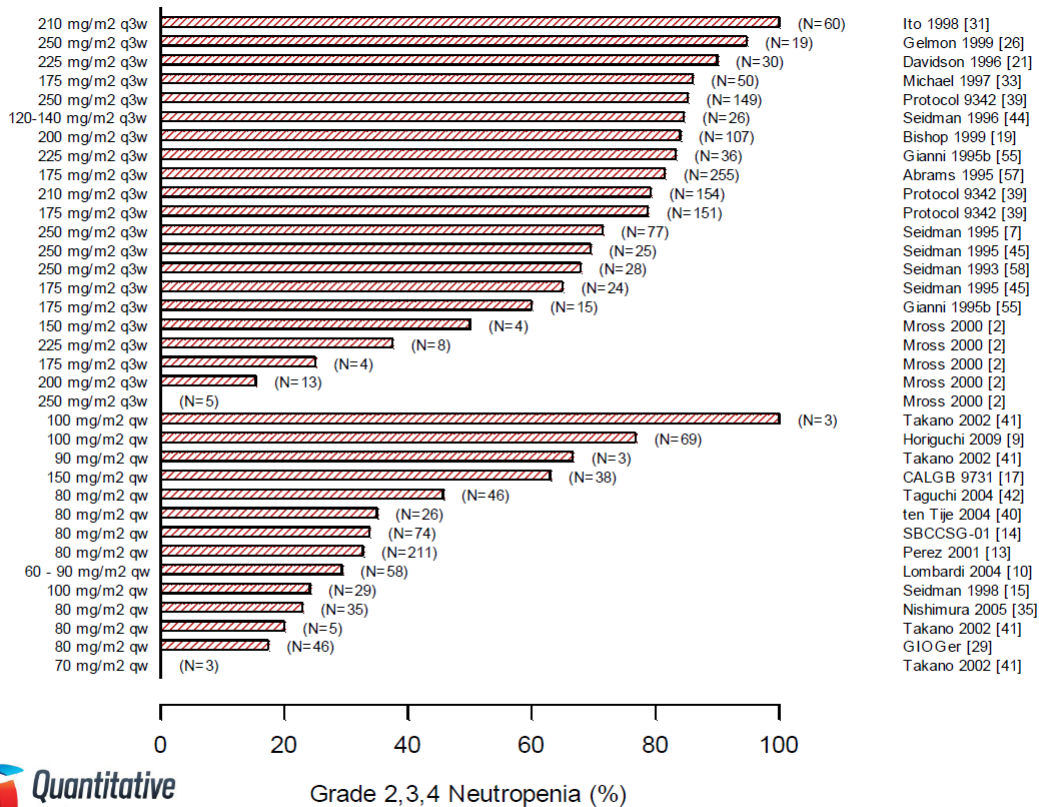
Table 1. Number of trials by infusion frequency, type of data and type of patients

Infusion frequency	Q3W		QW	SD	Total
	(1-3 hr)*	(6-168 hr)*			
N Trials	21	12	19	2	49
Breast/mixed or Others	14/8	8/5	14/5	1/1	35/16
PK/TOX/Efficacy	11/17/13	6/11/6	6/18/14	2/2/0	22/44/31
N Arms	44	23	23	6	95
N Patients	2038	900	1283	35	4256

1. Example plots of actual trial data

The following graphs show the overall survival curve and the percentage of grade 2,3,4 neutropenia, respectively, by treatment arm and trial. The trials are organized by dosing frequency and dose.





2. Outcome fields

The following endpoints are recorded in the database. For binary outcomes, the number of patients, percent of patients or rate is recorded.

- PK
 - Plasma concentration and time course
 - PK parameters (Cmax, AUC, T1/2, Cl, etc)

- Toxicity
 - Neutropenia and febrile neutropenia
 - Neutrophils (time course data)
 - Thrombocytopenia
 - Platelets (time course data)
 - Leucocytopenia
 - White blood cell counts (time course data)

- Efficacy
 - Complete Response
 - Partial Response
 - Complete and Partial Response
 - Stable Disease
 - Progressive Disease
 - Time to Progression
 - Progression Free Survival
 - Median survival
 - Overall Survival
 - Median Duration of Response
 - Median Duration of CR
 - Median Duration of PR
 - Median Duration of PR