qPharmetra
Better Decisions, Better Medicines

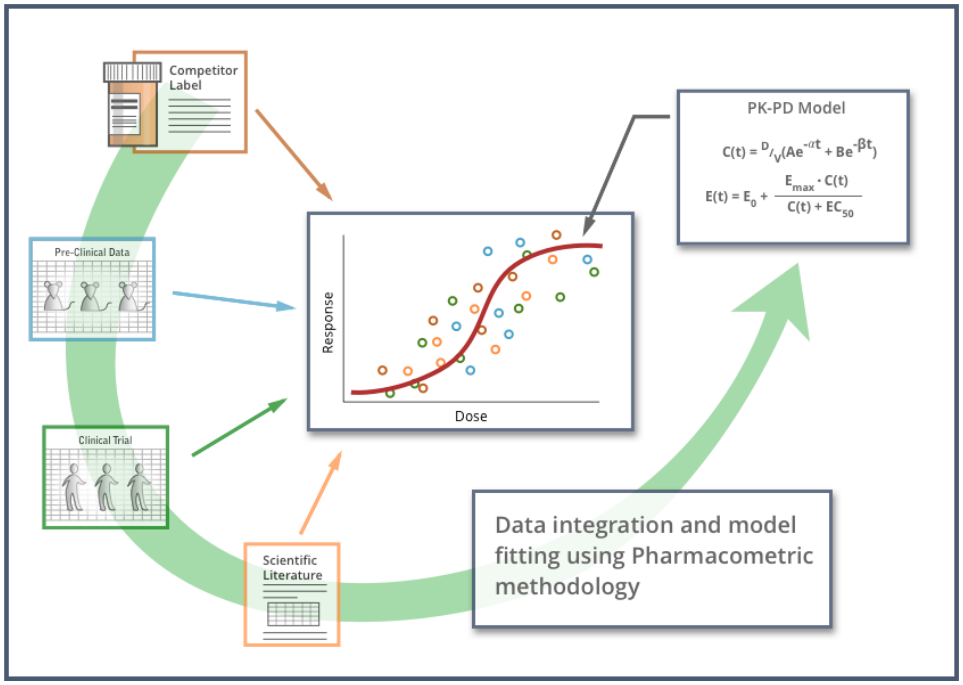
qPharmetra is helping the world's most sophisticated pharmaceutical and biotech companies develop better medicines using pharmacometrics.

- **Optimize dosing decisions**
- **De-risk late phase development programs**
- **Choose trial designs with higher probabilities of success**
- **Position your drug to compete effectively**
- **Develop robust regulatory submissions**
- **Produce compelling data packages for partners**

Pharmacometrics uses models to describe the beneficial and adverse effects of a drug therapy on a patient by combining multiple data sets in a logical way to get the most out of your data. Pharmacometrics is also known as Quantitative Clinical Pharmacology or PK/PD modeling.

"Pharmacometrics is an emerging science defined as the science that quantifies drug, disease and trial information to aid efficient drug development and or regulatory decisions."

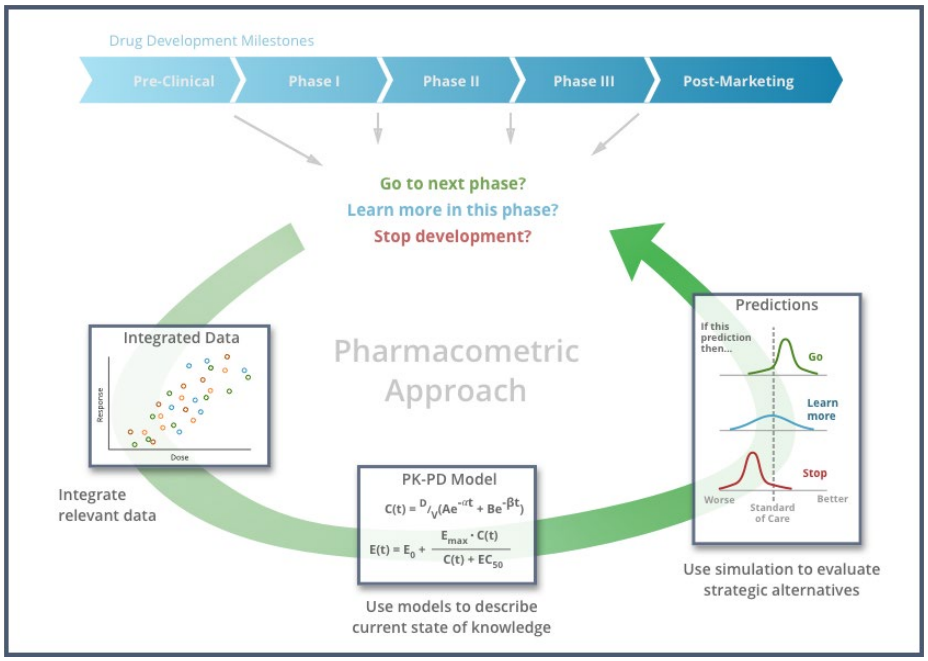
- U.S. Food & Drug Administration



The Pharmacometric Approach

Data → Models → Simulations → Decisions

By combining different types of models with a simulation step, a pharmacometrician brings quantitative insight to the strategic decisions arising in commercial drug development.



"The single-most important strength of pharmacometric analysis is its ability to integrate knowledge across the development program and compounds, and biology."

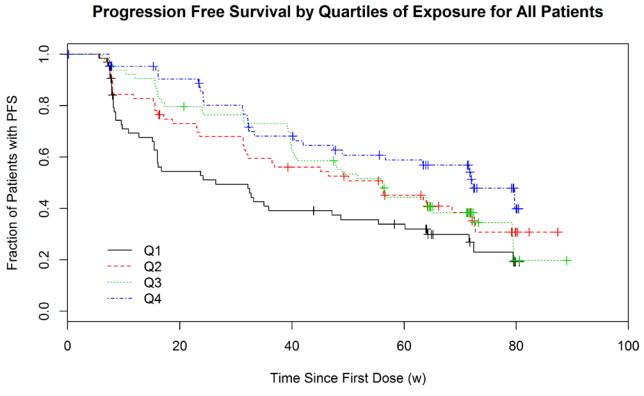
- U.S. Food & Drug Administration

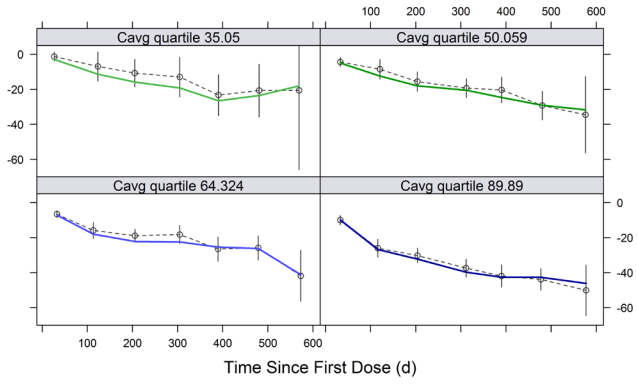
Mini-Case: Novanib Therapy for Solid Tumors

Development Context: Selection of registration dose and schedule

Available data:

- Pharmacokinetics
- Time to Disease Progression
- Reduction in Tumor Size (change in longest diameter of target lesion per RECIST)
- Historical relationship between tumor size and time to disease progression





qPharmetra's approach:

Decide how to decide

- Work closely with the company's clinical leadership to identify criteria defining optimal treatment outcome (adequate efficacy/acceptable safety and tolerability profile)

Modeling - Describe the data in a consistent mathematical framework

- Characterize PK and test patient characteristics for clinically important predictors of drug exposure
- Build exposure-response model to predict change in tumor size
- Use proportional hazards model to characterize relationship between change in tumor size and time to disease progression

Simulation - Examine alternative treatment regimens in large numbers of virtual patients using Monte-Carlo simulation to predict the outcome for different candidate treatment regimens

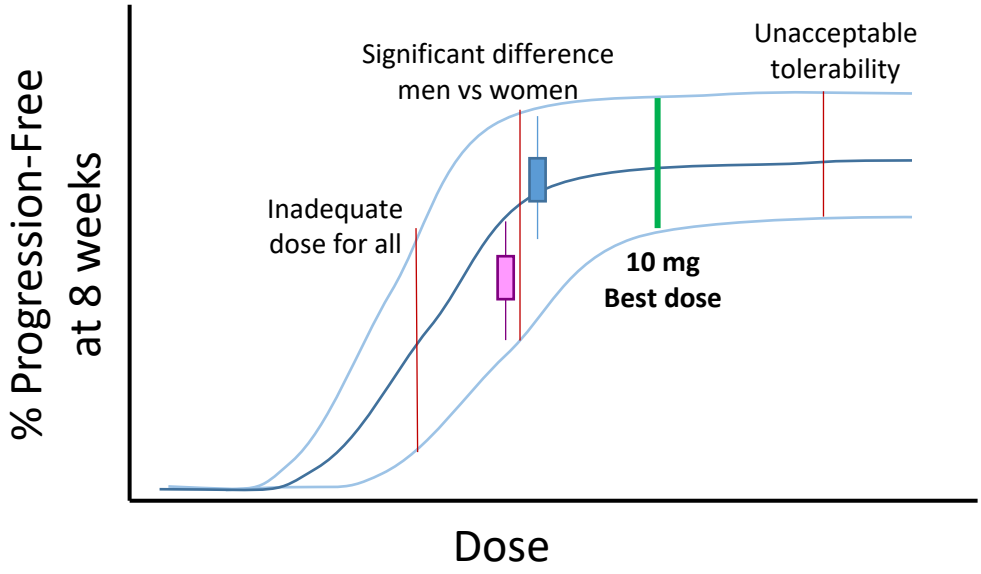
The pharmacometric approach is applied iteratively throughout the drug development process.

At each stage in the process, the relevant data is integrated to build models describing the current state of knowledge. This is the learning part of the iteration cycle.

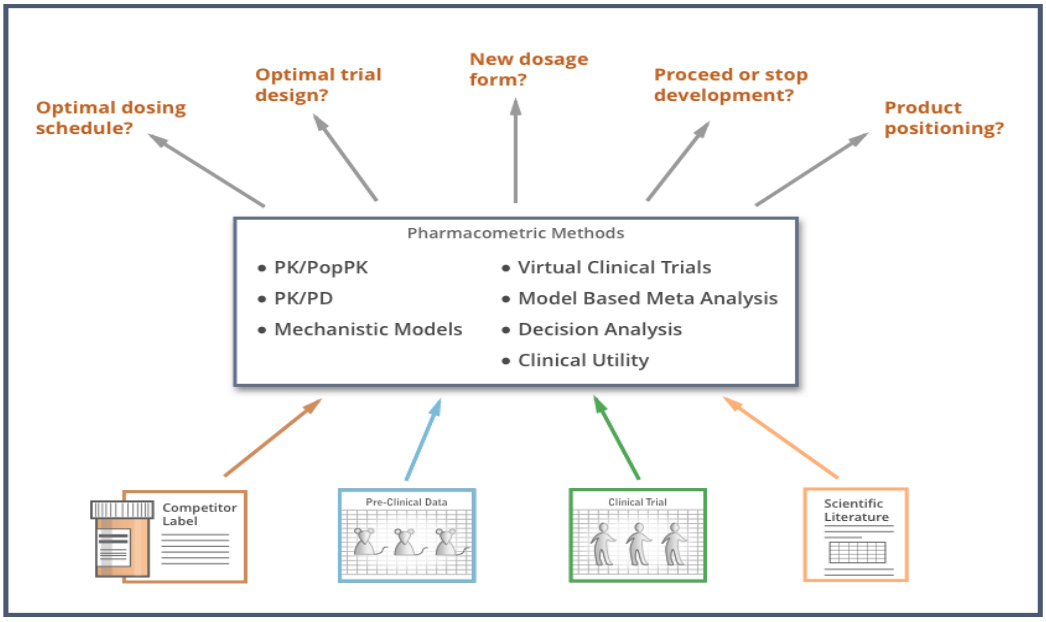
Next, these models are used to simulate strategic alternatives, producing quantified risk assessments of each option.

Impact:

Women were shown to have 35% lower exposure than men for a comparable dose. A dose of 10 mg daily was shown to give sufficient exposure to predict an 8-week progression-free survival advantage relative to standard of care in 85% of patients.



How can qPharmetra help improve the probability of success for your next clinical trial?



Clinical Pharmacology Consulting: We work closely with the company's clinical leadership to offer strategic guidance on the contents of the clinical pharmacology package, and help design the clinical pharmacology program.

Pharmacometrics: Data from pre-clinical and clinical studies, scientific literature and competitor regulatory filings are integrated into a full data package describing the characteristics of your drug. From this integrated data set, mathematical models of exposure and response are built and qualified to represent the drug's behavior. Simulation can then be used to optimize dose selection and trial design.

Data collected from subsequent trials are then used to confirm and improve the accuracy of the models. In this way, as the process moves forward, the ability to quantify development risks and improve the odds of success improve at each step.

qPharmetra is a global leader in pharmacometric analysis with offices in The Netherlands, Sweden and the United States.

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