**BACKGROUND**
- The therapeutic effectiveness of Drug X as a single agent has been clinically established.
- The efficacy of Drug X in a drug combination was evaluated in a clinical trial in the target patient population.

**STUDY DESIGN**
- Parallel, fixed doses
  - Group 1 (n=200 pts): Drug combination + Drug X
  - Group 2 (n=200 pts): Drug combination
- PK sampling
  - Up to 4 samples in weeks 1, 4, 12, 24
- Efficacy sampling
  - Up to 7 samples in weeks 0, 2, 4, 8, 12, 16, and 24.

**OBJECTIVE**
- To quantify the therapeutic value of Drug X in a drug combination.

**APPROACH**
- To evaluate the effect of Drug X by using modeling.

**METHODS (cont’d)**

**Characterizing Time Course of Response**
- Inhibitory (Emax) model
  - Drug effect is a function of time (t) and Drug X exposure (AUC)
  - Linear
    \[ \log(\text{Effect}) = V_0 + E_{\text{max}}(1 + \beta \times \text{AUC}_t) / \text{Th} + \epsilon_i \]
  - Non-linear
    \[ \log(\text{Effect}) = V_0 + E_{\text{max}} \frac{\text{AUC}_t}{\text{Th} + \epsilon_i} \]

**RESULTS (cont’d)**

**Time Course of Response**
- Estimate Probability of Response
  - Binary logistic regression model
    - Probability of response: achieve a target effect in a defined treatment period
    - Probability is a function of Drug X exposure (AUC)

**CONCLUSION**
- A model-based approach allows the evaluation of effect of a single drug in a combination therapy and is useful to
  - Assess the therapeutic value of Drug X in a drug combination.
  - Establish a scientific rationale for inclusion of Drug X in the combination therapy.