# Optimizing the sample size of a bridging study using Simulx, an application of the MonolixSuite

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**Watch webinar to see all steps live in Simulx**

## GOAL

Reference asthma treatment
- Current standard-of-care
- Approved globally (also in China)

New asthma treatment
- FDA approved
- does not include Chinese patients

Plan a bridging study for approval in China

*What is the sample size* required for a trial in Chinese patients to show a difference in response between the two treatments?

STANDARDIZE your workflow with MonolixSuite

## WORKFLOW

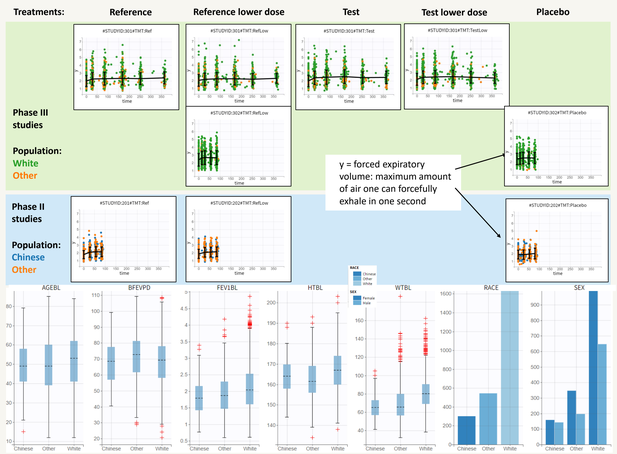
Data
- phase III, NEW treatment, NO Chinese patients
- phase III, REF treatment, NO Chinese patients
- phase II, REF treatment, ONLY Chinese patients

Population modeling in Monolix
- single population model covering the 3 datasets
- Investigate the impact of the covariates for Chinese and non-Chinese patients

Clinical trial simulations in Simulx
- Predict the response to the new treatment in Chinese asthma patients
- Suggest a minimal sample size for China bridging study

EXPORT your estimated model in one click

## DATA

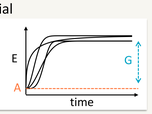



QUICKLY get a complete overview of all data with Monolix custom PLOTS

## PD MODEL ESTIMATED IN MONOLIX

Structural model: exponential

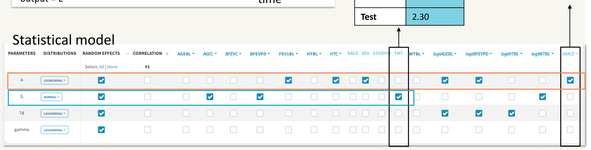
```
[LONGITUDINAL]
input = {A, G, Td, gamma}
EQUATION:
S = G * (1-exp(-(1/Td*t)^gamma))
E = max(1e-3, A + S)
OUTPUT:
output = E
```



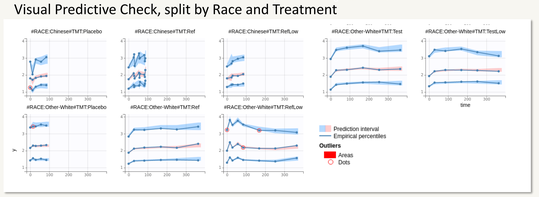

| TMT | Typical G |
|---|---|
| Placebo | 0.9 |
| RefLow | 1.34 |
| Ref | 1.59 |
| TestLow | 1.72 |
| Test | 2.30 |

| RACE | Typical A |
|---|---|
| White | 1.32 |
| Chinese | 1.26 |
| Other | 1.27 |

Statistical model



Visual Predictive Check, split by Race and Treatment

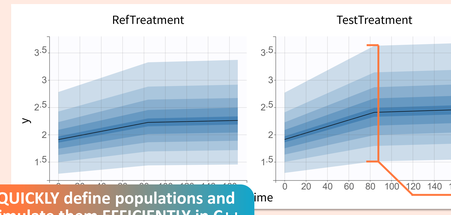



Save time with our AUTOMATED COVARIATE SEARCH strategies

## CLINICAL TRIAL SIMULATION IN SIMULX

### Simulation

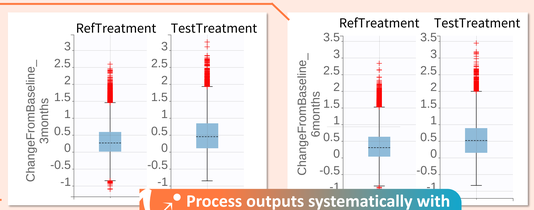
Comparing reference and new treatment in a population of **75 Chinese patients, during 3 months or 6 months**.




QUICKLY define populations and simulate them EFFICIENTLY in C++

### Quantitative Outcome and Endpoint

What is the **mean FEV1 change from baseline at the end of the study**?




Process outputs systematically with Simulx OUTCOMES & ENDPOINTS

### Trial Success

Is the mean FEV1 change from baseline **significantly higher with the new treatment**?

Unpaired t-test
H1: difference of arithmetic mean > 0
Success if p-value < 0.05

meanCFB_3months

| REP | TESTTREATMENT | | |
|---|---|---|---|
| | DIFFERENCE | P-VALUE | SUCCESS |
| 1 | 0.16 | 9.9e-3 | ✓ |

meanCFB_6months

| REP | TESTTREATMENT | | |
|---|---|---|---|
| | DIFFERENCE | P-VALUE | SUCCESS |
| 1 | 0.31 | 2.18e-5 | ✓ |

STATISTICAL TESTS to check trial success in a few clicks

### Power of the study = probability of success

**Variability between replicate studies and uncertainty** of our model can affect the results

meanCFB_3months

| REP | TESTTREATMENT | | |
|---|---|---|---|
| | DIFFERENCE | P-VALUE | SUCCESS |
| 1 | 0.16 | 9.9e-3 | ✓ |
| 2 | 0.13 | 6.92e-2 | ✗ |
| 3 | 0.27 | 5.75e-4 | ✓ |
| 4 | 0.2 | 3.93e-3 | ✓ |

meanCFB_6months

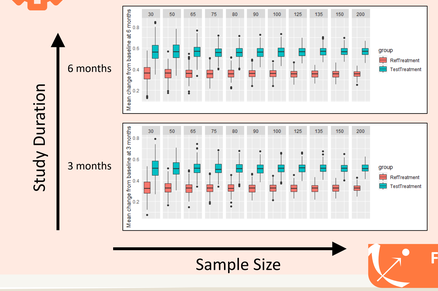
| REP | TESTTREATMENT | | |
|---|---|---|---|
| | DIFFERENCE | P-VALUE | SUCCESS |
| 1 | 0.31 | 2.18e-5 | ✓ |
| 2 | 0.087 | 1.45e-1 | ✗ |
| 3 | 0.18 | 1.23e-2 | ✓ |
| 4 | 0.16 | 1.93e-2 | ✓ |

Percentage of success over 300 replicates

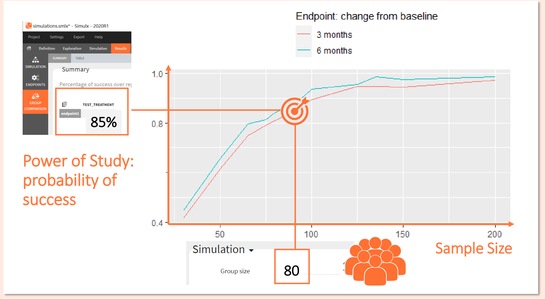
| TESTTREATMENT | |
|---|---|
| 3months | 79 |
| 6months | 81.33 |

Include replicates to get the POWER of your TRIAL

### Optimize trial design with LixoftConnectors




Fully AUTOMATE your workflow across apps with R




The required sample size is 80 individuals per group.

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