

CASE STUDY

Adding A Stratification Factor During The Study



Study Description

Phase III study randomized study comparing two drugs (Drug1 and Drug2) following chemotherapy in patients with newly diagnosed FLT3-mutated acute myeloid leukemia



Indication

Acute myeloid leukemia



Patient population

Large sample



Regions

North America



Situation

Randomized study using a 1:1 minimization algorithm based on six stratification factors

Early result review and observation:

- 187 patients randomized (94/Drug1 : 93/Drug2)
- 27 patients identified with an important biomarker that could potentially impact the outcome
 - 10 events were observed among the 27 patients
 - Imbalance treatment allocation for those patients (10/drug1 : 17/drug2)



Sponsor request: Integrate that biomarker as a stratification factor (replace or add stratification factor)



The Solution

- IDDI Biostatisticians advised to add this important biomarker as a stratification factor
- RTSM team imported the collected biomarker data for existing patients in the RTSM platform

Results

**IDDI has
successfully
delivered**

Adding a stratification factor & importing the collected biomarker data for existing patients allowed the sponsor to **reach overall balance amongst the two arms for these seven stratification factors**



Solution Detail (1)

Initially six stratification factors

Initial situation

Subject	Strat 1	Strat 2	Strat 3	Strat 4	Strat 5	Strat 6	Arm
1	1	0	1	1	0	0	Drug 1
2	0	1	1	0	1	0	Drug 2
3	1	1	0	1	0	1	Drug 1
4	1	0	1	0	0	0	Drug 1
5	0	1	0	0	1	0	Drug 2
6	0	0	0	1	0	1	Drug 1
7	1	0	1	0	1	0	Drug 2
8	0	1	0	1	1	0	Drug 2
9	0	0	1	1	0	1	Drug 1
10	1	0	0	1	1	0	Drug 2
11	0	1	0	0	0	0	Drug 1
...
Subject 187	0	1	0	1	0	1	Drug 1



Solution Detail (2)

Adding a stratification factor during the study

- Adding a new stratification factor results in having a second round of randomization not considering the information from the previous stratification.
 - ⇒ No overall balance: the balance will only be calculated for the upcoming next randomized patients

Adding Stratification Factor (no overall balance)

Subject	Strat 1	Strat 2	Strat 3	Strat 4	Strat 5	Strat 6	Strat 7	Arm
1	1	0	1	1	0	0		Drug 1
2	0	1	1	0	1	0		Drug 2
3	1	1	0	1	0	1		Drug 1
4	1	0	1	0	0	0		Drug 1
5	0	1	0	0	1	0		Drug 2
6	0	0	0	1	0	1		Drug 1
7	1	0	1	0	1	0		Drug 2
8	0	1	0	1	1	0		Drug 2
9	0	0	1	1	0	1		Drug 1
10	1	0	0	1	1	0		Drug 2
11	0	1	0	0	0	0		Drug 1
...
Subject 187	0	1	0	1	0	1		Drug 1
Next randomized 1	1	1	0	1	0	1	0	Drug 1
Next randomized 1	1	0	0	1	1	0	1	Drug 2



Solutions (3)

Importing the collected biomarker data for existing patients

- Importing the collected biomarker data for the previous subjects made it possible for the next randomization to consider all the stratification factors.

⇒ Overall global balance for all the subjects was reached as more patients got randomized through the minimization process

Importing collected data for overall balance

Subject	Strat 1	Strat 2	Strat 3	Strat 4	Strat 5	Strat 6	Strat 7	Arm
1	1	0	1	1	0	0	1	Drug 1
2	0	1	1	0	1	0	1	Drug 2
3	1	1	0	1	0	1	0	Drug 1
4	1	0	1	0	0	0	1	Drug 1
5	0	1	0	0	1	0	0	Drug 2
6	0	0	0	1	0	1	0	Drug 1
7	1	0	1	0	1	0	1	Drug 2
8	0	1	0	1	1	0	0	Drug 2
9	0	0	1	1	0	1	1	Drug 1
10	1	0	0	1	1	0	0	Drug 2
11	0	1	0	0	0	0	1	Drug 1
...
Subject 187	0	1	0	1	0	1	0	Drug 1
Next randomized 1	1	1	0	1	0	1	0	Drug 2
Next randomized 1	1	0	0	1	1	0	1	Drug1





Contact Us

Whether you need assistance with your clinical strategy, study design, clinical data management, or biostatistical analysis, IDDI's experts are here to help.

 iddi.com

 +32 (0) 10 61 44 44
+1 984 227 8599

 info@iddi.com

About IDDI

IDDI is a trusted clinical data science partner. With 35+ years of research-driven experience, we combine therapeutic expertise, biostatistical leadership, and regulatory insight to mitigate risk from design to registration and beyond.

We deliver uncompromising excellence in biostatistics, strategic consulting, clinical data management, IDMCs, and supporting eClinical technologies, because when every data point represents a patient, perfection is the only option.