**Term Project Outline**

### **1. Introduction**

*Rationale for the Study*

This study investigates the impact of Alpelisib dosing, scheduling, and the addition of endocrine therapy on treatment outcomes among breast cancer patients. Alpelisib, a PI3K inhibitor, has shown efficacy in treating hormone receptor-positive, HER2-negative breast cancer subtypes. By examining different dosing regimens and therapy combinations, we aim to identify factors that improve clinical outcomes, potentially guiding personalized treatment approaches.

Treatment outcomes for breast cancer can be influenced by both dosing patterns and the addition of combination therapies. Understanding the roles of Alpelisib dosage, scheduling, and co-administration with endocrine therapy could improve clinical benefits, help manage side effects, and inform treatment protocols for improved patient care.

*Objective*

Hypothesis (Impact of Endocrine Therapy):

* **Null Hypothesis (H₀)**: The addition of endocrine therapy to Alpelisib does not significantly affect treatment outcomes (e.g., weeks on study or best response).
* **Alternative Hypothesis (H₁)**: The addition of endocrine therapy to Alpelisib significantly affects treatment outcomes.

### **2. Method Section**

*Population of Interest*

The study population includes breast cancer patients with HR+/HER2- subtypes receiving Alpelisib treatment. Inclusion criteria ensure participants have measurable disease and are treated with Alpelisib, with or without concurrent endocrine therapy.

#### Variables of Interest

1. **Exposure Variables**:
   1. **Alpelisib Dose (mg)**: The specific dose of Alpelisib administered (e.g., 250 mg, 300 mg).
   2. **Alpelisib Scheduling**: Dosing patterns such as intermittent (7/7, 5/2) or continuous.
   3. **Endocrine Therapy**: Use of endocrine agents like Letrozole or Exemestane alongside Alpelisib.
2. **Outcome Variables**:
   1. **Clinical Benefit**: A binary measure indicating whether the patient experiences clinical benefit (yes or no).
   2. **Treatment Best Response**: Categorical response measures, including outcomes like stable disease, partial response, or disease progression.
   3. **Weeks on Study**: Total duration a patient remains engaged in treatment, measured in weeks.
3. **Covariates**:
   1. **Breast Cancer Subtype**: HR+/HER2- classification.
   2. **Mutation Count** and **TMB (nonsynonymous)**: Genetic markers that may influence treatment response.
   3. **Other Covariates**: Weight, kidney function, age, prior treatments, and comorbidities to adjust for potential confounding variables.

#### Study Design

This retrospective cohort study utilizes simple random sampling to explore relationships between dosing patterns, therapy combinations, and clinical outcomes. Although retrospective in nature, subgroup analyses and adjustments for covariates aim to mitigate bias and improve validity.

*Sample Size*

The dataset includes **140 patients** who received Alpelisib, distributed across various dosing schedules and therapy combinations. Statistical analyses will ensure adequate representation of each subgroup (e.g., dose levels and therapy status). Given the dataset size:

* Subgroup analyses (e.g., based on dose level and therapy combinations) will be carefully conducted to ensure sufficient representation.
* Statistical tests will account for the dataset's relatively moderate size, ensuring the robustness of the findings.
* Detailed descriptive statistics and exploratory analyses will provide insights before conducting inferential analyses.

### **3. Team Member Responsibilities and Contributions**

* **Klea:**
  + Literature review and formulation of the study rationale and hypotheses.
  + Compiled all sections, edited for coherence, edited, and ensured alignment with peer-reviewed feedback.
  + Will conduct sample size calculations and statistical modeling.
* **Bilal:**
  + Designed the methodology, including variables of interest and covariate selection.
  + Will conduct sample size calculations and statistical modeling.
* **Sureya:**
  + Literature review and formulation of the study design and sample size.
  + Will conduct sample size calculations and statistical modeling.