# Combining Bayesian Decision-Making with Frequentist Final Analysis in Phase 3 Oncology Trial

## Clinical Development Background

Our client is developing novel cancer immunotherapies for a range of oncologic indications. The company's lead candidate is a late clinical-stage cancer immunotherapy being developed to target hematologic cancers and solid tumors. The compound has been granted U.S. Food and Drug Administration (FDA) Fast Track Designation for the treatment of an extremely rare oncology indication. Clinical development of therapies in this indication faces inherent challenges of patient recruitment and scarcity of data.

## Sponsor Challenges

The sponsor had previously conducted a randomized, double-blind, placebo-controlled Phase 2 study. Moving into a confirmatory clinical trial setting, they came to Cytel for support with a trial design to address their key questions:

- How do we design a trial that makes most productive use of the prior information obtained from the Phase 2 study?
- Given the scant data available, how can we identify the best sample size to take forward to appropriately detect the effect size?

## Cytel Solution

- Cytel strategic consulting provided clinical trial design services including associated activities such as the development of simulations.
- Cytel ultimately proposed a 3-look adaptive study design to compare the efficacy of the compound versus control in patients with this rare indication after surgery and chemotherapy.
- The primary efficacy endpoint for the trial is Overall Survival (OS) and the design incorporates a first go/no-go interim analysis, with a subsequent sample size re-estimation interim analysis and a final analysis.
- While the primary endpoint is OS as there was not expected to be sufficient OS data at the first interim analysis, Progression Free Survival (PFS) is used combined with prior data to make a go/no-go decision.
- The second interim analysis is based on overall survival (OS) and at this point, a decision will be made to either stop the trial for efficacy or futility. Otherwise, the trial will be continued until reaching a specified number of events.
- If the trial is not stopped for efficacy a sample size adaptation will also be considered based on a promising zone design.[1]

## Outcomes

The design overcomes the challenges faced by the client of rarity of data within the indication and the assessment of sample size.

The design efficiently makes use of prior data to inform go/ no-go decision-making.

***References :*** *(1) Mehta, C. and Pocock, S. (2010). Adaptive increase in sample size when interim results are promising: A practical guide with examples. Statistics in Medicine, 30(28), pp.3267-3284.*