

TITLE: Bayesian Lalonde Go/No-Go Framework in Early Oncology: Selecting Neutral Priors and Controlling Risks

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ABSTRACT: Early oncology trials require robust Go/No-Go (GNG) decision frameworks that maximize information use and maintain statistical rigor. We piloted a fully Bayesian Lalonde GNG framework, enabling probability-based decision making throughout clinical development using predictive probability calculations. This approach aligns with cross-industry momentum toward Bayesian approaches. Through extensive simulations, we compared candidate priors – Beta(1, 1), Jeffereys prior, Beta(1/3, 1/3) to identify a neutral, weakly informative prior to use for the non-borrowing case in a single arm, binary endpoint (e.g., ORR) setting. Of the priors examined, Beta(1/3, 1/3) emerged as the most balanced choice in terms of decision operating characteristics, maintaining the risk of incorrectly stopping a promising drug within its desired level. We controlled false-go decisions by requiring the posterior median of the treatment effect to exceed a pre-specified 'critical value' from the Target Product Profile (TPP) for a GO decision, enhancing alignment between early phase decisions and the TPP. The framework applies to borrowing and non-borrowing designs and supports transparent sensitivity analyses, aiding consistent reporting and interpretation of results at each decision point throughout clinical development. Overall, this Bayesian GNG decision framework supports intuitive data synthesis and a continuous approach to de-risking across early clinical development.

PRESENTING AUTHOR BIO: Shreenidhi Soraba is a Statistician in Early Oncology Biometrics at AstraZeneca, experienced in clinical development and study design. Their work applies Bayesian Go/No-Go frameworks to enable transparent, risk-informed decisions in early oncology development.