STATISTICAL ANALYSIS PLAN

STUDY TITLE:

A PHASE II PILOT TRIAL OF HYDROXYCHLOROQUINE, EVEROLIMUS OR THE COMBINATION FOR PREVENTION OF RECURRENT BREAST CANCER ("CLEVER")

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Bayesian Poisson regression model

The number of DTCs observed by visit for each patient was analyzed with a Bayesian Poisson regression model that included treatment-by-visit effects and patient-level random intercepts to account for overdispersion in the outcomes. We denote observations within index $i \in 1, \ldots, N$ and patients with index $s[i] \in 1, \ldots, S$. Let y_i represent the number of DTCs for observation i. The Bayesian model is specified as follows:

$$y_i \sim Pois(\lambda_i)$$

$$\log(\lambda_i) = \alpha + \mu_{s[i]} + \boldsymbol{X}_i'\boldsymbol{\beta}$$

where α is an overall intercept, $\mu_{s[i]}$ is a patient-level intercept, $\boldsymbol{X_i}$ is a vector of treatment by visit effects, and $\boldsymbol{\beta}$ is a vector of treatment effects by visit. The following non-informative prior distributions are specified on the unknown model parameters:

$$\alpha \sim N(0, 10^2)$$

$$\beta_j \sim N(0, 10^2), j = 1{:}J$$

$$\mu_s \sim N(0, \sigma^2), s = 1{:}S$$

$$\sigma \sim t_3^+(0, 1)$$

Posterior sampling was done using the *brms* package (version 2.19.0) in the R programming language (version 4.3.1). Treatment effects for HCQ, EVE, and HCQ + EVE are presented by visit as the percent reduction in mean DTCs compared to observation alone at C3. Combination effects are evaluated by comparing the mean number of DTCs with HCQ + EVE to HCQ and EVE alone by visit. The estimated probability of DTC clearance is presented by visit and treatment group. Summaries of model parameters include the posterior mean, median, standard deviation (SD), and 95% credible interval (CrI).