2014-0255: Tumor mutation status will predict metabolic response to metformin in NSCLC

Statistical analysis plan

The objective will evaluate the correspondence of the RECIST and PERCIST tumor response methods. Each tumor’s relative change in maximum transaxial diameter on CT after 3 weeks induction metformin (N=60) will be matched with the corresponding relative change at 3-weeks from pre-treatment tumor SUV of [18F]-FDG-PET. The relationship among the pairs will be assessed for linear dependence using Pearson’s product moment correlation coefficient. The sample size of N=60 patients provides 80% power to detect a positive correlation of at least 0.32 using a one-sided test of null hypothesis of independence.

The objective will consider the predictive power of pre-treatment glucose utilization with mutation status for resultant metformin disease control (DC) using RECIST and PERCIST criteria. DC for RECIST will require CR, PR, or SD after 3 weeks induction metformin. DC for PERCIST will require a reduction in tumor SUV of [18F]-FDG-PET after 3 weeks induction metformin. The accuracy of pre-treatment SUV of [18F]-FDG-PET in predicting DC will be evaluated using area under the receiver operator characteristic curve (AUROC) for each tumor genotype independently and combined. For a one-sided test of the null hypothesis of indiscriminate prediction (AUROC=0.5), the sample size of N=60 patients provides at least 80% power to detect an AUROC of at least 0.71 at the 0.05 significance level given that the resultant disease control rate is at least 25% in the combined analysis. In addition, inference with multivariate logistic regression will be used to assess the effect of pre-treatment SUV of [18F]-FDG-PET in the presence of genotype status. Confounders of post-radiation chemotherapy and steroid use will be adjusted for using linear mixed regression modeling.