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

Version 11

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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 [^{18}F]-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 [^{18}F]-FDG-PET after 3 weeks induction metformin. The accuracy of pre-treatment SUV of [^{18}F]-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 [^{18}F]-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.