

Genetic and proteomic features associated with survival after treatment with erlotinib in first line therapy of non-small cell lung cancer.

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Background: An improved understanding of molecular features of cancers and cancer patients associated with benefit from targeted therapies could allow the rational personalization of therapies to increase the probability of efficacy and decrease toxicity and cost. Multiple biomarkers have been proposed for predicting benefit after therapy with EGF receptor targeted therapies in first line colon and second line lung cancer therapy.

Methods: In this study, we analyzed available tumor and serum samples from ECOG 3503, a single arm phase II study of erlotinib in first line lung cancer, for mutations in Kras and EGFR, as well as the previously described serum MALDI proteomic classifier (Veristrat™). Out of 137 enrolled patients, there were 93 serum samples and 43 tumor samples available.

Results: Molecular analysis of a subset of tumors from patients enrolled in ECOG 3503 shows that 10/43 (23%) contained Kras mutations and 3/43 (7%) harbored EGFR mutations. Classification of the 93 available sera for the pattern of proteins previously published as associated with survival after treatment with gefitinib identified 68/93 (73%) as predicted to be “good” and 25/93 (27%) predicted to have poor survival. Of the 6 responders with available serum, 5 were classified as MALDI good. Correlation with survival demonstrated a highly statistically significant correlation with MALDI status ($p < 0.001$), and a marginally significant association of EGFR mutation with survival ($p = 0.05$), but no correlation with ras mutation status. Median survival was 10.8 months in MALDI good patients and 3.9 in MALDI poor patients. MALDI status was independent of both ras and EGFR mutation status.

Conclusions: Thus, in distinct contrast to colon cancer, ras gene mutations do not appear to be associated with survival after first line EGFR-targeted therapy in lung cancer. The previously defined MALDI predictor is potent and highly clinically significantly associated with survival after first line treatment with erlotinib, and is independent of mutations in ras and EGFR in this dataset.