

Thoracic Malignancy Steering Committee (TMSC)

Lung cancer remains the deadliest cancer in the world despite the progress made with the approval of targeted and immunotherapies. With 5-year survival at a dismal 19% across all stages, there is dire need to conduct clinical research via innovative trial designs that are biomarker driven with clinically meaningful endpoints.

The Thoracic Malignancy Steering Committee (TMSC) has reviewed a robust portfolio of clinical trials over the last 5 years. Two novel paradigm-shifting trials in biomarker-driven molecularly targeted therapies were a direct result of the Joint FDA-NCI Clinical Trials Planning Meeting in February 2012. These trials, ALCHEMIST (randomized phase III adjuvant therapy) and LungMAP (a stepwise rapid evaluation of potential novel agents in stage IV non-small cell lung cancer (NSCLC)) are directing lung cancer care into an era of personalized medicine.

Treatment options approved for lung cancer have substantially increased in the last 5 years and with approval of multiple immunotherapies as single agents or in combinations upfront. However, treatment options for patients post progression after immunotherapies are limited.

The priorities have been reevaluated and modified periodically.

1) Innovative clinical trials that facilitate rapid development of therapies in immune-refractory patients and novel targeted agents for newly defined subsets in thoracic malignancies.

- a. Examine potential synergies between various agents in patients with advanced NSCLC who develop immuno-resistant disease.
- b. Evaluate tumor tissue for development of new biomarkers utilizing NGS and other emerging technologies that alter the efficacy and durability of response to genetically targeted therapies (e.g., EGFR TKIs) and or identify immune-refractory tumors.
- c. Validating ctDNA or other blood or sputum assays) for MRD and using it to personalize therapy would be valuable.
- d. Examine role for agents in adjuvant setting in resectable disease and as part of multimodality therapy for stage III disease as well as in other thoracic malignancies (mesothelioma, SCLC).

- 2) The rapid testing of new agents and strategies for the treatment of small cell lung cancer (SCLC) through innovative, real world trial designs that recognize the aggressive and widely metastatic nature of the disease and consequent patient disability.**
- 3) Exploration of neoadjuvant therapy for localized, resectable NSCLC, both as a method to potentially improve outcome as well as a way to evaluate the biological efficacy of new therapies.**
- 4) Rapid testing to determine the optimal role in terms of both efficacy and toxicity of new radiation approaches including protons, image-guided radiation therapy, stereotactic body radiation therapy (SBRT), etc.**