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) **Explore promising agents and combinations to find niches where industry is not active; examine markers of activity that could better drive precision IO and IO combinations, and evaluate the biological efficacy of new therapies.**

    a. Evaluate tumor tissue and biological fluids for development of new biomarkers that alter the efficacy and durability of response to genetically targeted therapies (e.g., EGFR TKIs), identify immune-refractory tumors, and maximize the use of banked tissue in a timely fashion in order to focus further therapies.

    b. Examine the role for agents in neoadjuvant and adjuvant settings in resectable disease and stage III unresectable disease and as part of multimodality therapy for locally advanced disease as well as in other thoracic malignancies (mesothelioma, SCLC).

2) **Validate ctDNA or other blood or sputum assays and consider prospective trials for MRD and using it to personalize therapy.**

3) **The rapid testing of new agents and strategies for the treatment of small cell lung cancer (SCLC) through innovative trial designs that recognize the aggressive and widely metastatic nature of the disease and consequent patient disability.**

4) **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.**
5) **Explore opportunities for more surgically-based trials.**
6) **Increase enrollment of underrepresented patients on clinical trials in the NCTN.**