# Next Generation Sequencing (NGS) Use Case 11.19.18

## M-CODE Working Group

Mr. A is a 58 year old Caucasian male (born in 1960) former smoker who presents with shortness of breath and pleuritic chest pain. He is referred to Dr. B, who performs a complete history and physical and orders a CT of the head and neck, chest, and abdomen, which shows multiple pulmonary and bone metastases. CBC with differential and comprehensive metabolic panel are all within 10% of normal limits. An FDG PET/CT confirms bone metastases. Brain MRI demonstrates 5 brain metastases all less than 1 cm, and no significant edema. Past medical history includes diabetes mellitus type II with neuropathy and congenital (hereditary) long QT syndrome. ECG shows normal sinus rhythm with QTc 490ms. Medications include insulin. His performance status is Eastern Cooperative Oncology Group (ECOG) 2.

To make a pathologic diagnosis and to obtain tissue for genomic analyses, tissue biopsy is performed on a lung lesion using CT-guided core biopsy. Pathology demonstrates non-small cell lung carcinoma (NSCLC). He is clinical Stage Group IVA (M1b): limited metastatic sites and definitive therapy for thoracic disease feasible. Genomic testing (next generation testing; NGS method) and PD-L1 biomarker testing (immunohistochemistry method) testing is ordered on the specimen using the FoundationOneCDx test from Foundation Medicine Inc.

Genomic testing results show actionable pathogenic variants in 4 genes: EGFR, BRAF, CDK4 and PDGFRA. PD-L1 testing is negative (<1%). The EGFR T790M variant makes him a candidate for osimertinib therapy (approved for NSCLC indication), but his history of long QT syndrome is a contraindication. In light of this, standard, non-targeted parenterally administered therapy e.g., carboplatin coupled with docetaxel, paclitaxel, or pemetrexed is under consideration.

The BRAF V600E variant provides a rationale to treat him with dabrafenib / trametinib combination therapy (approved for other cancers; would be used off-label for NSCLC; both are orally administered drugs). CDK4 amplification opens the possibility of treating him with palbociclib (FDA approved for breast cancer and liposarcoma; would be **off-label for NSCLC**; orally administered drug), and clinical trials are available (e.g., NCT03310879, NCT02896335). The PDGFRA I673M variant has no FDA-approved therapies, but clinical trials are available (e.g., NCT01306045; sunitinib; orally administered drug).

Mr. A and Dr. B discuss treatment options with shared decision making that takes into account current knowledge about potential outcomes such as **overall survival and progression free survival**; adverse effects; his own past medical history; the costs of therapeutic options; the modes of treatment delivery (oral or IV; frequency of visits to an infusion center; distance to an infusion center; and length of treatment); consideration of whether to participate in a clinical trial; and his own personal goals.

Implied facets of the case: The patient has received no prior treatments for this new diagnosis of lung cancer. The primary tumor is unresectable. Performance status is adequate to undergo treatment. ALK and ROS1 gene testing are negative. Tumor testing is somatic testing.