2015 Strategic Priorities

Head and Neck Steering Committee (HNSC)

Head and Neck Squamous Cell Carcinoma (HNSCC) is the sixth leading incident cancer worldwide. In the United States, the 2012 disease burden included 52,600 new cases and 11,500 deaths. Despite advances in surgical and radiotherapy techniques, as well as integration of chemotherapy into multimodality treatment paradigms, HNSCC is frequently lethal. Five-year overall survival (OS) is 40-60% and has increased only incrementally since 1990. Improved prognosis is largely attributable to the emerging epidemic of oral human papillomavirus (HPV) infection. An increasing proportion of oropharyngeal HNC is driven by oncogenic HPV, rather than the classic risk factors of tobacco and alcohol. HPV etiology is associated with improved survival after conventional treatments including surgery, cisplatin chemotherapy, and radiation. Although two distinct etiologies for HNSCC exist, environmental carcinogenesis or transformation by HPV oncogenes, in both instances HNSCC is associated with a fundamental failure of immune surveillance, tumor recognition and destruction. HNSCC has long been recognized as an immunosuppressive disease, inducing a permissive cytokine profile, poor antigen-presentation, low absolute lymphocyte counts, and anergy in the major effector cells of innate and adaptive immunity.

Currently available treatment options for HNSCCs consist of surgery, radiation and chemotherapy, administered in single or multi-modality regimens; however, the overall treatment efficacy still needs large improvements. Substantial clinical gains from further intensification or other variations using only these three modalities are unlikely. In addition, recently, immunotherapy has emerged as a highly promising fourth treatment modality in treatment of cancer, and its incorporation into HNSCC treatment can be readily explored now.

Thus, due to unique epidemiologic, anatomic, and clinical characteristics, HNSCC represents an ideal model among epithelial malignancies for studying the clinical trial concepts. These include:

1) HPV-associated oropharyngeal is highly responsive to conventional therapy, presenting the opportunity for reduced intensity treatment, including reduction in dose and schedule of

chemo-/radio-therapy or surgery. Current multimodality regimens designed for HPV-negative disease likely represent overtreatment and lead to substantial acute and long-term toxicities. A national priority in HNSCC is the development of rational de-intensification strategies which preserve the high cure rate while sparing late toxicity.

2) HPV-negative HNSCC is a model of a genetically heterogeneous, carcinogen-induced cancer. HPV-negative disease remains associated with a poor prognosis, despite treatment intensification.

The NCTN treatment trials approved by the Head and Neck Steering Committee should reflect the overarching clinical and scientific objectives of improving survival, decreasing morbidity and enhancing quality of life through development and refining of local, regional and systemic therapies for all solid tumors arising about the head and neck.

In the context of the Committee's principal goals, important trial design features may include definition and testing of biomarker-driven treatment algorithms and application of new agents useful in treating all stages of cancers arising about the head and neck. Incorporation of quality of life and patient reported outcome measures into Committee-approved trials is appropriate.

Enumerated without preference, current Strategic Priorities for NCTN treatment trials under the auspices of the Head and Neck Steering Committee are:

1) Facilitate the development and refine the use of systemic therapies for tumors arising in the head and neck and for thyroid cancers (including the testing of immune-modulating and molecularly targeted approaches in appropriately defined populations).

2) Design treatment trials to improve efficacy and survival, decrease morbidity, and increase quality of life.

- **a.** Improve the use and application of focused radiotherapy techniques (such as IMRT, IGRT, SBRT, and particle beam therapy)
- **b.** Improve the use and application of modern surgery (such as natural orifice

and minimally invasive approaches)

c. Minimize late treatment-related morbidity by rigorously testing strategies aimed at reducing treatment intensity for patients with good prognosis

3) Develop trials for treatment-resistant head and neck cancers.

4) Pursue trials of rare tumors arising about the head and neck, which can only be undertaken through the NCTN.