

2015 Strategic Priorities Genitourinary Cancer Steering Committee (GUSC)

The following summaries are based upon input from a series of strategic planning activities including multiple conference calls and in-person meetings among members of the GUSC and its Task Forces, and NCTN groups' appropriate disease committees, over several months from September 2014 to May 2015. Each of the groups presented their recent and ongoing development plans in the context of these meetings. Common themes that emerged from these discussions are summarized for each one of the Prostate, Bladder and Renal Task Forces.

Prostate Task Force

Prostate cancer is a disease affecting hundreds of thousands of Americans annually with a disease history that frequently traverses many decades and several distinct disease states, while being managed in a very multi-disciplinary fashion. The sheer prevalence of this disease and its long natural history mean that there are huge public health costs and policy implications that can arise from informative trials. The NCI GU Steering Committee, while interested in all aspects of prostate cancer, must of necessity focus on treatment, and within that still broad category, prioritize even further. Surveillance, imaging, and survivorship studies will be addressed elsewhere under the NCI trials structure. Within the treatment domain emphasis will be placed upon trials that aim to sharpen our selectivity for therapy, test the integration of new biologic agents, and improve survival. The two points in the "disease-arc" at which it is felt that an impact can be made and survival benefits felt within a reasonable timeframe are: the castration-sensitive advanced phase (including PSA-only recurrence and oligometastatic disease); and the castration-resistant phase. This is not to say that other points in the disease-arc will not be considered, they will, but they can only be prioritized if there is the potential for substantial practice change.

- 1) Integrate earlier, life-prolonging therapies into castration-sensitive metastatic disease directed toward improvement in survival, including multimodality strategies targeting oligometastatic disease.
- 2) Develop and validate predictive models and biomarkers of outcome for integration into the management of multiple stages of prostate cancer.
- 3) Screen, integrate, and optimize biological therapies in the management of prostate cancer within studies targeting unique high risk populations.
- 4) Develop trials with multimodality approaches or novel mechanistic strategies in castrate-resistant prostate cancer (CRPC).
- 5) Prioritize strategies for randomized or large scale testing studies that can lead to practice change.

Bladder Task Force

Bladder cancer is the most expensive cancer from diagnosis until death and ranks 18th in overall NIH funding representing an enormous unmet need in translational and clinical trials research. There has been no new approved drug in any stage since the approval of Valrubicin for BCG unresponsive CIS in 1998 and the 5-year survival probability for patients with muscle invasive (MI) cancer or visceral metastatic disease has not changed appreciably in the last 3 decades. The publication of specific guidance from the FDA regarding design of registration trials in non-muscle invasive bladder cancer (NMIBC) together with emerging data regarding the potential efficacy of immune based therapies and results from large scale integrative genomic profiling is rapidly accelerating drug development in all stages of bladder cancer. The field is poised to leverage these seminal events to design practice changing therapeutic trials with a rapid expansion of potential therapeutic targets in all phases of the disease. These clinical trials should provide a robust platform for validating predictive and prognostic biomarkers and molecular taxonomy.

- 1) Integrate, evaluate, and optimize molecularly targeted and immune-based therapies into the treatment of NMI and MI bladder cancer and/or other urothelial malignancies.
- 2) Evaluate novel primary treatment approaches alone or in combination with standard of care chemotherapy for high-risk or advanced/metastatic bladder cancer and other urothelial malignancies.
- 3) Identify patients at high risk for recurrence of bladder cancer (and/or other urothelial malignancies) following definitive local or loco-regional therapy, and, in this setting, optimize locoregional management as well as integrate novel treatment approaches (neoadjuvant, concurrent, or adjuvant).
- 4) Evaluate novel treatment interventions for patients suited for bladder-sparing therapy.
- 5) Incorporate and validate pathologic diagnosis and stage, risk stratification, predictive models and biomarkers of outcome into the management of bladder cancer, including integration of surgical innovations and evaluation of patient quality of life.

Renal Task Force

- 1) Evaluate agents and combinations for all clinically relevant histologic subtypes of renal cell carcinoma (RCC), guided by data from TCGA when available. There is a developing trial to evaluate Met inhibitors in papillary RCC.
- 2) Integrate immune-based therapies into the neoadjuvant, adjuvant, and metastatic treatment approaches for renal cell carcinoma. A proposal is in development to evaluate anti-PD-1 monoclonal antibody in the adjuvant and neoadjuvant setting.
- 3) Define mechanisms of resistance to active agents in RCC and identify and test strategies for overcoming this resistance, particularly with respect to anti-VEGF and anti-mTOR agents.
- 4) Develop and validate predictive models and biomarkers of outcome to specific, pathway-directed therapies in RCC. This will be evaluated concurrently with studies developed in priorities 1 and 2.

- 5) Identify biologic characteristics in non-metastatic RCC to guide approaches outlined above in neoadjuvant, adjuvant, and advanced disease settings. This is undergoing evaluation in the ongoing analysis of the intergroup study ECOG-ACRIN 2805.