GENITOURINARY CANCER STEERING COMMITTEE
SUMMARY OF DISEASE-SPECIFIC PRIORITIES

PROSTATE TASK FORCE

DISEASE-SPECIFIC PRIORITIZATION FOR PROSTATE CANCER

Preamble:

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 be addressed from informative trials. The NCI GU Steering Committee, while interested in all aspects of prostate cancer, must by necessity focus on treatment, and within that still broad category, prioritize even further based on unmet needs, which includes studying historically underrepresented and/or underserved populations. Strategies for randomized or large-scale testing studies that can lead to practice change will be emphasized. Surveillance, imaging, other biomarkers, and survivorship will not only be integrated into trials, but also have specific dedication elsewhere under the NCI trials structure. Within the treatment domain, emphasis will be placed upon trials for potentially lethal prostate cancer that aim to sharpen our selectivity for therapy, test the integration of new biologic agents, and improve survival. The parts of the “disease-spectrum” for which an impact can be made and survival benefits felt within a reasonable timeframe range from the castration-sensitive phase (including high-risk localized, PSA-only recurrence and oligometastatic disease) to the castration-resistant metastatic phase. This is not to say that other points in the landscape will not be considered; they will, but they can only be prioritized if there is the potential for substantial practice change.

1. Integrate promising therapies earlier into potentially lethal castration-sensitive prostate cancer directed toward improvement in survival or appropriate surrogates, including multimodality strategies targeting high-risk localized and oligometastatic disease.
2. Develop and validate predictive models, imaging, and other biomarkers for integration into selection and stratification of patients in the management of multiple stages of prostate cancer.
3. Identify, integrate, and optimize therapies in the management of prostate cancer within studies targeting specific, unique and high-risk populations, including historically underrepresented and/or underserved populations.
4. Develop trials with multimodality approaches or novel mechanistic strategies evaluating pharmacodynamics and elucidating mechanisms of treatment resistance.
5. Develop trials that study patient-centered outcomes, including quality of life, financial toxicity, and other patient-reported outcomes; and optimize existing strategies, including

treatment deintensification.

BLADDER TASK FORCE

DISEASE-SPECIFIC PRIORITIZATION FOR BLADDER CANCER

Preamble:

Bladder cancer is a common malignancy with substantial morbidity and mortality. There have been important therapeutic advances over the past several years, including the FDA approval of immune checkpoint inhibitors, antibody-drug conjugates and targeted therapeutics. These advances have led to many clinical trials investigating novel therapeutic approaches in non-muscle-invasive, muscle-invasive and metastatic disease. Future efforts will explore new therapeutic approaches in patients with immunotherapy-resistant disease, integration of biomarkers in all phases of disease, and innovative bladder preservation approaches in practice-changing trials. There will be an emphasis on social determinants of outcome (including financial) as well as the inclusion of underrepresented and underserved populations including but not limited to women, older adults, minority populations and patients with variant histology and rare tumor types.

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1. Evaluate and optimize novel therapies alone or in combination with standard of care treatment in the management of non-muscle-invasive, muscle-invasive and metastatic bladder cancer and/or other urinary tract malignancies.
2. Optimize local therapy approaches in the management of patients with bladder cancer by integrating innovative surgical techniques, novel drug delivery platforms, enhanced imaging technologies, and radiation, with an emphasis on bladder preservation approaches.
3. Develop, validate and integrate biomarkers and novel imaging modalities in the management of patients with non-muscle-invasive, muscle-invasive and metastatic bladder cancer and/or other urinary tract malignancies.
4. Incorporate measures to evaluate patient quality of life in clinical trials of patients with non-muscle-invasive, muscle-invasive and metastatic bladder cancer and/or other urinary tract malignancies.
5. Develop and integrate strategies to optimize the management of patients with upper tract disease, including innovative kidney sparing approaches and novel trials of perioperative therapy.

RENAL TASK FORCE

DISEASE-SPECIFIC PRIORITIZATION FOR RENAL CANCER

Preamble:

Kidney cancer (renal cell carcinoma, RCC) is among the 10 most common cancers in both men and women. The incidence has been increasing, in part due to increased use of imaging with detection of incidental renal masses, some of which are benign. Renal cancers have variable natural history of growth and progression. Despite treatment of early-stage disease, some patients ultimately develop recurrent/metastatic disease. There is also a subset of patients with overt *de novo* metastatic disease at presentation. While overall survival for patients with advanced disease has improved over recent years, the disease continues to have limited 5 year survival in the majority of patients. The introduction of immunotherapy-based treatment in the adjuvant and advanced disease settings has created opportunities for innovative clinical trials of combination and sequential therapies. Additionally, there are particular disease subsets, such as non-clear cell histology, that have worse survival compared to other subgroups and warrant special attention in future clinical trials. The NCI GU Steering Committee prioritizes therapeutic trials that strive to optimize the management of early RCC or improve clinical outcomes of RCC patients with advanced disease. Preferably these clinical trials should provide a platform for validating predictive and prognostic biomarkers and/or identifying mechanisms of drug resistance. In all clinical trials, the Committee encourages investigations that incorporate assessment of patient/caregiver factors, e.g., by including well-designed, adequately-powered evaluations of Quality of Life and patient-reported outcome measures, that can influence treatment compliance and impact the clinical outcomes.

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1. Develop and optimize therapeutic approaches for advanced kidney cancer:
   a) Develop novel therapies for kidney cancer
   b) Precision medicine approaches for all clinically relevant histologic subtypes
   c) Evaluate the role of surgery, radiation, ablation, and other therapies, alone and in combination
   d) Strategies to mitigate toxicity
   e) Optimize duration and treatment sequencing strategies
   f) Psychosocial and quality of life impact

2. Enhance knowledge of the biology and clinical management of localized renal tumors:
   a) Optimize management of early, localized, and locally advanced kidney cancer
   b) Biology and natural history of localized kidney cancer
   c) Prognostic and predictive biomarkers
   d) Economic/psychosocial burden of diagnostic interventions, surveillance and management

3. Address mechanisms of acquired resistance to existing and novel therapies in kidney cancer:
    a) Defining the pathways of resistance
    b) Biomarkers of resistance
    c) Strategies to overcoming resistance

4. Develop and validate prognostic and predictive models, including artificial intelligence and machine learning:
    a) Prognostic and predictive tissue-based (tumor, blood, urine) biomarkers
    b) Molecular/metabolomics/proteomics
    c) Pharmacogenomics
    d) Imaging biomarkers

5. Evaluate disparities in care of kidney cancer and develop strategies to mitigate them:
    a) Population differences by age, race/ethnicity, geography and access to care
    b) Differences by kidney or other organ dysfunction, autoimmune disease, immunosuppression associated with transplantation, etc.
    c) Pre-disposing risk factors due to genetics, health or environment
    d) Socioeconomic impact of therapy and disparity of care
    e) Strategies to improve equity, inclusion and access to care (e.g. virtual and various modalities of care delivery)