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# Editorial: Neoadjuvant systemic therapies in bladder, kidney, and prostate cancers

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**Editorial on the Research Topic**
Neoadjuvant systemic therapies in bladder, kidney, and prostate cancers

Clinically localized high-risk cancer typically fails after local therapy alone. To improve outcomes systemic treatment is frequently combined with local therapy. Systemic treatment can be given either before (neoadjuvant) or after (adjuvant) local treatment. The advantage of neoadjuvant treatment is that systemic therapy can be given early in the course of disease (rather than after local therapy which may delay systemic therapy and treatment of micrometastatic disease), the patient is typically in "better condition" to receive systemic therapy before rather than after local treatment, neoadjuvant therapy may reduce the size of size of the primary cancer rending local treatment more feasible/successful, and the genetic features of the cancer at diagnosis may be queried to determine which type of systemic therapy is best for an individual cancer. This series of articles reviews the current state-of-the-art for neoadjuvant therapy in bladder, kidney, and prostate cancers. Patient selection, treatment selection and duration, anticipated response, and outcomes are reviewed.

## Bladder cancer

More than 50% of patients with clinically localized muscle-invasive bladder cancer treated with surgery (radical cystectomy) or radiation therapy will die from metastatic cancer. This is most commonly the result of undetected micrometastatic cancer present at the time of diagnosis. To improve on outcomes with local therapy alone multiple studies investigated the role of neoadjuvant chemotherapy prior to radical cystectomy. Cis-platin based multiagent chemotherapy given neoadjuvantly has consistently been shown to improve overall survival in up to 10% of patients. Level 1 evidence from randomized clinical trials defines neoadjuvant chemotherapy prior to radical cystectomy as the standard of care. Unfortunately, only a minority of patients receive neoadjuvant treatment in this setting. While some may decline or be ineligible to receive cis-platin

chemotherapy many eligible patients simply are not being treated according to the current standard of care. An alternative to neoadjuvant chemotherapy is neoadjuvant immunotherapy. Current evidence suggests immune checkpoint inhibitors before radical cystectomy are well tolerated and result in pathologic complete response rates similar to neoadjuvant chemotherapy. The overview of neoadjuvant treatment in bladder cancer provides a thorough overview of these strategies.

## Kidney cancer

The accompanying overview discusses the role of neoadjuvant systemic therapy in kidney cancer. Immunotherapy shows the most promise in this setting. Preliminary studies demonstrate that neoadjuvant systemic therapy often results in cytoreduction potentially making a patient a candidate for partial rather than radical nephrectomy. Analogous to other cancers, neoadjuvant therapy may eradicate micrometastatic disease and allows for correlation of treatment with pathologic and systemic immune response. Several ongoing trials will continue to define the selection of which patients will benefit from neoadjuvant treatment, which treatment should be utilized, and the safety profile of this management strategy.

## Prostate cancer

Local therapy for clinically localized high risk prostate cancer is either radical prostatectomy (RP) or radiation therapy. Most studies investigating neoadjuvant treatment have focused on androgen deprivation therapy (ADT). Outcomes were different for surgery and radiation.

### Radical prostatectomy

Multiple studies have investigated the use of neoadjuvant ADT (LHRH agonist with/without a first-generation antiandrogen) prior to RP. The typical course of ADT was short, usually 3-4 months. Outcomes did show improvement in pathological features such as the likelihood of extraprostatic extension and positive surgical margins. Unfortunately, these pathologic changes have not improved biochemical outcomes after RP. Longer course ADT (8 months) showed better pathologic improvement but did not result in a clinically meaningful benefit. The addition of neoadjuvant chemotherapy to ADT has been investigated prior to RP. The primary endpoint, freedom from biochemical recurrence three years after RP, was negative. Newer hormonal agents (androgen synthesis inhibitors and second-generation antiandrogens) are under investigation. Early studies have shown promise and the results of randomized trials are awaited. Current guidelines do not support the routine use of any neoadjuvant treatment prior to RP in clinically localized high risk prostate cancer.

### Radiation therapy

Several well-designed studies have demonstrated that the addition of ADT to radiation therapy provides an overall survival benefit in high risk and unfavorable intermediate risk prostate cancer. The risk of the cancer determines the duration of treatment. ADT is typically initiated prior to radiation therapy and then continued in a concurrent and adjuvant approach. Select patients have been demonstrated to benefit from the addition of second line hormonal therapy to ADT. An in-depth overview of neoadjuvant strategies in prostate cancer accompanies this editorial.

## Summary

Neoadjuvant therapy offers the promise of improved patient outcomes compared to local treatment alone. Such approaches have proven to improve survival in patients undergoing radical cystectomy for bladder cancer and radiation therapy for prostate cancer. Continued research is required to better select which patients do and do not require systemic therapy, which systemic therapy is best, the duration of therapy, and how to minimize toxicity. The articles accompanying this editorial provide optimism for our patients but also highlight that much still needs to be done.

## Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note