Editorial

Adjuvant chemotherapy for locally advanced bladder cancer—a step closer to ending the ongoing controversy

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Comment on: Galsky MD, Stensland KD, Moshier E, *et al*. Effectiveness of Adjuvant Chemotherapy for Locally Advanced Bladder Cancer. J Clin Oncol 2016;34:825-32.

Submitted Jul 11, 2016. Accepted for publication Jul 29, 2016.
doi: 10.21037/tcr.2016.08.31
View this article at: http://dx.doi.org/10.21037/tcr.2016.08.31

The use of perioperative chemotherapy for patients undergoing radical cystectomy for invasive bladder cancer has been increasingly employed over the last several decades in an effort to improve survival. While neoadjuvant platinum based chemotherapy has level 1 evidence showing a survival benefit from randomized controlled trials and a meta-analysis, the existing evidence supporting the use of platinum-based chemotherapy in the adjuvant setting remains poorly defined and controversial (1,2). Attempts to answer the question regarding the benefit of adjuvant chemotherapy in patients with locally advanced disease after radical cystectomy (pT3/pT4 +/– node positive disease) through clinical trials have been fraught with poor accrual. Consequently, the existing evidence for adjuvant therapy relies on the data from various meta-analyses that demonstrates benefit for adjuvant chemotherapy (3-6).

Using the National Cancer Database (NCDB), the authors present a contemporary analysis of the comparative effectiveness of adjuvant chemotherapy *vs*. observation in 5,600 patients with locally advanced disease after radical cystectomy (pT3/pT4 +/– node positive disease) (7). Overall, 23% of patients received adjuvant chemotherapy; patients who were younger, had fewer comorbid conditions, and had node positive disease were more likely to be treated with adjuvant chemotherapy. Using various propensity scoring analysis to account for patient demographic and pathologic factors, the authors demonstrated a survival benefit at 5 years of 37% *vs*. 29% in the adjuvant chemotherapy group *vs*. observation. Similar to other administrative dataset studies, several important variables such as performance status are not captured by the database. Using a novel statistical technique, the authors account for a range of varying performance status with HR of 1.3 to 2.0 and determined that a survival benefit would still be demonstrated for adjuvant chemotherapy.

This study provides a snapshot on the current patterns adjuvant chemotherapy administration across the United States using a database that captures 70% of all cancer cases in the United States. As is the case with other retrospective cohort studies, there is inherent selection bias in the form of confounding by indication to treat in the patients who were ultimately treated with adjuvant therapy. Other data such as type and duration of chemotherapy used and information on recurrence of cancer are not captured by the NCDB and therefore is minor limitation of the study. The study is by no means a substitute for a well-designed randomized controlled trial; however, it does employ several statistical techniques (i.e., propensity matching) to account for missing data, and imbalances amongst treatment groups.

The decision to give adjuvant chemotherapy in patient's patients with locally advanced or node positive disease can be difficult due to the lack of high quality evidence supporting adjuvant therapy and lack of patient accrual in previously opened trials. Currently the treatment paradigm for patients with locally advanced or node positive disease involves a discussion between the surgeon, medical oncologist, and the patient on whether to pursue adjuvant therapy that includes chemotherapy and soon immunotherapy. Certainly, data from the current study provide further support for adjuvant chemotherapy.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned and reviewed by the Section Editor Zhenyu Ou, MD (Department of Urology, Xiangya Hospital, Central South University, Changsha, China).

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2016.08.31). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Grossman HB, Natale RB, Tangen CM, et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. N Engl J Med 2003;349:859-66.
2. Advanced Bladder Cancer Meta-analysis Collaboration. Neoadjuvant chemotherapy in invasive bladder cancer: a systematic review and meta-analysis. Lancet 2003;361:1927-34.
3. Sternberg CN, Skoneczna I, Kerst JM, et al. Immediate versus deferred chemotherapy after radical cystectomy in patients with pT3-pT4 or N+ M0 urothelial carcinoma of the bladder (EORTC 30994): an intergroup, open-label, randomised phase 3 trial. Lancet Oncol 2015;16:76-86.
4. Paz-Ares LG, Solsona E, Esteban E, et al. Randomized phase III trial comparing adjuvant paclitaxel/gemcitabine/cisplatin (PGC) to observation in patients with resected invasive bladder cancer: Results of the Spanish Oncology Genitourinary Group (SOGUG) 99/01 study. J Clin Oncol 2010;28:abstr LBA4518.
5. Cognetti F, Ruggeri EM, Felici A, et al. Adjuvant chemotherapy with cisplatin and gemcitabine versus chemotherapy at relapse in patients with muscle-invasive bladder cancer submitted to radical cystectomy: an Italian, multicenter, randomized phase III trial. Ann Oncol 2012;23:695-700.
6. Leow JJ, Martin-Doyle W, Rajagopal PS, et al. Adjuvant chemotherapy for invasive bladder cancer: a 2013 updated systematic review and meta-analysis of randomized trials. Eur Urol 2014;66:42-54.
7. Galsky MD, Stensland KD, Moshier E, et al. Effectiveness of Adjuvant Chemotherapy for Locally Advanced Bladder Cancer. J Clin Oncol 2016;34:825-32.

Cite this article as: Patel S, Cookson M. Adjuvant chemotherapy for locally advanced bladder cancer—a step closer to ending the ongoing controversy. Transl Cancer Res 2016;5(S3):S385-S386. doi: 10.21037/tcr.2016.08.31

