Bladder Cancer 3 (2017) 229–230
DOI 10.3233/BLC-179022
IOS Press

Clinical Trials Corner

Dear Readers,

Bladder-sparing strategies are actively sought by patients looking to preserve their quality of life. Urologists are softening to this approaches while radiation oncologists are becoming more precise in their treatment with fewer side effects. This month's issue of the Clinical Trials Corner of the Bladder Cancer Journal is devoted towards two actively recruiting radiation trials that hope to change treatment patterns for bladder cancer. In the future, if you feel that you would like to draw attention to a specific trial, please feel free to email us at: piyush.agarwal@nih.gov or cnsternberg@corasternberg.com and/or atBLC@iospress.com.

Sincerely,

Piyush K. Agarwal, MD
Head, Bladder Cancer Section
Urologic Oncology Branch
National Cancer Institute
Bethesda, MD, USA

Cora N. Sternberg, MD, FACP
Associate Editor, Bladder Cancer
Chair, Department of Medical Oncology
San Camillo Forlanini Hospital
Rome, Italy

Study Title: A Phase II Protocol for Patients With Stage T1 Bladder Cancer to Evaluate Selective Bladder Preserving Treatment by Radiation Therapy Concurrent With Radiosensitizing Chemotherapy Following a Thorough Transurethral Surgical Re-Staging

Clinicaltrials.gov identifier: NCT00981656

Sponsor: Radiation Therapy Oncology Group (RTOG)

Enrollment: 37

Rationale: Radiation combined with radiation-sensitizing chemotherapy has been effective in well-selected muscle-invasive bladder cancer patients. However, options for T1 bladder cancer refractory to BCG are limited and include radical cystectomy or experimental therapies. This trial applies trimodal therapy to T1 bladder cancer patients in the hope of sparing their bladders and effectively treating their disease.

Study Design: This is a single arm study treating patients with TURBT and then concurrent radiation therapy and chemotherapy. The chemotherapy regimen consists of either cisplatin or mitomycin plus fluorouracil, similar to that used by the MRC for locally advanced bladder cancer [1]. Eligibility is limited to patients with recurrent Ta or T1 high grade tumor after BCG therapy or patients in whom BCG is contra-indicated or patients that refuse BCG therapy.

Endpoints: The primary endpoint is the rate of freedom from radical cystectomy at 3 years. Secondary endpoints include: rate of freedom from radical cystectomy at 5 years, rate of freedom from the development of distant disease progression at 3 and 5 years, rate of freedom from progression of bladder tumor to stage T2 or greater at 3 and 5 years, disease-specific survival, overall survival, incidence of acute and late pelvic toxicity, recurrence of any local bladder tumor, potential prognostic value of tumor histopathology, molecular genetics, DNA content, and urine proteomics and the American Urological Association symptom scores at baseline and at 3 years.

ISSN 2352-3727/17/$35.00

Comments: BCG-refractory T1 bladder cancer can be quite aggressive and normally these patients are counseled to undergo radical cystectomy. This clinical trial presents a bladder-sparing option to these patients. This trial is nearing the end of its accrual and the results may establish a new standard of therapy. However, patient selection will be key as it is for chemoradiotherapy for muscle-invasive disease and patients without hydronephrosis, CIS, or variant histology are excluded from this trial. Importantly, patients require a radical and complete TUR for inclusion into this trial.

Study Title: A Phase II Trial of MK3475 in Combination With Gemcitabine and Concurrent Hypofractionated Radiation Therapy as Bladder Sparing Treatment for Muscle-Invasive Urothelial Cancer of the Bladder

Clinicaltrials.gov identifier: NCT02621151

Sponsor: New York University School of Medicine

Enrollment: 54

Rationale: Building on the success of chemoradiotherapy for muscle-invasive bladder cancer and immunotherapy in bladder cancer, this trial combines pembrolizumab with gemcitabine and radiation therapy for muscle-invasive bladder cancer. The hypothesis is that the addition of a checkpoint inhibitor can achieve better local and systemic control of disease.

Study Design: This is a single arm, Phase II study for muscle-invasive bladder cancer patients who are not cystectomy candidates or refuse cystectomy. Since the combination has not been evaluated together, there is a safety lead-in cohort of 3-6 patients.

Endpoints: The primary endpoint is the two-year bladder-intact disease-free survival rate. This is freedom from bladder recurrence, pelvic recurrence, distant metastases, bladder cancer-related death, and cystectomy. Secondary endpoints include the following: safety, complete response rate, overall survival, and metastasis-free survival.

Comments: This trial expands on traditional inclusion criteria for chemoradiotherapy by allowing up to T4a tumors to be included and there is no exclusion criteria for associated CIS or hydronephrosis. This is concerning as we know from radiation literature that patients with these adverse pathologic features do not respond as well to chemoradiotherapy. Finally, a complete TURBT is not required for inclusion and this is most concerning as the radical TUR may be a critical part of the bladder-sparing approach. Perhaps the addition of immunotherapy can compensate for these adverse features and possibly expand the role of chemoradiotherapy.

REFERENCES

[1] James ND et al N Engl J Med. 2012 Apr 19;366(16):1477–88.