Clinical trial: Extended lymph node removal does not benefit patients with localized muscle-invasive bladder cancer

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An extended lymphadenectomy—removal of additional lymph nodes beyond the extent of the standard procedure—in patients undergoing radical cystectomy (removal of bladder and nearby tissues) because of clinically localized muscle-invasive bladder cancer provides no patient benefit as measured by disease-free survival or overall survival times. It does, however, increase the risk of adverse events (side effects) and post-surgical death.

These primary results from the phase 3 SWOG S1011 clinical trial are being delivered in an oral presentation at the 2023 annual meeting of the American Society of Clinical Oncology in Chicago on June 5 (Abstract 4508).

The results will be presented by S1011 principal investigator Seth P. Lerner, MD, the Beth and Dave Swalm Chair in Urologic Oncology at Baylor College of Medicine and an investigator with the SWOG Cancer Research Network that led the study.

The results of S1011 are expected to change clinical practice in treating these patients.

"Extended lymphadenectomy is considered a standard of care and is increasingly used," Lerner said, "especially for patients with locally advanced bladder cancer, who have a higher risk of lymph node metastases."

Once cancer invades the muscle of the bladder, it can also get into the

blood and lymphatic system and can lodge in the lymph nodes. In about one-quarter of patients with muscle-invasive bladder cancer, the disease has already spread to regional lymph nodes.

For this reason, after removing the bladder in these patients, surgeons will also remove all of the lymph nodes in the primary landing zone from around the bladder. Removing those lymph nodes—known as a lymphadenectomy—significantly reduces the chances of the cancer returning within the pelvis.

The SWOG S1011 trial asked whether it was better to extend the lymphadenectomy to remove even more lymph nodes from a wider area, and whether this would reduce the risk of recurrent disease or death.

Surgeons participating in the trial had to first undergo a credentialing process designed specifically for the study. A total of 36 surgeons at 27 participating sites in the U.S. and Canada were credentialed, and they enrolled 658 patients, 618 of whom were eligible to be randomized.

These patients were randomized during their surgery, after the surgeon had determined the patient's disease had not spread beyond the pelvis. All patients underwent a standard bilateral pelvic lymphadenectomy; those randomized to the investigative arm then also had an extended lymph node removal, with nodes removed at least up to the aortic bifurcation.

The median number of nodes removed was greater in the patients on the extended lymphadenectomy arm—39 nodes vs. 24 nodes on the control arm—but the percentage of nodes found to contain metastatic disease was similar on the two arms—26 percent versus 24 percent, respectively.

Patients on the extended lymphadenectomy arm were more likely to experience grade 3 or 4 adverse events (serious side effects) within 90

days of surgery, regardless of attribution, than patients who received a standard lymphadenectomy—49 percent of patients versus 42 percent. Additionally, the number of deaths within 90 days of surgery was also greater on the investigative arm—19 patients versus 7 patients.

The SWOG S1011 team had hypothesized that the group of patients on the investigative arm would have improved disease-free and overall survival times compared to those on the control arm. However, no significant differences were seen between the extended versus standard lymphadenectomy arms in disease-free survival (HR = 1.10 [95% CI 0.87, 1.42], 2-sided p = 0.40) or in overall survival times (HR 1.15 [95% CI 0.89, 1.48] 2-sided p = 0.29).

Lerner noted that a definitive phase III surgical trial of this sort was an ideal fit for the NCI's National Clinical Trials Network (NCTN).

"SWOG S1011 addressed an important surgical question, and the federally funded NCTN is uniquely suited for such practice-changing trials led by surgical oncologists," Lerner said. "Collaboration across the NCTN was the key to success, as was equipoise from high-volume surgeons who recognized the lack of level I evidence supporting our current practice at the time we conceived the trial."

More information: Abstract 4508: Phase 3 SWOG S1011 clinical trial

Provided by SWOG Cancer Research Network