Postop Radiation Aids Survival In Some Endometrial Ca Patients

BY BRUCE WILSON
Contributing Writer

PHILADELPHIA — Adjuvant external beam radiation therapy with or without vaginal brachytherapy can lead to improved overall survival for some women with high-risk endometrial carcinoma, according to a study reported at the annual meeting of the American Society for Therapeutic Radiology and Oncology.

"Endometrial adenocarcinoma remains the most commonly diagnosed [gynecologic] malignancy in the United States, but optimal treatment for stage I and II disease remains controversial," said Dr. Christopher M. Lee of the department of radiation oncology, Huntsman Cancer Hospital, Salt Lake City. He noted that selected high-risk subgroups have increased local-regional recurrence rates and decreased survival, but which of those patients might benefit from adjuvant radiation is still controversial.

These data show that 'the improvement in overall survival is really due to the EBRT component' and not to the additional brachytherapy component.

In this retrospective analysis, Dr. Lee and colleagues utilized the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registry database to identify women with stage IC/grade 3 and stage II endometrial carcinoma without N1 or M1 disease. Specifically, they extracted data from the SEER 11 registries and Alaska data set containing data on patients diagnosed between 1988 and 2001. They identified 4,010 patients—all of whom had undergone hysterectomy with bilateral salpingo-oophorectomy—and analyzed prognostic factors such as age, race, cancer stage, tumor grade, extent of surgery, and whether or not they had received postoperative external beam radiation therapy (EBRT) with or without brachytherapy. Of the patients, 31.3% had received EBRT and 26.2% had received EBRT plus brachytherapy. "It was interesting to us that 42.5% of this population had received no further adjuvant treatment," Dr. Lee said.

A Kaplan-Meier analysis revealed that patients with stage II/grade 1 disease received no additional survival benefit from either EBRT or brachytherapy, alone or combined. However, patients with stage IC/grade 3-4, stage II/grade 2, and stage II/grade 3-4 disease all received additional benefit with EBRT plus or minus brachytherapy. "Of interest, there were significant improvements in overall survival between external beam radiation versus EBRT versus EBRT plus [brachytherapy] in both the stage IC high-grade and the stage II high-grade cohorts," Dr. Lee said.

Further analysis revealed that older age, late diagnosis, black race, and no nodal exam at the time of hysterectomy all had a detrimental effect on survival. After controlling for these factors, the authors found that there was a significant overall survival advantage with EBRT plus or minus brachytherapy for patients with stage IC/grade 3-4, stage II/grade 2, and stage II/grade 3-4 disease, but not with stage II/grade 1 disease. Contrary to the prior results, there was no improvement in overall survival with the addition of brachytherapy to EBRT. These data show that "the improvement in overall survival is really due to the EBRT component" and not to the additional brachytherapy component," Dr. Lee said.

Because of the retrospective nature of the trial, he cautioned against making too many conclusions about the data. "In the future, we would like to continue to look into and delineate the clinical and biological factors that would help us guide treatment and help us to account for the disparities we see between different patient cohorts, and to continue to develop a standardized and a risk-adaptive or stratified approach for adjuvant treatment for these patients," Dr. Lee said. ■

Dye-Colloid Combo Excels In Sentinel Node Mapping

BY ROBERT FINN
San Francisco Bureau

SANTA MONICA, CALIF. — A combination of patent blue dye and technetium-99m radiocolloid appears to be more accurate than patent blue dye alone in mapping sentinel lymph nodes in vulvar cancer, according to a study presented by Dr. Lukas Rob at the biennial meeting of the International Gynecologic Cancer Society.

Furthermore, a handheld gamma probe appeared to be more accurate and more convenient than lymphoscintigraphy in detecting "hot" nodes, said Dr. Rob of Charles University in Prague.

The nonrandomized study involved 59 women with stage T1 or T2 squamous cell cancers smaller than 4 cm in diameter. The investigators used blue dye alone in the first 16 women, and the combination of technetium-99m and blue dye in the remaining 43. Patients with suspicious or bulky lymph nodes were excluded from the study.

Of the 16 patients mapped with blue dye alone, sentinel lymph nodes were detected in 11 (69%), and there was one false negative (6%). In contrast, sentinel lymph nodes were detected in all of the patients mapped with the combination of blue dye and technetium-99m, and there were no false negatives. These differences were statistically significant.

In this second group of patients, investigators found a total of 98 sentinel lymph nodes. Of those, 82 were detected by both technetium and blue dye, 15 were detected by technetium alone, and one was detected by blue dye alone.

The investigators determined that the best time for injecting the radiocolloid was 3-4 hours before surgery. They performed the injection intradermally, peritumorally, and without local anesthesia. They used 0.2-0.4 mL of Sentiscint (15 MBq). About an hour before the operation, they conducted lymphoscintigraphy. They injected 2 mL of 2.5% Bleu Patente V 3-5 minutes before incision by the same route.

Although the handheld gamma probe showed a relatively good correlation with lymphoscintigraphy, the probe identified 14 "hot" nodes not seen in lymphoscintigraphy among the 43 women in the combination group. The investigators concluded that eliminating preoperative lymphoscintigraphy and using only the handheld probe during surgery would simplify management and result in lower costs without compromising the detection rate.

In all, the investigators detected 118 sentinel lymph nodes in 59 women. Of these sentinel nodes, 84% were in the superficial medial and intermedial inguinal chain, none were in the superficial lateral groin, and 16% were deep inguinal nodes. Dr. Rob said that one important message of the study was that it's crucial not to neglect a search for these deep inguinal nodes. ■

Gynecologic Cancer Patients in Clinical Trials Live Longer

BY ROBERT FINN
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SANTA MONICA, CALIF. — Patients with gynecologic cancer who chose to participate in phase I clinical trials survived for twice as long as similar patients who did not participate in such trials, according to a poster presentation by Dr. Francesco Legge at the biennial meeting of the International Gynecologic Cancer Society.

These results are surprising because phase I clinical trials are intended only to assess safety and to establish dosage ranges. Any clinical benefit would be a secondary consideration.

The retrospective analysis involved patients with gynecologic cancer who were referred to phase I clinical trials at the Royal Marsden Hospital in Sutton, England, over a 2-year period. Dr. Legge, who is affiliated with the Catholic University of the Sacred Heart in Rome and in Campobasso, Italy, and his colleagues compared 32 patients who chose to participate in those clinical trials with 36 patients who were referred but chose not to participate.

Median survival time of the patients who enrolled was 8 months, compared with 4 months for the patients who did not enroll, a statistically significant difference. After a multivariate analysis that controlled for various demographic measures and disease characteristics, three factors emerged as being significantly associated with a patient's decision on whether to enroll in a clinical trial.

Median survival time of patients who enrolled was 8 months, compared with 4 months for patients who didn't enroll, a statistically significant difference.

The longer the travel time from the patient's home to the hospital, the less likely she was to enroll. Of patients who lived within 1 hour of the hospital, 61% chose to participate, compared with 48% of the patients who lived 1-2 hours from the hospital, and 8% of patients who lived more than 2 hours from the hospital.

The better a patient's health was, as measured by her performance status, the more likely she was to participate. Of the patients with an initial Eastern Cooperative Oncology Group (ECOG) performance status of grade 0 (indicating a patient who is fully active), 59% chose to participate, compared with 51% of the patients with an initial performance status of grade 1 (indicating a patient who is able to carry out light or sedentary work). None of the patients with an initial performance status greater than grade 1 chose to participate in a trial.

Abnormal liver function tests also predicted nonenrollment in clinical trials.

Among the factors for which there was no significant relationship between enrollment or nonenrollment were age; marital status; occupation; ethnicity; interval from diagnosis; number of previous surgical procedures or previous courses of radiotherapy; and the junior or senior physician status of the individual discussing the phase I trial with the patient.

Ovarian cancer was the most common type of cancer among the patients in the study, accounting for 21 of 32 (66%) patients who chose to participate in the clinical trials and 21 of 36 (58%) patients who chose not to participate. The majority of the remaining patients had cervical cancer.

The patients participated in a wide variety of clinical trials, including those testing angiogenesis inhibitors, epidermal growth factor–receptor inhibitors, methyltransferase inhibitors, DNA-repair inhibitors, and new cytotoxics.

"The practical limitations imposed by long-distance travel, together with the potential clinical benefit due to the participation [in] these trials, should encourage more investigators to develop phase I units in major cancer centers," the investigators concluded. ■