Vaginal Brachytherapy for High-Intermediate Risk Endometrial Cancers

Data from a randomized phase 3 trial indicate that vaginal brachytherapy (VBT) may be a better option than pelvic radiotherapy for treating high-intermediate risk (age>60 and stage 1C grade 1-2 or stage 1B grade 3; any age and stage 2A grade 1-2 or grade 3 with <50% invasion) endometrial cancers because of a lower rate of side effects, leading to enhanced quality of life.

Remi A. Nout, MD, Leiden University Medical Center, Leiden, The Netherlands, reported the results of the PORTEC-2 trial (NCT00376844), in which patients were randomly assigned to either external beam radiation therapy (EBRT) (214 patients) or VBT (213 patients) as treatment for high-intermediate risk endometrial cancers following total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). EBRT consisted of 46 Gy that was delivered in 23 fractions; VBT was delivered at a high-dose rate of 21 Gy in 3 fractions or at a low-dose rate of 30 Gy in a single fraction. Vaginal relapse rate was chosen as the primary endpoint, because data from PORTEC-1 indicated that the vagina was the major site of relapse in patients with endometrial cancer who had no further treatment after TAH-BSO (Creutzberg et al. *Lancet* 2000).

Dr. Nout reported that at a median follow-up of 36 months, the vaginal relapse rates were not significantly different between the 2 arms (0.9% for VBT vs 1.9% for EBRT; p=0.97). The rate of pelvic recurrence was higher for patients in the VBT arm (3.5% vs 0.6%; p=0.03), but Dr. Nout pointed out that the majority of those pelvic recurrences was associated with distant recurrence. Both overall survival and relapse-free survival rates were similar for both arms of the study. The 3-year disease-free survival rate was 89.7% for VBT compared with 88.6% for EBRT (p=0.68). The overall survival at 3 years was 90.8% for VBT and 90.3% for EBRT (p=0.96).

While the efficacy of the 2 treatments was similar, VBT offered an advantage in terms of quality of life, said Dr. Nout. He noted that patients who received VBT after surgery reported significantly less diarrhea (moderate to severe: 6% vs 22%; p<0.001), which resulted in significantly fewer limitations in daily activities (p<0.001) and significantly better social functioning (p<0.002).

In addition to improved quality of life, VBT offers the benefit of a lower time commitment for treatment. Patients who receive 23 fractions of EBRT usually receive treatment 5 times per week for approximately 5 weeks. In contrast, treatment with VBT is usually given with high-dose rate brachytherapy, which requires three outpatient visits in a two week period.

"Vaginal brachytherapy is safe and effective for patients with high-intermediate risk features," said Dr. Nout, in conclusion. "[It] should be the treatment of choice for patients with high-intermediate risk endometrial carcinoma."

Evaluation of Doublet Chemotherapy Regimens for Advanced Cervical Cancer

The results of several Gynecologic Oncology Group (GOG) trials have established doublet chemotherapy with standard-dose cisplatin and paclitaxel as the preferred treatment for advanced or recurrent cervical cancer. The GOG 204 trial (NCT00064077) was conducted to evaluate 3 experimental cisplatin-containing doublet chemotherapy regimens against the standard of cisplatin and paclitaxel. The findings indicated that none of the doublet regimens was superior to cisplatin plus paclitaxel in terms of response rate, progression-free survival (PFS), or overall survival (OS).

The experimental arms in the phase 3 trial consisted of chemotherapy with cisplatin in combination with vinorelbine, topotecan, or gemcitabine. Bradley J. Monk, MD, University of California, Irvine, CA, presenting on behalf of the GOG investigators, noted that the study began as a 2-arm trial that was designed to compare cisplatin and vinorelbine against cisplatin and paclitaxel. The other arms of the trial were added when other studies suggested benefit of topotecan and gemcitabine. The trial was stopped prematurely in April 2007 after a planned interim futility analysis indicated that the 3 experimental arms were not likely to be superior to the standard arm by the end of the study, said Dr. Monk. At the time that the study was closed, 513 of a planned 600 patients had enrolled. Data on response and survival were available for 434 patients. The primary endpoint was OS.

OS was not significantly better for any of the experimental doublet regimens, with the relative hazard ratios (HRs) for all 3 regimens favoring cisplatin and paclitaxel (Table 1). Similarly, the HRs favored cisplatin plus paclitaxel with respect to PFS (a secondary endpoint). Dr. Monk reported that the median PFS for cisplatin plus paclitaxel was 12.9 months, compared with 10 to 10.3 months for the 3 other doublet regimens.