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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

New Treatments And Quality of Life Study For Ovarian Cancer Described At SGO

By Lawrence M. Prescott

SAN DIEGO—A number of promising treatment approaches for ovarian cancer, as well as a study demonstrating the value of assessing quality of life, were presented at the 35th Annual Meeting of the Society of Gynecologic Oncologists. Following are highlights of the presentations.

Gemcitabine and Cisplatin in Platinum-Resistant Disease

The combination of gemcitabine and cisplatin chemotherapy demonstrates effective synergistic activity in patients with platinum-resistant ovarian and peritoneal carcinoma, said Devansu Tewari, a fellow in the department of obstetrics and gynecology, University of California, Irvine Medical Center.

"The findings reported here are the highest response rate with this regimen, in an exclusively platinum-resistant group of patients with the

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Society of Gynecologic Oncologists:

Improved Therapies For Cervical Cancer Said To Show Promise In Clinical Trials

By Lawrence M. Prescott

SAN DIEGO—A range of new or improved therapeutic approaches, as well as a quality of life study in survivors, may prove to be of real benefit for patients with cervical cancer, stated investigators at the 35th Annual Meeting of the Society of Gynecologic Oncologists.

Paclitaxel in Advanced or Recurrent Disease

Results from a phase II study pointed out that paclitaxel (Taxol, Bristol-Myers Squibb) would be a positive addition to the oncologist's armamentarium for the treatment of advanced adenocarcinoma of the cervix, according to Sachin Apte, a fellow in the department of gynecologic oncology, The University of Texas M.D. Anderson Cancer Center.

"This report confirms the findings of a recent GOG study demonstrating that paclitaxel is an active and well-tolerated agent in recurrent or advanced adenocarcinoma of the cervix, with a response rate greater than that of reported cytotoxic agents," Apte said.

Several single-agent trials in cervical cancer have been published involving patients with adenocarcinoma who received prior radiation therapy, Apte said. Agents showing moderate activity included cisplatin, piper-azinedione, ifosfamide, gallium nitrate, and 5-fluouracil/leucovorin. A recent GOG study of single agent paclitaxel in non-squamous cervical

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Gemzar+Cisplatin Active In Platinum-Resistant Disease

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shortest platinum-free intervals," Tewari said. "The combination of gemcitabine and cisplatin chemotherapy is an active and tolerable regimen over a wide range of doses and patients can be retreated with this approach successfully."

While significant activity with the combination of gemcitabine and cisplatin chemotherapy in recurrent ovarian cancer has recently been reported, the majority of responses were in patients considered either platinum-sensitive or who had extended platinum intervals greater than 12 months, Tewari said. A study was designed to evaluate the activity of this regimen in women with recurrent ovarian and peritoneal cancer with more recent exposure to platinum.

Twenty-two platinum-resistant patients with a median of four prior chemotherapy regimens including two platinum-based regimens were treated with the combination of gemcitabine (Gemzar, Lilly) 450-600 mg/m^2 and cisplatin (Cisplatin, Baxter Anesthesia) 30 mg/m^2 on days 1 and 8 of a 21-day cycle. Dose adjustments were made based upon patient toxicity profiles. Response to this regimen was evaluated and the progression-free interval, survival, and toxicity of the treatment determined. Two patients were treated with the regimen on three and two separate occasions respectively, constituting 25 responses.

The overall response rate was 69%, with 8 complete responses, 9 partial responses, and 8 non-responders, Tewari said. The median progression-free interval in positive responders was 5.9 months and 3.8 months for the overall group. The median survival in the positive re-sponders was 15.8 months compared to 8.8 months in non-responders, with an overall group survival of 11.4 months.

Platinum-free intervals of less than 12 months were reported in 82% of positive responders, 71% of whom had intervals of less than 6 months.

With regard to the safety profile, a grade III or IV toxicity was encountered in 60% of treatments, with neutropenia grade III in 36% and grade IV in 28%; thrombocytopenia grade III in 28% and grade IV in 16%; anemia grade III in 12%; and peripheral neuropathy grade II in 4%. Two patients with partial reports discontinued the regimen secondary to drug toxicity. No treatment-related deaths occurred.

HA-CMC Barrier To Prevent Adhesions

Results from a pilot study demonstrate the usefulness of a sodium hyaluronate-carboxymethylcellulose (HA-CMC) barrier in women undergoing surgery for ovarian cancer, according to Robert Bristow, assistant professor of surgery, The Kelly Gynecologic Oncology Service, Johns Hopkins Medical Institutions.

"Placement of an HA-CMC barrier is associated with a significant reduction in the extent and density of pelvic adhesion formation following radical oophorectomy and pelvic peritonectomy for locally advanced epithelial ovarian cancer," Bristow said.

Locally advanced disease with contiguous extension to or encasement of the reproductive organs, pelvic peritoneum, cul-de-sac, and sigmoid colon can present a significant challenge to the surgeon operating on women with ovarian cancer, Bristow said. The retroperitoneal technique of radical oophorectomy is designed for the intact removal of a fixed ovarian tumor en bloc with attached peritoneum and attached structures and is a highly effective technique for resection of pan-pelvic disease due to ovarian cancer. The problem is that radical pelvic deperitonealization is necessarily associated with an increased risk of post-operative pelvic adhesion. This can potentially lead to small bowel obstruction, difficulty with re-operation, and suboptimal distribution of intraperitoneal chemotherapy. A pilot study was carried out, to investigate the efficacy of an HA-

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CMC barrier in preventing pelvic adhesions following a radical oophorectomy procedure for locally advanced ovarian cancer.

Between March 1, 2001, and March 1, 2002, Bristow said, all patients undergoing primary surgery for locally advanced FIGO stage III-IV epithelial ovarian cancer were prospectively offered study enrollment. Fourteen patients satisfied all inclusion criteria and underwent a radical oophorectomy en bloc with the internal genitalia and rectosigmoid colon. Intestinal continuity was re-established via circular end-to-end stapled anastomosis and placement of a closed suction drain following complete cytoreduction of pelvic disease, with no gross residual.

The entire pelvic peritoneal defect was covered with six separate subdivided HA-CMC sheets 6.5 cm X 5.0 cm each, using a quilting technique, with 1 cm overlap onto the abdominal peritoneum, Bristow said. The abdominal wall incision site was not treated with adhesion preventive measures. Post-operatively, patients received 6 to 8 cycles of platinum-based combination chemotherapy, according to community standard of care. Following completion of chemotherapy, the study participants underwent reassessment laparoscopy or laparotomy, as second-look surgery. Four quadrant pelvic (treated area) and abdominal wall (untreated internal control) adhesion scores were assigned using a previously validated scoring system, measuring the extent and density of adhesion formation.

Abdominal wall adhesions underlying the midline xypho-pubic incision were noted in 92.9% of patients and in 64.3% of abdominal wall quadrants, Bristow said. In the pelvis, post-operative adhesions were documented in 6 patients or 42.9% of the total group. Overall, both mean adhesion scores and the number of quadrants involved with adhesions were statistically significantly lower in the HA-CMC pelvis compared to the untreated abdominal wall, used as the internal control. There were no instances of intestinal anastomotic leak, and no peri-operative complications directly attributable to HA-CMC were observed.

Intraoperative Radiation Therapy

Intraoperative radiation therapy (IORT) is an effective treatment approach in patients with recurrent ovarian cancer, said Stephanie Yap, gynecologic oncology post-doctoral fellow, division of gynecologic oncology, gynecology and obstetrics department, Stanford University School of Medicine.

"Our institutional experience suggests that addition of intraoperative radiation therapy to surgical cytoreduction in patients with locally recurrent ovarian cancer offers an opportunity of improved disease control and salvage, contributing to the achievement of prolonged disease-free survival with acceptable toxicity," Yap said. "Patients with locally recurrent ovarian cancer should be counseled about the possible adjunctive use of intraoperative radiation therapy."

To evaluate disease outcome in recurrent ovarian cancer following treatment with surgical debulking and IORT, medical records of all patients with epithelial ovarian cancer who underwent secondary cytoreduction and were consented for IORT between January 1, 1994, and October 31, 2002, at a single testing care institution, were reviewed. Clinical, pathologic, surgical, and followup data were collected. A total of 55 patients were identified among whom 24 underwent tumor debulking and IORT. These 24 patients form the basis of this report.

Of the 24 patients, 22 were available for followup analysis, Yap said. Additional therapy at the time of and following IORT included whole abdominopelvic radiation in 9 patients, pelvic or locoregional radiation in 6 patients, chemotherapy in 6 patients, and no adjunct treatment in 2 patients. The IORT doses ranged from 9 to 14 Gy, with a mean of 11.6 Gy.

At a median followup of 19 months, 5 patients remain disease-free, while 17 patients have had a recurrence of disease, 4 of whom are still alive and 13 of whom have died of ovarian cancer. Five patients recurred within the radiation fields and 11 patients recurred at distant sites, with a median time to recurrence of 9.5 months. Overall, three patients were disease-free at 36 months. Nine patients experienced Grade 3 toxicities.

Monitoring Quality of Life

"Since patients are increasingly involved in their own healthcare, women with ovarian cancer should be monitored as their disease progresses or recurs to not only ensure that their psychosocial as well as treatment-related side effects are being met, but also that they do not increasingly use complementary and alternative medicines that may be contraindicated," said Vivian von Gruenigen, assistant professor of gynecologic oncology, Northeastern Ohio Universities College of Medicine (NEOUCOM), Rootstown, Ohio.

The goal of treatment for ovarian cancer is to

increase survival, disease-free interval, and ultimately, to improve quality of life, von Gruenigen said. While the need to assess outcomes in terms of patients' surgical and chemotherapy experience is progressively more recognized, because cancer patients now are altering their diets, taking nutritional supplements and using CAM, more attention should be paid to this relatively new development. A study conducted at NEOUCOM demonstrated that significantly more gynecologic oncology patients use CAM than gynecologic patients without a malignancy. Women who have been diagnosed with cancer may believe that they should be making major life style modifications in order to prevent a recurrence.

A study was designed, therefore, to prospectively evaluate quality of life, general health status, and the use of CAM in patients with ovarian cancer during the first six months after diagnosis, von Gruenigen said. Data from women with a benign adnexal mass studied earlier were used as a comparison. Overall, data from 26 patients with ovarian cancer and 41 patients with a benign adnexal mass were analyzed. All patients underwent surgical debulking and staging prior to chemotherapy, with the mean number of chemotherapy cycles being 45.

There were significant changes in physical, fatigue, and functional domains on the quality of life assessment using the Functional Assessment of Cancer Therapy (FACT-G), Gruenigen said. Physical and fatigue related scores decreased during chemotherapy but returned to baseline or higher levels following chemotherapy. There were no significant changes in social or emotional domain scores during or after chemotherapy. Both women with ovarian cancer and those with a benign diagnosis appeared to be responding well to their disease and treatment by six months, with significant increases over time seen in functional and emotional domain scores. In addition, results from the SF-36 Medical Outcomes Survey, administered at baseline and 6 months, showed improvements over time in bodily pain, social functioning, and mental health, with no significant differences between the two groups.

Use of megavitamins, antioxidants, and herbal alternative therapies increased significantly over time in both women with ovarian cancer and those with a benign diagnosis. There was no significant increase, however, in movement, mind-body, or diet therapies. The most prevalent reasons given for CAM use by both groups of women were to improve their quality of life, for a cure, or to live longer. CAM therapies were used at least once by close to three-quarters of these patients, data suggesting a pattern of women trying to cope with their disease and treatment.

Estrogen-Only HRT Little Risk In Endometrial Cancer, GOG Study Indicates

By Lawrence M. Prescott

SAN DIEGO—In a study conducted over a five-year period comparing estrogen replacement therapy (ERT) with placebo in more than 1,200 women with early stage endometrial cancer, ERT was associated with a very low incidence of disease recurrence or death, comparable to that seen in the placebo group, said Richard Barakat, speaking at the 35th Annual Meeting of the Society of Gynecologic Oncologists.

"Based upon the results of this study, I am prescribing estrogen-only hormone replacement therapy for interested patients who are experiencing symptoms of menopause and perimenopause following surgery for endometrial cancer," said Barakat, chief of the gynecology service, department of surgery, Memorial Sloan-Kettering Cancer Center, and associate professor of obstetrics and gynecology, Cornell Medical Center, New York, New York.

Adenocarcinoma of the endometrium is the most common malignancy of the female genital tract, Barakat noted. Standard therapy includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, and surgical staging. Further treatment is tailored to the presence or absence of various risk factors.

Studies in the 1970's reported possible links between the use of exogenous estrogen to an increased incidence of endometrial cancer, Barakat continued.

Women with a history of endometrial cancers were usually denied this therapy because it was thought that estrogen could theoretically stimulate occult disease.

Since there was no prospective data available to address the safety of ERT in women with endometrial cancer, albeit retrospective findings indicated that ERT could actually be safe in this group of women, Barakat said.

The Gynecologic Oncology Group decided to conduct a prospective randomized trial of estrogen versus placebo in women with early stage endometrial cancer to determine the effect of estrogen

replacement therapy in women who have undergone surgery for stage I or II endometrial cancer. Between June 1997 and January 2003, 1,240 women were randomized to receive either ERT or placebo after undergoing surgery for early-stage endometrial cancer. Both groups were treated for 3 years, with an additional 2 years of followup.

On July 9, 2002, following publication of the Women's Health Initiative clinical trial's results which reported that the overall risks of estrogen and progesterone exceeded the benefits, enrollment in the GOG study fell, although women in this study were receiving estrogen alone and the study was closed prematurely after it became clear that the accrual goal could not be reached in a reasonable amount of time. Data was collected for 1,236 evaluable patients rather than the 2,108 patients which were originally planned.

The median followup for all patients was 32.1 months, Barakat said. Stage, grade, histological subtype and percentage of patients receiving adjuvant therapy were similar. The median age at diagnosis for the 618 patients randomized to ERT was 57 years, while the median age for the 618 patients in the placebo group was 57.5 years. Compliance with therapy was similar in both groups, being 82.4% for those patients receiving estrogen compared to 78.9% of those in the placebo group.

In the ERT group, disease recurrence, new malignancy, and death were low, with 14 patients or 2.3% experiencing disease recurrence, six or 0.97% having a new malignancy, and five deaths or 0.8% due to endometrial cancer. Recurrences, new malignancies, and deaths from endometrial cancer were similarly low in the placebo group, with 10 patients or 1.6% experience a recurrence of their cancer, ,nine or 1.5% having a new malignancy, and four or 0.6% of these patients dying due to endometrial cancer.

The overall survival rate for the total study population was 96.6%.

At the completion of the study, all patients and physicans were asked to guess what treatment the patients had been receiving. Only 47.9% of patients and 46.4% of physicians who responded correctly guessed that the patient was on the estrogen arm of the study.

Similarly, only 36% of patients and 39.5% of physicians who responded correctly guessed that the patient was on placebo.

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carcinoma reported a response rate of 31%. That study included 36 adeno/adenosquamous carcinoma and treated patients with paclitaxel at 170 mg/m^2 over 24 hours.

Based on this earlier data, a single institution non-randomized phase II study was initiated to determine the activity and safety of paclitaxel in patients with advanced or recurrent adeocarcinoma of the cervix, Apte said. Twenty-six patients were enrolled into the study from December 1993 to February 2001, all of whom had measurable disease and pathologically confirmed disease that failed standard therapy. Paclitaxel was administered at 175 mg/m^2 over 3 hours every 3 weeks and continued until disease progression or toxicity.

Of the 26 patients enrolled in the study, 22 patients were evaluable for response, Apte said. The overall response rate was 36%, with 1 complete response and 7 partial responses. A median number of 5 cycles of paclitaxel was administered per patient, with the duration of response in responders being a median of 6 cycles and, in nonresponders, a median of 4.5 cycles. A total of 20 patients had previously received radiation therapy. Of the 8 responders, 6 patients had received prior radiation therapy.

Paclitaxel caused an acceptable level of toxicity, Apte said. In the GOG report, the incidence of grade IV neutropenia was 62%, with 8 febrile episodes requiring hospitalization. In this report, the incidence of grade IV neutropenia was only 18%, with no febrile episodes. There were no septic deaths. No patients required a dose reduction, while 10 patients tolerated a dose escalation to 200 mg/m^2.

Weekly vs. Three Weekly Cisplatin

A comparison of weekly vs three week concomitant cisplatin (Cisplatin, Baxter Anesthesia) and radiotherapy in patients with cervical carcinoma demonstrated that the three-week treatment approach is preferred, reported Paniti Sukumvanich, fellow, division of gynecologic oncology, department of obstetrics, gynecology, and women's health, Albert Einstein College of Medicine, Bronx, New York.

"In our experience, the intended dose of cisplatin was less frequently achieved when administered weekly versus a five days every 21 days regimen

with concomitant radiotherapy," Sukumvanich said. "Weekly cisplatin was less tolerable and more toxic, resulting in more treatment delays and unanticipated hospitalizations than in the three weekly regimen."

Multiple studies have shown concomitant cisplatin chemoradiotherapy to be more effective in the treatment of cervical cancer than radiotherapy alone, Sukumvanich said. In 1986, the division of gynecologic or oncology at Albert Einstein College of Medicine began administering cisplatin and radiotherapy concomitantly. From 1986 through 2001, cisplatin was administered at a dose of 20 mg/m^2 X 5 days every 21 days, for a planned 3 to 4 cycles. With the trend of administering chemotherapy in an outpatient setting, the 3 weekly dosing has become less popular than the weekly dose of 40 mg/m^2. The advantage of the weekly cis-platin dosing is fewer inpatient admissions for chemotherapy administration which results in a lower overall cost.

There have been no studies comparing different dosing regimens of cisplatin given with radiotherapy, so it is quite conceivable that the weekly cisplatin dose might results in higher chemo-related toxicity rates, Sukumvanich said. This would result in more admissions for chemotherapy-related side effects and would, in fact, negate any cost savings advantage of the outpatient regimen.

A retrospective review of data from 60 patients with cervical patients treated with cisplatin and radiotherapy was undertaken. Thirty consecutive patients treated from 1998 to 2001 with cisplatin 20 mg/m^2 daily for five days every 21 days and 30 patients from 2001 to 2003 with weekly cisplatin 40 mg/m^2 were evaluated. Patients treated for five days every 21 days were intended to receive 3 cycles of cisplatin, 2 with external beam radiotherapy and 1 with brachy-therapy. Patients treated weekly were intended to receive 6 to 7 cycles of cisplatin weekly through the prescribed course of chemotherapy. Patients were well matched for age, stage, and co-morbidities.

Overall, 83% of patients on the three weekly cisplatin/radiotherapy regimen completed therapy compared to 60% of those on the weekly regimen, Sukuvanich said. The median duration of radiotherapy was 50 days in the weekly cisplatin group versus 45 days in the three weekly cisplatin group. Radiotherapy was held in two patients in the weekly cisplatin group due to severe pancytopenia and grade 3 toxicity. No patients in the three weekly regimen experienced radiotherapy delays. Unplanned chemo-related hospital admission were higher in the weekly versus the three weekly group, being 13 and 4 respectively.

Pain Control During Low Dose Brachytherapy

An improved method of pain control appears to be promising during brachytherapy in patients with cervical cancer, said Joseph Santoso, associate professor and director, division of gynecologic surgery, obstetrics and gynecology faculty, University of Tennessee Health Science Center.

"Preliminary results show that epidural anesthesia offers superior pain control over the present standard of care using a PCA pump during brachytherapy treatment in patients with cervical cancer," Santoso said.

A pilot study was initiated to evaluate the efficacy of epidural anesthesia compared to PCA for pain control during low dose brachytherapy in patients with cervical cancer, Santoso said. Nine patients with stage III squamous cell carcinoma of the cervix, all qualified for brachytherapy, were randomized to PCA or epidural anesthesia for first implant insertion. Standard low dose brachytherapy for this population requires two implant insertions. Each patient became her own control by having one pain control regimen for the first insertion and then receiving the other regimen for her second insertion. Twice a day during hospitalization, each patient was asked to rate her pain using a pain scale, with "0" being no pain and "10" being the worst pain the patient had ever imagined. The pain scores were assessed with statistical analyses.

A reduction in pain scores was seen throughout the study with epidural anesthesia compared to the general anesthesia/PCA combination. The overall general/PCA pain score was 3.72 and the mean epidural pain score was 1.96. Decreased pain scores were seen with epidural anesthesia at all evaluation times in both study protocols.

Quality of Life in Survivors

In a survey of women treated for cervix cancer more than five years ago, the quality of life of these cervical cancer survivors varied significantly based on whether they were treated with radical hysterectomy and lymph node dissection (RHL) or radiation therapy (XRT), said Michael Frumovitz, fellow, department of gynecologic oncology, University of Texas M.D. Anderson Cancer Center.

"In our sample of women, cervix cancer survivors treated with radiation therapy had more

emotional distress and poorer quality of life compared with those treated with radical hysterectomy and lymph node dissection," Frumovitz said. "Our data suggest that cervix cancer survivors treated with surgery alone can expect an overall quality of life similar to peers with no history of cancer."

To compare quality of life in cervix cancer survivors treated by either RHL or XRT, three treatment groups of 38 women, two groups treated for cervical cancer more than 5 years ago and a control group with no history of cancer, were surveyed.

The XRT patients had statistically significantly poorer scores in 5 of the 6 psychological test summary measures when compared to RHL patients and controls, Frumovitz said.

New Treatment Modalities For Endometrial Cancer

By Lawrence M. Prescott

SAN DIEGO—Studies concerning such novel therapeutic approaches as intra-operative frozen section staging, systemic lymphadenectomy plus adjuvant radiotherapy, laparoscopy with CO_2 pneumoperitoneum and intraperitoneal radioactive phosphorous and vaginal brachytherapy all offer considerable promise in the treatment of endometrial cancer, according to investigators preventing their work at the 35th Annual Meeting of the Society of Gynecologic Oncologists.

Endometrial Biopsy, Frozen Section Analysis

The addition of intra-operative frozen section analysis to pre-operative endometrial biopsy appears to decease the risk of sub-optimal surgical management of endometrial cancer, said Kimberly Mark, fellow, department of obstetrics and gynecology, University of Minnesota.

"We feel that our data support the use of frozen section in all cases of grade 1 endometrial cancer prior to omitting a staging procedure, and that all endometrial cancer surgeries should be performed by a surgeon prepared to perform a staging procedure when indicated intraoperatively," Mark said.

Surgical staging including pelvic and para-aortic lymph node staging evolved from a pilot study carried out in 1976 which led to formal adoption by FIGO in 1988 as the definitive staging technique, Mark said. There is general agreement that staging is appropriate for all patients with grade 2 or 3 history, as well as those with significant myometrial invasion, cervical involvement, or suspicious lymph nodes. In addition, intraoperative frozen section has proven to be accurate for predicting final pathology, with a 90.9% accurate prediction in depth of invasion, and 91.9% accurate histological grade correlation to final pathology.

Patients with immediate or high risk endometrial cancer who do not undergo a staging procedure during their initial surgery must choose between additional surgery, radiation therapy or expectant management without complete information, Mark said. Identifying these "at-risk" patients before or during surgery should decrease unnecessary morbidity and cost. An attempt, therefore, was made to determine if surgical management of endometrial cancer is improved with the addition of intraperitoneal frozen section analysis when compared to routine pre-operative endometrial biopsy.

A retrospective review of patients with endometrial biopsy demonstrating endometrial cancer from June 1, 1999 through August 31, 2002 was performed, Mark said. Biopsy results were compared to corresponding intra-operative frozen section analysis, when performed, and final surgical pathology. The histologic subtype, FIGO grade, depth of myometrial invasion, extent of cervical involvement, presence of lymphatic or vascular invasion, pelvic washing cytology, and lymph node status were collected.

A total of 187 patients with endometrial cancer on endometrial biopsy who underwent surgery at three study institutions were identified, Mark said. Of these, 45 underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy alone and 142 underwent formal staging. Tumor grade on preoperative endometrial biopsy and final pathology report correlated in 156 of 187 patients or 83%. In 31 of 187 patients or 17%, the final pathology report demonstrated a grade 2 or grade 3 lesion when the preoperative endometrial biopsy was called grade 1. In this subgroup of 31 patients, 24 underwent staging, while 7 went unstaged.

When specimens were analyzed by inta-operative frozen section, tumor assessed pre-operatively to be grade 1 underwent an indicated staging procedure in 90% of patients (43/98). Overall correlation of grade on frozen section and final pathology was 82%. Overall correlation of depth of invasion on frozen section and final pathology was 92%.

Systemic Lymphadenectomy, Adjuvant XRT

Systemic lymphadenectomy and adjuvant radiotherapy are each important in providing a successful outcome in node positive endometrial cancer patients, reported Andrea Mariani, fellow, gynecologic surgery, oncology, Mayo Clinic.

"Optimal pelvic and periaortic lymphadenectomy and adjuvant radiotherapy are complementary in reducing failures in both the pelvic and periaortic areas in node positive endometrial cancer patient," Mariani said.

Between January 1984 to December 2001, 146 patients with endometrial cancer and documented lymph node metastases were treated at Mayo Clinic. Adequate lymphadenectomy was defined as the removal of more than 10 pelvic and more than 5 periaortic lymph nodes. Pelvic radiotherapy was administered to 78% of the patients and periaortic radiotherapy was given to 29%. Twenty-four patients who received adjuvant chemotherapy were excluded from the study. Median followup was 56 months.

In the whole cohort, 96 patients had stage III disease and 26 patients had stage IV endometrial caner, Mariani said. According to definition, 77% of patients received adequate pelvic lymphadenectomy, while 39% of patients had an adequate periaortic lymphadenectomy. The median number of pelvic lymph nodes was 4 in patients with inadequate pelvic lymphadenectomy and 23 in those with an adequate pelvic lymphadenectomy. The median number of periaortic lymph nodes was 0 in patients wit inadequate periaortic lymphadenectomy and 10 in patients with adequate periaortic lymphadenectomy.

Pelvic radiotherapy was administered to 78% of patients and 29% also received periaortic radiotherapy, Mariani continued. The median dose of pelvic radiotherapy was 5,040 cGy and of periaortic radiotherapy, 4,500 cGy.

For the total cohort, 24% experienced pelvic side wall failures and 27% had periaortic failures at 5 years. The 5-year pelvic side wall failure rate was 66% in patients not receiving radiotherapy compared to 18% in those who received radiotherapy. The 5-year pelvic side wall failure rates for patients managed with or without systemic lymphadenectomy were 18% and 38% respectively. Pelvic side wall failures were observed in 44% of patients who had suboptimal node dissection and/or no radiotherapy compared to 9% in those with both optimal lymphadenectomy and radiotherapy. Assessing numerous risk factors, only grade 1/2, stage III, and treatment with optional lymphadenectomy and radiotherapy were significant independent predictors of pelvic control.

The majority of patients received both periaortic radiotherapy and periaortic lymphadenectomy. In the periaortic region, 31% of patients failed within 5 years who did not receive radiotherapy versus 16% when adjuvant radiotherapy was administered to this region, Mariani said. Patients who received a suboptimal periaortic lymphadenectomy had a 36% failure rate at 5 years, compared to 11% when an optimal lymphadenectomy was performed. All periaortic failures occurred in patients whose management did not include optimal lymphadenectomy and radiotherapy to this area, 30% versus 0% at 5 years. Stage III and optimal joint therapy were the only independent predictors for disease control in the periaortic area.

"Overall, there was no efficacy demonstrable with pelvic and periaortic radiotherapy alone in endometrial cancer patients with inadequate lymphadenectomy and positive lymph nodes," Mariani said. "On the other hand, efficacy of pelvic and periaortic radiotherapy in steritizing lymph node disease was 86% and 100% in patients who had an adequate pelvic and periaortic lymphadenectomy respectively."

Clinical Trials Approved By NCI

The National Cancer Institute's Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase II

Phase II Study of hu14.18-IL2 In Children with Recurrent or Refractory Neuroblastoma. Children's Oncology Group, protocol ANBL0322, Sondel, Paul, phone 608-263-9069.

Phase II Study of Temodar (Temozolomide) and Radiation Therapy in Patients with Brain Metastasis from Non-Small Cell Lung Cancer. Eastern Cooperative Oncology Group, protocol E1F03, Robins, Ian, phone 608-263-1416.

Other

Gene Ratios for Prognosis in Lung Cancer. Cancer and Leukemia Group B, protocol CALGB-150303, Bueno, Raphael, phone 617-732-8148.

Ancillary Laboratory Protocol for Collecting Diagnostic Material on Patients Considered for ECOG Treatment Trials for Leukemia or Related Hematologic Disorders. Eastern Cooperative Oncology Group, protocol E3903, Paietta, Elisabeth, phone 212-920-4549.