by data that demonstrated a hazard ratio for EC of 89, when compared with benign endometrial biopsy during a period of 10 years.[2] Mutation of *PTEN*, a tumor suppressor gene, is implicated because the mutation rates for normal endometrium, endometrioid intraepithelial neoplasia (EIN), and endometrial carcinoma are 0%, 55%, and 83%, respectively. *PTEN* knockout mice demonstrate very high rates of EIN, and 20% develop EC. Progestins can achieve regression of precancerous lesions, which currently offer the best prospect for secondary prevention in predisposed women.

Molecular Genetics of Endometrioid EC

Type 1 and type 2 tumors (non–estrogen-related) have different genetic profiles.[3] In addition to *PTEN*, type 1 features mutations in mismatch repair genes as well as K-*ras* and β-*catenin*. Type 2 features aneuploidy and p53 mutations. Microarray technology has been used to demonstrate upregulated and downregulated genes in EC compared with normal endometrium. A variety of differentially expressed genes can also be identified between early and late stage diseases. Some of the most significant overexpressed genes are involved in key pathways: cell proliferation (eg, *CCNE1*), angiogenesis (eg, *MMPG*), and chromosomal instability (*BIRC5*). These have been confirmed as predicted target genes by means of microRNAs, most differentially expressed in EC compared with normal endometrium. Greater understanding of key genes involved in endometrial carcinogenesis will help in developing biomarkers of prognosis and therapeutic targets. Fundamental studies of these candidate genes will be important in elucidating mechanisms of causation, progression, and metastasis.

Serous and Clear Cell Carcinoma

Type 2 EC, which comprises around 5% to 10% of ECs, includes both serous carcinoma and clear cell carcinoma.[4,5] The term serous carcinoma is preferred to the commonly used as papillary serous carcinoma because a glandular variant exists without papillary formation. Unlike type 1 tumors, type 2 neoplasms are associated neither with estrogen excess nor with endometrial hyperplasia, although a proportion may evolve from a type 1 tumor via progression and mutation. Serous carcinomas are thought to arise in atrophic endometria from a precursor lesion known as serous endometrial intraepithelial carcinoma (serous EIC). They are, by definition, high grade and have a much poorer prognosis than type 1 tumors. The precursor lesion serous EIC has a propensity to arise in endometrial polyps and may give rise to extrauterine disease, even in the absence of endometrial stromal or myometrial invasion. Immunohistochemical studies have shown that p53 is diffusely positive in approximately 90% of serous carcinomas. Other markers such as HER-2 *neu* and ER/PR are inconsistently expressed (many cases are hormone receptor–negative). Most serous carcinomas are associated with mutations in the *p53* tumor suppressor gene. These mutations occur early in the evolution of uterine serous carcinoma and are demonstrable in the precursor lesion serous EIC. In clear cell carcinomas, which are also aggressive neoplasms and which are rarer than serous carcinomas, molecular events have been less well studied. *p53* and ER/PR are both inconsistently expressed. Mixed type 1 and type 2 carcinomas are not uncommon and may evolve from a type 1 neoplasm secondary to *p53* mutation.

Lynch Syndrome

The term Lynch syndrome is now used to encompass HNPCC and Lynch syndrome I/II. Endometrial cancer as a result of the Lynch syndrome accounts for 2% to 3% of all cases.[6] In women with EC below the age of 50 years, 9% have Lynch mutations. Individuals who exhibit the Lynch syndrome have around a 50-fold lifetime risk of developing EC compared with unaffected women, with studies suggesting a range of 40% to 60% lifetime risk for those with a mutation. The syndrome can be defined clinically using the Amsterdam criteria or genetically by germ line mutation in *MLH1*, *MSH-2*, or *MSH-6* defective DNA repair.

These mutations can be tested for on a tumor specimen to demonstrate a mutation carrier using immunohistochemistry and, if both normal and tumor tissue are available, microsatellite instability can be tested for, which, in hereditary cancer, is associated with a germ line mutation in the mismatch repair gene. In sporadic tumors, it is associated with hypermethylation of the *MLH1* promoter.

Thirty percent of individuals with Lynch syndrome will develop a second cancer within 10 years of the first cancer (compared with around 3%–4% of unaffected), and for women diagnosed with EC, the median time for a second cancer is 11 years. The only proven means of prevention of EC is hysterectomy; however, endocrine chemoprophylaxis is currently being explored in trials both in the United States and in the United Kingdom.

ER/PR Expressions

Two isoforms of both ER (ERα and ERβ) and PR (PRA and PRB) have been described.[7] Progesterone treatment is capable of inhibiting invasion of endometrial cells by down-regulating a number of genes, for example, *integrins* and *K-cadherin*. PRA is nuclear, whereas PRB shuttles between the nucleus and cytoplasm. Whereas ER and PR tend to be abundant in well-differentiated EC, they are sparse in poorly differentiated disease.

G-protein coupled with receptor for estrogen (GRP30), whose function is unknown, is highly expressed in some high-grade ECs, and its underexpression is significantly correlated with improved survival.

In GOG-119, tamoxifen in combination with medroxyprogesterone acetate was used in women with metastatic cancer; tumors with abundant ER had improved survival up to 5 years.[8] This hormonal regimen should be considered to be combined with temsirolimus, an M-TOR inhibitor, in a randomized study in women with advanced/metastatic disease.

Selective Estrogen Receptor Modulators and the Endometrium

Tamoxifen was the first selective estrogen receptor modulator.[9] It has a stimulating effect on uterine stroma and on epithelial cells, which may range from cystic change to proliferative, hyperplasic, to invasive cancer. These tissue-specific differential changes are dependent on differential ER conformation upon ligand binding, differential expression, and binding of coregulatory proteins to the ER.

Tamoxifen may also exert a carcinogenic effect via a genotoxic pathway through tamoxifen DNA adducts. Compared with non–tamoxifen-related tumors, a higher proportion of tamoxifen-related tumors exhibit *p53* mutations. It is not known whether some women are more susceptible to carcinogenesis by tamoxifen than other women, and if so, what may be the biomarkers for this.

Current State of Imaging

The most common event before the diagnosis of EC is postmenopausal bleeding, for which ultrasound examination of the uterus has considerable utility.[10] The negative predictive value of an endometrial echo less than 5 mm is 99%, which provides a very reliable means of excluding cancer. An ultrasound image that shows an abnormally thickened endometrium is not specific for benign or malignant lesions, which require further investigations, including hysteroscopy and biopsy. When a diagnosis of EC has

been made, magnetic resonance imaging can provide useful information for treatment planning for those cases not amenable to surgery. Magnetic resonance imaging can provide information on tumor bulk, depth of myometrial invasion, and cervical involvement and extrauterine spread.[11] Staging protocols are based on T2-weighted sequences, but contrast-enhanced T1-weighted sequences may be complementary and optimize the accuracy of interpretation. Magnetic resonance imaging has its limitations, including microscopic invasion and intranodal lymph node metastases; it is possible that sensitivity for detection of the latter will be improved by the use of ultrasmall particles of iron oxide (USP10) contrast agents. Evaluation of positron emission tomography, particularly for lymph node staging and early detection of recurrence, warrants evaluation.[12]

Treatment of EC

Role of Surgery

The role of primary hysterectomy for the treatment of endometrial carcinoma is well accepted. More controversial is the role of lymphadenectomy. Assignment of FIGO stage is based on presence or absence of metastatic disease in the retroperitoneal lymph nodes. As noted below, some gynecologic surgeons perform staging lymphadenectomies on all patients, some on no patients, and some tailor staging to include lymphadenectomy for patients thought to be at sufficiently high risk of lymph node involvement. In addition, the extent of lymphadenectomy remains a subject of debate.

Furthermore, understanding patterns of failure is critical in understanding how best to manage EC in postsurgical care. Of 612 women managed with hysterectomy and adjuvant radiotherapy (RT) at the Mayo Clinic, 141 (23%) relapsed and sites of recurrence were known for 132 cases; 60 hematogenous, 44 lymphatic, and 37 intraperitoneal.[13] Among women with myometrial invasion of less than 50%, 5% developed hematogenous spread compared with 23% in those with more than 50% invasion. Lymphatic embolization was found only in high-risk cases. Pelvic sidewall recurrence occurred at a rate of less than 1% in women without lymphovascular invasion (LVI) or positive nodes at presentation, and para-aortic recurrence was also as rare in women who were node-negative and had no LVI. In the presence of these, however, sidewall and para-aortic recurrences were 26% and 33%, respectively. Intraperitoneal spread was largely associated with advanced disease at presentation. Vaginal failure was associated with grade 3 histologic subtype and LVI.

GOG-99 is a randomized trial evaluating pelvic radiation to no further therapy among women considered at intermediate risk for recurrence after hysterectomy and lymphadenectomy.[14] Among those women with no evidence of disease in the retroperitoneal lymph nodes, age, grade, depth of myometrial invasion, and lymphovascular space invasion were independent predictors of recurrence. These same factors also predicted recurrence in the PORTEC 1 study that involved women who underwent hysterectomy but not lymphadenectomy as primary therapy for EC.[15]

Therefore, both hysterectomy and lymphadenectomy, if performed, can help determine both the risk of recurrent disease and the dominant patterns of failure, whether peritoneal or nodal. We do not know yet how to integrate adjuvant radiation therapy and chemotherapy to minimize the risk of recurrence.

Radical Hysterectomy

Unlike a simple hysterectomy, a radical hysterectomy will remove parametrial tissue, uppermost vagina, and pelvic ± para-aortic lymph nodes. As noted below, the optimal extent of lymphadenectomy is not well defined. This combined surgical procedure could have the effect of reducing central pelvic and vaginal failures, as well as define women at low risk of lymphatic site relapse. There is, however, no evidence to support radical hysterectomy for stage I disease. Radical hysterectomy should be confined to women with known bulky involvement of the cervix, that is, IIB.[16]

Role of Lymphadenectomy

The role of lymphadenectomy is to stage disease and in so doing to define prognosis and determine the need for adjuvant therapy. The extent of lymphadenectomy also remains controversial, including the optimal number of lymph nodes to remove, the sites for lymphadenectomy, and how high up the aorta the lymphadenectomy should extend. Some groups have advocated to above the aortic bifurcation, others to the level of the IMA, and others to the renal vessels. Whether lymphadenectomy is therapeutic in itself by removing involved nodes is a highly controversial issue. Nonrandomized, retrospective case series have been analyzed to determine whether removal of a greater or lesser number of nodes or indeed any nodes is associated with improved survival. A number of such studies from the United States have suggested a survival benefit in women undergoing surgical staging, but most of these studies have not controlled for standard of care, comorbidity, and stage migration, that is, node-positive women are moved out of stage I disease, leaving node-negative women being compared with women of unknown node status. A recently published study by Chan et al reported that among women who had been staged and found to have positive nodes, those in whom 11 to 20 nodes were removed and more than 20 nodes were removed had a relative hazard rate of 0.77 and 0.60, respectively, compared with those who had up to 10 nodes removed.[17] The benefit of lymphadenectomy among women whose hysterectomy specimens puts them at low risk for extrauterine disease seems to be small. As noted above, there is no consistent approach to lymphadenectomy even in North America.

Decisive proof of whether lymphadenectomy is therapeutic requires data from a randomized trial in which adjuvant therapy does not confound the findings. The recently reported, but as yet unpublished ASTEC trial, performed in the United Kingdom, was designed to address the effect of lymphadenectomy on survival and the effect of adjuvant RT on survival of at-risk women. The published results of ASTEC are eagerly awaited, although a preliminary analysis presented at the Annual Meeting of the Society of Gynecologic Oncologists (Palm Springs, Calif, March 2006) suggested no survival benefit associated with lymphadenectomy.

Sentinel Node Biopsy

The rationale of sentinel node surgery requires high negative predictive value as a means of avoiding the need for systematic lymphadenectomy in all and using a positive sentinel node to determine the need for full lymphadenectomy or adjuvant therapy. Sentinel nodes can be identified laparoscopically, which could precede definitive surgery. Sentinel nodes can be identified using either toluidine blue or radiolabeled technetium.[18]

Using both hysteroscopically presented marker and cervical or subserosal corpus injection has achieved negative predictive value approaching 100%.[19] Sentinel node detection rates are more than 90%, mostly pelvic with para-aortic nodes being the sentinel site on much rarer occasions. Although sentinel node surgery seems to be feasible in EC, its use has not become widespread. In addition, the utility of sentinel node surgery in EC management needs to be established in clinical trials.

Pelvic Radiotherapy and Chemoradiation

Both radiation therapy and chemotherapy have shown activity in preventing recurrence of EC, although their utility varies as to sites of failure. Trials evaluating different modalities of treatment in the adjuvant setting have been complicated by heterogeneity both of risk of recurrence and most likely sites for recurrence. We need to determine how best to integrate radiation and chemotherapy after primary surgery to take advantage of both modalities.

Pelvic RT, both external beam and brachytherapy alone or in combination, has been widely used for many years as adjuvant therapy in unstaged women, with either intermediate (stage IC/IIA, grades 1–2) or high risk (stage IC, grade 3), as well as in staged women with positive nodes and staged women with negative nodes but other high-risk factors. It has also been used for unresectable, advanced disease in the pelvis. Three randomized trials of RT for intermediate-risk disease have been completed: the Norwegian trial, PORTEC 1, and GOG-99.[14,15,20] These all demonstrated a reduction in pelvic recurrence but no effect on overall survival. Risk factors for recurrence were grade 3 disease, depth of invasion, lymphovascular space invasion, stage IC, and aged 60 years or older. The PORTEC 2 trial is currently evaluating whether pelvic external beam therapy can be safely replaced by brachytherapy with results expected late 2008. In light of these trials, there has been a reduction in the use of adjuvant RT for intermediate-risk disease. The principal challenge now is achieving higher survival rates in women with high-risk disease by virtue of age and primary tumor features whether unstaged or with negative nodes or those found to have nodal metastases.

In a recently published Italian trial, 345 women with stages IC/II (grade 3) and stage III were randomized to CAP or pelvic RT.[21] No difference in overall survival was found, but RT delayed pelvic relapse and chemotherapy delayed distal relapse. A recent phase 2 trial from the United States tested concurrent chemoradiation (cisplatin, 50 mg/m^2) with adjuvant cisplatin/paclitaxel (4 cycles of cisplatin 50 mg/m^2 and paclitaxel 175 mg/m^2).[22] This was feasible, and at 4 years, disease-free survival was 81%, indicating candidature for a phase 3 trial. On this basis, the PORTEC 3 trial opened as a collaborating PORTEC/NCRI intergroup study. It is planned to randomize 800 women with high-risk disease to either external beam RT or RT + concurrent cisplatin (weeks 1 and 3) followed by 4 cycles of carboplatin and paclitaxel (175 mg/m^2). The primary end point will be overall survival.

Whole Abdominal Radiotherapy

The rationale for whole abdominal RT (WART) is that the abdominal cavity is the commonest site of treatment failure in a number of studies involving with advanced disease, which included women with serous and clear cell tumors. Up to 30 gray is well tolerated, with shielding of the kidneys. In one of the largest reported studies, 132 women were treated with WART including 68% with stage III and 45% with serous or clear cell tumors.[23] Disease-free survival at 5 and 10 years was 55% and 45%, respectively; site of relapse was the abdominal cavity in 59%. Toxicity included 14% with gastrointestinal grades 3 to 4 and 2% renal.

In GOG-122, WART was compared with adriamycin/cisplatin in a phase 3 trial involving 396 women with stage III and IV endometrial carcinoma and less than 2-cm residual disease.[24] The results showed superiority for chemotherapy (hazard ratio, 0.71; 95% confidence interval, 0.54–0.94), although there was an excess of neurologic G_{1-2} and cardiac toxicity, with 8 treatment-related deaths compared with 4 in the WART arm. Eighty-four percent completed WART compared with 62% for chemotherapy. Almost twice as many women who had RT recurred outside the abdomen (18.3%) compared with AP (9.8%). We should note, however, that the survival curves for the 2 arms have grown together with time. Although WART is generally well tolerated, its role in the management of EC is not clear.

Vaginal Brachytherapy

The rationale of vaginal brachytherapy is that vaginal cuff recurrence is an important site of pelvic recurrence, and this type of treatment is very well tolerated. In studies reporting vaginal brachytherapy for adjuvant treatment of stage I disease, vaginal control approaches 100%. In PORTEC 1, 73% of recurrences among nonirradiated patients involved the vaginal cuff. Vaginal brachytherapy could substitute for external beam radiation if pelvic control rates were not compromised and, for higher-risk disease, could be combined with chemotherapy. An American survey of ASTRO and American Brachytherapy Society members produced 551 completed responses.[25] Most reported increased referral for vaginal brachytherapy with almost all treating the upper vagina only. Almost 70% of patients were treated with high–dose rate brachytherapy. The PORTEC 2 trial will determine whether brachytherapy can safely replace external beam RT for intermediate-risk disease. Future trials could combine vaginal brachytherapy with chemotherapy and better definition of the technical aspects of therapy.

Chemotherapy

Treatment of advanced/recurrent EC needs to take account of the proportion of women who may be obese, previously irradiated, and elderly. Among women who have not yet received chemotherapy, response rates in excess of 20% have been seen with the following drugs: doxorubicin/epirubin, paclitaxel/docetaxel, and cisplatin/carboplatin.[26] Two randomized trials have compared doxorubicin with doxorubicin/cisplatin. Response rates were higher for the combination (27% vs 45%; 17% vs 43%) with a median overall survival of 9 months for the combination arms in both trials.

GOG-177 compared the combination of doxorubicin and cisplatin with doxorubicin/cisplatin and paclitaxel with F-CSF support. There was an overall survival benefit. The response rate was 57% for the triplet compared with 34% for the doublet. The median overall survival rates were 15.3 and 12.3 months, respectively, but there was excess neurotoxicity with the 3-drug combination. The less-toxic combination of carboplatin and paclitaxel has been evaluated in several phase 2 trials with response rates in excess of 60%. This combination, which is now widely used in the community, is now being compared with doxorubicin/cisplatin/paclitaxel for women with stage III and IV diseases (GOG-209).

Role of Endocrine Therapy

The sex steroid hormones progesterone and estrogen bind to specific receptors with the resulting complex entering the nucleus and leading to specific patterns of gene expression, which lead to specific phenotypic effects, for example, progesterone leads to endometrial cell differentiation.

Endocrine therapy has been shown to have some activity in advanced/recurrent EC for more than 40 years. In clinical trials of single-agent progestogens (GOG-48 and GOG-81), response rates of approximately 20% were achieved with higher response rates in PR-positive and lower-grade tumors.[27] Combinations of progestogens and tamoxifen (which increases progesterone receptor expression and may therefore counteract resistance to progestogens) have been assessed. Phase 2 trials of such combination strategies (GOG-119 and GOG-153) have demonstrated overall response rates of 33% and 27%, progression-free survival of 3

and 2.7 months, and overall survival of 13 and 14 months, respectively.[8,28] The aromatase inhibitors, anastrozole and letrozole, have been assessed but demonstrated limited clinical activity.[29,30] Progestogen has been shown to be relatively ineffective as an adjuvant in primary therapy.[31]

Further trials are required to identify the optimal role of hormone therapy, before or after chemotherapy, and what biomarkers may be informative in predicting response.

Biotherapies

The hallmarks of endometrioid (type 1) uterine cancer are beginning to be understood, with *PTEN* inactivation, activating mutations within the PI3K pathway, K-*ras*–activating mutations, *MLH1/6* epigenetic inactivation, and β-*catenin* activation being well described. In contrast, type 2 (nonendometrioid) uterine carcinomas are characterized by aneuploidy, *p53* mutation, and defects in *p53* pathway genes (such as *p21/waf1* and *MDM2*). Targets for type 1 tumors include components of the PI3K pathway, the β-*catenin* pathway, the epidermal growth factor receptor family, endocrine therapy (PgR and ER), and antiangiogenic targets. Recently described mouse models that are heterozygously deleted for *PTEN* develop endometrial hyperplasia and endometrioid endometrial carcinoma at a high rate. The incidence of these endometrial carcinomas is drastically reduced by crossing with an AKT1-deficient mouse.[32] This suggests a case for exploring endocrine or biotherapy manipulation of endometrioid uterine cancer.

Phospho M-TOR and phospho S6 kinase are expressed in type 1 endometrial carcinoma. Rapamycin analogs were shown to inhibit endometrial carcinoma cell lines growth in vitro and inhibit the development of endometrial carcinoma in *PTEN* heterozygote knockout mice.[33] Trials of temsirolimus (CCI-779) and RAD001 have been undertaken, which have shown activity in uterine cancer, although surrogate molecular markers of response have remained elusive. For example, temsirolimus has shown a 26% response rate with a substantial additional stable disease fraction. Responses were not correlated with expression of receptors. Currently, there is a drive to integrate M-TOR inhibitors into chemotherapy schedules for EC.

Epidermal growth factor receptor and Her-2 are overexpressed in 50% and 60% of ECs, respectively. TKIs prevent multiple intracellular signaling pathways from being activated. Including mitogen-activated protein kinase pathway, protein kinase B (Akt), trastuzumab, cetuximab, and lapatinib have begun to be evaluated in phase 2 studies.

DEVELOPING A PORTFOLIO OF KEY TRIALS

This body of current knowledge provides a platform for determining the key questions, which need to be answered in an attempt to improve the standard of care and improve survival. This requires a set of clinical trials combined with translational research to demonstrate the optimal role of surgery, RT, and chemotherapy and to begin to evaluate biological targeted drugs and discover biomarkers for likely response/nonresponse to therapy.

The Consensus Group discussed the key questions where there was a dearth of information from trials and where new and additional data were needed. Through consensus, the group focused on questions of broad interest, which could advance knowledge and were most likely to attract intergroup and international collaborations. These are outlined below:

Prevention of Endometrioid Endometrial Carcinoma

As discussed above, EIN seems to be a precursor lesion to endometrioid endometrial carcinoma. A relative excess of estrogen, whether endogenous or exogenous, to progesterone can result in the development of EIN. Several trials to evaluate the therapeutic benefit of progestins in the treatment of EIN were discussed. The first, GOG-0224, randomizes women with EIN to continuous (megestrol, 40 mg twice a day for 12 weeks) or cyclic (megestrol, 80 mg twice a day for 12 weeks, 2 weeks on/2 weeks off) progestins for 3 months before hysterectomy. The primary end point of interest is the presence or absence of EIN in the hysterectomy specimen. A follow-up study would compare a commercially available progesterone-releasing intrauterine device, Mirena, to the best-performing arm of GOG-0224.

For women with Lynch syndrome, who face a high lifetime risk of EC, The UK NCRI is undertaking the POET trial, which randomizes eligible women either to the Mirena or to observation. The primary outcome is development of atypical hyperplasia or EC, whichever is detected first. Women in both arms will be observed for 12 months with transvaginal scanning ± uterine biopsy, up to 36 months.

Treatment of Endometrial Carcinoma

Adjuvant therapy after primary hysterectomy.

As discussed above, there seem to be 3 broad approaches to primary surgery and staging worldwide, namely, hysterectomy alone for most patients, hysterectomy and staging lymphadenectomy for most patients, and hysterectomy with staging lymphadenectomy for patients thought at sufficiently high risk for nodal metastasis. The group endeavored to design trials that might enroll patients with and without surgical staging for various risk groups.

For women with disease apparently confined to the uterus at time of hysterectomy (FIGO stage I–II), several trials were discussed. Overall, the goals of these studies was to delineate the appropriate roles for adjuvant pelvic RT, vaginal brachytherapy, systemic chemotherapy, and lymph node dissection in this patient population. Currently open to accrual is the PORTEC 3 trial, which randomizes women to pelvic RT versus chemoradiation and consolidation chemotherapy. Eligibility includes FIGO IB and IC/grade 3, II (occult) grade 3, IIIA or IIC, endometrioid, and stages IB to IIIC clear cell or serous histologic subtype. Chemoradiation includes concurrent cisplatin 50 mg/m^2 on days 1 and 22; after completion of chemoradiation, women will receive 4 additional cycles of carboplatin (AUC5) and paclitaxel 175 mg/m^2 thrice weekly. The planned accrual of 800 will detect a 10% difference in 5-year overall survival with 80% power.

One proposed trial would randomize women with node-negative EC defined as at high risk of recurrence to pelvic RT or chemotherapy plus vaginal brachytherapy. They would be stratified on the basis of lymph node evaluation, whether imaging or surgical dissection. A second proposal would randomize women who had undergone hysterectomy but not lymph node dissection to surgical staging and chemotherapy for positive nodes or pelvic RT and chemotherapy without surgical staging.

Consolidation Therapy After Hysterectomy for FIGO Stage III Disease

The recent studies documenting a role for systemic chemotherapy in women with advanced EC throw into question the benefits of local radiation treatment. The proposed trial would randomize women to systemic chemotherapy with or without radiation therapy targeted to the known or suspect sites of disease in the pelvis and/or para-aortic region.

Treatment of Isolated Pelvic Recurrence

About half of women with recurrent EC have their recurrences limited to the pelvis. Treatment approaches have included

surgical excision, pelvic radiation, and, more recently, chemotherapy. The proposed trial (GOG-0238) would randomize women experiencing pelvic recurrence of their ECs to radiation alone versus platinum-based chemoradiation. Surgical excision/debulking, but not exenteration, potentially curative surgery would be permitted before entry into the trial.

Treatment of Stage IV or Recurrent EC

The proposed trials seek to optimize chemotherapy regimens or decrease the toxicity of standard chemotherapy. In the United States, on the basis of GOG-177, paclitaxel seems to have been accepted as part of the standard treatment regimen for advanced EC. Outside the United States, paclitaxel is not widely used. In many countries, paclitaxel has not been approved for routine use among women with EC. In the United States, therefore, the GOG plans to complete accrual to GOG-0209, which compares a 3-drug combination of paclitaxel, doxorubicin, and platinum to a 2-drug regimen of carboplatin and paclitaxel. One proposed European trial would compare doxorubicin plus cisplatin with carboplatin plus liposomal doxorubicin. A novel agent, temsirolimus, an M-TOR inhibitor as described above, seems to have activity in EC. Two proposed studies would evaluate the addition of temsirolimus to chemotherapy or hormonal therapy in the treatment of women with stage IV or recurrent EC.

Treatment of Uterine CS

Uterine CS is a relatively rare histologic subtype compared with endometrial adenocarcinoma. Only intergroup and international collaborations will make possible timely completion of definitive trials for women with this disease.

Women with uterine CS are at high risk for both local and distant recurrences after primary hysterectomy. The proposed studies seek to define the benefit of pelvic RT, as well as the optimal chemotherapy regimen.

Adjuvant Treatment of FIGO Stage I to II Uterine CS

One proposed study would randomize women with CS after primary hysterectomy to pelvic RT or observation. A second proposed trial would use a bifactorial design to address both chemotherapy and radiation therapy questions. Women with CS after primary hysterectomy would be randomized to pelvic RT or not RT, as well as to paclitaxel plus cisplatin or paclitaxel plus cisplatin plus doxorubicin or epirubicin.

Consolidation Treatment for FIGO Stage II to IV Uterine CS

The proposed study would also use a bifactorial design to compare chemotherapy with or without a targeted agent and to compare pelvic radiation to no radiation.

CONCLUSIONS

The Endometrial Cancer Consensus process allowed a successful presentation of the current state of knowledge and resulted in an effective consensus to emerge regarding the progress that needs to be achieved to impact patient care.

As noted above, compared with ovarian and cervical cancer, EC and uterine CS have been studied much less extensively. Relatively few trials have been opened for women with these cancers, and accrual to those trials has been slow. Through intergroup and international collaborations, we hope to ensure that the best science informs trials for women with EC and uterine CS and that these trials are completed as rapidly as possible. We plan to work through the GCIG to promote accrual to those trials already open as well as the timely development of those trials proposed above. We will also need to educate our sponsors and partners in research, including national governments, charities, and the pharmaceutical industry about the importance of identifying more effective treatment of women with EC and uterine CS.

ACKNOWLEDGMENTS

The authors thank the help of the following individuals in preparing this paper: Chris Altgassen, Carien Creutzberg, Gini Fleming, Hani Gabra, Geoff Hall, Jane Hawnaur, Anuja Jhingran, Kim Leslie, Karen Lu, W Glen McCluggage, Scott McMeekin, Karl Podratz, William Small, and Gillian Thomas.

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Cancer Center (GOG); William Small, Northwestern University (RTOG); Gavin Stuart, University of Vancouver (NCIC CTG); Ann-Marie Swart, UK Medical Research Council (NCRI), Paul Symonds, University of Leicester (NCRI); Sun Kuie Tay, Singapore General Hospital; J. Tate Thigpen, University of Mississippi (GOG); Gillian Thomas, University of Toronto (GOG, ACRIN); Ian Tominson, Barts and the London NHS Trust (NCRI); Hemant Tongaonkar, Tata Memorial Hospital, Mumbai, India (GOG); Edward Trimble, NCI; Joan Walker, University of Oklahoma (GOG); Y.F. Wong, Chinese University of Hong Kong.

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Current Organ Topics:

Gynecologic Cancer
婦人科がん
婦人科がん治療ガイドライン策定の背景と今後の動向
Ⅳ．子宮体癌再発の治療

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〔*Jpn J Cancer Chemother* 36(2): 220-223, *February*, 2009〕

はじめに

子宮体癌の再発様式は，腟断端などの局所再発から肺転移などの遠隔再発，また孤立性の限局再発から腹膜播種などの多発性再発があり，化学療法は主に腹膜播種などの再発が対象となる。治療の原則として，再発子宮体癌に対しては，まず可能であれば腫瘍摘出術を試みる。腟断端再発のみであれば，腫瘍および腟の追加切除や，骨盤除臓術が有効である。さらに放射線療法として腔内照射や全骨盤外照射も行われ有効例も多い。しかし骨盤中央部から腟にかけての再発以外の腹腔内再発に対する摘出術の効果は期待できない。再発が多発性であったり，遠隔臓器たとえば肺・骨・脳などへの転移は孤立性の一部にしか手術対象とはされず，手術療法の可否にかかわらず全身化学療法などの併用を考慮する。以上のごとく，婦人科がん治療ガイドラインの内容をその策定の背景と現状ならびに今後の動向を簡単に考察する。

1．再発がんでの手術療法の適応

ガイドラインでの推奨は，切除可能で，他に転移を認めない症例に関しては積極的な外科的切除を考慮する。その大きさが4 cm以下の肺転移巣であれば，肺部分切除術を考慮するとされている。

積極的に手術療法を試みた報告は症例数が少ないながらも存在する。Morrisら[1]は20例の骨盤照射例に骨盤除臓術を行い，5年無病生存率45%，5年生存率56%であったと報告している。その他にも報告[2,3]が散見されるが，しかしながら実際に積極的な手術として骨盤除臓術は非常に侵襲の大きな手術であり合併症の危険性も高く，施設での環境の問題もあり，近年では実施されない傾向にある。さらに再発症例の多くが前治療に放射線治療や化学療法が行われている場合が多く，手術療法は再発巣の完全切除が可能な症例に限られる。肺転移に関しても，個数や所見で手術可能と診断しても手術不能症例も多く[4]慎重な適応が求められる。

2．再発がんでの放射線療法の適応

ガイドラインには，「放射線療法は腟断端再発には有用である」とある。局所療法である放射線療法も，手術療法同様，多発性や全身疾患としての再発の病態では明らかな限界がある。特に効果的な再発部位として腟断端再発があり，腔内照射や全骨盤外部照射を行うことで救済される率はPORTEC 1[5]では79%，Ackermanら[6]は2/3と報告し，MD Anderson[7]でも局所制御率は2年で82%という成績である。その他の再発転移病巣の治療として多数例に基づいた切除不能例に対する放射線療法の効果に関する報告はない。

さらにがんに伴う症状たとえば腟出血や疼痛に対する緩和医療として放射線療法は有用であり，姑息的治療効果は期待できるとされている。症状緩和のための放射線療法は，根治的よりも低い総線量30～40 Gy程度を10～20回に分割したり，1回当たりの線量を5～10 Gyと高くして，少ない照射回数で投与することが試みられている。子宮体癌では主として骨盤内の腫瘍進展による出血や疼痛，骨転移による疼痛などが終末期の緩和医療として放射線治療の対象になっている。具体的には，全骨盤外照射では1回10 Gyを3～4週おきに2～3回繰り返す方法[8,9]などが報告されており，出血は90%，疼痛も60%以上で緩和されたという。また骨転移に対する放射線療法では一般に80～90%で疼痛の緩和が得られる[10]。種々の線量投与スケジュールが症例の状態や，治療施設の規模などにより検討されている。

以上の手術療法や放射線療法は依然局所療法であり，適応はそれほど広くない。今後もそれらの予後改善効果に関する臨床試験の実施は可能性が低いが，個々の症例のQOL改善への応用がそれぞれの施設で種々検討が積み重ねられていくものと考える。

3．再発がんでの化学療法の適応

ガイドラインには不完全摘出の進行がんまたは遠隔転移例・再発がんに対して化学療法は有用であるとされている。そしてどのような薬剤が推奨されるかに関しては，これまでの標準は，アドリアマイシンとシスプラチンの併用であったが，1990年代後半より卵巣癌の標準治療薬であるパクリタキセルが試みられるようになり，これらをいかに併用するかが推奨されている。

Table 1 再発子宮体癌における併用化学療法の第Ⅱ相試験[14]

Study	Year of Publication	Regimen	No. of Patients	RR (%)	OS (months)
Dimopoulos	2000	Paclitaxel/cisplatin	24	67	18
Hoskins	2001	Carboplatin/paclitaxel	46	61	NA
Scudder	2005	Carboplatin/paclitaxel/amifostine	47	40	14
Gebbia	2001	Cisplatin/liposomal doxorubicin	35	57	8.5
Lorusso	2006	Carboplatin/liposomal doxorubicin	40	50	NA
Hilpert	2006	Carboplatin/liposomal doxorubicin	31	44	NA

Abbreviations: RR, response rate; OS, overall survival; NA, not available.

歴史的に進行・再発子宮体癌への化学療法の試みは盛んに行われてきたが，プラチナ製剤とアンスラサイクリン類の併用が長期にわたり標準治療とされてきた。近年ようやく卵巣癌での有用性が確立されたタキサン系薬剤の登場により，子宮体癌における化学療法ががぜん注目されてきている。その主なインパクトは1990年代に多数例で登録された進行子宮体癌の臨床試験GOG122の成績[11]が発表され，放射線療法と化学療法を直接比較したところ，それまでの標準治療であった放射線療法より化学療法AP療法が明らかに予後改善効果があったという報告以来である。時を同じくイタリアからも対象症例がやや進行がんが少ない対象にて放射線療法と化学療法は同様の治療成績であったという報告[12]もあり，さらにわが国でも1990年代に400例を超す症例を登録していたJGOG2033の報告[13]が2005年に報告され，両治療法の同等な治療成績と一部のより早期の症例群では明らかに化学療法が予後良好であった。これらの流れが欧米でも化学療法に対する期待の潮流となって今日に至っている。

Flemingらは総説[14]のなかで化学療法を総括し，以前に化学療法の既往のない症例に対する最も有効な薬剤はプラチナ製剤，タキサン系薬剤，さらにアンスラサイクリン類でありすべて20～30%の奏効率を示す。再発時に行う二次化学療法の効果は一般に低いが，タキサン系のみが20%以上の成績をいつも示してきたとしている。子宮体癌症例は多くは高齢で（診断時平均60～65歳）術後に放射線療法を受けてきた。したがってしばしば骨髄機能の予備能も少なく用量を上げた治療は注意を要することも指摘されている。その他の薬剤の単剤化学療法でもたとえばECOGのtopotecan単剤の第Ⅱ相試験の化学療法未実施の症例に対する効果は20%であったが，卵巣癌での使用量である1.5 mg/m^2 5日間を開始量としたが30例中4例に化学療法死を認め，結果的に放射線の前治療なしには1.0 mg/m^2，ありには0.8 mg/m^{2}が推奨された。また内服アンスラサイクリン類であるDoxilはドキソルビシンに比べ骨髄抑制は少ないが，残念ながら化学療法未実施症例には11%しか奏効せず，また化学療法既実施症例には9.5%しか効果がなく，ドキソルビシンより効果がなさそうである。単剤より併用化学療法がより有効であり，一部の無作為試験で生存率の改善が得られている。多くの併用療法が第Ⅱ相試験で検討され，たとえばcarboplatin/paclitaxel，carboplatin/liposomal doxorubicinやcisplatin/vinorelbineなどがある。最近の併用化学療法の第Ⅱ相試験をTable 1に列記した。

Table 2は大規模な再発・転移症例を対象にした臨床試験であり，これまでに無作為化試験で検討した最も有効なレジメンはcisplatin（50 mg/m^2），doxorubicin（45 mg/m^2），and paclitaxel（160 mg/m^2; TAP）の3剤併用療法[15]である。この治療法にはGCSFの併用が必要であり，2日間にわたる治療で1日目にpaclitaxelを2日目にdoxorubicin/cisplatinを使用する。その理由は乳癌での高い奏効率だがpaclitaxelとdoxorubicinの同日併用で心毒性が増加したことであげられている。このAP療法とTAP療法のランダム化比較試験GOG177が実施され，TAP療法が有意に有効であることが示されたが，TAP療法で死亡例も含む毒性の激しさより，標準療法としてのコンセンサスは得られていない。しかし臨床的にはpaclitaxel/carboplatin（TC）が実際には全米で広く使用され，投与が比較的容易であり多くの第Ⅱ相試験で証明されているからである。TAP regimenは現在Ⅲ/Ⅳ期や再発子宮体癌を対象に大規模GOG試験にてTAPとTCが比較検討されており，この結果が期待されている。

本邦でも術後あるいは進行・再発子宮体癌症例にはTC療法を実施している施設は多数に上り，JGOGではまずどのタキサン系薬剤とプラチナ製剤が有効なのかを検証すべく，docetaxel/carboplatin（DC），docetaxel/CDDP（DP），paclitaxel/carboplatin（TC）の3アームでの第Ⅱ相試験[16]を行い，奏効率でDC療法がやや劣り，他の二つの併用療法DPとTCと標準であるAP療法の比較を行うJGOG2043を実施中であり，600例の目標症例で現在300例を超そうとしている。この結果は世界的にも極めて注目され，子宮体癌治療の標準治療の確立に

Table 2 これまでの再発転移子宮体癌における無作為化比較試験[14]

Study and Regimen	No. of Patients	RR (%)	Median OS (months)
Thigpen	356		
Doxorubicin		22	6.7
Doxorubicin/cyclophosphamide		33	7.3
Aapro	177		
Doxorubicin		17	7
Doxorubicin/cisplatin		43	9
Thigpen	281		
Doxorubicin		25	9.2
Doxorubicin/cisplatin		42	9.0
Gallion	342		
Doxorubicin/cisplatin		46	11.2
Circadian-time doxorubicin/cisplatin		49	13.2
Fleming	317		
Doxorubicin/cisplatin		40	12.6
Doxorubicin/paclitaxel		43	13.6
Fleming	273		
Doxorubicin/cisplatin		34	12.3
Doxorubicin/cisplatin/paclitaxel		57	15.3

Abbreviations: RR, response rate; OS, overall survival

寄与するものと思われる。

さらに新しい分子標的剤も子宮体癌に対して研究されている。具体的にはerlotinib, sorafenib, bevacizumabなどが第Ⅱ相試験の最中であり，GOGは現在trastuzumabの第Ⅱ相試験も行っており，EGFR2（FISHでserousやG3で15～30%陽性）が増幅されている症例を対象にしている。NCICのtemsirolimus（ヒトでのrapamycin［mTOR］inhibitorの標的）第Ⅱ相試験が化学療法未実施症例を対象に行われ26%の奏効率を示している[17]。興味深いことに子宮体癌では*PTEN*遺伝子変異を頻繁に示すことからこれらの薬剤の治療効果に興味があるのだが，効果はPTEN染色とは有意に関連しなかった。他のmTOR inhibitorであるRAD001の報告[18]もあり，前治療にて奏効しなかった再発子宮体癌に対し，15例中8例で癌の進行を抑制した。

4．再発がんでの黄体ホルモン療法の適応

ガイドラインには，「黄体ホルモン療法は類内膜腺癌G1あるいはプロゲステロン受容体陽性の進行・再発症例に試みられる」とある。

進行・再発子宮体癌は1960～1980年代にはホルモン剤，特にプロゲステロン剤で治療される場合が多く，奏効率は18.9～56.3%[19]とされ，わが国でも，栗原ら[20]が55例の進行・再発子宮体癌で26.5%と報告している。medroxyprogesterone acetate（MPA）がわが国では唯一使用可能であり，GOGの検討[21]で経口MPAは子宮体癌に有効で，特に高分化型，プロゲステロン受容体陽性症例に奏効し，1,000 mg投与が200 mg投与に勝る効果を示さなかったことから，MPA 200 mg投与が妥当と結論している。これまで進行・再発子宮体癌に対する化学療法は前述のごとく満足すべき成績ではないために，化学療法に各種ホルモン剤を併用して治療する試みも行われてきたが有効率もさほど改善せず，ホルモン剤の併用効果についてのエビデンスは乏しい。このような状況の下，現在は欧米で分子標的療法との併用の試みも始められようとしている。しかしいずれにしてもホルモン剤は，ホルモン受容体の有無にかかわらず，せいぜい20%程度にしか効果はなく特定の症例にしか用いられない。個々の症例のQOLを考え，化学療法など毒性の強い治療法には耐えられない場合にはbest supportive careの一環として考慮すべきと考える。

まとめ

再発子宮体癌は手術療法，化学療法，さらに放射線療法，ホルモン療法などを工夫しながらあくまで治癒をめざし，それが不可能なら緩和医療としての応用も含め，できるだけの延命を目指した，症例や家族の希望を十分に取り入れた医療を実践するべきと考える。そのためにも最新の治療成績などを取り入れつつ，情報収集に努めなければならない。化学療法では，タキサン類，プラチナ類，さらにアンスラサイクリン類などが有効な薬剤であり，再発や転移性腫瘍には化学療法の有用性はあまり大きくはないが，高齢者の多いことからも毒性は重点的に管理されるべきである。さらに最近の流れとして，副作用の少ない分子標的治療の試みも散見されるようになり，卵巣癌同様，種々の分子標的を狙いにした治療法の開発が進むものと考える。世界の流れを十分に把握しつつ，少しでも症例の延命を願いつつ日々の日常臨床に取

り組んでいきたい。

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Gynecologic Cancer Intergroup だより

Homepage: http://www.gcig.igcs.org/

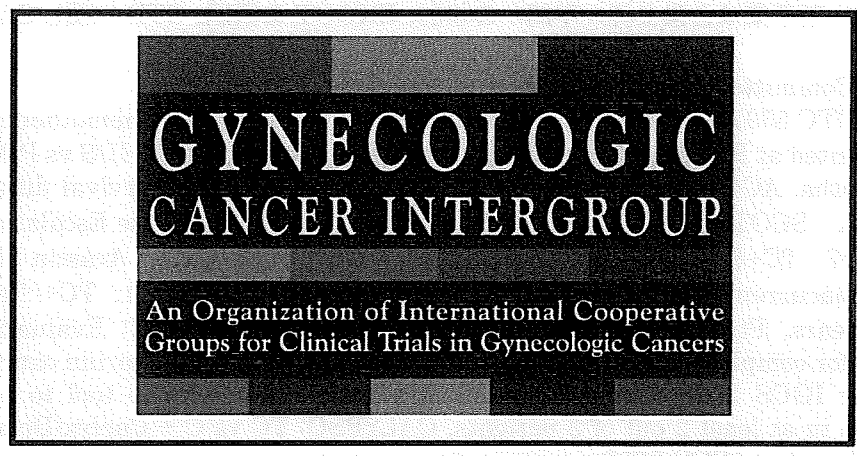
第5号 2009年総集号

JGOG GCIG委員会 編集

寒河江 悟 委員長

委員: 青谷恵利子、岡本愛光、竹内正弘、進 伸幸、藤原恵一

(2010,2,18)



GCIG 委員会 2009 年活動報告書

1. 平成 21 年 1 月 30 日、teleconference が開催された。Membership: ACRIN が加入, 予定: ICORG, TRSGO, GICOM., S. Africa Webmaster IGCS website へ移動 GCIG Q+A は IGCS "case report" で、Ongoing Business: 次回 General Assembly は NCI US Ovarian Cancer 特集と topics, 企業試験と学問的試験のあり方を議論 Highlights Kitchener to ESGO for 秋 2009, Trimble to SGO for 2010. 今後 Cervix Cancer State of the Science, 4th Ovarian Cancer Consensus Conference, Ovarian Cancer State of the Science を予定。

2. 平成 21 年 2 月 28 日アストラゼネカ社の MT 薬臨床試験のアドバイザリーボード会議が中国上海にて開催され、杉山、紀川、寒河江が出席。Olaparib(PARP 阻害剤)については平成 21 年 5 月 ASCO にて Olaparib の BRCA 卵巣癌 Phase II 結果を発表、この演題は Best of ASCO にも取り上げられた。平成 22 年 1 月 JGOG 開発治験・臨床試験推進委員会(東京)にて Olaparib の漿液性卵巣癌 Phase II に関する審議が行われ、JGOG の参加について検討中。

3. 平成 21 年 5 月 28-29 日 ASCO 総会(オーランド)時に開催された GCIG 春季総会が開催されたが、新型インフルエンザの影響で正式参加が出来ず、一部の個人的参加のみとなった。
EXECUTIVE BOARD MEETING 5.28 Membership: GICOM (Mexico), ICORG (Ireland) and TRSGO (Turkey)が暫定参加.Secretariat: Chair-Elect に ANZGOG の Quinn が候補に Website は IGCS の HP に移動。Governance ならびに Statutes を更新。総会: 10 月の topic に臨床試験での画像診断。業績:FIGO 論文発刊済み(Petru)、勧誘:東欧 group 代表が秋季総会に参加。Highlights を ESGO (Oct.2009)、SGO(Mar.2010)で.Cervix Cancer SOTS は June 18 – 19, 2009, Manchester, UK に開催。4th Ovarian Cancer Consensus Conference は June 2010, Vancouver, B.C.で。新事業は企業主導か学問かの検討、ENGOT の説明、GTD に関して ISSTD 会長をご招待など。
Ovarian Cancer Committee Marth /Harter
登録終了試験:EORTC 55971 CHORUS Upfront Surgery vs Neoadjuvant Chemotherapy Pts closed / 550, Presented at IGCS 2008, no difference of PFS between NACT+IDS vs PDS was seen with 12 months. AGO-OVAR-9: CT ± GEM Pts closed 1742, no survival difference between two arms, SCOTROC-4 :Carbo Flat Dosing vs Intrapatient Dose Escalation Pts closed 932, ICON-7: TC+/- Avastin Pts closed / 1520, GOG-218: CT +/- Avastin Placebo vs CT + Avastin concurrent and extended Pts closed / 1800, EORTC 55041: TC+/-Tarceva consolidation 2 years, Pts closed / 835, AGO-OVAR OP-2 Desktop II: Evaluation of predictive factors for complete resection in platinum-sensitive recurrent ovarian cancer Pts closed/412, Report IGCS 2008. The AGO-Score is a useful and reliable tool to predict complete resection in at least 2 out of 3 patients, CALYPSO: TC vs C + Caelyx(Doxil) Pts closed / 976, Presented at ASCO 2009
現在登録中の臨床試験: AGO-OVAR OP-3 LION study: systemic LN vs no LN in IIB-IV OVCA Pts: 26 / 640 pts, First line; JGOG3017: CT vs CDDP + Irinotecan Patients 360 / 652, mEOC:oxaliplatin + capecitabine ± Avastin vs carboplatin + paclitaxel ± Avastin Pts 0/332 MITO-7: Weekly CT vs 3-weekly CT (QoL) Patients 25 / 500, JGOG ip trial: IP vs IV carboplatin + weekly Paclitaxel, NCIC CTG OV.21: IP/IV Platinum/T vs IV CT optimally debulked following NACT, AGO-OVAR-12: Carbo Paclitaxel +/- BIBF 1120 (Vargatef) , AGO-OVAR-16: 1st line + Pazopanib consolidation 1 yr, そのほか、ICON8: weekly vs tri weekly and early reduction or late one、AGO-OVAR OP-7Desktop III:

Cytoreductive surgery vs NO surgery in platinum-sensitive recurrent EOC, HECTOR: C-Topo vs CT or CG in recurrent Pt-sensitive ovarian cancer Pts 452 / 550, MITO-8: PLD vs CT cross-over in 6-12 m Pt-free interval Pts 25 / 253 , SGCTG / NCRI:A Randomised Phase III Trial of Weekly CT vs Doxil In Recurrent, Platinum Resistant, Ovarian Cancer
まとめ:GCIG は卵巣癌の標準治療を変えうる重要な試験を遂行してきた。主眼は初回化学療法で、手術の試験も始めてきたし、耐性再発癌の検討も進んでいる。
Symptom Benefit working group (see attached)Friedlander/B.Miller
再発癌の症状の管理は重要で、QOL 評価法の選定 stage1 の後、実際の治療での有用性を検討する試験に参加依頼が来ているので stage2 を検討予定。緩和的化学療法での QOL の評価を国際的に行い、方法と症状の改善を目指す。
Endometrial Cancer (+GTD) Standing Committee report (see attached) D.Miller
現在登録中:摘出後試験: GOG-0249: A Phase III Trial of Pelvic Radiation Therapy versus Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High Risk, Early Stage Endometrial Cancer, GOG-0258: A Randomized Phase III Trial of Cisplatin and Tumor Volume Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial: PORTEC-3: Randomized Phase III Trial Comparing Concurrent Chemoradiation and Adjuvant Chemotherapy with Pelvic Radiation Alone in High Risk and Advanced Stage Endometrial Carcinoma: 再発癌 GOG-0238: A Randomized Trial of Pelvic Irradiation with or without Concurrent Weekly Cisplatin in Patients with Pelvic-only Recurrence of Carcinoma of the Uterine Corpus 進行・再発癌: NCIC: EN 8: Randomized Phase III Study of progestational hormone therapy *versus* deforolimus in women with recurrent or metastatic endometrial cancer: 癌肉腫: GOG-0261 (UC-0701): A Randomized Phase III trial of Carboplatin plus Paclitaxel VERSUS Ifosfamide plus Paclitaxel in Chemotherapy Naïve Patients with Newly Diagnosed Stage I-IV, Persistent or Recurrent Carcinosarcoma (Mixed Mesodermal Tumors) of the Uterus: 平滑筋肉腫:GOG-0250 (DTM0720): A Randomized Phase III Evaluation of Gemcitabine-Docetaxel plus Bevacizumab (NSC#704865, IND #7921) in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus
Cervix Cancer (+ vulvar, vagina) Committee Small/Sagae
Cervix Cancer State of the Science, June 18-19,2009 開催、Fractionation Survey 論文へ。
現在進行中試験: *GOG 0219:*A phase III, randomized trial of weekly CDDP and RT versus CDDP, Tirapazamine and RT in stage IB2-IVA cervical carcinoma limited to the pelvis. 薬剤の供給に問題あり。JGOG Phase III study of S-1 + Cisplatin in cervical cancer 52 of 360 pts. *EORTC 55994*: Randomized phase III study of neoadjuvant chemotherapy followed by surgery vs. concomitant radiotherapy and chemotherapy in FIGO stage Ib2, IIa>4 cm or IIb cervical cancer. さらに 100 例の登録が必要。*GOG 240:* Cis/Taxol +/- Bev vs Topo/Taxol +/- Bev in stage IVB cervix cancer 内容的に問題あり。
検討中試験: *RTOG 0724:* ChemoRT with and without adjuvant chemotherapy in high risk cervix cancer after hysterectomy 現在放射線治療医の最も関心ある試験、*KGOG 0801:*RT vs CRT in intermediate risk cervix cancer after hysterectomy GOG 試験として accept され、近く開始予定. *GOG A Phase III Trial of 12 months of Oral Pazopanib versus Placebo Among Women With FIGO Stage IB2, > 4 cm IIA and IIB-IVA Cervical Cancer Limited to the Pelvis After Responding to Front-Line Weekly Cisplatin Chemotherapy and Pelvic Radiation 分子標的薬の頸がんへの応用例。GOG CVM0503: CRT vs CRT + Cetuximab in patients with para-aortic metastasis* さらに Cetuximab の応用も企画されている。新しい試みと

して、OUTBACK trial (ANZGOG) から a concept for delivering adjuvant carboplatin/paclitaxel chemotherapy after completion of chemo/RT in cervical cancer が提案されﾌﾟﾛﾄｺｰﾙ作成中。EMBRACE (AN INTERNATIONAL STUDY ON MRI-GUIDED BRACHYTHERAPY IN LOCALLY ADVANCED CERVICAL CANCER)も説明された。

Harmonization – Operations Elser Statisticians Brady

Operations: GCIG への参加グループ間での臨床試験の標準化に向けて以下の問題を議論した。1 Definition of Protocol Signature/Site Acceptance Form、2 Survey of policies / processes - Queries / Deficiencies / Monitoring、3 CALYPSO 試験に基づき TMF compilation in Intergroup trials を議論した。Statistician: 1. 今後のトピックス a.主要な予後解析因子の標準化 b.グループ間での方法の説明文を作成。2. 非劣性試験の結果の解析、3. 明快な第三相試験デザインの確立

Rare Tumours (incl. carcinosarc. and borderline) Gershensen/Reed

現在進行中 Trials: GOG 0187: Phase II study of paclitaxel for ovarian stromal tumors as second-line therapy. GOG 0239: A phase II trial of AZD6244 (NSC 741078) in women with recurrent low-grade serous carcinoma of the ovary and peritoneum. GOG 0251: A phase II trial of bevacizumab (rhuMAB VEGF) for recurrent sex cord-stromal tumors of the ovary.

企画中: GOG 0241: A GCIG Intergroup multicentre phase III trial of open label carboplatin and paclitaxel +/- bevacizumab compared with oxaliplatin and capecitabine +/- bevacizumab as first line chemotherapy in patients with mucinous epithelial ovarian cancer (mEOC). GOG 0254: A phase II evaluation of SU11248 (sunitinib malate) in the treatment of persistent or recurrent clear cell ovarian carcinoma. RTM0602: A phase II trial of paclitaxel and carboplatin vs. bleomycin, etoposide, and cisplatin for newly diagnosed advanced stage sex cord-stromal tumors of the ovary. RTM0905: A phase II study of Imatinib Mesylate (SRI571; Gleevec; NCI-supplied agent NSC#716051; IND 61135) in the treatment of vulvo-vaginal melanoma harboring somatic alterations of c-KIT. RTM0907: A phase II evaluation of Sunitinib Malate (Sutent ® SU11248, NCI-Supplied agent, NSC#736511, IND #74019) in combination with carboplatin and paclitaxel as first-line therapy in the treatment of clear cell carcinoma of the ovary. ANZGOG: Phase 2 study of ARomatase inhibitors in women with potentially hormone responsive recurrent/metastatic Gynaecological Neoplasms (PARAGoN). さらに Q&A Format は IGCS web 上で議論される予定。稀少症例の登録試験の試みも検討中。.

Translational Research Birrer/McNeish

組織材料: 多くの組織収集がされているが、多くはフォルマリン固定パラフィン包埋組織であり、凍結材料はすこし。この情報を web にのせ内膜癌や卵巣癌での材料収集に役立て、trial/non trial, type of tissue, numbers and contact person に分類する。材料の質、臨床経過、臨床情報が重要で、採取部位が最も重要である。 TR projects の review: TGCA (US) and IGC projects の議論を行った。 Clear Cell Study での TR 案: Biomarker studies 血清中 HNF1 Beta と HIG2、ZNF217 の免染. Chemoresistance: Proliferation markers such as P27, CDK2, Ki67, MCN all by IHC. Chemoreistance genes e.g. ABC transporter (MDR1, MRP TOPO1 by IHC and RTPCR, H1Fα, VEGF, again by IHC and RTPCR. さらに UTG1 polymorphisms based on leucocyte DNA などを検討予定。 共同研究と今後の方針:GCIG 試験への TR の提案を早期に行う。GCIG の bank を基盤にした研究を開始する。遺伝子解析の検証試験を開始する。

4. 平成 21 年 6 月 子宮頸癌の SOTS が英国ﾏﾝﾁｪｽﾀｰにて開催され、琉球大戸板先生が参加。

6/17 1. Global Issues in Cervical Cancer 途上国で頸癌の罹患が高率であり治療水準が不十分であり、UICC や IAEA の取り組みが紹介された。2. 予防ワクチン接種が急激に増加している。3.

2007 年の SOTS での合意点：予後因子としては、貧血、低酸素関連、腫瘍径(MRI がベスト)と LN status の重要性を確認。4. 早期癌(1a-1b1 期) 1)手術 AR trache の総説(2008 GO)の解説後、低侵襲手術の試験(対象：IA-IB1 (2cm>), LVSI 50%>)や NAC+縮小手術の試験も紹介。2) 術後 HR 症例の治療は CCRT + adjuvant chemotherapy の有効性を示唆(RTOG7204, KGOG/GOG0801)された。5. 早期癌(IB2) NAC+手術の意義が再評価されつつあり、TP vs TIP の data などが議論された。6. 2B-4A 期 1)CCRT CDDP 以外でもよい、CCRT 後の Adjuvant CT 追加がよいなどが戦略立案に重要。さらに、今後の国際臨床試験の展開は先進国・途上国に分けて戦略を考える。2) IMRT, hyperthermia などの現状と問題点が紹介。7. 再発癌 手術、CCRT、化学療法(特に分子標的薬)の現状と今後について報告。8. 腔内療法 国際調査の結果が報告され、多くの施設で IGBT が普及しつつあること(特に US ガイド)が報告された。また、Central pelvis に対する線量にかなりのばらつきがあったことが示された。9. CCRT 後の G3/4 の late toxicity は 5-18%であり、許容範囲内であることが示された。

6/18 4つの subgroup (1:Early/Surgical, 2:Advanced/Chemoradiation, 3: Recurrent disease, 4: Accrual from developing countries)に分かれ今後の国際協調試験の方向性と可能性、問題点が討議され、1. 早期/手術 低侵襲手術、NAC＋手術、2. 進行癌 1)症例選択: 進行期での層別はせず、腺癌、リンパ節は PET、腫瘍径は MRI で層別を。2)再発様式から、局所治療の用量をあげるより、全身的治療(遠隔転移予防)に重点をおいた治療戦術が重要。3)CCRT 後の追加化学療法の戦術が有効であり、今後 RTOG7204(術後 CCRT vs CCRT+adjuvant CT)への参加が広く求められた。NAC+CCRT の再評価を目的とした試験の提案もあった。

5. 平成 21 年 10 月 10-11 日 セルビア・ベオグラードにて ESGO にて同時開催の GCIG 秋季総会に出席した。参加者：寒河江、藤原、進、岡本、青谷、青木 Observer：松村(京大)

Executive Board & General assembly Membership アイルランド、トルコ、メキシコ 準会員 上海、ブラジル、その他 準備中 Web: Clinical Trial Update は充実してきている。最新情報の提供が呼びかけられた。GCIG 会議への Web based registration system を構築する予定。Criteria for GCIG Trial の定義: Academic vs. Industrial trial：Pure Academic Trial は公的財源が十分確保できているグループについては、明確な定義が可能であるが、その他のグループでは、グループの運営が企業からの寄付で成り立っていることを考えると、その遂行はほぼ不可能である。現状を考慮すると、Academic Trial の定義を過大に厳格化することは、現状では無理であろう。すなわち現時点で Pure Academic Study のみを GCIG Trial をすることは不可能ではないか。GCIG の各グループの運営状況に関する懸念として、各国ともに Regulation は厳しくなる一方、funding の状況は悪化している。臨床試験の現状と funding 増加を訴える Publication が必要であろうという提案が行われた。一方、研究者管理や SAE 報告に IT を導入したり、IRB を中央化するなどの効率化を目指すことによって無駄を省くことも重要であることが指摘された。米国方式であるが、これを構築するにも財源が必要である。似たような臨床試験デザインが各グループで重複しないように配慮することも重要であることが指摘された。

Ovarian Cancer Committee C. Marth/P. Harter

GOG218, ICON7 は TC に Bevacizumab の上乗せ、維持療法の効果を検証する試験で、最近登録終了し結果待ちである。AGO-OVAR OP 4/DESKTOP III study は開始されており、各グループの協力要請あり。ICON 8: Weekly Paclitaxel の検証試験。

JGOG で検討している iPocc 試験を紹介:Dose-dense paclitaxel + IV Carboplatin AUC6 vs. dose-dense paclitaxel + IP Carboplatin AUC6 を phase II/III として行う。対象は II-IV 期の上皮性卵巣癌(JGOG3017 を行っている間は clear cell は登録しない)で、初回手術後 optimal, suboptimal の両者を適格とする。NCIC CTG OV21: A phase II/III study of IP plus IC

chemotherapy versus IV carboplatin plus paclitaxel in patients with epithelial ovarian cancer optimally debulked at surgery following neoadjuvant IV chemotherapy: 初回手術不能進行卵巣癌症例に対して NACT を行い、その後 IV TC 療法、IV paclitaxel + IP carboplatin, IV paclitaxel + IP cisplatin + IP paclitaxel の比較を行う。Phase II 部分で IP を行う2群のうち一つを pick the winner として取り上げ、Phase III として IC TC 群と比較する。この試験ではすべての症例で Day 8 に paclitaxel が投与されることになった。GOG0252: A PHASE III CLINICAL TRIAL OF BEVACIZUMAB WITH IV VERSUS IP CHEMOTHERAPY IN, OVARIAN, FALLOPIAN TUBE AND PRIMARY PERITONEAL CARCINOMA. Arm I: IV Paclitaxel (weekly) + IV Carboplatin + IV Bevacizumab → IV Bevacizumab、Arm II: IV Paclitaxel (weekly) + IP Carboplatin + IV Bevacizumab → IV Bevacizumab、Arm III: IV Paclitaxel + IV Cisplatin + IV Bevacizumab + Day8 IP Paclitaxel→ IV Bevacizumab の試験が、ちょうど開始されたことが報告された。iPocc Trial の評価:GOG, NCI Canada の IP 試験とは異なり、比較するパラメターが一つに絞ってあるので結果の解釈が単純である点が高く評価された。GCIG 試験として ANZGOG が参加の可能性を示唆してくれている。来年度のグラント申請をしてくれることになった。サマリーの英訳を送ることにした。

Rare Tumours (carcinosarcoma) (borderline) (IGCS Education) N.Reed/D. Gershensen

GOG0241: Mucinous Carcinoma に対する TC, XEROX, ±Bevacizumab の2x2ランダム化比較試験は US と UK (UK MIO trial)の政府審査に提出されており、承認され次第登録開始予定。US と UK のデータセンターで別個のデータベース作成し、最終的に統合解析を行う(UK)。(Target 332) GOG0254: Clear Cell Carcinoma に対する Sunitinib の第 II 相試験 (Target 40)。日本では薬剤提供の問題が障壁となっている。RTM0602 (GOG): Sex cord stroma tumor of ovary に対する BEP 対 TC のランダム化第 II 相試験が計画中。RTM0905 (GOG): Dasatinib (Sprycel)の膣外陰メラノーマに対する第 II 相試験が提案されたが、メラノーマはメラノーマ試験グループに任せた方が効率的であることが指摘された。ANZGOG: ホルモン感受性の可能性のある転移製・再発婦人科がん(体癌、ESS、肉腫、顆粒膜細胞腫など)を一括して aromatase inhibitor である Anastrozole の効果を評価する第 II 相試験が計画されている。JGOG3017: 登録 416/652、うち韓国から 18 症例。UK, GINECO, MITO が近々参加することを報告。JGOG3017, CCC trial のフォローアップ試験や CCC の再発症例に対する新薬の Phase II trial を行う必要ありとの議論がある。GOG で計画している Carcinosarcoma に対する TC 対 TI (Taxol 対 Ifosfamide)のランダム化第III相比較試験に JGOG が GCIG international group study として行えないかどうかを打診したところ、Mark Brady (GOG)と Ted Trimble (NCI)から NCI でその方法論について検討するとの回答を得たが、JGOG としての FWA を取得、すべての研究者の NCI 登録が必要になるなど、かなりハードルが高くなりそうである。一方 MITO から Carcinosarcoma に対する TC 対 Ifosfamide + Cisplatin の比較試験への参加を打診された。レギュレーション等を考えると、こちらの方が参加しやすい可能性が高い。

Symptom Benefit Michael Frielander によって提案された、化学療法抵抗性または3rd Line 以降の化学療法を行う症例に対する、症状調査が第一段階から、第二段階に移行することが発表され、各国のグループが協力を申し出ている。詳細なプロトコルを取り寄せた上で、JGOG として参加可能かどうかを検討したい。

Translational Research M. Birrer/I.McNeish

1. 新しい TR の方向性:GOG262 (weekly dose dense TC +/- beva vs standard TC + beva)、GOG252 (IP chemotherapy)などの2つの trial が新たなトランスレーショナルリサーチを組み入れる絶好の trial である。trial のプロトコールに TR が入るのは多くの場合最終段階であり、もっと早い時期からプロトコールに組み込まれるべきである。採取検体による相違が生じている。2. Pharmacogenomics (新薬開発に有用な遺伝子情報学)NCI, GOG からの提案で卵巣癌において個

人や人種による遺伝的背景が第一次化学療法の奏功率・有害事象・QOL・予後に影響するのではないかとの仮定の下、進行卵巣癌のジェノミックDNAと臨床データから検討する研究で、東京大学と理化学研究所が無料で解析する予定である。検体としては全血が質的にも量的にも一番適していることで一致した。3. Clear cell study JGOG 岡本・進・松村 3 人から、Array CGH-GISTIC 解析の検討および細胞周期関連分子の検討、UGTA1 研究、遺伝子発現プロファイリングアプローチによる新規分子標的薬の開発の発表があり、賞賛された。さらに1)日本人・欧米人における clear cell の頻度の違い、2)なぜ日本において子宮内膜症と clear cell が増加傾向なのか、3)遺伝子発現プロファイルによる卵巣癌と腎癌の類似性などが討論された。4. 粘液性 trial mEOC/GOG241 trial が TR を組み入れる絶好の trial であり、次回討論予定。

Endometrial Cancer Standing Committee Report (+ GTD) Chair: David Miller

Resected endometrial: GOG-0249: A Phase III Trial of Pelvic Radiation Therapy versus Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High Risk, Early Stage Endometrial Cancer – RTOG would like to participate 対象は Stage I, IIA with high-intermediate risk PORTEC-3: Randomized Phase III Trial Comparing Concurrent Chemoradiation and Adjuvant Chemotherapy with Pelvic Radiation Alone in High Risk and Advanced Stage Endometrial Carcinoma – Participating groups: MaNGO, ANZGOG, NCRI, and NCIC-CTG. NSGO interested.対象:stage IB grade 3 with documented LVSI、stage IC or IIA grade 3、Stage IIB、stage IIIA or IIIC GOG-0258: A Randomized Phase III Trial of Cisplatin and Tumor Volume Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial – RTOG would like to participate 対象:patients with either surgical stage III or IVA endometrial carcinoma After 4: A Phase III intergroup trial on adjuvant therapy in radically operated endometrial cancer patients with high risk for micro-metastatic disease: 4 courses of adjuvant *CT* (CT) followed by radiation therapy (RT) versus 2 more courses of CT (Hogberg) 対象は PORTEC3 とほぼ同じ、組織型は endometrioid のみ。 Pelvic recurrence: GOG-0238: A Randomized Trial of Pelvic Irradiation with or without Concurrent Weekly Cisplatin in Patients with Pelvic-only Recurrence of Carcinoma of the Uterine Corpus 対象は再発子宮体癌(骨盤・腟に限局) Advanced/recurrent: GOG0248 Randomized Phase II Trial of Temsirolimus or the Combination of Hormonal Therapy & Temsirolimus in Women With Advanced or Recurrent Endometrial Cancer Accrual 43/42 (stageIcompleted) NCIC EN 8: Randomized Phase III Study of progestational hormone therapy *versus* Ridaforolimus in women with recurrent or metastatic endometrial cancer (Oza) 対象: recurrent or metastatic endometrial cancer Carcinosarcoma: GOG-0261: A Randomized Phase III trial of Carboplatin plus Paclitaxel VERSUS Ifosfamide plus Paclitaxel in Chemotherapy Naïve Patients with Newly Diagnosed Stage I-IV, Persistent or Recurrent Carcinosarcoma (Mixed Mesodermal Tumors) of the Uterus Sarcoma GOG0250: Randomized Phase III Evaluation of Docetaxel, Gemcitabine, & G-CSF +/- Bevacizumab in the Treatment of Recurrent or Advanced Leiomyosarcoma 以上、RT や CT、あるいはその併用など混沌とした状況である。

Cervix Cancer Report (+ vulvar, vagina) W. Small/S.Sagae

まず Cervix Cancer State of the Science Meeting report (June 18-19, 2009)H. Kitchener が行われた。昨年の SOTS の報告論文は Trimble, E.L. Meeting Report: Cervical cancer state-of-the-clinical-science meeting on pretreatment evaluation and prognostic factors, September 27-28,2007: Proceedings and recommendations. Gynecology Oncology, 2009 August; 114(2); 145-150.である。 現在進行中の臨床試験: *GOG 0219 (NCIC- CTG)* : A phase III, randomized trial of weekly CDDP and RT versus CDDP, Tirapazamine and RT in stage

IB2-IVA cervical carcinoma limited to the pelvis. Tirapazamine の供給に問題が生じている。*EORTC 55994*: Randomized phase III study of neoadjuvant chemotherapy followed by surgery vs. concomitant radiotherapy and chemotherapy in FIGO stage Ib2, IIa>4 cm or IIb cervical cancer. EORTC 独自に試験終了を目指している。*JGOG (KGOG) Phase III study of S-1 + Cisplatin* in cervical cancer: アジアで進行中である。*GOG trial (MANGO, NCIC-CTG, NSO):* Cis/Taxol +/- Bev vs Topo/Taxol +/- Bev in stage IVB cervix cancer. 近く開始される臨床試験: *RTOG 0724 (GOG):* ChemoRT with and without adjuvant chemotherapy in high risk cervix cancer after hysterectomy (Jhingran). *KGOG 0801 (GOG)*: RT vs CRT in intermediate risk cervix cancer after hysterectomy. 新しい試み: ASGO: Randomized trial of weekly VS triweekly plaitinum with radiotherapy (Sarikapan)、MANGO: Early neoadjuvant trial (Zola)、The OUTBACK ANZGOGtrial: Chemoradiotherapy +/- adjuvant chemotherapy/GOG 219 Replacement (Linda Mileshkin)、NCIC-CTG: Less radical surgery in early stage cervical cancer (Marie Plante)、NCRI: Neoadjuvant chemotherapy (Mary Mccormack)、Uniform toxicity criteria for GCIG trials: (Zola)、Cervical Cancer in underdeveloped Nations (Gillian Thomas) などであり、CCRT のあとにさらに CT を追加する試験や低侵襲手術の試験など多彩な提案がなされている。

Harmonization (Ops and Stats) G. Elser/M. Brady JGOG 参加者: 青谷恵利子

ハーモナイゼーション・グループでは、各国の法規及び異なる臨床試験グループポリシーに関する互いの理解を深め、国際共同試験を円滑に行うために必要となる「調整」を行っている。特に今回のミーティングでは、実際に複数の GCIG 試験が実行されたことにより見えてきた運用上の調整に関する議題が多く取り上げられた。【継続的審議事項】1. 施設の認定基準の明確化、施設とグループの契約関係の証明、必須文書の整理、2. JGOG Investigator としてのクオリフィケーション基準の明確化、3. JGOG 試験関係者の名簿管理(施設および事務局)、4.「被験者保護に関する教育」と「利益相反に関する管理」「試験に関するする機密保持契約」に関する JGOG ポリシーと実践、5. プロトコル単位での教育の提供、6. モニタリングの実施体制(＊欧州では訪問モニタリングが必須であるが、米国 GOG では日本と同様に治験以外はセントラルモニタリングを中心に実施している。)、効果安全性評価委員会の責務の明確化、手順書の整備、これらを網羅する JGOG グループポリシーについて、GCIG へ最新版の提出が求められている。 さらにその他の議題として、1. Group Contacts & Summaries 全ての参加グループの試験実施体制や運営上の取り決めについては、GCIG の HP に公開されている。JGOG の情報についても更新作業を行なう必要がある。2. ヘルシンキ宣言 2008 年版ヘルシンキ宣言の"The patients are entitled to be informed the results of the research"という解釈が各国で異なっている現状が指摘された。臨床試験が終了し、結果が公表された段階でどこまで、どのような方法で患者に伝達する必要があるのか、GCIG 標準を定めるのか等が話し合われた。3. CTC AE Version 4.0 最新版は 4.0 であるが、欧州のグループは未だ 3.0 を使用している。年に 1 度メジャー改訂が行われる 4.0 にどのように対応するかが検討された。①有害事象名(カテゴリーを含む)は version にあわせて変更せざるを得ない、②NCI の作成者を招聘して Q&A セッションをもつことが提案された。4.「逸脱」Violation, Deviation (Major/Minor), Deficiency など「逸脱」を意味する用語は、各々のグループで異なり、この定義を GCIG として統一化しようという動きがある。5.「モニタリング」方法に関する要求事項 引き続き、各グループのモニタリング体制を公開・評価していくことが確認された。6.「Group Specific Appendix」記載事項の統一、7. Current GCIG Studies 各グループで現在実施している GCIG 試験について、その進捗状況が報告された。JGOG からは、JGOG3017 および GOG0218 試験、AGO 試験および IP 試験の進捗状況について青谷が報告した。

11:30am Education Session: Imaging and Clinical Trials E.Sala HP で閲覧可能

12:30pm　GCIG Executive Board meeting　1:00pm　GCIG presentation at ESGO
2:00pm – 6:00pm Satellite GCIG Trial Meetings
GSK の Pazopanib/AGO 試験の会議に藤原、青谷が出席。本試験は、GCIG の管轄下で、ドイツの AGO の主導により実施される国際共同試験です。 本邦では、2009 年 2 月に GOG-Japan の各施設を対象に説明会がおこなわれ、同 4 月に JGOG の開発治験・臨床試験推進委員会で実施が承認されております。 目標症例数は全体で 900 例、本邦では 50 例であり、いずれかが目標症例数に到達した時点で本邦での登録を終了する予定です。全体では2009年6月に1例目の症例が登録され、これまでに 318 例が登録されています。 また、本邦でも同様に 6 月に 1 例目の症例が登録され、これまでに 24 例が登録されています。(2010 年 1 月 18 日現在)

6.第 7 回国内 GCIG 委員会　横浜 JSCO 2009,10,23
Belgrade での秋季総会の各 working group 報告を参加 GCIG 委員より行われた。

7.JGOG 総会において GCIG 会議報告 2009,12,4
子宮体癌、卵巣癌について報告、子宮頸癌については頸癌委員会報告にて時間をいただいた。
内容は、昨年 ASCO で発表した JGOG3016 臨床試験について、欧米での評価がますます高まり、新規の臨床試験の arm に weekly の idea が多数採用され、GCIG 秋季総会にて最新 Lancet 論文は高く評価されていた。今後の追試の成績が IP 試験とともに注目される。また JGOG3017 を GCIG 研究として進行中であり、KGOG からの登録があり、さらに英、仏、伊などの参加目前である。さらに JGOG3017 関連で TR 研究の内容にも注目された。現在独自に進行中の JGOG2043 子宮体癌臨床試験について化学療法の標準療法は何かの議論を深め、術後療法の最善策の討論が沸騰している

8.今後の GCIG 会議の予定

Spring meeting	6 月 2-3 日	at ASCO 2010	Chicago
Fall meeting	10 月 22-23 日	at IGCS 2010	Prague

9. 2010 年の課題
1. 6 月卵巣癌 SOTS 会議が(ﾊﾝｸｰﾊﾞｰ)が開催予定であり、IP と dose-dense、分子標的治療が注目され、今後も3極の一翼として婦人科癌の共同研究の議論を続ける。
2. GCIG 活動の発展に JGOG の役割を十分に果たすべく委員会活動を強化し、卵巣癌 JGOG3017 に続いて、体癌や頸癌試験への参加を各国のグループと協議を続ける。
3. さらに JGOG からの委員として GCIG 頸癌委員会 co-chair の重責をはたす。

Gynecologic Oncology 115 (2009) 456–459

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Practice pattern for postoperative management of endometrial cancer in Japan: A survey of the Japanese Gynecologic Oncology Group

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ARTICLE INFO

Article history:
Received 2 July 2009
Available online 17 September 2009

Keywords:
Endometrial cancer
Adjuvant therapy
Survey
Japanese Gynecologic Oncology Group

ABSTRACT

Objective. To determine the current status of postoperative management of endometrial cancer in Japan by surveying members of the Japanese Gynecologic Oncology Group (JGOG).

Method. We conducted an original mail survey regarding the status of postoperative treatment including indication criteria, treatment procedures, and chemotherapeutic regimen among all 226 active member institutions of the JGOG.

Results. A total of 199 institutions (88.1%) responded to the survey. A total of 4063 patients with endometrial cancer were treated at the member institutions of the JGOG over a year. As adjuvant therapy, chemotherapy (79.9%) was significantly ($p<0.01$) preferred over radiotherapy (13.0%) or hormonal therapy (7.1%). Furthermore, more than 50% of respondent institutions performed adjuvant therapy when patients exhibited International Federation of Gynecology and Obstetrics (FIGO) stage IB/G3/positive lymph-vascular space invasion (LVSI)/endometrioid adenocarcinoma or FIGO IB/G3/non-endometrioid histology, and more than 90% institutions administered adjuvant therapy when patients exhibited FIGO IC/G3/positive LVSI/endometrioid adenocarcinoma or FIGO stage IC/G3/regardless of LVSI/non-endometrioid histology. A combination of paclitaxel and carboplatin was the most preferred first-line regimen for adjuvant chemotherapy followed by combination regimens consisting of anthracycline and platinum.

Conclusion. The present survey provides relevant information regarding the current status of adjuvant therapy in Japanese patients with endometrial cancer.

Introduction

The prognosis of patients with advanced endometrial cancer is determined by the administration of adequate adjuvant therapy based on surgical staging and clinicopathologic prognostic factors such as histologic subtype, histologic grade, or lymph-vascular space involvement (LVSI). Therefore, surgery for endometrial cancer has both a therapeutic and diagnostic role. A previous survey by the Japanese Gynecologic Oncology Group (JGOG) revealed that standard surgical procedures such as simple or type II hysterectomy with systematic pelvic lymphadenectomy or para-aortic lymph node sampling are routinely performed in most patients with endometrial cancer in Japan [1]. However, although the Japan Society of Gynecologic Oncology (JSGO) has published treatment guidelines for endometrial cancer [2] to reduce the differences in treatment modalities across institutions in Japan, the optimal therapeutic modality for postoperative endometrial cancer remains debatable. Furthermore, patient selection criteria for adjuvant therapy and optimal chemotherapeutic regimens for endometrial cancer have not yet been established in clinical practice. To evaluate the current clinical practice patterns for postoperative management of endometrial cancer in Japan, we conducted a survey among the JGOG member institutions.

Patients and methods

The questionnaire used in this study was designed by members of the Disease Committee of Uterine Endometrial Cancer in the JGOG. The final instrument included clinical questions to determine both the

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0090-8258/$ – see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.ygyno.2009.08.016