Oral Etoposide for Refractory or Recurrent Epithelial Ovarian Cancer

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Objective: *To study the response rate (RR), toxicity, progression-free survival (PFS), and overall survival (OS) of the patients with recurrent or refractory epithelial ovarian cancer (EOC), who had oral etoposide at dosage of 75 mg/day.*

Material and Method: *Patients with recurrent or refractory EOC who were treated with oral etoposide between January 1998 and December 2007 were identified from the Archive of the Gynecologic Oncology Unit of the institution. Clinical and pathological data were reviewed.*

Results: *During the present study period, 38 patients receiving oral etoposide were identified. Median age was 51 years (range, 33-72 years). Seven patients could not tolerate chemotherapy side effects during the first cycle, leaving 31 patients evaluable for response. The overall RR was 25.8% (8/31 patients), 19.4% complete (6/31) and 6.4% partial responses (2/31). Stable diseases were demonstrated in 19.4% (6/31) while progressive diseases were found in 54.8% (17/31). The median PFS was 4.8 months (range, 3.3-6.4 months) with 2-year PFS of 16.7% (95% confidence interval [CI], 2.1-31.4%) while median OS was 12.0 months (range, 0.75-25.5 months) and 2-year OS was 36.4% (95% CI, 17.4-55.3%). The main toxicity was gastrointestinal side effect.*

Conclusion: *Oral etoposide at a daily dosage of 75 mg is an active agent for refractory or recurrent EOC. Gastrointestinal symptom is the most common side effect. This oral chemotherapeutic agent has some advantages over other drugs in terms of convenience for administration and fewer visits.*

Keyword: *Oral etoposide, Recurrent, Epithelial ovarian cancer*

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Epithelial ovarian carcinoma (EOC) is the third leading cause of gynecologic cancer deaths after breast and cervical cancers all over the world[1]. The expected global incidence in 2008 is 21,650 new cases of ovarian cancers, with 15,520 deaths. The high mortality rate partly lies on fact that most cases are diagnosed when their disease is in the advanced stages[1-3]. The standard treatment of all EOC is primary surgery, which serves as a diagnostic means for staging and as a therapeutic procedure to remove as much of the tumors as possible. Patients with early stage disease and risk factors for recurrence, and those in advanced stage will have adjuvant chemotherapy to prevent tumor recurrence or to eradicate residual tumors, respectively. The most common chemotherapy in the primary treatment is platinum drug, either alone or in combination. Despite the high objective response rate to surgery and primary chemotherapy, these patients still have a high rate of relapse and require additional treatment either with the same drug or with other drugs.

The choice of chemotherapeutic agents depends mainly on the duration of responses to the primary treatment, which is reflected as the treatment-free interval. The patients in remission with longer treatment-free intervals than 6-12 months (platinum-sensitive diseases) may be re-treated with platinum drugs. Those who have shorter treatment-free intervals

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(platinum-resistant) or had never been in remission (refractory ovarian cancer) should be given the other chemotherapeutic agents. Aside from the treatment-free interval, other factors are also of importance such as the toxicity during primary chemotherapy treatment, the residual toxicity, the cost-effectiveness of the chemotherapy, the financial resource of the patients, the convenience of administration, the expected response of the disease to the planned chemotherapy regimen based on prior reports, the experience and the preference of the caregiver, and the patients themselves[2-4]. The response rates to subsequent chemotherapeutic drugs would associate with the efficacy of drugs themselves, cross resistance with previous administered drugs, and mainly with the primary tumor response to platinum compounds or platinum sensitivity status. The platinum-sensitive patients are expected to have higher response rates (30% to > 50%) than those of platinum-resistant or refractory cancer who would have lower response rates (10-30%)[2,3].

Aside from the response rates, the aim of treatment after relapse might also be different among these patients. The platinum-sensitive patients may have a main objective to extend survival while those with platinum-resistant or refractory cancer have aims to control the disease, extend the period of progression-free, to palliate symptoms, and to maintain a good quality of life.

With emerging technologies, various options of chemotherapy agents have been developed and are used as the second- or further-lines of treatment for refractory or recurrent EOC, such as, paclitaxel (if has not been used as the first line drug), liposomal doxorubicin, gemcitabine, docetaxel, topotecan, oral etoposide, etc. Among these chemotherapies, oral etoposide yields advantages over the other drugs in terms of more convenience to administer and fewer expenses because the patients do not require hospitalization. In Western countries, the dosage of oral etoposide being used is approximately 100 mg/m^2 per day[5,6]. However, severe neutropenia of grade 3 and 4 were experienced in more than two-thirds of the patients[7]. Theoretically, this dosage regimen might be relatively high for the patients who have smaller body habitus like Asian women. However, there are still limited data regarding the appropriate dose for this population. With the pharmaceutical availability of the 25 mg capsule of etoposide in Asia including Thailand, the authors modified the dose of etoposide to a fixed daily dose of 75 mg (or 50 mg upon discretion of the physician based on the patients'performance status).

The aim of the present study was to assess the response rate (RR), progression-free survival (PFS) and overall survival (OS) of the patients with refractory or recurrent EOC who received 75 mg oral etoposide per day. The side effects or drug toxicity were also evaluated.

Material and Method

The present study was conducted after an approval from the Ethic Committee for Researches Involving Human Subjects of Bangkok Metropolitan Administration. Patients with refractory or recurrent EOC between January 1998 and December 2007 were identified. Eligibility criteria included patients who had histopathologic diagnosis of EOC, had persistent, progressive, or recurrent diseases after primary chemotherapy, and had oral etoposide. Etoposide may be used as the second- or further-lines of treatment after the other chemotherapeutic agents. Patients who had incomplete data of treatment were excluded.

Patient's clinical and pathological data were collected from the in-patient and out-patient charts. Data were collected on: age; International Federation of Gynecology and Obstetrics (FIGO) stage; tumor histologic cell type and grade; first line chemotherapy including the particular type of platinum drug; other chemotherapies preceding or after etoposide; number of cycles of oral etoposide; BSA of the patients; side effects or toxicity of oral etoposide particularly hematologic and gastrointestinal systems. The main outcomes to evaluate drugs efficacy were RR, PFS, and OS. The clinical response was determined according to the Gynecologic Oncology Group response criteria based on findings from the physical examinations, radiologic imaging, or CA125[8]. Complete response (CR) was defined when there was no clinical evidence of tumor after chemotherapy treatment while partial response (PR) was defined when tumor reduction was > 50%. Stable disease (SD) was defined as a tumor that was unchanged in size or was decreased < 50% or increased < 25%. Progressive disease (PD) was defined as an increase in tumor size > 25% or development of a new lesion. In the patients who had no evidence of solid tumor but the diagnosis was made from elevated CA 125 level, the serologic response was assessed with serial CA 125. Rate of response was derived from the rates of CR and PR. Since the present study involved more of the patients who had platinum-resistant disease, the authors were also interested in

the overall control rate of disease, which was obtained from summation of the response rate and rate of SD.

PFS was defined as the interval from the date the oral etoposide was started to the date of disease progression. For patients who were lost to follow-up, PFS data were right-censored at the time of the last evaluation or contact when the patient was known to be progression-free. Overall survival was defined as the interval from the date of oral etoposide started to the date of death or last follow-up visit. For patients who were alive at the end of the present study, overall survival data were right-censored at the time of the last evaluation or contact.

Platinum-sensitive disease was defined as a response to initial platinum-based chemotherapy that lasted more than six months after treatment ended. Platinum-resistant disease encompassed those who did not respond with stable or progressive diseases to primary platinum treatment or those who had primary response but recurred within six months after the end of therapy[9].

The clinical practice to administer chemotherapy to EOC patients in the authors' institution are the patients have to have Zubrod performance status 0-2, measurable disease or ascites or pleural effusion with cytologic proven malignant cells, and serially progressive elevated CA-125 level in the patients (with value > 100 mu/ml) without measurable disease. Pre-treatment evaluation prior to each treatment includes physical examination, complete blood count (CBC), and blood chemistry including CA 125 level. Chest radiography, optional pelvic or abdominal ultrasonography or computerize tomography are performed at an interval of every 2-3 cycles or earlier if indicated. Specifically to oral etoposide, interval CBC and side effects from chemotherapy are to be assessed weekly and then every two weeks in first two cycles and as usual as described earlier. Hematologic and other toxicities are graded to 0-4 according to WHO criteria[10]. Pretreatment evaluation is to be repeated before the next cycle.

Daily oral etoposide (25 mg/capsule) was given to the patients for 21 days, followed by one-week interlude before starting the next cycle. The dose was given at a daily dosage of 75 mg in three divided dose. Dose reduction was allowed according to the patient's performance status. The patients would be informed for the possible side effects and were instructed to have an earlier hospital visit as necessary. All patients were to receive a minimum of two cycles of oral etoposide before the first evaluation for clinical response, unless progression of diseases was clearly evidenced or unacceptable toxicity was experienced. The therapy was continued until the disease completely responded. In the circumstances of partial response or stable disease, the drug was continued upon discretion of the physician, patients' tolerability to side effects, and their preference.

Data were analyzed using SPSS statistical software version 11.5 (SPSS, Chicago, IL). Descriptive statistics were used for demographic data and summarized as mean with standard deviation or frequency with percentage. PFS and OS were analyzed with the Kaplan-Meier method. The outcomes were significant only if $p < 0.05$.

Results

Forty-one EOC patients received oral etoposide between January 1998 and December 2007. Medical records of three patients were unavailable. Hence, 38 patients were enrolled in the present study. Median age of patients was 51 years (range, 33-72 years). Most patients were in stage III. All patients had platinum-based chemotherapy as the first line treatment: 28 patients (73.7%) had platinum plus cyclophosphamide and ten had platinum in combination with paclitaxel (26.3%). Out of 38 patients, 28 (73.7%) were classified as platinum-resistance while ten (26.3%) were classified as platinum-sensitive. Nine of the ten patients with platinum-sensitive diseases had reinduction with platinum with cyclophosphamide or with paclitaxel while one patient who had a disease-free period of 6 months had new second-line chemotherapeutic regimen of weekly paclitaxel. Out of 28 platinum-resistant patients, 20 had oral etoposide while the remaining had paclitaxel, gemcitabine, liposomal doxorubicin, or ifosfamide. These 38 patients either had some responses to second-line treatment or had progressive diseases; 32 of them eventually received other chemotherapy as the third-setting while the other six declined or had poor performance status to have further specific treatment. With persistence or progression of diseases to the third-line drug, 17/32 patients did not have any treatment further while 15 patients subsequently had other chemotherapeutic agents. Characteristic features of the EOC patients including the types of chemotherapy given in each setting are shown in Table 1.

Focusing on the oral etoposide, the drug was given to 38 patients as the second-, third-, or fourth-line chemotherapy (Table 1). The average BSA of the 38 patients was 1.46 m^2 (range, 1.22-1.79 m^2).

Table 1. Characteristic features of epithelial ovarian cancer who received oral etoposide (n = 38)

Characteristic features	Number	%
Histopathology of ovarian cancer		
Serous cystadenocarcinoma	10	26.3
Mucinous cystadenocarcinoma	5	13.2
Endometrioid carcinoma	11	28.9
Clear cell carcinoma	6	15.8
Adenocarcinoma, not otherwise specified	6	15.8
FIGO stage		
I	8	21.0
III	25	65.8
IV	5	13.2
Primary chemotherapy		
Platinum[a] plus cyclophosphamide	28	73.7
Carboplatin plus paclitaxel	10	26.3
Type of primary platinum-sensitivity		
Platinum-sensitive (treatment-free interval > 6 months)	10	26.3
Platinum-resistant (treatment-free interval ≤ 6 months)	28	73.7
Chemotherapy used in the second setting (n = 38)		
Oral etoposide	20	52.6
Re-induction with platinum plus cyclophosphamide or paclitaxel	9	23.7
Paclitaxel	7	18.5
Liposomal doxorubicin	1	2.6
Ifosfamide	1	2.6
Chemotherapy used in the third setting (n = 32)		
Oral etoposide	15	46.9
Platinum plus cyclophosphamide	2	6.2
Megestrol acetate	6	18.9
Gemcitabine	5	15.6
Liposomal doxorubicin	2	6.2
Paclitaxel, oxaliplatin	2	6.2
Chemotherapy used in the fourth setting (n = 15)		
Oral etoposide	4[c]	26.8
Megestrol acetate	3	20.0
Single paclitaxel or combined with carboplatin	2	13.3
Gemcitabine	2	13.3
Alkeran	2	13.3
Liposomal doxorubicin, hexamethylmelamine	2	13.3
Number of cycles of oral etoposide		
≤ 1 cycle	7	18.4
2 cycles	10	26.3
3 cycles	10	26.3
4 cycles	5	13.2
6 cycles	6	15.8

[a] Platinum included cisplatin or carboplatin
[b] Paclitaxel was given weekly in five and tri-weekly in two patients
[c] One patient who had had etoposide in the second setting had the drug again in the fourth setting

Daily dosage of 75 mg oral etoposide was prescribed in 35 patients (all had BSA > 1.3 m^2) while the dose was modified to 50 mg in three patients due to several prior chemotherapy regimens with some residual toxicities and their low BSA (BSA < 1.30 mg/m^2). Seven patients (18.4%) received fewer than two cycles of oral etoposide due to intolerable gastrointestinal or hematologic side effects. All of these seven patients, with BSA ranged

from 1.30-1.55 m^2, had oral etoposide 75 mg/day as the second-line drug in four patients, third-line in two, and as the fourth-line drug in one patient. The gastrointestinal side effects in five patients were nausea (grade 4) on day 13 of the first cycle (one patient), obstructive jaundice from gall stone requiring surgical correction (one patient), bowel obstruction from tumor seeding (two patients), and severe abdominal pain from tumors (one patient). The other two patients had severe hematologic side effects leading to severe pulmonary infection (one patient), or pneumonia with pleural effusion (one patient).

Median number of etoposide treatment was 3 cycles (range, 1-6 cycles). Excluding the seven patients who had < 2 cycles of etoposide, 31 patients were assessed for response. Dosage of etoposide was given at 75 mg/day in 35 patients while three patients who had BSA < 1.3 m^2 had etoposide dose 50 mg/day. The overall response rate was 25.8% (eight patients) with 19.4% (six patients) CR and 6.45% PR (two patients). Each four of these eight patients had etoposide as the second- or third-line drug. Stable disease was achieved in six patients (19.3%), giving the overall control rate of 45.2%. Seventeen patients (54.8%) experienced disease progression. In relation to the sensitivity status to primary platinum treatment, patients with platinum-sensitive diseases had a higher response rate compared to those with platinum-resistant diseases, 4/10 patients (40.0%) compared to 4/21 patients (19.1%). The responses of EOC patients to oral etoposide according to the sensitivity status to primary platinum treatment are presented in Table 2.

Among the six patients who had complete response to etoposide, one patient was lost to follow-up after 2 months while five patients had disease-free interval for 1-24 months before recurrences of diseases were evidenced. All were treated with other chemo- or hormonal therapy. Two patients who had PR and 2/6 patients who had SD as the best response from etoposide received further chemo- or hormonal therapy. Among patients with PD and those who were not assessable for response, only 7/17 and 5/7 patients respectively had further-lines of chemotherapy.

The median PFS of all 38 patients was 5.5 months (95% confidence interval [CI], 3.4-7.6 months) with 1-year and 2-year PFS of 33.3% (95% CI, 15.3-51.3%) and 19.0% (95% CI, 3.1-35.0%), respectively. PFS of the eight patients who had responded to oral etoposide was significantly longer than those who did not respond, 19.2 months (95% CI, 5.5-32.9 months) compared to 4.1 months (95% CI, 2.4-5.7 months) ($p = 0.004$).

By the time of the present study, 26 of the 38 patients (68.4%) had died. Median overall survival (OS) was 18.8 months (95% CI, 6.9-30.6 months) with 1-year and 2-year OS of 63.2% (95% CI, 47.1-79.2%) and 46.5% (95% CI, 29.3-63.7%), respectively. OS of the eight patients who had responded to oral etoposide was not reached and was significantly longer than those who did not have responses, 15.3 months (95% CI, 1.0-29.6 months) ($p = 0.045$).

Aside from the gastrointestinal side effects in the five patients and pulmonary infection in two patients, which occurred within the first two cycles as mentioned earlier, the other pertinent finding was the hematologic toxicities. From the 113 cycles of oral etoposide, grade 3 and 4 hematologic toxicities were encountered in 18 cycles (15.9%) in 11 patients (28.9%). Ten of them had BSA < 1.5 m^2. Grade 3-4 hematologic toxicities were leucopenia in six cycles (6/38 patients or 15.8%) and severe neutropenia in nine cycles (7 patients or 18.2%). All of them withheld their next cycles of chemotherapy for 7-14 days until spontaneous recovery from neutropenia occurred. Dosage was also reduced in two patients in the following cycle to 50 mg/day. Grade 3 hemoglobinemia requiring

Table 2. Response to treatment with oral etoposide according to the primary response to platinum-based chemotherapy (n = 31)

Responses to oral etoposide	Response to primary platinum drug as first-line treatment	
	Platinum-sensitive (n = 10)	Platinum-resistance (n = 21)
Complete response	3 (30%)	3 (14.3%)
Partial response	1 (10%)	1 (4.8%)
Stable disease	2 (20%)	4 (19.0%)
Progressive disease	4 (40%)	13 (61.9%)

Table 3. Hematologic toxicity after oral etoposide according to the World Health Organization (WHO) criteria in 38 patients (n = 113 cycles)

Hematologic components	Grade of hematologic toxicity (number of cycles, %)				
	0	1	2	3	4
Hemoglobinemia	53 (46.9%)	33 (29.2%)	24 (21.2%)	3 (2.7%)	-
Leucopenia	74 (65.5%)	18 (15.3%)	15 (13.3%)	3 (2.7%)	3 (2.7%)
Neutropenia	79 (69.9%)	16 (14.1%)	9 (7.9%)	6 (5.4%)	3 (2.7%)
Thrombocytopenia	109 (96.5%)	4 (3.5%)	-	-	-

blood transfusion was encountered in three cycles (2 patients or 5.3%). No grade 3-4 thrombocytopenia was observed. The details of all degree of hematologic toxicities are demonstrated in Table 3.

Discussion

Single chemotherapy is a reasonable cost-effective treatment for patients with recurrent EOC in both platinum-sensitive and platinum-resistant group[11,12]. This is true especially in platinum-resistant patients when the objectives for treatment are to reduce symptoms in case of symptomatic disease, without or have minimal accumulation of toxicity, convenient of administration without hospitalization or premedication, and low cost. Nevertheless, the drug should have certain efficacy in terms of demonstrable response rate, prolonged progression-free duration, and survival. Oral medication is an interesting option that is convenient for administration, lesser numbers of visits, and lower cost for chemotherapy and associated drugs. In long-term users, it may improve quality of life that the patients can have home therapy while maintaining their normal daily lives.

Etoposide is a long known chemotherapy obtained from a natural product, which acts to inhibit topoisomerase II resulting in DNA damage. One profit of etoposide is its availability in both parentheral and oral forms. Oral etoposide was reported to have efficacy for EOC with response rates ranging from no objective response to 34%[5-7,13,14]. One study by Hoskin et al used fixed dose 100 mg oral etoposide for 14 days every 21days in 31 EOC patients[5]. The 100 mg dosage was alternating with 50 mg in the patients with BSA < 1.2 m^2. The response rate was 26% but myelotoxicity grade 3-4 was evident in up to 16% of patients (leading to one septic death). Another study by Seymour et al also found a similar rate of response at 24% from oral etoposide dose 100 mg in 41 patients[6]. However, only 50% of patients could have full 14-day regimen, and approximately 10% experienced grade 4 neutropenia. In the following years, Kavanagh et al from MD Anderson Cancer Center modified the dose of oral etoposide to 50 mg/m^2[7]. No objective responses were demonstrated in all 14 patients while the toxicity was very high with two-third of the patients having grade 3 or grade 4 neutropenia. One Gynecologic Oncology Group study by Rose et al used 50 mg capsule of oral etoposide (escalated from 30 to 60mg/m^2/day) for 21 days every 28 days for 82 EOC patients: 41 patients had platinum-resistant disease while 41 had platinum-sensitive tumors[13]. The response rate for the platinum-sensitive tumors was higher than that of the platinum-resistant, 34.1% and 26.8% respectively.

The present study evaluated the EOC patients who used the oral etoposide of 75 mg/day as a salvage therapy for those with recurrent or refractory ovarian cancer. This dosage was proposed based on the following backgrounds. These women generally have smaller body builds than the women in Western countries, so the dose of 100 mg/day was expected to be too high for patients. With the 50 mg pharmaceutical oral capsule, which was the only capsule strength available in the past, it would be hard or impossible to adjust the dose despite a high hematologic toxicity from the 100 mg daily dose. When the pharmaceutical drug company has launched the 25 mg capsule of oral etoposide, the authors modified the dose for the presented patients. The authors found that the presented response rate was in the range that was reported from the other studies using higher daily doses of 100 mg total or 50 mg/m^2, 25.8% compared to 20-34%[5,6,13,14]. In recurrent EOC, especially the platinum-resistant diseases, the patients and the physician might be satisfied with the diseases that remained stable or controlled without any progression[9]. When the authors added the rate of stable disease

with the response rate, these added up to 45.2% of the rate of disease control.

Median PFS recurrent EOC patients in the present study, wherein the majority was platinum-resistant, were 4.8 month. This figure was similar to the PFS reported from a previous study using oral etoposide 50-100 mg/day which found median PFS of 4.3 months in platinum-resistant and 7.5 months for platinum-sensitive diseases[13]. This was also comparable to the PFS yielded from the other second-line monotherapy, such as, paclitaxel, liposomal doxorubicin, topotecan, doxetaxel, hexamethylmelamine, or melphalan, which reported PFS in the range of 5 to 8 months[2,15-20].

Gastrointestinal toxicity was the main cause of early chemotherapy discontinuation (< 2 cycles) in the present study (5/38 patients or 13%). This side effect was also encountered in 10.3% of the patients in the GOG study[13]. For the hematologic toxicity, severe or grade 3 and grade 4 myelosuppression occurred as leucopenia (especially neutropenia) and hemoglobinemia. Leucopenia occurred in 12.9% of the patients (4.7% of 113 cycles) and neutropenia in 12.9% (8% of the cycles) which were much lower than 41% and 45% of patients reported from the other study using a daily dosage of 50 mg/m^2 [13]. Grade 3 anemia requiring blood transfusion was found in the present study in only 5.3% of the patients while the study by Rose and De Jong reported this side effect as high as 20-23.5%[13,21]. Lower hematologic toxicity in the present study compared to other studies might be due to obvious lower total dose in each patient (50 or 75 actual dose in the present study) versus 50 mg or 100 mg of actual dose in their studies. One obvious advantage of the low dose of etoposide being used in the present study was there was no grade 3 or 4 thrombocytopenia while the prevalence in previous reports using a higher dose were found in up to 9-18%[13,14].

Because of the impact of global economical crisis, the cost of the health service system is of concern in Thailand. Nevertheless, the quality of care and the aim for the best practice offering to the patients are not of lesser importance[11,12]. Despite the low cost of chemotherapeutic drugs and other medical utilities in the authors' institution, which serves for the public service, the cost of oral etoposide administration was lowest among the chemotherapeutic drugs, with comparable efficacy in terms of response rates, PFS, and OS, such as paclitaxel, liposomal doxorubicin, topotecan, doxetaxel, and hexamethylmelamine. This issue should be discussed with the EOC patients in the counseling process for their treatment option.

Few limitations of oral etoposide were to be noted. Its use in any patients who had a gastrointestinal problem might result in a suboptimal absorption or intolerability from the gastrointestinal side effect. Another is the hematologic toxicities that were more frequently encountered in the patients with very small body habitus as in those with BSA less than 1.3 m^2 compared to those with higher BSA. These should be precautions in using oral etoposide.

In conclusion, oral etoposide at a daily dose of 75 mg for 21days every 4 weeks is an active agent for refractory or recurrent EOC. The response rate, PFS, and OS are comparable to the other chemotherapy for recurrent EOC and the oral etoposide itself at a higher dose. The side effects are minimal especially in those with a BSA of > 1.5 m^2. The advantages over the other parenteral chemotherapy were the convenience for administration, lesser visits, lower cost for chemotherapy, and pre-medications.

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การใช้ยาอีโตโปไซด์ชนิดรับประทานในการรักษาผู้ป่วยมะเร็งรังไข่ ชนิดเยื่อบุผิวที่ดื้อยา หรือกลับเป็นซ้ำ

เถาวลัย ถาวรามร, ศิริวรรณ ตั้งจิตกมล, สุมนมาลย์ มนัสศิริวิทยา, สุรวุฒิ ลีฬหะกร

วัตถุประสงค์: *เพื่อศึกษาอัตราการตอบสนอง ผลข้างเคียงจากยาระยะเวลาที่โรคไม่ดำเนินต่อ และระยะอัตราการอยู่รอดของผู้ป่วยมะเร็งรังไข่ชนิดเยื่อบุผิว หลังจากได้รับยาเคมีบำบัดอีโตโปไซด์ ชนิดรับประทานขนาด 75 มก. ต่อวัน*

วัสดุและวิธีการ: *ทำการศึกษาผู้ป่วยมะเร็งรังไข่ชนิดเยื่อบุผิวที่ก้อนมะเร็งไม่ตอบสนองหรือดื้อต่อยาเคมีบำบัดขั้นแรก หรือมีการกลับเป็นซ้ำ และได้รับยาเคมีบำบัดอีโตโปไซด์ชนิดรับประทานขนาด 75 มก. ต่อวัน ตั้งแต่ เดือนมกราคม พ.ศ. 2541 ถึง เดือนธันวาคม พ.ศ. 2550 ที่หน่วยมะเร็งนรีเวชวิทยา วิทยาลัยแพทยศาสตร์กรุงเทพมหานครและวชิรพยาบาล สำนักการแพทย์ กรุงเทพมหานคร*

ผลการศึกษา: *ในช่วงเวลาที่ศึกษามีผู้ป่วยที่ได้รับยาเคมีบำบัดอีโตโปไซด์ชนิดรับประทาน ที่หน่วยมะเร็งวิทยานรีเวช 38 ราย มัธยฐานของอายุเท่ากับ 51 ปี (พิสัย 33-72 ปี) ผู้ป่วยมีอาการข้างเคียงจากยาเคมีบำบัดชุดแรก 7 ราย จึงมีผู้ป่วย 31 รายที่สามารถประเมินผลการตอบสนองต่อยา พบอัตราการตอบสนองโดยรวมร้อยละ 25.8 (8 ราย) เป็นการตอบสนองโดยสมบูรณ์ ร้อยละ 19.4 (6 ราย) และการตอบสนองเป็นบางส่วน ร้อยละ 6.4 (2 ราย) มีการอยู่คงที่ของโรคร้อยละ 19.4 (6 ราย) และการดำเนินเพิ่มของโรค ร้อยละ 54.8 (17 ราย) ค่ามัธยฐานระยะเวลาที่โรค ไม่ดำเนินต่อเท่ากับ 4.8 เดือน (พิสัย 3.3-6.4 เดือน) มีระยะเวลาที่โรคไม่ดำเนินต่อ 2 ปี ร้อยละ 16.7 (มีค่าความเชื่อมั่นที่ร้อยละ 95 [95%CI] เท่ากับร้อยละ 2.1-31.4) และมัธยฐานของระยะอัตราการอยู่รอดเท่ากับ 12 เดือน (0.75-25.5 เดือน) มีระยะอัตราการอยู่รอด 2 ปี เท่ากับร้อยละ 36.4 (มีค่าความเชื่อมั่นที่ร้อยละ 95 [95% CI] เท่ากับร้อยละ 17.4-55.3) ผลข้างเคียงรุนแรงจากยาส่วนใหญ่เป็นอาการทางระบบทางเดินอาหาร*

สรุป: *ยาเคมีบำบัดอีโตโปไซด์ชนิดรับประทานขนาด 75 มก. มีประสิทธิภาพในการออกฤทธิ์ในผู้ป่วยมะเร็งรังไข่ชนิดเยื่อบุผิวที่ก้อนมะเร็งไม่ตอบสนองหรือดื้อต่อยาเคมีบำบัดขั้นแรก รวมถึงมีข้อดีถึงความสะดวกในการใช้ยาจำนวนครั้งที่มาตรวจน้อย โดยผลข้างเคียงจากยาส่วนใหญ่จากระบบทางเดินอาหาร*