Thai Journal of Obstetrics and Gynaecology
December 1998, Vol. 10, pp. 231-234

## GYNAECOLOGY

# Interferon Alpha-2b in the Pathological Complete Response Advanced Epithelial Ovarian Cancer

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**ABSTRACT**

**Objective** To evaluate the efficacy of the interferon alpha-2b for prophylaxis of recurrence in advanced epithelial ovarian cancer.

**Design** Open.

**Setting** Siriraj Hospital.

**Subjects** The pathological complete response advanced epithelial ovarian cancer patients between August 1995-1997.

**Main outcome measure** Recurrence rate, duration of recurrence, survival, and drug toxicities.

**Results** The evaluable patients included 20 cases of the advanced epithelial cancer, achieved PCR after postoperative chemotherapy. Interferon alpha-2b was administrated 5 million units subcutaneously, 3 times a week for 6 months. The recurrence occurred 6 out of 20 cases (30.0%) (95% CI 0.099, 0.501). The histopathology and chemotherapeutic regimen showed no significant relationship with the recurrence. Almost of patients had fever grade 1-2 in 1-3 weeks of treatment. The haematologic toxicity was found, haemoglobin level grade 3 of 15.0% and thrombocytopenia grade 2 of 5.0%.

**Key words :** prophylaxis, interferon alpha-2b, PCR epithelial ovarian cancer

Ovarian cancer is the third common cancer in female, during 1992-1996, the incidence at our institute was 10.17%, 86.27% was epithelial cancer. [1] The platinum base regimens for advanced epithelial cancer achieved a pathological complete response (PCR) ranging from 33.3-77.7%. [2-8] Even after PCR, the recurrence following first-line chemotherapy occurred in 20.0-60.0%.[8-9] The interferons are glycoproteins which inhibit malignant cell proliferation and phenotypic transformation in laboratory[10] There is antiproliferation effect of the epithelial ovarian cancer both in vivo and in vitro,[11-14] and has efficacy in the epithelial ovarian cancer not only minimal residual cancer but also in the recurrence and refractory cancer by intraperitoneal application plus chemotherapy.[14-17] The study was designed to evaluate the efficacy and toxicity of the interferon alpha-2b for prophylaxis of the recurrence of PCR advanced epithelial ovarian cancer.

## Materials and Methods

Patient selection : Eligible criteria included the histological proof of epithelial ovarian cancer stage III-IV disease, which achieved PCR after postoperative chemotherapy of cisplatinum or paraplatin or paclitaxel combination regimen. The patient should have an adequate bone marrow function (a leukocyte count greater than 3,500/Cu.mm, a platelet count greater than 100,000/Cu.mm, haemoglobin level greater than 8 gm/100ml.), and should signed the consent form.

Drug administration : Interferon alpha-2b was given immediately after the evaluation of the histopathology of the second-look laparotomy with the dosage of 5 million units subcutaneously, 3 time a week for 6 months. The patient should have oral acetaminophen 500-1000 mg. before interferon. The haemotologic and non haematologic toxicity especially fever was recorded according to WHO classification. The blood count was repeated every 4 weeks after treatment : if the total white count was less than 3,500/Cu.mm., platelets less than 100,000/Cu.mm., or haemoglobin less than 8 gm/100 ml., the treatment would be delayed for one week. If these values were not reached after one week, the supportive treatment was required.

Assessment of recurrence : Patients were evaluated by physical and gynaecological examination every 4 weeks. Chest radiograph, abdominopelvic ultrasonogram, and serum CA-125 were performed after treatment 3 and 6 months. After discontinuation of interferon the patients were evaluated every 4 weeks for 12 months and every 12 weeks for 36 months.

Statistical analysis : The comparison of recurrence related to histopathology, stage of diseases, and chemotherapeutic regimen using Fisher exact test. Kaplan and Meier's method were used to estimate the survival, which measured from beginning of the interferon treatment.

## Results

From August 1995-1997, 20 evaluable patients were included. Patient characteristics and recurrence are summarized in Table1. The serum CA-125 levels ranged from 2.4-24.4 U/ml (median 10.4) before second-look laparotomy. The histopathology, stage of diseases, and chemotherapeutic regimen showed no significant relation with the recurrence (Table 1). The recurrence was found 6 out of 20 cases (30.0%) (95% CI 0.099, 0.501) one patient showed recurrence in 3 months after administration of interferon. After discontinuation of drug the recurrence occurred at one month 2 cases, 3 months 1 case, 8 months 1 case, and 14 months 1 case. There was pelvic recurrence in 5 cases and brain metastasis one case. Three patients expired with survival time of 4.0-37.0 months, and 3 patients are alive with disease under second line drugs treatment. The Kaplan and Meier's survival curve were constructed in Figure 1.

The non-haematologic toxicity was fever grade 1-2 in 1-3 weeks of the interferon treatment in all cases. The haemoglobin level grade 3 requiring blood transfusion occurred in 3 cases (15.0%). The thromocytopenia grade 2 caused delay of treatment occurred in one case (5.0%).

## Discussion

Theoritically interferon has the antiproliferative, immune-moduration activity, and showing efficacy in residual or recurrence epithelial ovarian cancer. These effects of interferon alpha-2b could not improved the PCR or prolonged median survival in advanced epithelial cancer comparing with cisplatinum combination.[18] This trial of interferon alpha-2b could not decreased the recurrence of PCR advanced epithelial ovarian cancer. Of those may be due to small number of cases or small dosage of interferon or inadequate period of drug administration, the higher dose and longer period of drug administration will have higher cost. The immune suppressant effect of chemotherapy may be masked the immune modulating activity of interferon. The other factors including diet, environment, physical activity may be the role of immune responsiveness.[19] The median age of patients of 46 years, non elderly will be not the cause of unfavourable immune activity.

**Table 1.** Patient characteristics and recurrence after interferon alpha-2b

| Characteristics | | | Recurrence number (%) | P-Value |
|---|---|---|---|---|
| 1. Ages | median | 46 years | | |
| | range | 32-68 years | | |
| 2. Cell types | serous cystadenocarcinoma | 7 (35 %) | 1 (14.28) | 0.627 |
| | endometrioid adenocarcinoma | 6 (30 %) | 3 (50.00) | 0.627 |
| | clear cell adenocarcinoma | 3 (15 %) | 1 (33.33) | 1.00 |
| | mixed (serous + endometrioid) | 4 (20 %) | 1 (25.00) | 1.00 |
| 3. Stages | III A | 3 (15 %) | 0 | 1.00 |
| | B | 6 (30 %) | 2 (33.33) | 1.00 |
| | C | 10 (50 %) | 4 (40.00) | 0.652 |
| | IV | 1 (5 %) | 0 | 1.00 |
| 4. Chemotherapy | CDDP + CTX | 7 (35 %) | 2 (28.57) | 1.00 |
| | CBP + CTX | 7 (35 %) | 2 (28.57) | 1.00 |
| | CBP + TAXOL | 6 (30 %) | 2 (33.33) | 1.00 |

CDDP = cis-diamine dichloroplatinum, CTX = cyclophosphamide,
CBP = carboplatin or paraplatin, TAXOL = paclitaxel

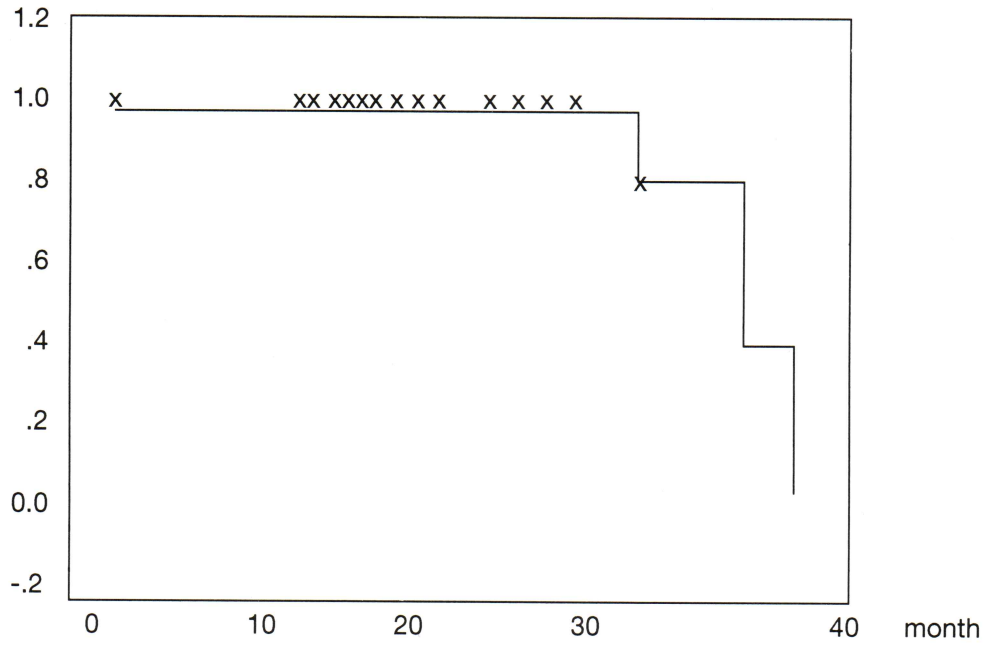



**Fig. 1.** Survial curve of the patients.

**Acknowledgement**

The authors wish to thank Miss Suowalak Hunnangkul from clinical epidemiology unit for statistical analysis, the assitants (Miss Montha Hangsubcharoen, Miss Pattanart Watcharaswee, Mrs. Kanjana Thamiltorn) and Schering – Plough Ltd. for partial support of interferon alpha-2b.

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