SINGLE-AGENT TOPOTECAN IN PLATINUM-RESISTANT RECURRENT OVARIAN CANCER: A STUDY IN VIET NAM NATIONAL CANCER HOSPITAL

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ABSTRACT

Platinum-based doublet chemotherapy is still supposed as standard regimen in ovarian cancer. However, the rate of relapse or refractory is also very high and vary from 80-85% with stage III-IV ovarian cancer [1]. The prognosis of platinum-resistant ovarian cancer (relapse or refractory within 6 months after initial treatment) has a median survival of 9–12 months and less than 15% respond to subsequent chemotherapy [2]. Thesedays, there are several agents were introduced to control this disease such as Docetaxel, Etoposid, Gemcitabine, Liposomal doxorubicin with overall response rate vary from 12-27% [3] [4] [5]. The objective of this study was to evaluate response and toxicity of 5-day Topotecan chemotherapy in women with primary and secondary platinum-resistant epithelial ovarian cancer.

Keyword: *Topotecan, Ovarian Cancer, Platinum-Resistant.*

I. INTRODUCTION

Ovarian cancer is the second most common gynecologic malignancy. According to Globocan 2018, there are around 295,414 new cases and 184,799 deaths of ovarian cancer annually [6]. The primary treatment for ovarian cancer is surgery combined with platinum-based chemotherapy, which is considered the standard of care. Despite initial therapy, the majority of women will relapse and require retreatment. The rate of relapse or refractory is also very high and vary from 80-85% with stage III-IV ovarian cancer [1]. The management of relapsed disease is based upon the amount of time that has elapsed between the completion of platinum-based treatment and the detection of relapse. Patients with a platinum-free interval (PFI) of six months or longer are considered to have "platinum-sensitive" disease while patients with a PFI of less than six months are considered to have "platinum-resistant" disease. There are a number of active treatment options available for women with platinum-resistant ovarian cancer, and the ideal treatment is not known. A Cochrane systematic review of trials (n =1323) with platinum-resistant ovarian cancer concluded that topotecan, paclitaxel, and pegylated liposomal doxorubicin (PLD) have similar efficacy, but different patterns of side effects [7]. We conducted this study to evaluate response and toxicity of 5-day Topotecan chemotherapy in women with primary and secondary platinum-resistant epithelial ovarian cancer.

II. PATIENT AND METHOD

This is the retrospective study, including 31 platinum-resistant recurrent ovarian cancer patients at Viet Nam National Cancer Hospital from February 2023 to February 2024. The criteria of inclusions were histologically or cytologically confirmed ovarian carcinoma, underwent plainum-based doublet chemotherapy in the past, and now

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relapse or refractory confirmed by CTScanner or MRI. Patients were treated for at least 3 cycles of Topotecan. Topotecan is 1.5 mg/m^2 intravenous days 1-5 of 21-day cycles. Treatment was continious until progressive disease or unacceptable toxicity.

Primary outcome was overall response rate (ORR) which evaluated by using RECIST 1.1. Secondary outcome was toxicity which evaluated byusing the NCI Common Toxicity Criteria.

III. RESULT

3.1.Patients characteristics

The median age was 51,1 ± 7,5 with priority stage III, IV (83,9%). Most patient's histology is adeno serious carcinoma (83,9%). There is 80.6 % paticipants showing progressive diseases within 3 months from discontinution of platinum-based chemotherapy in ovarian cancer (Table 1)

Variables	No of patients (%)
Age, mean± SD	51,1 ± 7,5
Staging	
II	16,1
III	71
IV	12,9
Histologic type	
Serous carcinoma	83,9
Mucinous carcinoma	9,7
Endometrioid carcinoma	3,2
Other	3,2

3.2. Single-agentTopotecan in platinum-resistant Ovarian Cancer

3.2.1. Efficacy: In 31 patients, 20 patients were treated with 3 cycles of Topotecan, 1 patient was treated with 4 cycles of Topotecan, 1 patient with 5 cycles, and only 9 patients who continued treatment for 6 cycles Topotecan.

1 patient reached complete response (3.2%), 10 patients reached partially responded (32.3%), 4 patients had stable disease (12.9%), and 16 patients progressed after 6 cycles (accounted for 51, 6%). The overall response for the treatment regimen is 35.5% (Table 2). Thus, the clinical benefit rate was 48,4% (Complete response+ Partial response+ Stable disease).

Response		
	No of patients	**(%)**
Complete response	1	3,2
Partial response	10	32,3
Stable disease	4	12,9
Progressive disease	16	51,6
Sum	31	100

3.2.2. Side effects of Topotecan

Neutropenia, Erythropenia, and Thrombocytopenia occurred mainly grade I, II. There was no neutropenia grade IV (Table 3). Hepatotoxicity was found mainly in grade 1. There were 2 patients with grade 2 of increase in SGPT, accounted for 6.4%. Toxicity in kidney was less common, only 25.8% increased Ure. No patients were increased creatinine (Table 4).

Table 3: ***Hematological Toxicity***

		Grade 0	Grade I	Grade II	Grade III	Grade IV	Sum
Neutropenia	**Number**	16	5	7	3	0	31
	%	51,6	16,1	22,6	9,7	0	100
Erythropenia	**Number**	2	12	12	3	2	31
	%	6,5	38,7	38,7	9,7	6,5	100
Thrombocytopenia	**Number**	19	9	0	0	0	28
	%	67,9	32,1	0	0	0	100

Table 4: ***Liver and kidney toxicity***

		Grade 0	Grade I	Grade II	Grade III	Grade IV	Sum
SGOT	**Number**	23	8	0	0	0	31
	%	74,2	25,8	0	0	0	100
SGPT	**Number**	22	7	2	0	0	31
	%	71	22,6	6,4	0	0	100
Bilirubin	**Number**	23	8	0	0	0	31
	%	74,2	25,8	0	0	0	100
Ure	**Number**	23	8	0	0	0	31
	%	74,2	25,8	0	0	0	100
Creatinin	**Number**	31	0	0	0	0	31
	%	100%	0	0	0	0	100

IV. DISCUSSION

Topotecan is a commonly used agent in recurrent ovarian cancer, especially relapse or refractory platinum-resistant ovarian cancer. Some prospective studies showed the emerging efficacy as well the good tolerance with five-day schedule topotecan in this population.

According to a study of Jalid Sehouli (2011): 94 Platinum-resistant ovarian cancer patients treated with Topotecan at a dose of 1.25 mg / m2 / day, IV infusion from day 1 to day 5, 21-day cycle showed: overall response rate was 3%, partial response was 15%, stable disease was 39% and progressive disease was 43%. Clinical benefit was 48.4% [8]. A study by Bokkel (1997) was conducted in 112 recurrent ovarian cancer patients, showed that the overall response rate was 20.5%, the complete response was 4.5% [9]. The study of Alan Gordon (2001) also showed that patients with recurrent ovarian cancer or not responding to line 1 regimen had an overall response rate of 17% [10]. Once again our study revealed substantial effectiveness of topotecan as first-line therapy after failure with platinum-based regimen to control ovarian cancer. In addition, we found that a safe profile of topotecan when continuously indicating during five-day intravenous infusion. Neutropenia was mainly in grade 1 and 2. No patient had neutropenia grade 4 and 9.7% of patients had neutropenia grade 3. Hepatotoxicity and renal toxicity were generally uncommon and only mild grade 1-2 (2 cases). None of the cases in grade 3.4 which affect the patient or had to stop treatment. These encouraging results support the crucial role of topotecan in patients with platinum-resistant ovarian cancer.

V. CONCLUSION

A total of 31 patients were enrolled, with a median age of 51.1 years. Objective responses were 35.5% (3.2% of complete responses and 32.3% of partial responses). Stable disease was noted in 4 patients (12.9%) and progression of disease occurred in 16 patients (51.6%). The most common adverse event was anemia observed in 93.5% of patients. Grades 3 and 4 anemia were observed in 9.7% and 6.5% of patients. 9.7% patients with grade 3 neutropenia and no patient was admitted with grade 4 neutropenia or neutropenic fever. Thrombocytopenia was rare, mostly in grade 1 and 2. No patients had significant side effects that warranted discontinuation of therapy.

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