Original Article

A retrospective clinical study of bevacizumab combined with gemcibabine or paclitaxel in the treatment of recurrent ovarian cancer

Wu MD*, Wang Y[1]*, Ding T, Zhou YF, Song J, Liu XH[2], Wei MH, Yang QH[3], Zhou J[1], Wang SH, Lv QY[4]

Departments of Clinical Pharmacy and [4]Gynaecology and Obstetrics, Lishui People's Hospital of Zhejiang Province, [1]Department of Gynaecology and Obstetrics, Lishui Maternal and Children Care Hospital, Lishui 323000, Departments of [2]Pharmacy and [3]Onclology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang 453100, PR China

*Wu MD and Wang Y contribute equally to this work

Correspondence to: Dr. Lv QY, E-mail: qingyuan_lv@126.com

Abstract

BACKGROUND: Bevacizumab, a recombinant humanized monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor A, was described to be effective in the treatment of recurrent or platinum-resistance ovarian cancer. The present retrospective study was performed to further evaluate the clinical efficacy and toxicity of bevacizumab in the treatment of Chinese recurrent ovarian cancer patients who had been previously treated by platinum-based chemotherapy. **MATERIALS AND METHODS:** We reviewed the hospital database and finally included 26 recurrent ovarian cancer patients who were treated with bevacizumab combined with gemcibabine or paclitaxel or single agent. All included patients received >3 cycle of bevacizumab treatment. The tumor response, overall survival, and toxicities were documented. **RESULTS:** Under the treatment of bevacizumab combined with gemcibabine or paclitaxel, 2 complete response (7.7%), 8 partial response (30.8%), 7 stable disease (26.9%) and 9 progression disease (34.6%) was documented with the objective response rate of 38.5% and disease control rate of 65.4%. The median overall survival from the first application of bevacizumab was 15.3 months [Figure 1] for all of the 26 patients. The median overall survival time was 16.2 and 14.0 months for bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment schedule respectively. The overall survival was not different between bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment regimen hazard ratio = 0.80 (95% confidence interval: 0.32–2, $P = 0.64$). The hypertension and proteinuria were the major bevacizumab related toxicities. **CONCLUSIONS:** Bevacizumab combined with gemcibabine or paclitaxel was a promising treatment schedule for platinum-resistance recurrent ovarian cancer.

Key Words: Bevacizumab, efficacy, gemcibabine, paclitaxel, platinum-resistance, recurrent ovarian cancer, toxicity

Introduction

Ovarian cancer remains the most lethal gynecological malignancy worldwide, and survival rates have remained unchanged in spite of medical advancements.[1] For most of the patients, the postoperative platinum base systematic chemotherapy was recommended. But after several cycles of systematic chemotherapy, a certain part of the patients became platinum-resistance recurrent ovarian cancer.[2,3] The treatment strategy for this type of ovarian cancer was formidable.[3] Recent studies showed that bevacizumab combined with chemotherapy or single agent alone can improve the prognosis of patients with ovarian cancer especially for platinum resistance patients.[4,5] We performed the present retrospective study in order to evaluate the clinical efficacy and toxicity of bevacizumab in the treatment of Chinese recurrent ovarian cancer patients who had been previously treated by platinum-based chemotherapy.

Materials and Methods

We reviewed the hospital database and finally included 26 recurrent ovarian cancer patients who were treated with bevacizumab combined with gemcibabine or paclitaxel or single agent. The general characteristic of the included 26 ovarian cancer patients are demonstrated in Table 1. Totally, 13 patients administered with bevacizumab + paclitaxel treatment schedule, 10 cases treated with bevacizumab + gemcitabine treatment modality and other 3 patients were treated with bevacizumab single agent.

Access this article online

Quick Response Code:

Website: www.indianjcancer.com

DOI: 10.4103/0019-509X.154096

Patients with measurable disease were evaluated by the Response Criteria in Solid Tumors.[6] The overall survival for the 26 cases were calculated by Kaplan–Meier survival curve and difference between bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment modality was test by Cox Proportional-Hazards Regression analysis. All the data were analyzed by SPSS 16.0 software (http://www.spss.com/corpinfo/).

Results

Treatment regiment

Totally, 26 cases with recurrent ovarian cancer were analyzed in this retrospectively study. 13 patients administered with bevacizumab 7.5 mg/m^2 + paclitaxel 70 mg/m^2, 10 cases with bevacizumab 7.5 mg/m^2 + gemcitabine 1 g/m^2 and other 3 patients were treated bevacizumab 7.5 mg/m^2 or 10 mg/m^2 single regimen [Table 2].

Tumor response

The tumor response rate was divided into complete response (CR), partial response, stable disease (SD) and progression disease (PD). Under the treatment of bevacizumab combined with gemcibabine or paclitaxel, 2 complete response (7.7%), 8 partial response (30.8%), 7 SD (26.9%) and 9 PD (34.6%) was documented with the objective response rate (ORR) of 38.5% and disease control rate (DCR) of 65.4% [Table 3].

Survival

The median overall survival from the first application of bevacizumab was 15.3 months [Figure 1] for all of the 26 patients. The median overall survival was 16.2 and 14.0 months for bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment schedule respectively. The overall survival was not different between bevacizumab + gemcitabine and bevacizumab + paclitaxel treatment schedule hazard ratio = 0.80 (95% confidence interval: 0.32–2, $P = 0.64$).

Table 1: General characteristics of patients

Characteristics	Cases (*n*=26) (%)
Age (year)	51.2±8.8
Stage	
I	2 (7.7)
II	3 (11.5)
III	14 (53.8)
IV	5 (19.2)
Unknown	2 (7.7)
Baseline CA125 (U/mL)	
Median	423.6
Range	62.3-3884.1
Grading	
G1	1 (3.8)
G2	11 (42.3)
G3	12 (46.2)
Unknown	2 (7.7)

Table 2: Treatment regimen of the 26 cases

Patients	Bevacizumab (mg/m²)	Chemotherapy
1	7.5	Paclitaxel 70 mg/m²
2	7.5	Gemcitabine 1 g/m²
3	10	None
4	7.5	Paclitaxel 70 mg/m²
5	7.5	Paclitaxel 70 mg/m²
6	10	None
7	7.5	Gemcitabine 1 g/m²
8	7.5	Paclitaxel 70 mg/m²
9	7.5	Gemcitabine 1 g/m²
10	7.5	None
11	7.5	Gemcitabine 1 g/m²
12	7.5	Paclitaxel 70 mg/m²
13	7.5	Paclitaxel 70 mg/m²
14	7.5	Paclitaxel 70 mg/m²
15	7.5	Gemcitabine 1 g/m²
16	7.5	Gemcitabine 1 g/m²
17	7.5	Paclitaxel 70 mg/m²
18	7.5	Paclitaxel 70 mg/m²
19	7.5	Gemcitabine 1 g/m²
20	7.5	Paclitaxel 70 mg/m²
21	7.5	Gemcitabine 1 g/m²
22	7.5	Paclitaxel 70 mg/m²
23	7.5	Paclitaxel 70 mg/m²
24	7.5	Gemcitabine 1 g/m²
25	7.5	Paclitaxel 70 mg/m²
26	7.5	Gemcitabine 1 g/m²

Table 3: Response rate for the patients

Response	Number	Percentage
CR	2	7.7
PR	8	30.8
SD	7	26.9
PD	9	34.6
ORR	10	38.5
DCR	17	65.4

CR=Complete response; SD=Stable disease; PD=Progression disease; PR=Partial response; ORR=Objective response rate; DCR=Disease control rate

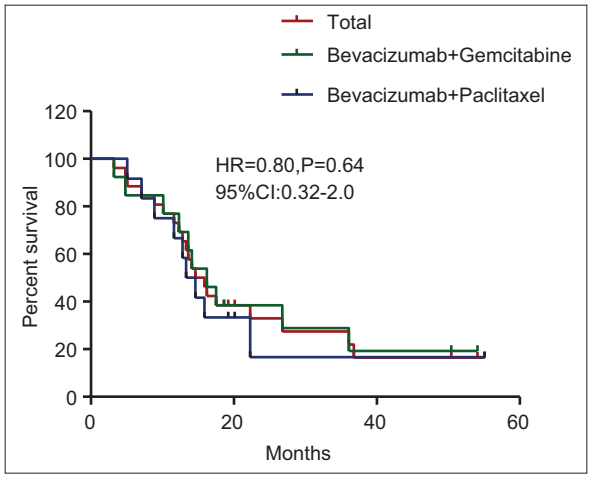

Figure 1: The Kaplan–Meier survival curve for overall survival

Toxicities

The median administered bevacizumab cycle was 6.8 with the range of 3–18 treatment cycles. One patient was found to have gastrointestinal perforation with the incidence rate of 3.8%. Totally, 8 cases were documented hypertension with the incidence of 30.8%. Proteinuria occurred in 6 patients.

Discussion

Ovarian cancer is the 5th most common diagnosed cancer in women.[7] It is usually diagnosed at an advanced stage and is the leading cause of death from gynecologic cancers in women. The overall survival rate at 5 years is 50%, and its treatment is still poor. For most of the patients, the platinum base systematic chemotherapy was recommended. But some patients finally became platinum-resistance recurrent ovarian cancer. The treatment strategy for this type of ovarian cancer was formidable. After recurrence, response rates to second-line chemotherapy for platinum-sensitive patients are 30% or higher.[3] However, patients with platinum-resistant disease have significantly lower response rates of 10–25% to chemotherapeutic agents.[3] Previously randomized controlled trails (RCTs) evaluated the bevacizumab combined with platinum-based chemotherapy compared to platinum-based chemotherapy alone in the treatment of ovarian cancer. The median PFS (progression-free survival) was significantly increased by 4 months in patients treated with bevacizumab combined treatment modality. But the PFS was not statistical different between bevacizumab + placebo and chemotherapy alone.[8]

Bevacizumab, a recombinant humanized monoclonal antibody that blocks angiogenesis by inhibiting vascular endothelial growth factor A, was described to be effective in the treatment of recurrent or platinum-resistance ovarian cancer.[9] The use of bevacizumab for recurrent ovarian cancer has been reported response rates of 16–21% with an additional 39–55% of patients exhibiting SD.[10] In the present retrospective study, we found 2 CR (7.7%), 8 partial response (30.8%), 7 SD (26.9%) and 9 PD (34.6%) with the ORR of 38.5% and DCR of 65.4%, which was a little

bit higher to the previously study. The reason for the higher response and DCR may associate with the small number patients and retrospective study design, which was prone to heterogeneity and bias. So, well-designed prospective RCTs were needed for further evaluation the clinical value for bevacizumab combined with gemcibabine or paclitaxel in the treatment of recurrent ovarian cancer.

References

1. Cramer DW. The epidemiology of endometrial and ovarian cancer. Hematol Oncol Clin North Am 2012;26:1-12.
2. Luvero D, Milani A, Ledermann JA. Treatment options in recurrent ovarian cancer: Latest evidence and clinical potential. Ther Adv Med Oncol 2014;6:229-39.
3. Vargas-Hernández VM, Moreno-Eutimio MA, Acosta-Altamirano G, Vargas-Aguilar VM. Management of recurrent epithelial ovarian cancer. Gland Surg 2014;3:198-202.
4. Eisenhauer EL, Zanagnolo V, Cohn DE, Salani R, O'Malley DM, Sutton G, *et al.* A phase II study of gemcitabine, carboplatin and bevacizumab for the treatment of platinum-sensitive recurrent ovarian cancer. Gynecol Oncol 2014;134:262-6.
5. Gonzalez-Martin A, Gladieff L, Tholander B, Stroyakovsky D, Gore M, Scambia G, *et al.* Efficacy and safety results from OCTAVIA, a single-arm phase II study evaluating front-line bevacizumab, carboplatin and weekly paclitaxel for ovarian cancer. Eur J Cancer 2013;49:3831-8.
6. Agrawal A, Purandare N, Shah S, Puranik A, Banavali S, Rangarajan V. Response assessment in metronomic chemotherapy: RECIST or PERCIST? Indian J Nucl Med 2014;29:74-80.
7. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. CA Cancer J Clin 2014;64:9-29.
8. Burger RA, Brady MF, Bookman MA, Fleming GF, Monk BJ, Huang H, *et al.* Incorporation of bevacizumab in the primary treatment of ovarian cancer. N Engl J Med 2011;365:2473-83.
9. Monk BJ, Pujade-Lauraine E, Burger RA. Integrating bevacizumab into the management of epithelial ovarian cancer: The controversy of front-line versus recurrent disease. Ann Oncol 2013;24:X53-8.
10. Barber EL, Zsiros E, Lurain JR, Rademaker A, Schink JC, Neubauer NL. The combinationofintravenousbevacizumabandmetronomicoralcyclophosphamide is an effective regimen for platinum-resistant recurrent ovarian cancer. J Gynecol Oncol 2013;24:258-64.

How to cite this article: Wu MD, Wang Y, Ding T, Zhou YF, Song J, Liu XH, *et al.* A retrospective clinical study of bevacizumab combined with gemcibabine or paclitaxel in the treatment of recurrent ovarian cancer. Indian J Cancer 2014;51:103-5.

Source of Support: Nil. **Conflict of Interest:** None declared.