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Real-World Efficacy and Safety of Endostar-Platinum versus Bevacizumab-Platinum Intracavitary Perfusion for Serous Cavity Effusions

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Abstract: *Retrospective analysis of 71 patients with malignant serous cavity effusions (MSE) treated with either Endostar-platinum or bevacizumab-platinum regimens revealed that bevacizumab combined with platinum yielded superior objective response rate (ORR: 56.76% vs 45.16%, P<0.050) and significantly prolonged median progression-free survival (mPFS: 13.0 vs 10.0 months, HR=0.409, 95% CI: 0.219–0.764, P=0.001) compared with Endostar-platinum. The two regimens showed comparable disease control rate (DCR), quality of life (QOL) and adverse events profiles. Multivariate analyses identified absence of pulmonary metastasis, completion of ≥3 treatment cycles, and 200 mg bevacizumab dose as independent prognostic factors for longer mPFS in MSE patients.*

Keywords: *Endostar; Bevacizumab; Intracavitary perfusion; Malignant Serous Effusions; Malignant ascites; Malignant pleural effusion*

1. Introduction

Serous effusion is defined as the pathological accumulation of excess fluid in the body's serous cavities (such as the pleural, abdominal, and pericardial cavities). This condition arises from either increased fluid production or decreased fluid absorption within these spaces[1]. Malignant ascites (MA) is most common in patients with abdominal malignancies. It presents with marked abdominal distension, dyspnea, and impaired immune system, which increases the difficulty of anticancer therapy[2], and often signals tumour recurrence. Malignant pleural effusion (MPE) occurs most frequently in lung and breast cancers. Small effusions may cause mild symptoms or none at all. As fluid volume increases[3], severe cases may present with palpitations, dyspnea, or jugular venous distension. About 10%–30% of lung cancer patients develop MPE; pericardial effusion is rarer (~5%). Early-stage breast cancer rarely presents with effusions, but as the disease progresses—especially with distant metastases—effusions appear more frequently: MPE in about 10%–20% of recurrent/metastatic breast cancer and pericardial effusion in about 5%–10%, while peritoneal (ascites) effusion occurs in 8%–15% if there is peritoneal metastasis. Lymphomatous pleural involvement rates are about 7%–30%; both Hodgkin and non-Hodgkin lymphoma, as well as lymphosarcoma, can cause pleural effusions. Variances in incidence are modulated by tumor type and study methodology. A review of global literature finds that the median survival for MPE is generally between 4 and 10 months[4]. Recurrence and poor prognosis in MPE and MA patients impose significant physical burdens and reduce quality of life, highlighting the urgent need for effective, clinically impactful solutions.

Malignant serous effusions (MSE) are common complications in terminal stage of cancer. Diagnosis of MSE entails both pathological confirmation (detection of exfoliated tumour cells in effusion) and supportive evidence (biochemical analysis of effusion, imaging of tumour foci, or exclusion of non-malignant causes). The prognosis for malignant tumour patients with serous cavity effusions is inferior. Big data and epidemiological studies show that primary lung cancer has the shortest median survival with effusion. In 2018, Pallidas et al. published a predictive scoring system in Lancet Oncology to estimate 3-month mortality in these patients[5]. The system incorporates factors including hemoglobin level, leukocyte count, C-reactive protein, Eastern Cooperative Oncology Group (ECOG) Performance Status score, and tumor type—enabling more accurate prediction of both median and overall survival. This advancement also depends on standardized data collection and reduced subjective bias[6]. Technological and pharmaceuticals have greatly empowered the treatment of MSE, with Endostar

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(recombinant human endothelial cell suppressor) as a notable example[7]. First-line drug choices should be tailored to the underlying malignancy. For tumours with pronounced angiogenic features, such as renal cell carcinoma, colorectal tumours, lung cancer, breast cancer, and glioblastoma, vascular endothelial cell inhibitors have demonstrated significant efficacy[8]. Intracavitary chemotherapy has been used since the mid-twentieth century. Compared with intravenous or oral administration, this route offers lower systemic toxicity, more targeted regional delivery, and higher local drug concentrations, especially valuable for cancers of the serous membrane (pleural, peritoneal, etc.).

Endothelial Cell Suppressors (ECS) are key biological factors that inhibit both the proliferation and migration of vascular endothelial cells and are considered important regulators of tumor angiogenesis[9]. Under physiological conditions, ECS participate in neovascularisation, in pathological conditions, they affect the uncontrolled growth and metastasis of tumors[10]. While the biology of ECS is not fully elucidated, its mechanisms are believed to include: a. Blocking endothelial cells from entering the cell cycle to inhibit proliferation. b. The Kringle domain is a vital structural region, interacting with multiple signaling pathways of endothelial cells to inhibit degradation of the basement membrane, thus affecting cell migration[11]. c. ECS are cytotoxic to endothelial cells and can induce apoptosis[12]. ECS were first discovered in 1997 during collagen research, but large-scale, high-purity extraction for clinical use remains technically challenging. Recombinant human ECS was introduced in China in 2006, and subsequent clinical studies confirmed its efficacy, especially in combination with chemotherapy for solid tumours [13].

In murine models, Endostar significantly inhibits ascites formation, reduces the number of tumours and erythrocytes in effusion, decreases peritoneal permeability (as measured by spectrophotometry)[14], downregulates VEGF expression, and prolongs survival[15]. Similarly, evidence exists that Bevacizumab is efficacious for ascites associated with lung, ovarian, and gastric cancers. A review of domestic and international literature, as well as expert consensus and most recent guidelines for serous effusion management, reveals no prior studies directly comparing Endostar and Bevacizumab in intraperitoneal infusion for effusion control. The indications for these agents differ: Endostar is primarily used intravenously for non-small cell lung cancer (NSCLC) but is contraindicated in patients with cardiac or renal insufficiency; Bevacizumab is widely indicated for metastatic colorectal cancer (mCRC), advanced/recurrent/metastatic NSCLC, recurrent glioblastoma (rGBM), and hepatocellular carcinoma (HCC) via the intravenous route. Notably, the present study's administration route is off-label, but since 2010, related studies and guideline recommendations have supported its use in this setting[16]. This research thus provides robust evidence to inform potential updates to drug labelling and to support standardized clinical adoption, furthering optimization of patient care.

2. Study Methods and Patient Selection

2.1 Study Design

This retrospective case–control study included patients treated at two sites of the Third Affiliated Hospital of Anhui Medical University between January 1, 2021 and January 1, 2025. Eligible subjects were patients with pathologically or cytologically confirmed malignancy and massive malignant serous effusions, treated with Endostar or Bevacizumab in combination with platinum-based chemotherapy by intracavitary perfusion.

2.2 Quality Control

Missing values of key variables—including treatment regimen, Eastern Cooperative Oncology Group (ECOG) performance status, age, gender, and treatment cycle—were assessed. As the variables in this study are not influenced by themselves or other confounding factors, they are classified as completely random variables. Using SPSS 26.0, the missing data rate was determined to be 6%. Multiple imputation (MI) was employed for data supplementation: the data were stratified by multiple dimensions, 5 imputed datasets were generated, and the dataset with a high Cronbach's alpha coefficient (α) was selected for subsequent statistical analysis.

2.3 Patient Selection

From the two wards, malignant tumour patients with massive serous effusions (primarily pleural or peritoneal) who had completed at least two continuous treatment cycles at our hospital were included.

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An initial pool of 410 patients with malignant pleural/peritoneal effusion was screened (Figure 1). Inclusion criteria were: a. age 18–85 years. b. ECOG 0–4. c. expected survival >16 weeks. d. pathologically or cytologically proven malignant serous effusion. e. preserved bone marrow, coagulation, hepatic and renal function, with tolerance to endothelial cell suppressors and platinum chemotherapy. f. imaging-confirmed massive serous effusion by ultrasound or CT. g. chest/abdominal drainage catheter in situ. h. signed informed consent for intracavitary perfusion. i. regular follow-up via clinic, hospitalisation, or telephone. Exclusion criteria: a. prior radiotherapy, chemotherapy, immunotherapy, targeted therapy, or major organ surgery within 4 weeks of intracavitary perfusion. b. uncontrolled esophageal/gastric varices, peptic ulcers, end-stage disease/multiorgan failure, or other high gastrointestinal perforation risk. c. uncontrolled hypertension. d. presence of massive hemorrhagic effusion on drainage. e. pre-treatment leucocytes <3.0×10^9/L, neutrophils <1×10^9/L, platelets <100×10^9/L, or hemoglobin <65g/L (except transfused patients). f. no efficacy data available. The Ethics Committee of the Third Affiliated Hospital of Anhui Medical University approved the study.

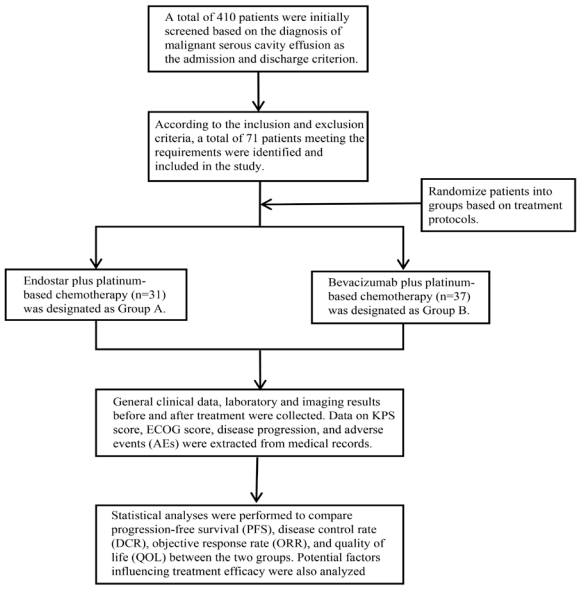

Figure 1: Research Methodology Flowchart

2.4 Treatment

Of the 410 screened patients, 71 eligible patients were included from the 410 screened: 31 in Group A (Endostar plus platinum) and 37 in Group B (Bevacizumab plus platinum). Group A received Endostar 45 mg plus platinum administered via intracavitary perfusion on days 1, 4, and 7 of a 21-day cycle. Group B received Bevacizumab 5 mg/kg plus platinum on day 1 of a 21-day cycle. Treatment in both groups continued until disease progression, unacceptable toxicities, or withdrawal of consent. Efficacy was assessed every two cycles by RECIST Version 1.1, and adverse events (AEs) were evaluated per cycle. All pre- and post-treatment chest/abdominal CT or ultrasound, effusion drainage volume, routine blood counts, hepatic/renal function, and coagulation profiles.

2.5 Study Objectives

Baseline evaluation included gender, age, medical history, ECOG score, primary tumour, clinical stage, metastatic sites, and treatment cycles, among others. The primary endpoint was progression-free survival (PFS) of serous effusion following both regimens. Secondary endpoints included quality of life (QOL), objective response rate (ORR), disease control rate (DCR), and AEs.

2.6 Statistical Analysis

2.6.1 Primary Study Endpoint

The patient's effusion status was evaluated at the end of each treatment cycle or during the subsequent visit. Treatment efficacy for serous effusion was assessed per WHO criteria: Complete response (CR)—effusion disappears and persists for at least 4 weeks. Partial response (PR)—effusion reduced by ≥50%

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and symptom relief for ≥4 weeks. Stable disease (SD)—effusion not reduced by ≥50% nor increased by ≥25%, with no significant symptom changes. Progressive disease (PD)—effusion increased by ≥25% or patient death. Primary endpoints: ORR—proportion of patients with CR or PR. DCR—proportion of patients achieving CR, PR, or SD. PFS—time from initiation of effusion treatment to disease progression or death.

2.6.2 Quality of Life Assessment

The Karnofsky Performance Status (KPS) score of patients before and after treatment was collected. Changes in these scores were used to assess quality of life, classified as: improvement (an increase in KPS score by ≥10 points), stability (no change in KPS score), and worsening (a decrease in KPS score by ≥10 points).

2.6.3 Evaluation of Adverse Reactions

Grading and assessment of adverse reactions were performed according to the Common Terminology Criteria for Adverse Events, Version 5.0 (CTCAE v5.0), established by the National Cancer Institute (NCI) of the United States.

2.6.4 Statistical Analysis

Data were processed using SPSS 26.0 software. Normality and homogeneity of variance tests were first performed for each group. Depending on whether data conformed to normality and variance homogeneity assumptions, either t-tests or nonparametric tests were used to compare the means and probability of differences between groups. Survival curves were generated using the Kaplan-Meier method. COX regression was used to identify factors affecting the PFS of serous cavity effusion. $P < 0.050$ was considered statistically significant.

3. Results

3.1 Patient Characteristics and Treatment

A total of 71 eligible patients were ultimately enrolled in this study. There were no significant differences in demographic or clinical characteristics between the two groups (Table 1). Patients were divided into two groups based on treatment: 31 patients received Endostar (Endu) combined with platinum-based intrapleural/intraperitoneal therapy for serous cavity effusions, with a median age of 71 years (range: 27–87 years), including 21 males and 8 females; the majority had an ECOG score of 2. Thirty-seven patients received bevacizumab (Bev) combined with the platinum-based agent for pleuroperitoneal effusion, with a median age of 66 years (range: 33–86 years), including 23 males and 15 females. The majority had an ECOG score of 3. Most patients in both groups had stage IV tumours, and a minority had not undergone tumour staging. The most common primary tumour among the enrolled patients was lung cancer, followed by gastric cancer. Forty-four patients had metastatic lesions in other organs, whereas 26 patients had no metastatic tumours.

3.2 Efficacy of Treatment

In the Endostar group, there was 1 patient with CR of serous cavity effusion, 13 with PR, 14 with SD and 3 with PD, the ORR was 45.16% and the DCR was 90.32%. In the bevacizumab group, there were 2 patients with CR, 26 with PR, 7 with SD, and 2 with PD, the ORR was 56.76% and the DCR was 94.60% (Table 2). There was a statistically significant difference in ORR between the two groups ($P<0.050$), but no significant difference in DCR. Survival analysis showed that the median progression-free survival (mPFS) in the bevacizumab group was longer (13 months, 95% CI: 0.678-0.981) than in the Endostar group (10 months, 95% CI: 0.329-0.818) (HR=0.409, 95% CI: 0.218–0.764, P=0.001) (Figure 2). One patient with lung cancer in the Endostar group died from cardiopulmonary arrest. In the bevacizumab group, two patients died: one from respiratory failure (lung cancer) and one from cachexia (gastrointestinal malignancy). Review of the cases of these three patients indicated that their deaths were unrelated to the study treatment.

Regression analysis was performed on the data using SPSS version 26.0. Univariate Cox regression was performed on factors in both groups; details are shown in Table 3. In univariate analysis, no pulmonary metastasis (HR=0.611, 95% CI: 0.338-0.504, P=0.010), treatment cycles ≥ 3 (HR=0.724, 95% CI: 0.363–0.644, P=0.035), bevacizumab dose of 200mg (HR=0.545, 95% CI: 0.091–0.553, P=0.025), and Bev group (HR=0.659, 95% CI: 0.363-0.897, P=0.017) had higher PFS. For multivariate Cox

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regression analysis: no pulmonary metastasis (HR=0.457, 95% CI: 0.257-0.878, P=0.018), treatment cycles ≥ 3 (HR=0.337, 95% CI: 0.134-0.845, P=0.020), bevacizumab dose of 200mg (HR=0.684, 95% CI: 0.090-0.304, P=0.043), treatment with bevacizumab (HR=0.505, 95% CI: 0.375-0.604, P=0.046). Compared with the Endostar group, the bevacizumab group malignant serous effusion progression, corresponding to an approximate 49.5% reduction in risk.

Table 1 Baseline clinical characteristics of patients.

Characteristics	Endo Group, n=31(%)	Bev Group, n=37(%)	P-value
AGE			0.234
≥66	9(29.0)	19(51.4)	
18-66	22(71.0)	18(48.6)	
Gender			0.294
Male	23(74.2)	23(62.2)	
Female	8(25.8)	14(37.8)	
Medical history			0.546
Hypertension	9(29.0)	9(24.3)	
Diabetes	4(12.9)	4(10.8)	
cerebral infarction	1(3.2)	0	
ECOG SCORE			0.303
1 Score	4(12.9)	2(5.3)	
2 Score	12(38.7)	12(31.6)	
3 Score	12(38.7)	21(55.3)	
4 Score	3(9.7)	3(7.9)	
Primary tumor			0.940
Lung cancer	14(45.2)	14(37.9)	
Liver cancer	3(9.7)	3(8.1)	
Gastric carcinoma	5(16.0)	6(16.2)	
Intestinal cancer	0	4(10.8)	
Ovarian cancer	0	2(5.4)	
Appendiceal cancer	0	1(2.7)	
Cervical cancer	0	1(2.7)	
Pancreatic cancer	3(9.7)	2(5.4)	
Esophagus cancer	0	4(10.8)	
Abdominal tumor	2(6.5)	0	
Bone cancer	1(3.2)	0	
Skin cancer	1(3.2)	0	
Endometrial Cancer	2(6.5)	0	
Metastatic carcinoma			0.226
Have transfer	16(51.6)	20(54.1)	
No transfer	15(48.4)	17(45.9)	
Serous effusion			0.227
Hydrothorax	15(48.4)	27(73.0)	
Ascites	16(51.6)	10(27.0)	

ECOG, Eastern Cooperative Oncology Group. Endo: Endostar. Bev: bevacizumab.

3.3 Analysis of toxicity

AEs in this study were graded according to the CTCAE Version 5.0. No treatment-related deaths occurred in either group. Table 4 summarises the adverse events in both groups, showing no statistically significant difference between them(P>0.050). Approximately 64.5% of patients in the endostar group and 83.7% in the bevacizumab group experienced grade 1–2 AEs. The incidence of grade 3–4 AEs in the endostar group 25.8%, and 16.2% in the bevacizumab group. All AEs were managed with symptomatic treatment, and no treatment-related deaths occurred. The common adverse events of Endostar include chest/abdominal pain, gastrointestinal reactions, fatigue, etc., for bevacizumab, common AEs include hypertension (new-onset or exacerbation), proteinuria, and epistaxis/gingival bleeding; among special populations (such as age ≥65 years), the risks of arterial thrombosis or hypertension are increased. This study did not include assessment of newly developed hypertension or proteinuria before and after treatment, and the reported adverse event rates are based solely on data from this study.

3.4 Quality of Life Assessment

Changes in patients' KPS scores before and after treatment in both groups are summarized in Table 5. The improvement rate of quality of life for the bevacizumab group (78.37%) was higher than that of the Endostar group(58.06%), but the difference was not statistically significant (P>0.05).

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Table 2:Response rate of clinical treatment of serous effusion.

	Endo group,n=31(%)	Bev group,n=37(%)	P value
CR	1(3.21)	2(5.41)	
PR	13(41.94)	26(51.35)	
SD	14(45.16)	7(18.92)	
PD	3(9.68)	2(5.41)	
ORR	14(45.16)	28(56.76)	0.013
DCR	28(90.32)	35(94.60)	0.653

CR, complete response. PR, partial response. SD, stable disease. PD, progression disease. ORR, objective response rate. DCR, disease control rate.

Table 3:Progression-free Survival in Malignant Serous Effusions.

ITEM	Univariate PFS			Multivariate PFS		
	HR	95% CI	Log-rank P	HR	95% CI	Log-rank P
Age						
≤66 vs >66	1.145	0.620-2.116	0.665			
Gender						
Male vs female	0.568	0.293-1.909	0.093			
ECOG performance status						
≤1 vs >1	1.006	0.355-2.848	0.991			
Histology						
HBP (yes or no)	0.642	0.320-1.407	0.160			
DM (yes or no)	1.353	0.412-4.447	0.618			
Metastases						
Lung (yes or no)	0.611	0.338-0.504	**0.010**	0.457	0.257-0.878	**0.018**
Liver (yes or no)	1.614	0.494-5.266	0.428			
Gastrointestinal tumors (yes or no)	1.255	0.613-2.571	0.535			
Reproductive system tumors(yes or no)	4.260	0.585-31.029	0.153			
Treatment cycle						
2 vs ≥ 3	0.724	0.363-0.644	**0.035**	0.337	0.134-0.845	**0.020**
Dose of bevacizumab						
200mg (yes or no)	0.545	0.091-0.553	**0.025**	0.684	0.090-0.304	**0.043**
300mg (yes or no)	0.775	0.422-1.423	0.411			
400mg (yes or no)	0.552	0.133-2.293	0.413			
Type of effusion						
MA vs MPE	0.998	0.523-1.907	0.996			
Therapeutic regimen						
Endo vs Bev	0.659	0.363-0.897	**0.017**	0.505	0.375-0.604	**0.046**

Abbreviation: HBP: High Blood Pressure, DM: Diabetes Mellitus, CVA: Cerebrovascular Accident, MA: Malignant ascites, MEP: Malignant pleural effusion, Endo: Endostar, Bev: bevacizumab.

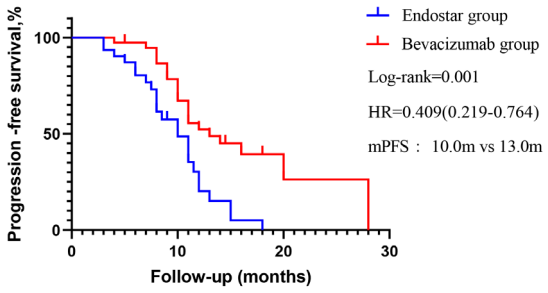

Figure 2: Kaplan-Meier survival curves of mPFS in the Endostar and bevacizumab groups.

The bevacizumab group achieved a longer mPFS of serosal effusion compared with the endostatin group: The bevacizumab group had an mPFS of 13.0 months (95% CI: 0.678–0.981), while the Endostar

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group had an mPFS of 10.0 months (95% CI: 0.329–0.818).

Table 4:Comparison of main adverse reactions between the two groups [n(%)].

Event	Endostar (n=31)		Bevacizumab (n=37)		P Value
	Grade1/2	Grade3/4	Grade1/2	Grade3/4	
Any	20(64.5)	8(25.8)	31(83.7)	6(16.2)	0.900
Impaired renal function	1(3.2)				0.456
Impaired liver function	7(22.6)	4(12.9)	9(24.3)	2(5.4)	0.795
Hypoalbuminemia	26(83.9)		23(62.2)	1(2.7)	0.100
Leukopenia	7(22.6)	2(6.5)	8(21.6)	3(8.1)	1.000
Anemia	23(74.2)	5(16.1)	23(62.2)	4(10.8)	0.120
Neutropenia	3(9.7)	3(9.7)	2(5.4)	2(5.4)	0.494
Thrombocytopenia	9(29.0)	2(6.5)	9(24.3)	3(8.1)	0.803
Feeble	27(87.1)		36(97.3)		0.170
Malnutrition	16(51.6)		13(35.1)		0.221
Abdominal distention	30(96.7)		36(97.2)		1.000
Diarrhoea	9(29.0)		8(21.6)		0.578
Constipation	5(16.1)		5(13.5)		1.000
Fever	4(12.9)		4(10.8)		1.000
Nausea and Vomiting	7(22.6)		10(27.0)		0.782
Bone ache	3(9.7)		4(10.8)		1.000

Table 5:Comparison of KPS scores between the two groups.

Group	N	Improve	Stabilise	Reduce	Improvement rate,%
Endostar	31	18	8	5	58.06
Bevacizumab	37	29	6	2	78.37
P-value					0.317

4. Conclusions

Malignant serous cavity effusions most commonly present as pleural or peritoneal effusions. Despite advances in medicine, the control and recurrence of malignant serous cavity effusions remain unresolved challenges [17,18]. In recent years, anti-angiogenic agents have demonstrated significant efficacy in intraperitoneal/pleural therapy[19].

Studies have shown that there is no statistically significant difference in QOL between patients with malignant ascites treated with Endostar combined with cisplatin and those treated with cisplatin alone[20]. In this study, both groups demonstrated improvement in QOL after treatment. However, when comparing the improvement rates, there was no statistically significant difference in the improvement of QOL between patients treated with Endostar and those treated with bevacizumab perfusion for malignant serous cavity effusion across different tumour types. In 2021, a retrospective study of 90 gastric cancer patients with malignant ascites explored the efficacy and safety of Endostar combined with chemotherapy. The trial and control groups had 37 and 53 patients, respectively; the median overall survival for the experimental group was 9.7 months, with an ORR of 75.7% and a DCR of 94.6%, based on the tumour remission and control rates of participants. QOL was significantly improved compared with the control group[21].

An exploratory study investigated different dosages of bevacizumab in the treatment of MPE, reporting that the mPFS was 10 months with a dosage of 5 mg/kg and an ORR of 50%. In the 2.5 mg/kg group, the mPFS was 4.5 months, and in the 7.5 mg/kg group, the mPFS was 6.0 months. The bevacizumab dosing in this study is consistent with previous optimal dosages, and the resulting mPFS was similar[22]. Furthermore, studies have found that the total cure rate of bevacizumab combined with lobaplatin perfusion in lung cancer-induced malignant pleural effusion is 83.72%. After treatment, levels of vascular endothelial growth factor (VEGF) and hypoxia inducible factor-1α (HIF-1α) in pleural effusion were significantly decreased compared to lobaplatin alone; expression of markers related to T cell recognition and attack of tumor cells was higher in the bevacizumab combination group; the mPFS was 7.6 months, longer than the 5.1 months in the control group[23].

In our preliminary study, compared with Endostar combined with platinum perfusion therapy for malignant serous cavity effusion, bevacizumab provided longer PFS of serous cavity effusions (10.0 months vs 13.0 months), with no significant difference in AEs, and grade 3-4 AEs accounted for only 11.36%, with no treatment-related deaths observed. Studies have additionally reported that ascites typically recurs within a short period after initial regression by cancer therapy. Currently, no studies have

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explored the quantitative relationship between treatment and the recurrence rate of effusion.

The final results of this study suggest that bevacizumab combined with platinum-based drugs via intraperitoneal/intrapleural administration in malignant serous cavity effusion leads to a longer mPFS for effusion. Both drug perfusion approaches are safe, show no significant difference in adverse effects, and no treatment-related deaths occurred. The no pulmonary metastasis is a potential factor influencing the PFS of serous effusion. The efficacy of 200 mg of bevacizumab is superior to other dosages. After ≥3 cycles of treatment, patients achieved a 66.3% higher PFS of serous effusion compared to those receiving <2 cycles, a statistically significant difference (P=0.020). Suggesting that a minimum of three treatment cycles is required to achieve meaningful control over effusion recurrence.

This study has certain limitations, First, the sample size of this study is insufficiently large, with minimal geographical variation, failing to reflect the overall characteristics of the population. Data from a small sample size introduces bias into the results of normality distribution and homogeneity of variance tests. Additionally, the confidence intervals used to estimate the range of population parameters are relatively wide, leading to low precision of the results. Therefore, more large-sample, prospective, multi-center clinical trials are required second, during the statistical analysis of adverse reactions, the lack of data on common adverse reactions associated with the two drugs (Endostar and bevacizumab) has impaired the observation of adverse reactions. This may result in unaccounted factors that potentially affect patients' survival duration. Hence, in the process of clinical drug research, close monitoring and documentation of adverse reactions are essential to improve data accuracy.

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