

## ORIGINAL ARTICLE

# The efficacy and safety of irinotecan combined with nedaplatin in the treatment of small cell lung cancer

Jun Fu, Sanyou Fang, Yin Wen, Yanbing Wang, Xin Yin, Daofeng Wang

Department of Respiration, Taixing People's Hospital, Taixing 225400, P.R. China.

## Summary

**Purpose:** To investigate the efficacy and safety of irinotecan combined with nedaplatin in the treatment of small cell lung cancer (SCLC).

**Methods:** 64 patients diagnosed with SCLC in our hospital from April 2013 to June 2015 were retrospectively analyzed. Thirty-two patients in group A were treated with irinotecan combined with nedaplatin, while 32 patients in group B were treated with irinotecan combined with cisplatin. The treatment efficacy was evaluated after 3 cycles of chemotherapy. Abbott ARCHITECT i2000SR chemiluminescence microparticle immunoassay analyzer was used to detect serum CEA, CA19.9 and CA125. The levels of serum CEA, CA19.9 and CA125 were assessed before and after treatment.

**Results:** In the two groups, the levels of serum CEA, CA19.9 and CA125 of the patients after treatment were lower than those before treatment ( $p < 0.05$ ). The main toxic side effect of the patients was gastrointestinal reaction in both groups. The total incidence of toxic side effects in group A was lower than that in group B ( $p < 0.05$ ).

**Conclusion:** The efficacy of irinotecan combined with nedaplatin is good and the safety is high in the treatment of SCLC and it can be used as a clinical treatment method of SCLC and is worthy of being generalized.

**Key words:** efficacy, irinotecan, nedaplatin, safety, small cell lung cancer

## Introduction

Lung cancer is the most common primary malignant tumor in the lung. It mainly appears in the bronchial epithelium [1]. 1.8 million people are diagnosed with lung cancer each year, and 1.6 million people die of this disease [2]. Some reports indicate that smoking is still the main reason for many patients to get lung cancer [3]. SCLC accounts for 15-20% of all lung cancers [4]. Of SCLC patients 95% are smokers [5]. SCLC is a neuroendocrine form of lung cancer and is one of the most metastatic and lethal cancers [6]. The main treatment methods of SCLC are radiotherapy and chemotherapy [7]. Although the efficacy of the first-line treatment of SCLC patients is good, the efficacy is transient, thus the disease of almost all patients relapses when they are treated or within a few months after treat-

ment. Patients have to be treated by second-line treatment, but currently there are no other treatments apart from the first-line treatment [8].

Irinotecan is a drug that contains camptothecin and facilitates the death of cancer cells by interfering with the topoisomerase 1 $\beta$  enzyme. Also, it can interfere with the synthesis of DNA and affect mitosis [9]. In the study of Kondo et al [10], it was shown that the tolerance of patients treated with irinotecan monotherapy was good and could be used as a treatment method for SCLC patients. Some studies [11] show that irinotecan combined with cisplatin have some antitumor activity and controllable toxicity for patients with metastatic and unresectable esophageal cancer. In the study of Zhong et al [12], the efficacy and toxicity of ne-

Corresponding author: Daofeng Wang, M.M. Department of Respiration, Taixing People's Hospital, No. 1 Changzheng Rd, Taixing 225400, P.R. China.

Tel: +86 18952679908, Email: fqngk@163.com

Received: 01/03/2020; Accepted: 26/03/2020

daplatin and cisplatin in the treatment of malignant pleural effusion were compared. The results showed that nedaplatin was an analogue of cisplatin, although the efficacy of nedaplatin was worse than that of cisplatin. Its toxicity was much lower than that of cisplatin. In this study, it was speculated if nedaplatin combined with irinotecan could replace irinotecan combined with cisplatin in the treatment of SCLC.

Therefore, this study aimed to prove that irinotecan combined with nedaplatin is a feasible and alternative treatment protocol compared with irinotecan combined with cisplatin.

## Methods

### General data

This was a prospective study. Sixty-four patients with SCLC were the study objects, and were diagnosed by the pathology department in our hospital from April 2013 to June 2015. There were 42 males and 22 females, aged between 43 and 68 years on average ( $59.84 \pm 8.15$ ). Thirty-two patients in the combined treatment group (group A) were treated with irinotecan combined with nedaplatin, while 32 patients in the conventional treatment group (group B) were treated with irinotecan com-

bined with cisplatin. This study was approved by the medical ethics committee of our hospital. All patients signed informed consent form before treatment entry.

Inclusion criteria: patients diagnosed with lung cancer by biopsy in our hospital; patients undergoing chemotherapy after surgery; patients with normal coagulation function; patients agreed to cooperate with the work of the medical staff in our hospital; patients didn't have other serious organ diseases affecting this study and received chemotherapy in our hospital after diagnosis; patients with complete cases; patients or their immediate relatives signed informed consent form. Exclusion criteria: patients with chronic inflammatory intestinal diseases, glaucoma, severe cardiopulmonary dysfunction, liver dysfunction, kidney dysfunction, nerve dysfunction, and cardiovascular and cerebrovascular diseases; patients complicated with other tumors; patients with immune diseases, infectious diseases, and physical disability; bedridden patients; patients in gestation; patients with poor compliance; patients transferred to another hospital during the treatment.

### Methods

The patients in the two groups were treated with symptomatic supportive treatments such as nutrition and analgesia. *Group A*: The patients were treated with irinotecan (purchased from Shanghai Acebright Pharmaceutical Co., Ltd., SFDA approval number: H20123191)

**Table 1.** Comparison of clinical data

Data	Group A (n=32)	Group B (n=32)	t/ $\chi^2$	p
Age, years	58.54±8.64	59.05±8.20	0.242	0.809
BMI (kg/cm <sup>2</sup> )	22.62±5.24	23.15±5.91	0.379	0.706
Disease course (day)	15.42±5.21	15.20±5.84	0.159	0.874
Gender, n (%)			0.277	0.599
Male	22 (68.75)	20 (62.50)		
Female	10 (31.25)	12 (37.50)		
Smoking, n (%)			0.474	0.491
Yes	26 (81.25)	28 (87.50)		
No	6 (18.75)	4 (12.50)		
Education background, n (%)			0.064	0.800
<High school	18 (56.25)	19 (59.37)		
≥High school	14 (43.75)	13 (40.63)		
Residence, n (%)			0.291	0.589
City	21 (65.63)	23 (71.88)		
Countryside	11 (34.38)	9 (28.12)		
Nationality			0.736	0.391
Han	30 (93.75)	28 (87.50)		
Minority	2 (6.25)	4 (12.50)		
Tumor size (cm), n (%)			0.063	0.802
>3	17 (53.13)	18 (56.25)		
≤3	15 (48.87)	14 (43.75)		
Tumor stage, n (%)			0.251	0.616
I-II	16 (43.75)	18 (48.65)		
III-IV	16 (56.25)	14 (51.35)		

combined with nedaplatin (purchased from Nanjing Chemical Book Pharmaceutical Co., Ltd., SFDA approval number: H20051987). On the first and the eighth day, the patients were intravenously injected with 250 ml of irinotecan at a concentration of 60 mg/m<sup>2</sup> combined with 0.9% normal saline. On the second day, the patients were intravenously injected with nedaplatin at a concentration of 85 mg/m<sup>2</sup>. One cycle was 21 days, and the patients were treated for 3 cycles (1 treatment course). *Group B*: The patients were treated with irinotecan combined with cisplatin. On the first and the eighth day, the patients were intravenously injected with 250 ml of irinotecan at a concentration of 60 mg/m<sup>2</sup> combined with 0.9% normal saline). On the first day, the patients were intravenously injected with 250 ml of cisplatin at a concentration of 75 mg/m<sup>2</sup> combined with 0.9% normal saline. Cisplatin was purchased from Yunnan Phytopharmaceutical Co., Ltd. (SFDA approval number: H53021740). One cycle was 21 days, and the patients were treated for 3 cycles (1 treatment course). After the patients were treated for 3 cycles, the chemotherapy efficacy was evaluated. When the patients had toxic side reactions, such as severe myelosuppression or gastrointestinal reaction, they were treated with symptomatic supportive treatments, and the chemotherapy was stopped if necessary. Fasting venous blood (5 mL) of all patients was collected in the morning. After the blood stayed still at room temperature for 30 min, it was centrifuged, and the serum was extracted and was stored in a refrigerator at -80°C. An Abbott ARCHITECT i2000SR chemiluminescence microparticle immunoassay analyzer and matched reagents were used to detect serum CEA, CA19.9 and CA125. The detection processes

were carried out strictly in accordance with the manufacturer's instructions.

#### Observation indicators

The expression levels of serum CEA, CA19.9 and CA125 of the patients in two groups were observed before and after treatment. The clinical efficacy in the two groups was observed. CT was used to evaluate the changes in lesions of the patients. According to the evaluation criteria of efficacy [13], three indicators were constructed, they were markedly effective, just effective or ineffective. Markedly effective: the disease condition of the patients improved completely; effective: the disease condition of the patients improved partially and was stable; ineffective: the disease condition of the patients worsened and relapsed. Toxic side effects: the incidence of nausea, vomiting and diarrhea of the patients in two groups was recorded during treatment. Prognosis: All patients were followed up for 1 year by letters, telephone calls, home visit, and reexaminations. The deadline was June 30th, 2014, and the terminal event was the death of patients. Six-month survival curves and 1-year survival curves of the patients were plotted after prognosis, and survival rates were calculated.

#### Statistics

All experimental results were statistically calculated by SPSS24.0 (Beijing Strong Vinda Information Technology Co., Ltd.). All graphs were plotted by Graphpad8 (Shenzhen Softhead Software Technology Co., Ltd.), and the results were checked twice. The count data were ex-

**Table 2.** Comparison of levels of serum CEA of the patients in two groups before and after they were treated (U/mL)

	Group A	Group B	t	p
Before treatment	26.54±10.74	26.78±10.33	0.091	0.928
After treatment	18.42±7.76	19.01±6.85	0.322	0.748
t	3.467	3.546		
p	0.001	<0.001		

**Table 3.** Comparison of serum CA19.9 levels of the patients in two groups before and after they were treated (U/mL)

	Group A	Group B	t	p
Before treatment	39.15±13.33	40.32±12.57	0.361	0.719
After treatment	16.72±2.36	17.14±2.15	0.744	0.459
t	9.373	10.280		
p	<0.001	<0.001		

**Table 4.** Comparison of levels of serum CA125 of the patients in two groups before and after treatment

	Group A	Group B	t	p
Before treatment	73.59±34.88	74.21±34.23	0.072	0.943
After treatment	54.33±26.61	55.16±26.41	0.125	0.901
t	2.483	2.493		
p	0.016	0.015		

pressed as rates, and chi-square ( $\chi^2$ ) test was used in the comparison between groups. The measurement data were expressed as mean $\pm$ standard deviation. Repeat ANOVA test was used in the comparison at different time points. T-test was used in the comparison between groups. Survival rates were calculated by Kaplan-Meier method and were compared by Log-rank test. When  $p < 0.05$ , differences were considered to be statistically significant.

## Results

### Comparison of clinical data

The clinical data of the patients in the two groups were compared. It was found that there were no significant differences in age, BMI, disease course, gender, smoking history, education background, residence, nationality, tumor size, and tumor stage ( $p > 0.05$ ). These results proved that the

clinical data of the patients in the two groups were comparable (Table 1).

### Comparison of levels of serum CEA, CA19.9 and CA125 of the patients in the two groups before and after treatment

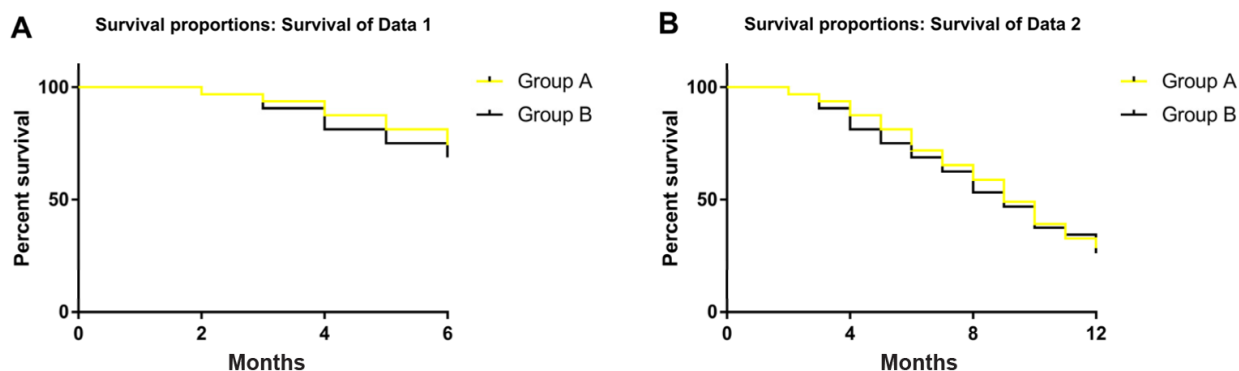
Chemotherapy was not discontinued during treatment in both groups. The levels of serum CEA, CA19.9 and CA125 were observed before and after treatment. In both groups, the levels of serum CEA, CA19.9 and CA125 after treatment were lower than those before treatment ( $p < 0.05$ ). There were no obvious differences in the levels of serum CEA, CA19.9 and CA125 between the two groups before treatment, and there were no obvious differences in the levels of serum CEA, CA19.9 and CA125 between the two groups after treatment ( $p > 0.05$ ) (Tables 2, 3 and 4).

**Table 5.** Comparison of the clinical efficacy of the patients in two groups n (%)

Group	n	Markedly effective	Effective	Ineffective	Total effective rate
Group A	32	10 (31.25)	18 (56.25)	4 (12.50)	28 (87.50)
Group B	32	8 (25.00)	16 (50.00)	8 (25.00)	24 (75.00)
$\chi^2$					1.641
p					0.200

**Table 6.** Comparison of toxic and side reactions of the patients in two groups

Group	n	Nausea and vomiting n (%)	Diarrhea n (%)	Total incidence n (%)
Group A	32	2 (6.25)	3 (9.38)	5 (15.63)
Group B	32	7 (21.88)	9 (28.12)	16 (50.00)
$\chi^2$				8.576
p				0.003



**Figure 1.** Survival results of the patients in the two groups. **A:** 6-month survival rates of the patients in the two groups: the 6-month survival rate of the patients was 71.88% in group A, while the 6-month survival rate of the patients was 68.75% in group B. Survival rates of the patients in the two groups were compared, and it was found that the differences were not statistically significant ( $p > 0.05$ ). **B:** 1-year survival rates of the patients in the two groups: the 1-year survival rate of the patients was 28.13% in group A, and 28.13% in group B. Survival rates of the patients in two groups were compared, and it was found that the differences were not statistically significant ( $p > 0.05$ ).

### *Comparison of the clinical efficacy of the patients in the two groups*

In group A, the efficacy of 10 patients was markedly effective. The efficacy of 18 patients was effective. The efficacy of 4 patients was ineffective. The total effective rate was 87.50%. In group B, the efficacy of 8 patients was markedly effective. The efficacy of 16 patients was effective. The efficacy of 8 patients was ineffective. The total effective rate was 75.00%. There were no significant differences between the efficacy of the patients in group A and in group B ( $p>0.05$ ) (Table 5).

### *Comparison of toxic side reactions of the patients in the two groups*

The main adverse reaction was gastrointestinal. The digestive tract reactions were mainly nausea and vomiting and delayed diarrhea, but patients didn't have serious liver injury and kidney injury. The above adverse reactions were tolerable, and could be improved after administration of symptomatic treatments. There were no differences in adverse reactions of the patients in the two groups before treatment. After treatment, 2 patients had nausea and vomiting and 3 patients had diarrhea in group A. Seven patients had nausea and vomiting and 9 patients had diarrhea in group B. The incidence of toxic side reactions in group A was significantly lower than in group B ( $p<0.05$ ) (Table 6).

### *Survival results of the patients in two groups*

Kaplan-Meier survival curves revealed that the 6-month survival rate and the 1-year survival rate of the patients were 71.88% and 28.13% in group A. The 6-month survival rate and the 1-year survival rate of the patients were 68.75% and 28.13% in group B. Survival rates of the patients in the two groups were compared and it was found that the differences were not statistically significant ( $p>0.05$ ) (Figure 1).

## **Discussion**

SCLC is a histological subtype of lung cancer, with unique biological and clinical characteristics. Although the morbidity of SCLC has been decreasing over the past few years, its malignant degree is high, and the 5-year survival rate of patients is less than 5% [14]. Chemotherapy generally can relieve symptoms and improve the quality life of SCLC patients. However, the remission period of SCLC is very short. The median survival period of patients is from 8 to 10 months, and their 1-year survival rate is only 30-40% [15]. SCLC relapses

in almost all of the patients because of resistance to chemotherapy [16]. Therefore, it is imperative for patients to choose a suitable treatment plan in order to treat SCLC.

Irinotecan is a topoisomerase-1 inhibitor and when it is combined with cisplatin, it can show a synergistic effect *in vitro* [17]. Currently, platinum-based chemotherapy (platinum combined with etoposide or irinotecan) is the main treatment method of extensive SCLC [18]. In recent years, topotecan, irinotecan and other drugs have been combined with platinum drugs to treat SCLC, and this approach achieved some efficacy [19]. In the study of Liu et al [20], the efficacy and safety of irinotecan combined with cisplatin and etoposide combined with cisplatin were researched in the treatment of untreated patients with extensive SCLC. The results showed that irinotecan combined with cisplatin improved the 1-year and 2-year survival rate of the patients, but they still had toxic and side reactions caused by the drugs. In the study of Xu et al [21], irinotecan combined with platinum was evaluated in the treatment of untreated patients with extensive SCLC. It was demonstrated that irinotecan combined with platinum could improve the overall survival rate, progression-free survival rate, and total effective rate of patients with extensive SCLC compared with etoposide combined with platinum, but they still had toxic and side reactions. Nedaplatin is a second-generation platinum analogue developed by Shionogi pharmaceutical company. Some reports show that nedaplatin has a similar efficacy, but the water solubility of nedaplatin is 10 times greater than that of cisplatin, and the nephrotoxicity and gastrointestinal toxicity are lower than those of cisplatin [22,23]. Therefore, the efficacy and safety of irinotecan combined with nedaplatin in the treatment of SCLC were investigated in this study.

In this study, irinotecan combined with nedaplatin was used to treat recurrent SCLC. The levels of serum CEA, CA19.9 and CA125 were compared before and after treatment. In both groups, the levels of serum CEA, CA19.9 and CA125 of the patients after treatment were lower than those before treatment ( $p<0.05$ ). There were no obvious differences in levels of serum CEA, CA19.9 and CA125 between the two groups before treatment, and there were no obvious differences in the levels of serum CEA, CA19.9 and CA125 between the two groups after treatment ( $p>0.05$ ). This result suggests that irinotecan combined with nedaplatin and irinotecan combined with cisplatin have efficacy in the treatment of recurrent SCLC. In the study of Lyu [24], the higher the levels of serum CEA, CA19.9, and CA125, the better the treatment efficacy. This result

can prove our study results. The clinical efficacy of the patients in the two groups was evaluated. In group A, the efficacy of 10 patients was markedly effective. The efficacy of 18 patients was effective. The efficacy of 4 patients was ineffective. The total effective rate was 87.50%. In group B, the efficacy of 8 patients was markedly effective. The efficacy of 16 patients was effective. The efficacy of 8 patients was ineffective. The total effective rate was 75%. There were no significant differences between the efficacy of the patients in group A and B ( $p>0.05$ ). After treatment, 2 patients had nausea and vomiting and 3 patients had diarrhea in group A. Seven patients had nausea and vomiting and 9 patients had diarrhea in group B. The incidence of toxic and side reactions in group A was significantly lower than in group B ( $p<0.05$ ). This result indicates that the toxicity of nedaplatin combined with irinotecan is significantly lower than that of cisplatin combined with irinotecan, and this result is consistent with the study of Li et al [25], that is: the toxicity of nedaplatin combined with irinotecan was lower than that of cisplatin combined with irinotecan in the treatment of SCLC. Then, the 6-month survival rate and the 1-year survival rate of all patients were recorded through a 1-year follow-up. Kaplan-Meier survival curves showed that the 6-month survival rate and the 1-year survival rate of the patients were 71.88% and 28.13% in group A. The 6-month survival rate and the 1-year survival rate of the group B patients were 68.75% and 28.13%. Survival rates of the patients in the two groups were compared and it was found that the differences were not statistically significant ( $p>0.05$ ). This result indicates that nedaplatin combined with irinotecan and

cisplatin combined with irinotecan can improve the survival rate of patients with SCLC.

However, there are still some shortcomings in this study. Firstly, it was unclear whether any other factors could affect the data. For example, the collected samples were few and the follow-up time was short. In addition, in the study of Tang et al [26], the results showed that adverse reactions of patients were also significantly different when nedaplatin and cisplatin were used to carry out a chemoradiotherapy regimen in the treatment of patients with stage II-IVB nasopharyngeal carcinoma. In this study, nedaplatin and cisplatin were combined with irinotecan in the treatment of SCLC. It was speculated that the results might be different when nedaplatin and cisplatin were used to treat SCLC respectively. Therefore, it is expected that the number of samples will be increased and the follow-up time will be prolonged in later studies. Moreover, different treatment protocols are expected to supplement the condition of patients with SCLC and perfect the results of this study.

## Conclusion

In summary, the efficacy of irinotecan combined with nedaplatin in SCLC is good, and the incidence of toxic and side reactions of patients is low and can be controlled. Irinotecan combined with nedaplatin can be used as a clinical treatment method of SCLC and is worthy of being generalized.

## Conflict of interests

The authors declare no conflict of interests.

## References

1. Popper HH. Progression and metastasis of lung cancer. *Cancer Metastasis Rev* 2016;35:75-91.
2. Hirsch FR, Scagliotti GV, Mulshine JL et al. Lung cancer: current therapies and new targeted treatments. *Lancet* 2017;389:299-311.
3. Novello S, Barlesi F, Califano R et al. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016;27:v1-27.
4. Zhao XL, McCutcheon JN, Kallakury B, Chahine J. Prognostic factors and combined histologies in 205 resected small cell lung cancer (SCLC) patients. *J Clin Oncol* 2017;35:e20009.
5. Alvarado-Luna G, Morales-Espinosa D. Treatment for small cell lung cancer; where are we now?-a review. *Transl Lung Cancer Res* 2016;5:26.
6. Yang D, Winslow MM, Sage J. Influence of cancer initiation on tumor progression in SCLC. *Clin Cancer Res* 2018;24:Abstr no. IA07.
7. Turrisi AT 3rd, Kim K, Blum R et al. Twice-daily compared with once-daily thoracic radiotherapy in limited small-cell lung cancer treated concurrently with cisplatin and etoposide. *N Engl J Med* 1999;340:265-71.
8. Chen HZ, Bonneville R, Krook MA et al. Genomic characterization of recurrent small cell lung cancer through research autopsy reveals clonal diversity and candidate driver of chemoresistance. *Proc AACR Annu Meet* 2019;748.
9. Meisenberg C, Ashour ME, El-Shafie L et al. Epigenetic changes in histone acetylation underpin resistance to the topoisomerase I inhibitor irinotecan. *Nucleic Acids Res* 2016;45:1159-76.

10. Kondo R, Watanabe S, Shoji S et al. A phase II study of irinotecan for patients with previously treated small-cell lung cancer. *Oncology* 2018;94:223-32.
11. Kim M, Keam B, Kim TM et al. Phase II study of irinotecan and cisplatin combination chemotherapy in metastatic, unresectable esophageal cancer. *Cancer Res Treat* 2017;49:416.
12. Zhong LZ, Xu HY, Zhao ZM, Zhang GM, Lin FW. Comparison of efficacy and toxicity between nedaplatin and cisplatin in treating malignant pleural effusion. *Onco Targets Ther* 2018;11:5509.
13. Tsuchida Y, Therasse P. Response evaluation criteria in solid tumors (RECIST): new guidelines. *Med Pediatr Oncol* 2001;37:1-3.
14. Berghmans T, Scherpereel A, Meert AP et al. A phase III randomized study comparing a chemotherapy with cisplatin and etoposide to an etoposide regimen without cisplatin for patients with extensive small-cell lung cancer. *Front Oncol* 2017;7:217.
15. Hu Q, Wang Q, Zhu H, Yao Y, Song Q. Irinotecan compared with etoposide in combination with platinum in previously untreated extensive stage small cell lung cancer: An updated systemic review. *J Cancer Res Ther* 2016;12:881.
16. Wagner AH, Devarakonda S, Skidmore ZL et al. Recurrent WNT pathway alterations are frequent in relapsed small cell lung cancer. *Nat Commun* 2018;9:3787.
17. Shibutani T, Takano M, Miyamoto M et al. Combination of irinotecan and platinum for platinum-resistant or refractory recurrent ovarian cancers: A preliminary case series. *Mol Clin Oncol* 2017;7:51-5.
18. Chen Y, Chen L, Zhong D. Comparing the adverse effects of platinum in combination with etoposide or irinotecan in previously untreated small-cell lung cancer patients with extensive disease: A network meta-analysis. *Thorac Cancer* 2017;8:170-80.
19. Tsoukalas N, Aravantinou-Fatorou E, Baxevanos P et al. Advanced small cell lung cancer (SCLC): new challenges and new expectations. *Ann Transl Med* 2018;6:145.
20. Liu ZL, Wang B, Liu JZ, Liu WW. Irinotecan plus cisplatin compared with etoposide plus cisplatin in patients with previously untreated extensive-stage small cell lung cancer: A meta-analysis. *J Cancer Res Ther* 2018;14:1076.
21. Xu F, Ren X, Chen Y et al. Irinotecan-platinum combination therapy for previously untreated extensive-stage small cell lung cancer patients: a meta-analysis. *BMC Cancer* 2018;18:808.
22. Wang H, Zhu X, Huang J, Chen P, Han S, Yan X. Nedaplatin sensitization of cisplatin-resistant human non-small cell lung cancer cells. *Oncol Lett* 2016;11:2566-72.
23. Lin Z, Lv WZ, Wang SY et al. Efficacy and safety of pemetrexed and nedaplatin followed by pemetrexed maintenance therapy in advanced lung adenocarcinoma. *Cancer Manag Res* 2017;9:671.
24. Lyu J. The value of combined detection of serum CEA, CA125 and CA19-9 in the treatment of lung cancer patients. *Int J Lab Med* 2018;39:1322-5.
25. Li CG, Huang XE, Li Y. Phase II trial of irinotecan plus nedaplatin (INP) in treating patients with extensive stage small cell lung cancer. *Asian Pac J Cancer Prev* 2011;12:487-90.
26. Tang LQ, Chen DP, Guo L et al. Concurrent chemoradiotherapy with nedaplatin versus cisplatin in stage II-IVB nasopharyngeal carcinoma: an open-label, non-inferiority, randomised phase 3 trial. *Lancet Oncol* 2018;19:461-73.