The efficacy of amrubicin salvage chemotherapy in patients with relapsed extensive-disease small-cell lung cancer: A retrospective study

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Introduction

The efficacy of amrubicin for relapsed small-cell lung cancer (SCLC) has been reported in previous studies. Little information is available, however, regarding efficacy and survival benefits of third-line amrubicin chemotherapy in patients with extensive-disease (ED)-SCLC compared with what is known about second-line amrubicin.

Methods

We retrospectively analyzed the clinical records of ED-SCLC patients treated with amrubicin salvage chemotherapy as a third-line chemotherapy between January 2005 and July 2016 (amrubicin salvage group). The efficacy and toxicities of amrubicin were evaluated. Overall survival (OS) in the amrubicin salvage group was compared with OS among ED-SCLC patients treated with at least second-line chemotherapy between May 2000 and July 2016 and without subsequent amrubicin salvage chemotherapy (No-amrubicin group).

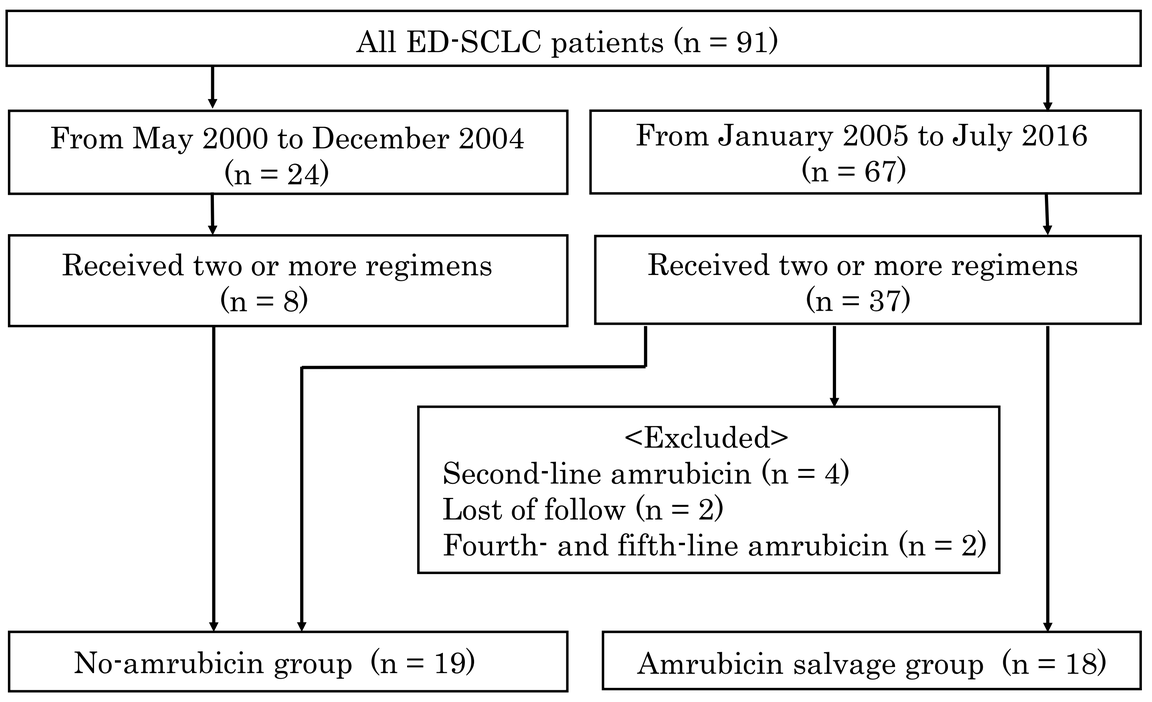
This retrospective study was approved by the institutional review board of Shinshu University School of Medicine (approval number: 3503)

Patients characteristics

Category	Number (%)	Number (%)
Treatment content	with amrubicin	without amrubicin
Total number of patients	18	19
Gender, Male/Female	14 (77.8)/4 (22.2)	17 (89.5)/2 (10.5)
Median age (range), years	69 (56-81)	68 (48-84)
ECOG performance status	first-line/third-line	first-line
0	5 (27.8)/2 (11.1)	3 (15.8)
1	10 (55.6)/12 (66.7)	13 (68.4)
2	2 (11.1)/4 (22.2)	2 (10.5)
3	1 (5.5)/0 (0.0)	1 (5.3)
Smoking history		
current+former	16 (88.9)	17 (89.5)
never	2 (11.1)	2 (10.5)
Metastasis		
Brain yes/no	2 (11.1)/16 (88.9)	3 (15.8)/16 (84..2)
Liver yes/no	6 (33.3)/12 (66.7)	4 (21.1)/15 (78.9)
Bone yes/no	4 (22.2)/14 (77.8)	6 (31.6)/13 (68.4)
Pleural yes/no	5 (27.8)/13 (72.2)	7 (36.8)/12 (63.2)
Prior regimen (first/second)		
platinum+CPT-11/platinum+VP-16	12 (66.7)	8 (42.1)
platinum+VP-16/platinum+CPT-11	3 (16.7)	2 (10.5)
platinum+VP-16/platinum+VP-16	3 (16.7)	6 (31.6)
platinum+VP-16/CPT-11	—	1 (5.3)
platinum/platinum+NGT+CAV	—	1 (5.3)
Clinical trial/platinum+CPT-11	—	1 (5.3)

CPT-11 irinotecan, *VP-16* etoposide, *NGT* topotecan, *CAV* cyclophosphamide+doxorubicin+vincristine

Flow chart of patients



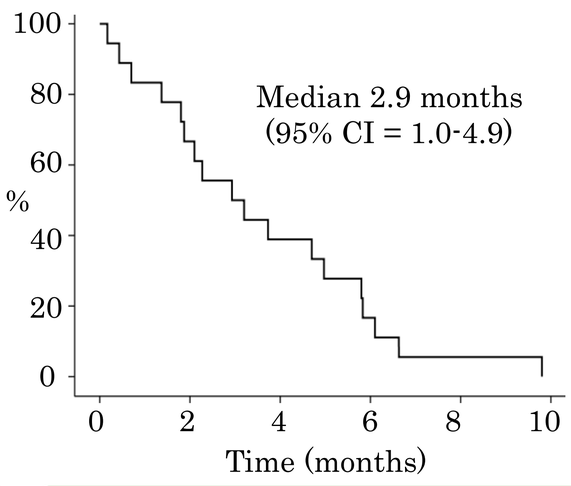
Efficacy and dose of amrubicin

Category	Number (%)
Best overall response	
Complete response	0 (0.0)
Partial response	5 (27.8)
Stable disease	7 (38.9)
Progressive disease	6 (33.3)
Overall response rate (%) (95% CI)	27.8 (7.1-48.5)
Disease control rate (%) (95% CI)	66.7 (44.9-88.4)
Cycles of chemotherapy, Median (range)	4 (1-10)
Starting dose (mg/m^2 daily day1-3)	
40	11 (61.1)
35	3 (16.7)
30	4 (22.2)

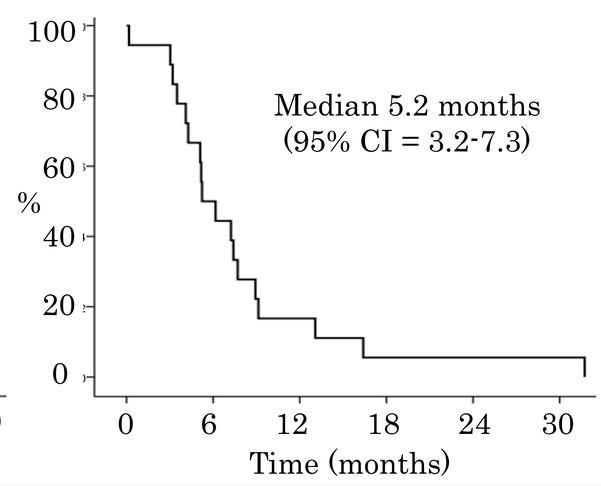
Toxicity of amrubicin

Adverse event	Any grade (%)	Grade1 (%)	Grade2 (%)	Grade3 (%)	Grade4 (%)
Neutropenia	15 (83.3)	0 (0.0)	2 (11.1)	4 (22.2)	9 (50.0)
Febrile neutropenia	7 (38.9)			7 (38.9)	
Leukopenia	15 (83.3)	3 (16.7)	0 (0.0)	8 (44.4)	4 (22.2)
Anemia	16 (88.9)	4 (22.2)	10 (55.6)	2 (11.1)	0 (0.0)
Thrombocytopenia	14 (77.8)	10 (55.6)	2 (11.1)	2 (11.1)	0 (0.0)
Fatigue	4 (22.2)	1 (5.5)	3 (16.7)	0 (0.0)	0 (0.0)
Nausea	4 (22.2)	4 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)
Constipation	5 (27.8)	5 (27.8)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhea	2 (11.1)	2 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)
Elevated AST/ALT	1 (5.5)	0 (0.0)	1 (5.5)	0 (0.0)	0 (0.0)
Elevated total bilirubin	2 (11.1)	1 (5.5)	1 (5.5)	0 (0.0)	0 (0.0)
Infection	2 (11.1)	0 (0.0)	2 (11.1)	0 (0.0)	0 (0.0)
Pulmonary toxicity	1 (5.5)	0 (0.0)	0 (0.0)	1 (5.5)	0 (0.0)

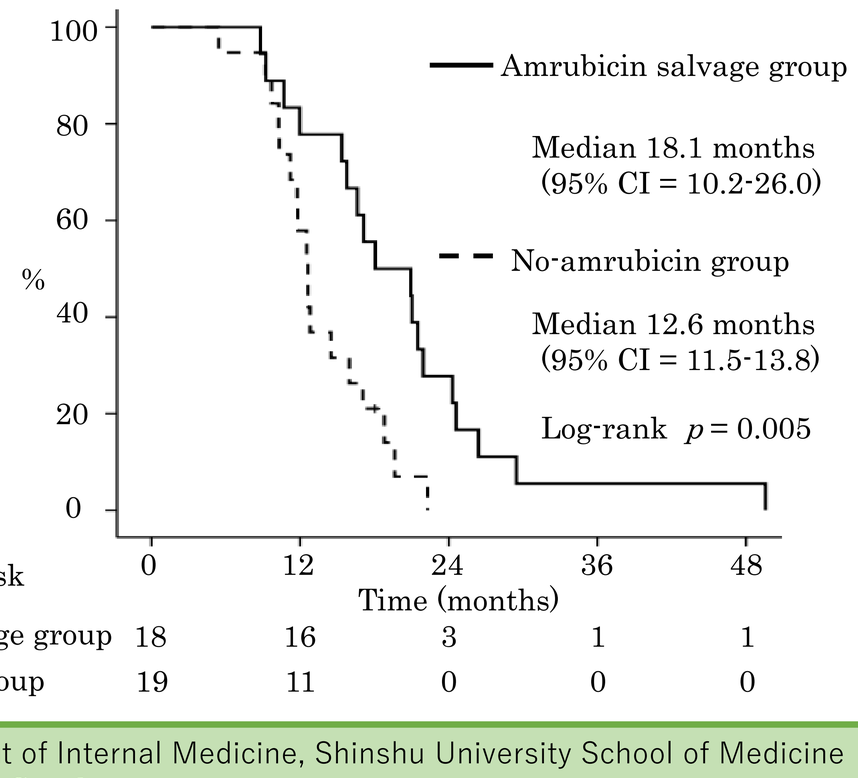
PFS



MST from third-line



OS



Discussion

With regard to the treatment of amrubicin as third-line chemotherapy, there are two retrospective clinical studies in Japan. The response rates were 14% [1)] and 44% [2)], respectively. In the present study, the response rate (27.8%) and the time from amrubicin monotherapy until time of death (5.2 months) were comparable to the above studies.

With regard to toxicity, the frequency of febrile neutropenia (FN) was high (38.9%), but there were no treatment-related deaths. The frequency of grade 3 or higher hematologic toxicities in our study were equivalent to the previous study [3) 4)].

<References>

1. J Thorac Oncol. 2007; 2: 741-4. 2. J Cancer Res Ther. 2012; 8: 266-71.
3. Thorac Cancer. 2018; 9: 1279-84. 4. Invest New Drugs. 2017; 35: 642-8.

Conclusion

Third-line amrubicin chemotherapy for relapsed ED-SCLC could be an effective regimen.

Although the frequency of FN was high, reduction of the starting dose and prophylactic use of G-CSF may reduce the frequency of FN.

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