

RESULTS

Demographic characteristics of patients are shown in Table 1. The mean \pm S.D of age (yr), weight (kg), height (cm) and body surface area (BSA, kg/m^2) of patients were 54.67 ± 8.02 (range 38-66), 54.75 ± 12.48 (36-77), 161.54 ± 8.06 (152.5-180) and 1.56 ± 0.19 (1.29-1.95), respectively. Performance status (PS) values were between 70% to 90%. Seven patients had squamous cell carcinoma, while five had adenocarcinoma and one had large cell carcinoma. Randomization sequences of cisplatin and cisplatin plus fosfomycin treatment cycles are shown in Table 2. During September 1998-October 1999, single dose per cycle of 100 mg/m^2 cisplatin plus vinblastine every 4 weeks are given to 13 male NSCLC cisplatin naïve patients for a total of 35 cycles (Table 2). The urinary NAG activities, CL_{cr} and Scr at baseline and after cisplatin therapy are shown in Table 3, 4 and 5, respectively. Table 6, 7 and 8 show the mean values (\pm S.D.) and statistic analysis of urinary NAG activities, CL_{cr} and Scr, respectively.

Missing data in Table 3, 4 and 5 were due to patients who dropped out from (patient no. 8, 10-13), had PS less than 70% (patients no. 9) or died during the study (patients no. 1, 5, 6). Urinary NAG activities at baseline in both cisplatin and cisplatin plus fosfomycin groups showed great variations among different patients and few patients had abnormally high urinary NAG values at baseline (Table 3). Since urinary NAG activities were not normally distributed, the non-parametric Mann-Whitney test was therefore selected for statistic analysis as described earlier. Most patients in both groups had their

urinary NAG activities increased on Day 3 after cisplatin treatment and these activities tended to return toward baseline on Day 6. Their mean urinary NAG activities increased significantly from their own baseline values only on Day 3 for both groups but the values at the same time points of both groups were not different (Table 6). There were much less variations in CL_{cr} and Scr in both groups and cisplatin or cisplatin in combination with fofomycin did not affect the patients' CL_{cr} and Scr (Table 4 and 5). The mean values of these two parameters did not change significantly from their baseline after either cisplatin or cisplatin plus fofomycin treatments (Table 7 and 8) and there were no significant differences in both groups between the corresponding values of CL_{cr} and Scr at the same time.

Table 1. Demographic characteristics of lung cancer patients in the study.

Patient no.	Age (yr)	Weight (kg)	Height (cm)	BSA (m ²)	PS (%)	Type
1	55	63	160	1.66	70	adenocarcinoma
2	59	56	163	1.58	90	squamous cell carcinoma
3	51	77	180	1.95	70	squamous cell carcinoma
4	51	61	173.5	1.72	70	adenocarcinoma
5	56	47	154.5	1.43	70	large cell carcinoma
6	66	45	152.5	1.38	80	squamous cell carcinoma
7	38	46	159	1.44	70	adenocarcinoma
8	48	52	162	1.54	70	adenocarcinoma
9	48	39	156.5	1.32	70	squamous cell carcinoma
10	47	50	159	1.5	80	squamous cell carcinoma
11	61	36	159	1.29	70	adenocarcinoma
12	63	48	153	1.42	80	squamous cell carcinoma
13	61	76	163	1.82	80	squamous cell carcinoma
Mean	54.67	54.75	161.54	1.56		
S.D.	8.02	12.48	8.06	0.19		

Table 2. Randomization sequences of treatment cycle.

Patient no.	Cycle of treatment			
	1	2	3	4
1	C+F	C+F	^a –	–
2	C	C	C+F	C+F
3	C+F	C	C+F	C
4	C+F	C	C+F	C
5	C	C+F	^a –	–
6	C+F	C	C	^a –
7	C	C+F	C+F	C
8	C	C+F	^b –	–
9	C+F	^c –	–	–
10	C	C+F	^b –	–
11	C	C+F	^b –	–
12	C	C+F	^b –	–
13	C+F	C	^b –	–

C = Cisplatin

C+F = Cisplatin + fosfomycin

^a death

^b drop out

^c PS < 70%

Table 3. Urinary NAG activities (unit/gram creatinine) of lung cancer patients treated with cisplatin and cisplatin plus fosfomycin.

Cisplatin				Cisplatin plus fosfomycin			
Patient no.	Day 0	Day 3	Day 6	Patient no.	Day 0	Day 3	Day 6
1	^a -	-	-	1	3.78	12.70	9.00
1	^a -	-	-	1	11.31	48.92	20.52
2	0.24	0.61	2.13	2	53.46	75.85	52.36
2	24.66	47.46	34.47	2	17.09	11.64	11.86
3	2.41	1.40	1.06	3	2.81	5.64	3.37
3	2.41	0.18	0.19	3	0.32	14.92	6.91
4	3.28	6.19	5.85	4	6.83	12.01	18.64
4	3.09	0.71	1.26	4	0.32	13.45	1.42
5	3.40	7.14	10.55	5	1.89	7.57	0.69
6	0.19	38.25	0.46	6	4.28	15.90	5.38
6	3.12	62.81	41.71	6	^a -	-	-
7	6.71	2.55	0.12	7	0.00	4.08	0.00
7	0.65	5.21	0.47	7	6.40	14.01	4.18
8	0.00	1.71	0.00	8	1.19	1.15	1.37
9	^b -	-	-	9	0.00	15.16	3.49
10	0.75	11.68	0.55	10	1.55	13.27	1.61
11	0.00	30.80	0.21	11	0.42	8.94	0.27
12	6.72	25.07	11.06	12	6.72	6.53	2.49
13	0.00	10.72	1.24	13	3.88	12.70	3.33
Mean	3.60	15.78	6.96	Mean	6.79	16.36	8.16
S.D.	6.03	19.38	12.73	S.D.	12.47	17.86	12.54
S.E.	1.51	4.84	3.18	S.E.	2.94	4.21	2.96

^a death

^b PS < 70%

Table 4. Creatinine clearance (mL/min) of lung cancer patients treated with cisplatin and cisplatin plus fosfomycin.

Cisplatin				Cisplatin plus fosfomycin			
Patient no.	Day 0	Day 3	Day 6	Patient no.	Day 0	Day 3	Day 6
1	^a -	-	-	1	63.50	66.80	63.10
1	^a -	-	-	1	30.60	57.00	36.30
2	60.00	52.80	48.10	2	40.70	41.60	40.30
2	54.00	69.60	36.50	2	32.70	46.40	32.80
3	44.00	58.20	81.60	3	64.10	49.60	54.60
3	67.00	41.90	44.50	3	56.00	55.40	52.30
4	62.10	63.00	62.90	4	60.30	78.00	34.10
4	49.10	181.90	42.80	4	46.10	55.00	47.20
5	36.70	35.00	28.50	5	45.10	27.30	182.80
6	46.60	50.20	34.60	6	58.80	46.20	33.60
6	46.30	35.10	31.70	6	^a -	-	-
7	41.80	52.50	203.40	7	63.80	41.40	45.80
7	21.90	61.10	48.30	7	28.40	51.10	58.00
8	82.90	70.90	70.80	8	74.10	82.10	63.00
9	^b -	-	-	9	53.10	60.80	31.10
10	53.00	43.00	32.20	10	40.90	29.20	21.20
11	48.40	36.60	52.20	11	43.70	37.40	39.50
12	44.70	37.60	36.80	12	47.10	48.50	46.50
13	47.60	58.00	51.00	13	55.30	95.60	75.20
Mean	50.38	59.21	56.62	Mean	50.24	53.86	53.19
S.D.	13.60	34.83	41.82	S.D.	12.85	17.84	35.11
S.E.	3.40	8.71	10.45	S.E.	3.03	4.20	8.27

^a death

^b PS < 70%

Table 5. Serum creatinine (mg/dL) in lung cancer patients treated with cisplatin and cisplatin plus fosfomycin.

Cisplatin				Cisplatin plus fosfomycin			
Patient no.	Day 0	Day 3	Day 6	Patient no.	Day 0	Day 3	Day 6
1	^a -	-	-	1	1.20	1.00	0.90
1	^a -	-	-	1	1.60	1.00	1.10
2	1.00	0.90	1.10	2	0.90	0.90	0.80
2	0.80	0.70	1.00	2	1.00	0.80	0.90
3	1.00	1.00	0.70	3	0.90	1.00	0.80
3	1.10	1.30	1.10	3	0.90	1.00	0.90
4	0.70	0.70	0.70	4	0.70	0.80	0.70
4	1.10	1.10	1.00	4	0.80	0.70	0.90
5	1.10	1.20	1.20	5	1.20	1.20	1.10
6	1.10	0.90	0.90	6	0.90	1.00	1.10
6	1.20	1.20	1.10	6	^a -	-	-
7	0.90	1.10	0.90	7	0.90	0.90	0.90
7	0.80	0.90	0.80	7	0.90	0.90	0.90
8	0.70	0.60	0.70	8	0.70	0.70	0.80
9	^b -	-	-	9	1.00	0.70	1.10
10	1.00	1.20	1.40	10	1.30	1.80	1.90
11	0.80	1.00	0.80	11	0.80	0.90	0.80
12	1.00	1.30	1.10	12	1.00	0.90	0.90
13	0.90	1.00	0.90	13	1.00	0.80	0.90
Mean	0.95	1.01	0.96	Mean	0.98	0.94	0.97
S.D.	0.15	0.21	0.20	S.D.	0.22	0.25	0.26
S.E.	0.04	0.05	0.05	S.E.	0.05	0.06	0.06

^a death

^b PS < 70%

Table 6. Urine NAG activities before and after 100 mg/m² cisplatin administration.

Treatments	Urine NAG activities (unit/gram creatinine) before and after cisplatin therapy		
	Before (Day 0)	Day 3	Day 6
Cisplatin	3.60±6.03	15.78±19.38 (<i>p</i> = 0.0142) ^a	6.96±12.73 (<i>p</i> = 0.6369) ^a
Cisplatin plus Fosfomycin	6.79±12.47 (<i>p</i> = 0.1828) ^b	16.36±17.86 (<i>p</i> = 0.0010) ^a (<i>p</i> = 0.1898) ^b	8.16±12.54 (<i>p</i> = 0.5267) ^a (<i>p</i> = 0.1164) ^b

^a compared to Day 0 in the same cycle.

^b compared to cisplatin in the same day.

Table 7. Creatinine clearance (mL/min) before and after 100 mg/m² cisplatin administration.

Treatments	Creatinine clearance (mL/min) before and after cisplatin therapy		
	Before (Day 0)	Day 3	Day 6
Cisplatin	50.38±13.60	59.21±34.83 (<i>p</i> = 0.7063) ^a	56.62±41.82 (<i>p</i> = 0.4975) ^a
Cisplatin plus Fosfomycin	50.24±12.85 (<i>p</i> = 1.0000) ^b	53.86±17.84 (<i>p</i> = 0.6809) ^a	53.19±35.11 (<i>p</i> = 0.6127) ^a

^a compared to Day 0 in the same cycle.

^b compared to cisplatin in the same day.

Table 8. Serum creatinine (mg/dL) before and after 100 mg/m² cisplatin administration.

Treatments	Serum creatinine (mg/dL) before and after cisplatin therapy		
	Before (Day 0)	Day 3	Day 6
Cisplatin	0.95±0.15	1.01±0.21 (<i>p</i> = 0.3798) ^a	0.96±0.20 (<i>p</i> = 0.9542) ^a
Cisplatin plus Fosfomycin	0.98±0.22 (<i>p</i> = 1.0000) ^b	0.94±0.25 (<i>p</i> = 0.4753) ^a	0.97±0.26 (<i>p</i> = 0.5339) ^a

^a compared to Day 0 in the same cycle.

^b compared to cisplatin in the same day.