TOLERANCE AND EFFICACY OF PEMETREXED-CISPLATIN FOR ADVANCED NON-SQUAMOUS NON-SMALL CELL LUNG CANCER: A GALICIAN LUNG CANCER GROUP STUDY

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PURPOSE

Advanced stage non-small cell lung cancer (NSCLC) represents a 80% all lung cancer. Recently a noninferiority phase III study was proved that in adenocarcinoma and large-cell carcinoma histology advanced NSCLC, cisplatin/pemetrexed provides better efficacy than cisplatin/gemcitabine. This was the first prospective phase III study in NSCLC to show survival differences based on histologic type. We conducted a multicenter study in advanced NSCLC to evaluate the tolerance and efficacy of first-line pemetrexed-cisplatin in non-epidermoid arcinoma.

PATIENTS AND METHODS

Patients with pathologically confirmed non-epidermoid histology and stage IIIB (pleural effusion) and IV NSCLC were eligible for study. Patients received pemetrexed (500 mg/m2 day 1) and cisplatin (75 mg/m2 day 1) every 21 days. All patients received oral folic acid daily and a vitamin B12 injection every 9 weeks. The first restaging was performed after three cycles. Toxicity was assessed at each cycle, according to the National Cancer Institute Common Toxicity Criteria. In the absence of progression or undue toxicity, treatment was continued for a maximum or six cycles. Disease status was assessed according to Response Evaluation Criteria in Solid Tumors.

PATIENT CRITERIA	No. of Patients	(%)
Patient number	94	
Median age (Range)	57	34-80
Sex		
Male	77	82
Female	16	17
Stage		
IIIB	10	10.6
IV	78	83
ECOG Performance Status		
0	17	18
1	62	66
2	7	7.4

Table 1.
Demographic data for non-squamous NSCLC patients treated with Pemetrexed/Cisplatin

RESULTS

From May 2008 to October 2010, 94 patients with non-squamous carcinoma were accrued from seven centers across Galicia, Spain (patient demographic data shown in Table 1). Of the 94 patients treated with cisplatin/pemetrexed, 70 were assessable for response. There was a complete response in 1 patient (1.4%), partial response in 29 patients (41.4%), a stable disease in 25 patients (35.7%) and a progression disease in 15 patients (21.4%). The median time to disease progression was 4.17 months (95% CI, 3.3 to 5) and the median overall survival was 12.6 months (95% CI, 6.76 to18.43) (see table 2 and figures 1 and 2).
Patients received a median of 5 cycles of therapy (range 1-8 cycles). Eight received a single cycle before discontinuing treatment. In 5 of these, treatment was stopped due to rapid disease progression. In the other 3 patients, treatment was discontinued on the basis of an adverse event. Sixteen other patients discontinued treatment following an adverse event after a range of 2-6 cycles of pemetrexed/cisplatin.
The median dose of weekly pemetrexed delivered was 166 mg/m2 and of cisplatin 25 mg/m2. In 4 patients (4.5%) dose reduction was required due to toxicity (febrile neutropenia, 2 patient; mucositis, 1 patient; nausea, 1 patient). Dose delay occurred in 8 patients. Eighty-nine patients were assessable for toxicity (see Table 3).

	No. of patients	Percent (%)	Valid Percent (%)
Overall response rate	30	32	42,9
Complete response	1	1,1	1,4
Partial Response	29	30,9	41,4
Progression Disease	15	16,0	21,4
Stable Disease	25	26,6	35,7
Total assessable	70	74,5	100,0
Not assessable	24	25,5	
Total	94	100,0	

Table 2.
Response rates for non-squamous NSCLC patients treated with Pemetrexed/Cisplatin

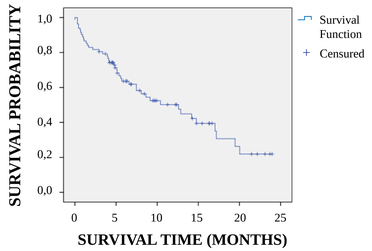

Fig. 1 (left).
Kaplan Meier overall survival curve

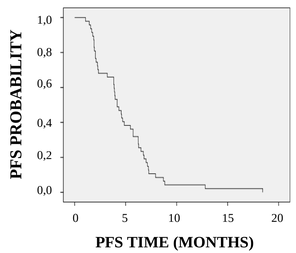

Fig. 2 (right).
Kaplan Meier progression-free survival curve

GRADE	1	(%)	2	(%)	3	(%)	4	(%)
Anemia	26	29.2	14	15.7	2	2.2	0	0
Leukopenia	0	0	1	1.1	0	0	0	0
Neutropenia	1	1.1	5	5.6	3	3.4	0	0
Febrile Neutropenia	0	0	2	2.2	1	1.1	3	3.4
Thrombocytopenia	1	1.1	0	0	0	0	0	0
Renal Dysfunction	0	0	0	0	0	0	0	0
Liver Dysfunction	0	0	0	0	0	0	0	0
Nausea	20	22.5	7	7.9	2	2.2	0	0
Vomiting	14	15.7	7	7.9	5	5.6	0	0
Alopecia	2	2.2	1	1.1	0	0	0	0
Mucositis	5	5.6	7	7.9	0	0	0	0
Constipation	5	5.6	4	4.5	0	0	0	0
Diarrhea	5	5.6	1	1.1	1	1.1	0	0
Neuropathy	1	1.1	0	0	0	0	0	0
Skin	1	1.1	1	1.1	0	0	0	0
Edema	1	1.1	0	0	1	1.1	0	0
Asthenia	29	32.6	24	27	2	2.2	0	0
Anorexia	15	16.9	7	7.9	0	0	0	0

Table 3.
Main toxic effects following treatment with Pemetrexed/Cisplatin

CONCLUSION

Combination with pemetrexed-cisplatin is well tolerated and has activity comparable with other agents approved for use in first-line in advanced adenocarcinoma and large-cell carcinoma lung cancer.

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