Multitargeted antifolate LY231514 as first-line chemotherapy for patients with advanced non-small-cell lung cancer: A phase II study. National Cancer Institute of Canada Clinical Trials Group.

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Abstract

PURPOSE: To evaluate the efficacy and safety of the multitargeted antifolate LY231514 (MTA) in patients receiving initial chemotherapy for unresectable, advanced non-small-cell lung cancer (NSCLC).

PATIENTS AND METHODS: Patients with measurable, advanced NSCLC who had not received previous chemotherapy for advanced disease were considered for this study. Eligible patients who gave written informed consent initially received MTA 600 mg/m(2) intravenously (IV) for 10 minutes every 3 weeks. After three patients received treatment at this dose, the dose was reduced to 500 mg/m(2) IV at the same infusion time and frequency because of toxicity seen in this study and another Canadian MTA trial in colorectal cancer. Patients received up to four cycles after complete or partial remission or six cycles after stable disease was documented.

RESULTS: Thirty-three patients were accrued onto the study. All were assessable for toxicity, and 30 patients were assessable for response. All but one patient had an Eastern Cooperative Oncology Group performance status score of 0 or 1, 18 patients (55%) had adenocarcinoma, and nine patients (27%) had squamous cell carcinoma. Twenty-five patients (76%) had stage IV disease, and the remainder had stage IIIB disease at trial entry. Seven patients experienced a confirmed partial response and no complete responses were seen; thus, the overall response rate was 23.3% (95% confidence interval, 9.9% to 42.3%). The median duration of response was 3.1 months (range, 2. 3 to 13.5 months) after a median follow-up period of 7.9 months. Four (67%) of six patients with stage IIIB disease and three (12.5%) of 24 with stage IV disease responded to treatment. Four patients (13.3%) experienced febrile neutropenia and 13 (39%) experienced grade 3 or 4 neutropenia, whereas only one patient (3%) developed grade 4 thrombocytopenia. Nonhematologic toxicity was generally mild or moderate, but 39% of patients developed a grade 3 skin rash. Most other toxicities comprised grade 1 or 2 stomatitis, diarrhea, lethargy, and anorexia. Ten patients stopped protocol therapy because of toxicity.

CONCLUSION: MTA seems to have clinically meaningful activity as a single agent against advanced NSCLC. Toxicity is generally mild and tolerable. Further study of this agent in combination with cisplatin and other active drugs is warranted in this disease.

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MeSH Terms:

Heading	Qualifier
Adult	
Aged	
Antineoplastic Agents	adverse effects
	*therapeutic use
Carcinoma, Small Cell	*drug therapy
Female	
Glutamates	adverse effects
	*therapeutic use
Guanine	adverse effects
	*analogs & derivatives
	therapeutic use
Humans	
Infusions, Intravenous	
Lung Neoplasms	*drug therapy
Male	
Middle Aged	
Survival Analysis	
Treatment Outcome	

0	Antineoplastic Agents
0	Glutamates
04Q9AIZ7NO	pemetrexed
5Z93L87A1R	Guanine

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