Docetaxel plus Gemcitabine as First-line Treatment in Malignant Pleural Mesothelioma: A Single Institution Phase II Study

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Abstract. *Background: The cisplatin-pemetrexed and cisplatin-gemcitabine combinations are considered the standard treatment for malignant pleural mesothelioma. The purpose of this study was to examine the efficacy of gemcitabine plus docetaxel in the first-line setting, as this combination has not been investigated in mesothelioma before. Patients and Methods: Twenty-five consecutive patients with malignant pleural mesothelioma were enrolled. They received 80 mg/m^2 of docetaxel and 1,000 mg/m^2 of gemcitabine on days 1 and 14 of a 28-day cycle. The treatment was scheduled for a maximum of 6 cycles or until disease progression or unacceptable toxicity. Results: A total of 7 out of our 25 patients (28%) responded to treatment. In 14 patients (56%), the disease remained stable, while in 4 (16%) it progressed. The median time to progression was 7 months (range: 5.4-8.6 months) and the median overall survival was 15 months (range: 12.4-17.5 months). Conclusion: The administration of gemcitabine and doctaxel appears to be promising first-line therapy for patients with mesothelioma, as it is well tolerated and appears to improve survival.*

Malignant pleural mesothelioma (MPM) is a rare aggressive tumor caused mainly by occupational asbestos exposure. Its incidence reaches 100 cases/million/year in occupationally exposed populations as opposed to 1 case/million/year in the general population and data show that it will continue to increase until 2020-2030 (1).

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The rarity of MPM and its often subtle clinical manifestation may lead to a missed or delayed diagnosis. The current treatment of advanced malignant pleural mesothelioma is platinum-based combination chemotherapy (2, 3). The landmark trial that compared the combination of cisplatin plus pemetrexed to cisplatin monotherapy demonstrated a survival benefit of 2.8 months for the combination arm (4). A subsequent trial showed a 2.6 month improvement in the survival of patients who were treated with cisplatin plus raltitrexed when compared to the survival of those who received cisplatin alone (5). Response rates for the combination treatments were 41.3% and 23.6%, while median overall survival time was 12.1 and 11.4 months respectively (6). The combination of cisplatin and gemcitabine has demonstrated comparable response and survival rates in several phase II trials (7-10), although it has not yet been evaluated in any randomized clinical trial.

A phase II trial examining the effectiveness of docetaxel in patients with MPM had been launched but was terminated early, after the first accrual stage, because of an insufficient number of patients with complete or partial disease response. There is no evidence of docetaxel being an effective agent as monotherapy in malignant mesothelioma (11). The efficacy of gemcitabine as a single-agent against mesothelioma is also limited when used in clinical practice (12). Bi-weekly administration of a docetaxel/gemcitabine combination constitutes a tolerable and convenient regimen for the treatment of advanced non-small cell lung cancer, with efficacy similar to most standard-platinum based therapy (13-15) but there have been no clinical trials investigating this combination in MPM therapy. We therefore conducted a preliminary phase II trial to evaluate the anti tumor efficacy of this double treatment, as determined by objective response, time to progression, overall survival and quality of life.

Patients and Methods

Twenty-five patients with measurable, histologically confirmed MPM were enrolled in the present study. Patients were older than 18 years of age and had an Eastern Cooperative Oncology group performance status of 0-1. They had no uncontrolled cardiac or