RESEARCH ARTICLE

Docetaxel and Cisplatin in First Line Treatment of Patients with Unknown Primary Cancer: A Multicenter Study of the Anatolian Society of Medical Oncology

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Abstract

Background: The overall prognosis for cancers of unknown primary (CUP) is poor, median overall survival (OS) being 6-12 months. We evaluated our multicentric retrospective experience for CUP administered docetaxel and cisplatin combination therapy. Materials and Methods: A total of 29 patients that were pathologically confirmed subtypes of CUP were included in the study. The combination of docetaxel (75 mg/m2, day 1) and cisplatin (75 mg/m2, day 1) was performed as a first line regimen every 21 days. Results: The median age was 51 (range: 27-68). Some 17 patients had multimetastatic disease on the initial diagnosis. Histopathological diagnoses were well-moderate differentiated adenocarcinoma (51.7%), undifferentiated carcinoma (27.6%), squamous cell cancer (13.8%), mucoepidermoid carcinoma (3.4%) and neuroendocrine differentiated carcinoma (3.4%). Median number of cycles was 3 (range: 1-6). Objective response rate was 37.9% and clinical benefit was 58.6%. Median progression free survival (PFS) and overall survival (OS) were 6 months (range: 4.3-7.7 months) and 16 months (range: 8.1-30.9 months), respectively. Fourteen patients (60.8%) were treated in a second line setting. There was no treatment related death. Most common toxicities were nausia-vomiting (44.6%) and fatigue (34.7%), serious cases (grade 3/4) suffering nausia-vomiting (10.3%), neutropenia (13.8%) and febrile neutropenia (n=1). Conclusion: The combination of cisplatin and docetaxel is an effective regimen for selected patients with CUP. Keywords: Cancer of unknown primary - docetaxel - cisplatin - combination - clinical benefit

Introduction

Cancer of unknown primary (CUP) accounts for 2-10% of all malignancies and accepted as metastatic cancer (Fizzazi et al., 2011; Pavlidis et al., 2012; Greco et al., 2012). Incidence of CUP is decreased secondary to advances of pathology and imaging methods (Greco et al., 2012; Hemminki et al., 2012). In many patients, pathologic diagnosis is adenocarcinoma and the disease is on the multimetastatic sites. Except selected patients, survival benefit of the treatments are limited and the intent of treatment is palliative. The prognosis of CUP is poor, response rate (RR) is 20-35%, median overall survival (OS) is 6-12 months and one year OS is 15-35% (Fizzazi et al., 2011; Greco et al., 2012; Pavlidis et al., 2012). Although different chemotherapy regimens were evaluated, there is no standard treatment, currently. Platinum based regimens are mostly used and the results of phase II taxane studies are promising in patients with CUP (Poussel et al., 2004; Adenis et al., 2010; Hainsworth et al., 2010). Here-in, we evaluated our multicentric retrospective experience for CUP administering docetaxel and cisplatin in combination therapy.

Materials and Methods

Between 2007 and 2010, totally 29 patients that were pathologically confirmed subtypes of CUP was evaluated in the five institutions, retrospectively. The treatment naive patient has pathologically confirmed CUP and although detailed examinations (physical examination, chest graphy, thoraco-abdominal computarized tomography (CT), mammography, if necessary pozitron emission tomography/ computarized tomography- PET/CT) and diagnostic sample, the primary was unable to identify. Female patient with alone axillary lymph node

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involvement and adenocarcinoma of the peritoneal cavity, midline carcinoma that suspected with germ cell tumor and patient with SCC at single site involvement were not included the study.

The patients were treated with the combination of docetaxel (75 mg/m², day 1) and cisplatin (75 mg/m², day 1) every 21 days. The evaluation for the treatment response in CUP was assessed by both clinical and radiological criteria using Response Evaluation Criteria in Solid Tumors (RECIST) (Eisenhauer et al., 2009). Toxicities were recorded based on National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 3.0.

Data were expressed with median values with range. While progression free survival (PFS) is defined from the initial day of treatment to first progression, OS is defined from the initial of treatment to last control or death. All statistical analyses were based on ‘intent to treat’. The Kaplan Meier survival estimates were calculated. Survival curve were compared with logrank test. A p-value was accepted statistically significant if the value less than 0.05. SPSS 15 was used for statistical analysis.

Results

The median age of four female (13.8%) and 25 male (86.2%) totally 29 patients was 51 (range: 27-68). Performance status (PS) were based on World Health Organization (WHO); 0 in 6 patients, 1 in 18 patients, and 2 in 5 patients. While histopathological samples were achived from brain (n=7), bone (n=7), lymphadenopathy (n=6), liver (n=4), lung (n=3), in one patient from soft tissue metastasis and in one patient from intraabdominal metastasis. In 17 patients (58.6%) had multmetastatic (more than two different sites) disease on the initial diagnosis. Brain metastasis was detected in 8 (27.6%) of all patients and they were treated with cranial radiotherapy. Liver metastasis was detected in 5 (17.2%) of all patients. Histopathological diagnoses were; well-moderate differantiated adenocarcinoma (n=15, 51.7%), undifferantiated carcinoma (n=8, 27.6%), SCC (n=4, 13.8%), mucoepidermoid carcinoma (n=1, 3.4%) and neuroendocrine differantiated cancer (n=1, 3.4%) (Table 1).

Twenty-nine patients who were treated with docetaxel and cisplatin combination at least one cycle as a first line setting of in the patients with CUP, median number of cycle was 3 (range: 1-6). There was no complete response. Although objective response rate (ORR) was 37.9% (n=11), clinical benefit was 58.6% (partial response (n=11), stable disease (n=6)). Median PFS and OS were detected 6 months (range: 4.3-7.7 months) and 16 months (range: 8.1-30.9 months) respectively (Figure 1, 2). Totally 14 patients (60.8%) were treated on second line setting; regimens were gemcitabine and its combination (n=7), oral etoposide (n=3) and others (n=3). There was no treatment related death and unexpected toxicity. Dose reduction and treatment discontinuation were performed in two patients because of serious toxicities. The treatment well tolerated in generally. Although most common toxicities were nausue-vomiting (n=13, 44.8%) and fatigue (n=9, 314%), serious toxicities (grade 3/4) were nausue-vomiting (n=3, 10.3%), neutropenia (n=4, 13.8%) and febrile neutropenia (n=1) (Table 2). In univariate log rank analysis, sex, age, PS and number of metastatic sites were no independent prognostic factors for PFS and OS (Table 3).

Discussion

CUP are heterogeneous group of disease that characterised poor prognosis and short treatment response duration. There is no clear standard treatment approach (Fizziangi et al., 2011; Pavlidis et al., 2012). Although RR and median OS were 10% and 4 months with single agent 5 fluorouracil, doublet regimen that contain third generation cytotoxic agents (taxane, gemcitabine) were achieved higher RR and one year OS 30-40% and 50% respectively.

References


National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. 2009.


