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Article title; Three cases of advanced cutaneous squamous cell carcinoma treated with a combination of carboplatin and epirubicin.

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TEXT

Dear Editor,

Advanced cutaneous squamous cell carcinoma (cSCC) with nodal and/or distal metastases or large local spreading is inoperable and treatment options for patients are limited usually to chemotherapy and radiation. The National Comprehensive Cancer Network (NCCN) Guidelines® include some regimens of cisplatin (CDDP)-based systemic therapies, but no chemotherapy has yet been established for advanced cSCC[1]. Peplomycin sulfate, bleomycin, and irinotecan are licensed for cSCC in Japan, but are not commonly used in actual clinical practice because of their low efficacy and severe side effects, such as interstitial pneumonia, myelosuppression, and adverse digestive symptoms. CA regimen, the combination of CDDP and adriamycin (ADM), has been reported to show a response rate of about 60% for advanced cSCC[2,3], whereas other regimens, such as CDDP plus 5-fluorouracil or CDDP plus cetuximab, have shown less than 20% response rate[4]. Suzuki et al.[3] and Nakamura et al.[5] previously reported a C'A' regimen, modified from CA regimen, using carboplatin (CBDCA) and epirubicin (EPI). This regimen is preferable for elderly and patients with underlying disorders, because it reduces nephrotoxicity of CDDP and cardiac toxicity of ADM[3]. Nevertheless, as the number of reported cases treated with this regimen remains scant, further validation is required. Here, we report three cases of advanced cSCC treated with the combination of CBDCA and EPI.

Clinical profiles of the patients are summarized in Table 1. They had a past history of burn scar, lichen sclerosus et atrophicus, and external injury, respectively. Patient case 3 was complicated with mild kidney failure. In all cases, primary cSCC lesions were surgically resected aiming for local control. The patients then received chemotherapies with an area under the curve (AUC) 5 dose of CBDCA and 60 mg/m^2 of EPI, because

of the high-risk characteristics of the primary lesions mentioned in the NCCN Guidelines®, such as potential of nodal metastases or distal metastases. As the tumor of case 2 transformed into a granulocyte colony-stimulating factor (G-CSF)-producing tumor and rapidly progressed shortly after the initial course of the chemotherapy, it was impossible for the patient to receive a second course. Patients in the other two cases received 4 courses of the regimen and their progression-free survival was 4 and 6 months, respectively. Neutropenia (over grade 3) was observed in every course in all cases.

Although the risk of nodal metastases and distal metastases in cSCC is relatively low, currently licensed cSCC chemotherapies and radiation therapy are unsatisfactory in terms of both efficacy and safety. Two out of three cases treated with C'A' regimen in this report achieved a progression-free period of several months without serious adverse events except for hematological toxicity. Notably, all three cases avoided death by C'A' regimen in spite of their poor Eastern Cooperative Oncology Group (ECOG)-Performance Status (PS) (from Score 2 to 3), suggesting a good tolerability of this regimen. Further documentation of cases of cSCC treated with C'A' regimen is warranted to establish this regimen as an option for the treatment of advanced cSCC.

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Table 1. Clinical profiles of the patients

Case No.	Age /Gender	Primary site	Stage	Prior therapy	Metastatic site at initial C'A' therapy	Best Response*	PFS (months)	OS from C'A' therapy (months)	Adverse event (Grade) **
1	64/M	Leg	III	surgical excision	none	PD	4	21	Gastric ulcer (G2) Neutropenia (G3)
2	64/F	Vulva	IV	surgical excision	LN	PD	0	2	Neutropenia (G4)
3	71/M	Leg	IV	surgical excision	LN, Lung	SD	6	10	Anemia (G3) Neutropenia (G4) Thrombopenia (G2)

PFS, progression-free survival; OS, overall survival; M, male; F, female; LN, lymph node(s); PD, progressive disease; SD, stable disease

* according to the Response Evaluation Criteria in Solid Tumours (RECIST) guideline version 1.1. (Eisenhauer E.A. et al. Eur J Cancer 45 (2009) 228-247)

** according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 5.0. (https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_50)