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Safety and efficacy of the combination chemotherapy consisting of S-1 and cisplatin (CDDP) on patients with advanced/recurrent head and neck cancer (HNC) (phase I/II study)

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Background: S-1 is an oral anticancer agent, contains tegafur (FT), gimeracil (CDHP) and oteracil potassium (Oxo). Response rate of S-1 for HNC is 28.8% as single agent treatment in phase II. In a preclinical study, and clinical study of other cancer, it has shown synergistic effects with CDDP. The purpose of this study was to determine the maximum tolerated dose (MTD) and recommend dose (RD) in the combination treatment with S-1 and CDDP (Phase I), and evaluate the efficacy and toxicity using defined RD (Phase II) for HNC patients.
Methods: Patients with histological or cytological diagnosis of advanced/recurrent HNC with evaluable lesions were eligible for this study. Other criteria; adequate organ function, Performance Status 0–1, age <80 years, and written informed consent. S-1 was administered orally at 40 mg/sqm twice a day for 14 consecutive days, and CDDP (Level.1–2: 60–70 mg/sqm, within approved dose in JPN) was infused over 2 hours on day 8. Each course was repeated every 3–4 weeks. Dose limiting toxicities (DLT) were determined as grade 4 hematological and grade 3 non-hematological.
Results: 10 patients for Phase I and additional 28 patients for Phase II were registered. Although DLT was not observed in Level 1 (n = 4), fatigue and diarrhea of grade 3 (DLT) occurred in Level 2 (DLT:2/6). MTD was not achieved in Phase I. Level 2 (70 mg/sqm of CDDP) was considered as RD for phase II. In 34 patients, administered 70 mg/sqm of CDDP in phase I and II, 16 patients were recurrent HNC. At the termination of treatment, response rate was 67.6% (7 complete response included). Confirmed responses with adequate duration time (d28) were 2 complete responses and 13 partial responses with an overall response rate of 44.1% (95% CI: 27.4–60.8). Hematological toxicities of grades 3 and 4 included neutropenia (11.8%), thrombocytopenia (11.8%) and anemia (8.8%). Non-hematological toxicity of grades 3 and 4 included anorexia (26.5%), nausea (14.7%), fatigue (8.8%) or diarrhea (2.9%). Since the observation period is short, the median survival time and the 1-year survival rate is not obtained so far. However, 1-year survival rate will be presented.
Conclusions: In HNC patients, S-1 plus CDDP combination chemotherapy demonstrated synergistic effects with acceptable toxicity. These results warrant further investigations of this regimen.

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Preliminary result of proton beam therapy for olfactory neuroblastoma

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Background: Olfactory neuroblastoma (ONB) is a rare disease, and standard treatment strategy has not been established. Radiation therapy for ONB is challenging because of its proximity to critical organs such as optic pathway and brain stem. Proton beam therapy (PBT) can provide better dose distribution compared to X-ray irradiation because of its physical characteristics. We retrospectively reviewed our experience to analyze the feasibility and efficacy of PBT for ONB.
Materials and Methods: From November 1999 to April 2004, 13 patients with Kadish stage A-C disease underwent PBT for ONB. There were 4 men and 9 women, with median age of 56 years (range, 29–84). PBT was done using 150–190 MeV of proton beam of which the relative biologic effectiveness was estimated as 1.1. The optimization of dose distribution was performed with spread-out Bragg peak method. Neck dissection was performed for patients with node positive disease. Adverse events were assessed according to the RTOG/EORTC acute and late radiation morbidity scoring criteria. Survival was estimated by the Kaplan-Meier method.
Results: Median follow-up period was 32 months (10–61 months). A total dose of PBT was 65 cobalt Gray equivalent (GyE) with 2.5 GyE once daily fractionation (4 to 5 fractions per week). Four patients were treated with PBT alone, 4 received prior chemotherapy, and 5 underwent volume reduction surgery prior to PBT. All patients completed PBT as planned without interruptions. One patient died from disseminated disease. Two local recurrences were observed, one of which was salvaged surgically. Three year overall survival rate was 92% (95% CI, 76–100%), and 3-year local progression free survival rate was 82% (95% CI, 59–100%). In one patient with Kadish C disease (destroying skull base), liquorrhea was observed after shrinkage of tumor. Otherwise no late adverse events of ⩾Grade 3 had been observed including cataract, visual impairment, brain necrosis, and brain stem damage.
Conclusions: Our preliminary results of PBT for ONB showed excellent local control and survival outcomes, without serious adverse events. PBT is deemed to be a preferable treatment modality, although further accumulation of patients and longer follow-up is required.

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Pre-operative radiation therapy combined with super selective intra-arterial infusion chemotherapy for head and neck cancers

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Purpose: To report the results of pre-operative radiation therapy combined with super selective intra-arterial infusion chemotherapy for patients with head and neck cancers.
Material and Method: From March 2002 to August 2004, pre-operative radiation therapy combined with super selective intra-arterial chemotherapy was performed for head and neck cancers in 26 patients (18 male, 8 female patients, 29–74 years old). 15 maxillary sinus carcinomas, 4 tongue carcinomas, and 7 oropharyngeal carcinomas were treated. Histropathology revealed 21 squamous cell carcinomas, 3 adenoid cystic carcinomas, 1 mucoepidermoid carcinoma, and 1 neuroendocrine tumor. CDDP (50–100 mg/body) was administered weekly by super selective intra-arterial infusion into tumor vessels for 4 weeks via a transfemoral approach by the Seldinger technique. Radiation therapy delivered was 40 Gy (2 Gy per day) in 4weeks with 4 or 6 MV X-ray.
Result: 21 patients (80.8%) completed this treatment regimen. Treatment was stopped or interrupted in 5 patients due to bone marrow suppression (1/5), stomatitis (1/5), allergic reaction to contrast medium (1/5), and vasospasm (1/5). The radiographically response rate was 92.3% (complete response; 11/26, partial response; 13/26). Surgical operation was performed in 12 patients, and histopathrogical complete response rate was 75.0% (9/12). Grade 3 or 4 toxic events were noted in 12 patients (included 4 hematologic toxicities, and 10 mucositis). 3 patients with Grade4 hematological toxicity were noted in the following 3 patients. One had liver cirrhosis, one received 400 mg CDDP intra-arterial infusion, and one received systemic chemotherapy for esophageal carcinoma. There were no catheter-related complications.
Conclusion: Pre-operative radiation therapy combined with super selective intra-arterial infusion chemotherapy for head and neck cancers showed good efficacy in our study. Further investigations should be carried out with larger series to evaluate long-term survival rate with this treatment.

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Are reoperations effective in biochemical palliation of persistent and recurrent hyperparathyroidism in patients with parathyroid carcinoma?

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Background: Parathyroid Carcinoma (PC) is a rare functioning neoplasm, accounting for 1% to 5% of cases of primary hyperparathyroidism (PHPT). To date, surgery is the only effective treatment. However, in spite of apparent radical resection, recurrences occur in most of case. Since the main cause of death in these patients is usually represented by the metabolic complications of hypercalcemia rather than local tumor invasion or distant, reoperations are often required to take hypercalcemia under control and possibly improve the prognosis.
Patients and Methods: Six out of 19 patients (12 men and 7 women, median age 65 years, range 30–78 years) with confirmed PC underwent one or more reoperations because of persistent or recurrent PHPT. After each operation, the relative efficacy to reduce serum calcium and PTH levels was analysed and compared.