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POSTER

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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POSTER

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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POSTER

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. Histopathology 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 4 weeks 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 histopathological 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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POSTER

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.

Results: Repeated surgery never achieved a definitive cure, and a temporary biochemical remission (5 months) occurred only in 1 case. Initial surgery significant reduced calcemia ($36 \pm 5.9\%$) and PTH levels ($79.7 \pm 13.5\%$, $p < 0.05$), although all patients persisted or recurred. In case of repeated surgery, the first and second reoperations significantly reduced serum calcium ($22.4 \pm 6\%$ and $13.7 \pm 3\%$, respectively) and PTH levels ($80.5 \pm 6\%$ and $69 \pm 7\%$, respectively; $p < 0.05$), but the reduction became not statistically significant ($P = NS$) after the second reoperation. The first reoperation was less effective in reducing the serum calcium levels than initial surgery ($p = 0.005$), while no differences were found for PTH levels ($p = 0.91$). The second reoperations were progressively less effective in reducing both calcemia and PTH levels ($p = 0.03$ and 0.04 , respectively), while no difference were found between further operations.

Conclusions: Repeated surgery is effective to achieve significant biochemical palliation; although it is never followed by definitive cure. Initial surgery achieve the best results, because reoperations became progressively less effective. For these reasons, in case of recurrent PC, the use of other adjuvant treatment (calcimimetic agents) should be considered in addition to repeated surgery.

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POSTER

The treatment result of hypopharyngeal cancer

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Introduction: To evaluate the treatment result of hypopharyngeal cancer and find the prognostic factors.

Material and Patients: There were 430 hypopharyngeal cancer received treatment in Chang Gung Memorial Hospital from January 1994 to May 2004. Four hundred and seventeen (96%) patients are male and the median age is 56 ranging from 15 to 87. The majority (88%) of patients had habits of smoking, 73% of patients alcohol drinking and 51% of patients had betel quid chewing. The stage distribution is stage I: 4(0.9%), stage II: 20(4.7%), stage III: 57(13.3%) and stage IV: 349(81.2%). Thirty five patients refused radical treatment so there were 395 patients entering analysis. Eight one (20.5%) patients received radical surgery and the others (79.5%) received organ preservation treatment.

In organ preservation patients, 46 patients received radiotherapy alone; 156 patients received chemotherapy then radiotherapy and 112 patients received concomitant chemoradiotherapy.

Result: The 5-year disease specific survival for stage I, II, III and IV were 67%, 74%, 44% and 20% respectively ($p = 0.000$). Patients received radical surgery first or organ preservation treatment did not have significant difference in disease specific survival. The 5-year survival for radical surgery and organ preservation are 31% and 34% respectively. Patients who received concomitant chemoradiotherapy had 61% of chance for organ preservation but only 52% for those patients who received induction chemotherapy.

Discussion: The majority of hypopharyngeal cancer is stage IV disease. There was no survival difference between organ preservation and radical surgery. It may hint that organ preservation may be considered for hypopharyngeal cancer patients.

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POSTER

Management of medullary thyroid carcinoma

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Aim: To establish the optimal treatment modality for Medullary thyroid carcinoma.

Material and Methods: 182 patients have been treated for Medullary Thyroid Carcinoma at the NNBRCC. 142 out of them were followed-up for 5 years and more. As per the TNM the patients had the following stages of disease: T₁N₀M₀ – 7, T₂N₀M₀ – 13, T₃N₀M₀ – 19, T₀N₁M₀ – 4, T₁N₁M₀ – 11, T₂N₁M₀ – 13, T₂N₁M₁ – 2, T₃N₁M₀ – 47, T₃N₁M₁ – 20, T₄N₁M₀ – 9, T₄N₁M₁ – 19, T₃₋₄N₁M₁ – 8.

The results of treatment of patients with regional metastases were analyzed. 69 patients underwent surgical treatment. Combined treatment including surgery + pre- or post-operative radiotherapy of 40 to 70 Gy was administered to 65 patients. Palliative radiotherapy was administered in 36 patients having inoperable disease. Chemotherapy was administered in 18 patients. Chemotherapy included different combinations of adriablastin, bleomycin, cyclophosphamide and cisplatin. At least two cycles of treatment was given to each patient.

Results: In the group of patients who underwent surgery alone, 60.9% are alive for five or more years; combined treatment with preoperative

radiotherapy – 61.5%; combined treatment with postoperative radiotherapy – 57.7%. The difference between these figures are statistically non-significant. In the group of patients who were border-line operable, this figure was 28.2%. Palliative effect was attained in 11% cases. Only one patient responded to chemotherapy.

Conclusions: Surgery is still the main modality of treatment of medullary thyroid cancer. Radiotherapy has restricted indications namely border-line operable cases – established microscopically or macroscopically or palliative and symptomatic treatment of inoperable forms of tumor spread like bone metastases. Chemotherapy is so far a tertiary option and new drugs and/or new combinations are needed to be tested.

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POSTER

Effect of zinc on improving mucositis and dermatitis caused by radiotherapy of head and neck cancer – results of randomized study

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Purpose: Zinc is known to be very important in the context of metabolic response to injury and wound healing. If zinc can improve the healing of mucositis and dermatitis, patients will be more willing to complete the treatment course, and hopefully, the survival rate will increase.

Materials and methods: Oral zinc adopted in this study was Pro-Z, extracted from bovine prostate, containing amino acid chelated zinc. A double-blind, randomized, placebo-controlled study processed from Jan. 2003 to Aug. 2004. Ninety-seven patients with head and neck cancers received radiotherapy and were enrolled in this study. Among them, 49 patients took 3 capsules of Pro-Z per day during the entire course of radiotherapy while the other 48 patients took 3 capsules of placebo per day.

Results: Patients of both groups are similar in gender, age, body weight, pre-treatment serum zinc, pre-treatment serum transferrin. Tumor characteristics such as tumor type, pathology, recurrence and stage are comparable in both groups. About the treatment of both groups, the details are similar also. The patients of placebo arm suffered from grade 2 mucositis and grade 2 dermatitis earlier than those of Pro-Z arm ($p = 0.017$ and 0.014 , respectively). Between patients of those 2 groups, there was also significant difference in the development of grade 3 mucositis ($p = 0.003$) and grade 3 dermatitis ($p = 0.0092$). The mucositis and dermatitis were milder on patients of Pro-Z arm (both $p = 0.003$). Though the milder mucositis and dermatitis, patients of Pro-Z arm were unable to receive more courses of weekly concurrent chemotherapy than those of placebo arm ($p = 0.46$). The weight loss among both groups was similar ($p = 0.44$). The common side effects of zinc, such as gastrointestinal discomfort, did not occur in all the patients.

Conclusion: During the period of radiotherapy, severe mucositis and dermatitis developed later and milder on patients with zinc supplement than on those without zinc. However, the weight loss and courses of weekly concurrent chemoradiotherapy were not different significantly between patients who took Pro-Z and those who didn't. In this randomized study, Pro-Z is promising in the improvement of radiation mucositis and dermatitis. But its impact on treatment results such as local control and overall survival is under further investigated.

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POSTER

Submandibular gland sparing using intensity modulated radiotherapy (IMRT) for head and neck cancer: Effect on the basal saliva flow and clinical symptoms of xerostomia

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Background: We evaluated the effect of submandibular gland sparing achieved by intensity modulated radiotherapy (IMRT) on the basal salivary flow rate and the symptoms of xerostomia at 6 and 12 months following completion of radiation therapy for head and neck cancer.

Methods: 35 patients with head and neck cancer were treated with IMRT between July 2000 and April 2004. The mean age at study entry was 53 years (range, 29 to 78), and 17 were male. Patients were required to have normal salivary gland function at study entry. Eight patients had nasopharyngeal and 27 oropharyngeal cancer. Five patients had stage II, 5 stage III, 22 stage IVA, and 3 stage IVB tumor at presentation. Nineteen patients received postoperative RT and 16 definitive chemo-

RT with concurrent cisplatin, either 40 mg/m² once weekly ($n = 9$) or 100 mg/m² ($n = 7$) on days 1, 22 and 42 of the radiation course. All patients received a minimum total dose of 50 Gy with 2 Gy daily fractions to the primary tumor site and the locoregional lymph nodes (PTV1),