A Novel Concurrent Chemoradiotherapy with TS-1/Nedaplatin for Esophageal Cancer Showing Better Quality of Life During Treatment

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Abstract

Concurrent chemoradiotherapy (CRT) for esophageal cancer is expected to achieve adequate quality of life (QOL) and to improve the survival of patients. As a QOL-oriented therapy for esophageal cancer, concurrent CRT with TS-1/nedaplatin (CDGP) was developed and evaluated.

Between June 2001 and September 2002, 18 patients with esophageal cancer were enrolled in a clinical study of concurrent CRT with TS-1/CDGP. To evaluate the impact of treatment on the QOL, the patients were asked to answer QOL Questionnaire for Cancer Patients Treated with Anticancer Drugs (QOL-ACD) before and after therapy.

The response rate was 66.7%, with a complete response occurring in 9 (50.0%) of the 18 patients.

Patients with improved global, functional, or mental QOL after therapy showed or tended to show a significant, longer survival. Compared to patients previously treated by the same regimen with 5-FU instead of TS-1, those receiving the present therapy were able to leave hospital more frequently during treatment. TS-1/CDGP-based CRT for esophageal cancer exhibited comparable antitumor activity and survival benefit as with standard 5-FU/CDDP-based CRT without causing serious side-effects. The patients receiving the present therapy seemed to have a better chance of maintaining their QOL.

Key words

Esophageal cancer, TS-1, nedaplatin, Chemoradiotherapy, QOL

Introduction

Concurrent chemoradiotherapy (CRT) for esophageal cancer has been usually based on cisplatin (CDDP) as the key drug, and CDDP/5-fluorouracil (5-FU) remains the most common chemotherapy regimen for concurrent CRT based on the concepts of biochemical modulation and radiosensitization.\(^3\)\(^4\)

Nedaplatin (CDGP) is a derivative of CDDP with far less nephrotoxicity and gastrointestinal toxicity and it has been reported to achieve a better response as a monotherapy for esophageal cancer (objective response rate: 51.7%).\(^5\) Since 1999, we have used concurrent CRT with 5-FU/CDGP to treat a few patients with esophageal cancer and have obtained a good outcome.\(^6\) We also found that all toxicities of this therapy resolved spontaneously with dose omission or could be counteracted by standard treatments. However, 5-FU must be administered by continuous infusion over several days, which limits a patient’s activity and impairs the quality of life (QOL) during treatment. TS-1 is an oral anticancer agent that is composed of tegafur, the prodrug of 5-FU, plus two modulators (gimestat and otastat potassium),\(^7\)\(^8\) and it has been...
designed to provide prolonged tumor exposure to 5-FU with only moderate toxicity. With the aim of establishing a CRT regimen to improve the QOL of patients with esophageal cancer, we devised a CRT protocol using TS-1/CDGP and initiated clinical evaluation in June 2001. As we observed improvement in the QOL through our pilot study, we increased the number of patients and conducted a detailed statistical analysis. This report presents the therapeutic outcome in the initial 18 patients treated with TS-1/CDGP-based CRT, including the effect on QOL evaluated using the QOL Questionnaire for Cancer Patients Treated with Anticancer Drugs (QOL-ACD).10-11

This therapy demonstrated a similar antitumor activity to the standard 5-FU/CDDP-based CRT for esophageal cancer. During treatment with this regimen, the patients seemed to have a better chance of maintaining their QOL.

QOL scores may be correlated with survival and/or tumor response and may be of prognostic significance in patients with esophageal cancer undergoing CRT.

Materials and Methods

1. Eligibility criteria

Between June 2001 and September 2002, 18 patients with esophageal cancer were enrolled in a clinical study of concurrent CRT with TS-1/CDGP.

Men and women aged between 20 and 79 years who were inpatients with histologically or cytologically proven esophageal cancer were eligible for TS-1/CDGP-based concurrent CRT. The conduct of and protocols for study were approved by the institutional review board and all participating patients gave their informed consent. Other eligibility requirements included the absence of any carry-over toxicity of previous therapy, a projected life expectancy ≥3 months, and baseline data obtained within 2 weeks before entry indicating the following: i) the presence of a measurable or evaluable lesion on endoscopy, barium esophagography, or computed tomography; ii) a performance status (PS) ≤2 according to Zubrod criteria; iii) adequate hematological function with a hemoglobin ≥9.0 g/dL, a white cell count of 3,000–12,000/mm³, a neutrophil count of ≥1,500/mm³, and a platelet count of ≥80,000/mm³; and iv) adequate hepatic and renal function with a total bilirubin <3 mg/dL, aspartate transaminase alanine transaminase <100 IU/L, and serum creatinine not greater than the upper limit of normal.

2. Methods

1) Chemotherapy

This clinical study was started at 80~100 mg/day of TS-1 plus 5~6 mg/m²/day of CDGP. TS-1/CDGP was given 5 days per week for a 2- or 4-week course, and 1 or 2 courses were administered every 4 weeks. CDGP was infused in 1.5~2h.

2) Radiotherapy

Radiotherapy was initiated on day 1 and was performed 5 days a week. Antero-posterior portals encompassing the primary tumor with a 5-cm margin as well as the regional and any other radio graphically visible lymph nodes were used to deliver 1.8~2.0 Gy daily to a total dose of about 40 Gy. Based on the tumor size and response, two oblique portals limited to the tumor volume were used to deliver an off-cord boost of about 20 Gy in 2.0-Gy daily fractions on 5 days per week.

3) Evaluation of response and toxicity

Tumor response was rated according to the Response Evaluation Criteria in Solid Tumors (RECIST).12 The objective response rate (the percentage of patients with a complete or partial response) was determined. Survival time was measured from the start of treatment and the survival rate was estimated by the Kaplan-Meier method.

Toxicities were assessed and graded according to the Japan Clinical Oncology Group (JCOG) toxicity criteria,13 which are similar to the National Cancer Institute Common Toxicity Criteria (NCI-CTC).

4) Evaluation of the influence of QOL on prognosis

Before the start and after completion of CRT, the patients were asked to complete the QOL-ACD10-11 (Fig. 1). The QOL-ACD assesses four domains of QOL (functional, physical, mental and psychosocial domains, which are covered by Questions 1~6, 7~11, 12~16, and 17~21, respectively) together with the global quality of life (using a “face” scale, Question 22). Each question was scored from 1 point (worst) to 5 points (best). Using the 22 individual score obtained before and after CRT, total QOL score as well as sub-total scores for each of the 4 QOL domains were calculated.

Cox regression and logistic regression models that included survival time (in days) and the tumor response (categorized as “response” and “no response”) as response variable and global or domain QOL scores as explanatory variable were used to determine whether any QOL score influenced on
QOL-ACD
This questionnaire will help us understand your current condition. Please circle the number that best describe your condition in the past few days. (This information will remain strictly confidential and will not in any way affect your therapy. Please answer exactly the way you feel.)

1. How much were you able to accomplish your daily activity?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Fully accomplished

2. How often were you able to go out without help?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Fully accomplished

3. Were you able to take a half hour walk?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Without any problem

4. Did you feel any difficulty walking even a short distance?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Very much

5. Were you able to walk up and down the stairs?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Very much

6. Were you able to take a bath by yourself?
   - 1: Not at all
   - 2: A little
   - 3: Moderately
   - 4: Mostly
   - 5: Yes without any help

7. How well did you feel?
   - 1: Very poor
   - 2: Poor
   - 3: Slightly poor
   - 4: Slightly well
   - 5: Very well

8. Did you have a good appetite?
   - 1: Very much
   - 2: Much
   - 3: Slightly
   - 4: Slightly less
   - 5: Very much less

9. Did you enjoy your meals?
   - 1: Very much
   - 2: Much
   - 3: Slightly
   - 4: Slightly less
   - 5: Very much less

10. Did you experience any vomiting?
    - 1: None
    - 2: Very slight
    - 3: Slight
    - 4: Moderate
    - 5: Very much

11. Did you lose any weight?
    - 1: No
    - 2: Very little
    - 3: Little
    - 4: Moderate
    - 5: Very much

12. Did you sleep well?
    - 1: Yes
    - 2: No

13. Were you able to devote yourself on (become enthusiastic about) something?
    - 1: Very well
    - 2: Slightly well
    - 3: Poorly
    - 4: No

14. How well were you able to deal with your stress?
    - 1: Very well
    - 2: Slightly well
    - 3: Poorly
    - 4: No

15. Did you feel you could not concentrate on something?
    - 1: No
    - 2: Very little
    - 3: Little
    - 4: Moderate
    - 5: Very much

16. Did you get any encouragement from something/somebody you believe/trust (e.g. family, friends, religion, hobby)?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

17. Did you worry about your disease?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

18. Did you have any problem dealing with people outside your family?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

19. Did you think your family was troubled by your getting treatment?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

20. Do you worry about your social life in the future?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

21. How much do you worry about your financial problem caused by your treatment?
    - 1: Very much
    - 2: Slightly
    - 3: Very little
    - 4: No

22. Please circle the number of the face that best fits your feelings in the past few days?

   ![Faces](image_url)

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Fig. 1. QOL Questionnaire For Cancer Patients Treated With Anticancer Drugs.
survival time and tumor response, respectively. In the respective models, the relationship was evaluated in terms of adjusted hazard ratio (HR) and odds ratio (OR). In both models, separate analyses were performed using the pre-CRT score and the pre-CRT to post-CRT change of the score as the explanatory variable.

First, we evaluated the influence of each of the 4 QOL domains using the model having one explanatory variable, separately (univariate analysis). Then, we evaluated the effect of each of the 4 QOL domains using the model having the 4 QOL domains simultaneously as explanatory variables (multivariate analysis).

The influence of demographic and clinical parameters on survival time and tumor response was also evaluated with the Cox and logistic regression analysis, respectively. The demographic and clinical parameters used were age and clinical stage at enrollment, as well as albumin (ALB), cholinesterase (CHE), squamous cell carcinoma related antigen (SCC), cytokeratin 19 (CYFRA), and body weight at enrollment and the changes of these parameters after treatment.

The number of days that each patient could take leave from hospital during concurrent CRT was compared by Welch’s t-test between patients treated with TS-1/CDGP-based CRT in the present studies and patients previously treated with 5-FU/CDGP-based CRT.

In all the tests, significance level was set at 0.05 for convenience. However, considering the small sample size and the observational nature of the study, in case p values between 0.05 and 0.10 are obtained we used expressions, such as “rather significant” or “slightly better” as appropriate.

Results

1. Clinical profile

All 18 patients were men and their mean age was 60.4 years (range: 43–77 years). The PS was 0 in 8 patients and 1 in 10 patients. One patient had non-small-cell carcinoma, while the histological diagnosis was squamous cell carcinoma with varying degrees of differentiation in the other 17 patients (1 well differentiated, 11 moderately differentiated, 4 poorly differentiated, and 1 moderately/poorly differentiated carcinoma). The primary tumor was located in the upper thoracic esophagus in 4 patients, the middle thoracic esophagus in 9 patients, and the lower thoracic esophagus in 5 patients.

According to the International Union Against Cancer (UICC) TNM classification,14 4, 2, 10, and 2 of the patients, had T1, T2, T3, and T4 tumors, respectively, with N1 disease in 11 patients, M1a in 2 patients, and M1b in 4 patients. There were 3 patients with stage I disease, 3 with stage IIA disease, 2 with stage IIB disease, 3 with stage III disease, 3 with stage IV A disease, and 4 with stage IV B disease. (Table 1)

2. Tumor response and survival

All of the patients enrolled received the full scheduled doses of chemotherapy and were assessable for response. Among these patients, 9 (50.0%) achieved a complete response (CR) and 3 achieved a partial response (PR), for an overall response rate of 66.7%. The remaining 6 patients showed progressive disease (PD). The breakdown of response was as follows: 10 CRs (55.6%), 6 incomplete responses (IRs), and 2 PDs for the primary tumor; 4 CRs, 2 PRs, 2 stable diseases (SDs), and 3 PDs for posi-

Table 1. Patient and Tumor Characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>60.4</td>
</tr>
<tr>
<td>Range</td>
<td>43-77</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18(100%)</td>
</tr>
<tr>
<td>Female</td>
<td>0(0%)</td>
</tr>
<tr>
<td>WHO performance status</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>8(44.4%)</td>
</tr>
<tr>
<td>1</td>
<td>10(55.6%)</td>
</tr>
<tr>
<td>2</td>
<td>0(0%)</td>
</tr>
<tr>
<td>UICC TNM stage</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>4(22.2%)</td>
</tr>
<tr>
<td>T2</td>
<td>2(11.1%)</td>
</tr>
<tr>
<td>T3</td>
<td>10(55.6%)</td>
</tr>
<tr>
<td>T4</td>
<td>2(11.1%)</td>
</tr>
<tr>
<td>NO</td>
<td>78(38.9%)</td>
</tr>
<tr>
<td>N1</td>
<td>11(61.1%)</td>
</tr>
<tr>
<td>Distant metastasis</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>2</td>
</tr>
<tr>
<td>Liver</td>
<td>2</td>
</tr>
<tr>
<td>Cervical node</td>
<td>3</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Thoracic-upper</td>
<td>4(22.2%)</td>
</tr>
<tr>
<td>Thoracic-middle</td>
<td>9(50.0%)</td>
</tr>
<tr>
<td>Thoracic-lower</td>
<td>9(27.8%)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>17(94.4%)</td>
</tr>
<tr>
<td>Undifferentiated carcinoma</td>
<td>1(5.6%)</td>
</tr>
<tr>
<td>WHO: World Health Organization, UICC: International Union Against Cancer</td>
<td></td>
</tr>
</tbody>
</table>
tive lymph nodes (≥1 cm on radiograph); and 1 SD and 5 PDs for distant metastases. (Table 2) After a mean follow-up period of 539.2 days, the 1-year survival rate and the median survival time were estimated to be 61.1% and 433 days, respectively (Fig. 2).

3. Toxicity

The toxicities observed were leukopenia (n=18), neutropenia (n=16), thrombocytopenia (n=17), anemia (n=13), fever ≥38°C (n=3), esophagitis (n=8), and radiation pneumonitis (n=10) (Table 3). The incidence of grade 3 or 4 hematological toxicity was 61.1% (n=11) for leukopenia, 55.6% (n=10) for neutropenia, 44.4% (n=8) for thrombocytopenia, and 25.0% (n=4) for anemia. Non-hematological toxicities were grade 1 in all patients. All toxicities resolved after dose omission or standard treatment such as medicine of granulocyte-colony stimulating factor(G-CSF), blood transfusion, antibiotics.

4. Evaluation of influence of QOL on prognosis

Among the 18 patients, 15 completed the QOL-ACD before and after concurrent CRT. The analyses of QOL scores were performed for the 15 patients. More than half of the patients (53.3% [8/15]) had an unchanged or improved total QOL score after treatment. Table 4 shows a summary of statistics of QOL scores before and after treatment.

1) Relationship between QOL and survival

1. Pre-CRT QOL

We examined whether survival was influenced by pre-CRT QOL (Table 5-a, 5-b).

Univariate analysis showed no significant influence of the pre-CRT QOL of the 4 domains and global QOL on survival. In multivariate analysis, it was suggested that the patients with higher functional QOL score before CRT had insignificant, but slightly worse prognosis (adjusted HR 1.226 [95% CI, 0.966–1.556]; p=0.0938).

2. Change of QOL score attributable to CRT

Tables 6-a, 6-b show the results of analysis examining the relationship between changes of the QOL scores and survival time.

The changes of total and functional QOL scores were of significant predictive value in the respective univariate analysis (adjusted HRs were 0.951 and 0.855 and corresponding p-values were 0.0271 and 0.0312, respectively). While, multivariate analysis showed significant and rather significant relationship with survival time for the

![Fig. 2. Survival of patients with esophageal cancer. After a mean follow-up period of 539.2 days, the 1-year survival rate was estimated to be 61.1%, respectively (n=18)](image-url)
change of the functional QOL score (adjusted HR 0.748; p=0.0174) and that of the mental QOL score (adjusted HR 0.735; p=0.0802). The HRs suggest that the patients with an increased global, functional, or mental QOL score after CRT had a longer survival time.

2) Relationship between QOL and tumor response

Pre-CRT QOL

We examined whether tumor response was influenced by the pre-CRT QOL.

In univariate analysis, the patients with higher psychosocial QOL score tended to show better tumor response to treatment (OR 1.412; p=0.0728).

Change of QOL attributable to CRT

Changes of the QOL score showed no significant relationship with the tumor response.

3) Relationship between clinical predictors and survival

Table 4 also shows a summary of the age and clinical stage at enrollment as well as data on several clinical parameters (ALB, CHE, SCC, CYFRA, and body weight) obtained before and after treatment.

Table 5-a. Effect of Pre-CRT Score on Prognosis (Univariate Analysis)

Table 5-b. Effect of Pre-CRT Score on Prognosis (Multivariate Analysis)

We tried to find out whether survival was influenced by age, clinical stage, or other clinical factors before CRT. As a result, the clinical stage was the only significant predictor of survival (HR 2.110, p=0.0171 in univariate analysis) (Table 5-a, 5-b).

Change attributable to CRT

Similar regression analyses failed to identify any parameter for which the change was significantly related to survival.

4) Relationship between clinical predictors and tumor response

Pre-CRT variables

We tried to find out whether the tumor response to CRT was influenced by the patient’s age, clinical stage, or other clinical factors before CRT. As a result, age was the only parameter showing a tendency to be significant predictor of the tumor response to CRT (OR 1.165, p=0.0747 in univariate analysis) (Table 7).

Change attributable to CRT

Similar regression analyses failed to identify any parameter for which the change was significantly related to survival.

Table 4. A summary of QOL data

Table 5-a. Effect of Pre-CRT Score on Prognosis (Univariate Analysis)

Table 5-b. Effect of Pre-CRT Score on Prognosis (Multivariate Analysis)
any parameter for which the change was significantly related to the tumor response.

5) Leave during treatment

A retrospective comparison between the 18 patients treated with TS-1/CDGP-based CRT and 18 age-matched (p=0.0512) historical controls who received 5-FU/CDGP-based CRT showed that the TS-1 containing regimen allowed patients to leave the hospital on significantly more days during treatment (mean: 8.1 days [range 0–20 days] vs. 1.2 days [range 0–12 days]; p=0.0003).

Discussion

In an early phase II study on head and neck cancer,15 TS-1 monotherapy achieved a high response rate (45.8%) of squamous cell carcinoma and was active against primary as well as metastatic tumors; 50% of positive cervical lymph nodes showed an objective response and partial response of a hepatic metastasis was obtained in 1 patient.

Recently, a combination of CDDP with TS-1 instead of 5-FU has been shown to be effective for the treatment of gastric cancer.16–19 Koizumi et al.20 Reported that during phase I/II studies, TS-1/CDDP combination achieved an overall response rate of 74% in patients with gastric cancer. These findings suggested that combining TS-1 with a platinum compound could enhance antitumor activity due to biochemical modulation.

The primary toxicity of TS-1/CDGP-based CRT was myelosuppression, which tended to be slightly more severe than that due to 5-FU/CDDP-based CRT. However, all hematological toxicity resolved after dose omission or standard treatment. With the exception of grade 1 anorexia in 1 patient, no gastrointestinal toxicity occurred during treatment with TS-1/CDGP-based CRT and the other non-hematological toxicities were relatively modest.

Five reports21–25 documented the use of TS-1 combined with radiation for the treatment of esophageal cancer. However, clinical studies have never been conducted on TS-1 and CDGP-containing CRT for esophageal cancer.

According to the report by Ishikura et al.,26 the patients with clinical stage I to IVA without T4 disease using 5-FU/CDDP-based CRT for the esophageal cancer showed CR of 69%.

The present clinical study demonstrated that TS-1/CDGP-based CRT had a comparable efficacy against esophageal cancer to standard 5-FU/CDDP-based CRT with acceptable toxicity.

Many different tools and questionnaires have been developed to assess the QOL of cancer patients. The questionnaires widely used in Europe and the USA include the Functional Living Index for Cancer (FLIC),27 the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30,28,29 and the Functional Assessment of Cancer Therapy (FACTS).30 The QOL-ACD10–11 that adapts the FLIC and EORTC QLQ-C30 to

Table 6-a. Effect of Amount of Change on Prognosis (Univariate Analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Hazard Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (FLIC)</td>
<td>Functional</td>
<td>0.955</td>
<td>0.741</td>
<td>1.260</td>
<td>0.6912</td>
</tr>
<tr>
<td>Physical</td>
<td>0.910</td>
<td>0.769</td>
<td>1.051</td>
<td>0.6088</td>
<td></td>
</tr>
<tr>
<td>Mental</td>
<td>0.980</td>
<td>0.859</td>
<td>1.108</td>
<td>0.5300</td>
<td></td>
</tr>
<tr>
<td>Psychosocial</td>
<td>0.986</td>
<td>0.886</td>
<td>1.103</td>
<td>0.5867</td>
<td></td>
</tr>
<tr>
<td>Total (FLIC)</td>
<td>1.049</td>
<td>0.897</td>
<td>1.214</td>
<td>0.6258</td>
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</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Hazard Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (EORTC)</td>
<td>Face</td>
<td>2.797</td>
<td>1.249</td>
<td>5.463</td>
<td>0.0121</td>
</tr>
<tr>
<td>Total (EORTC)</td>
<td>2.052</td>
<td>1.203</td>
<td>3.444</td>
<td>0.0471</td>
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</tbody>
</table>

Table 6-b. Effect of Amount of Change on Prognosis (Multivariate Analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Hazard Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (FLIC)</td>
<td>Functional</td>
<td>0.746</td>
<td>0.588</td>
<td>0.950</td>
<td>0.0174</td>
</tr>
<tr>
<td>Physical</td>
<td>1.133</td>
<td>0.922</td>
<td>1.343</td>
<td>0.2648</td>
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<tr>
<td>Mental</td>
<td>0.705</td>
<td>0.521</td>
<td>0.938</td>
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<tr>
<td>Psychosocial</td>
<td>1.230</td>
<td>0.943</td>
<td>1.628</td>
<td>0.1212</td>
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<th>Hazard Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (EORTC)</td>
<td>Face</td>
<td>2.023</td>
<td>0.820</td>
<td>5.000</td>
<td>0.1261</td>
</tr>
<tr>
<td>Total (EORTC)</td>
<td>1.038</td>
<td>0.553</td>
<td>1.992</td>
<td>0.3715</td>
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</tbody>
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Table 7. Effect of Pre-CRT Score on Response Rate (Univariate Analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Odds Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (FLIC)</td>
<td>Functional</td>
<td>0.946</td>
<td>0.805</td>
<td>1.119</td>
<td>0.3204</td>
</tr>
<tr>
<td>Physical</td>
<td>1.014</td>
<td>0.783</td>
<td>1.304</td>
<td>0.9228</td>
<td></td>
</tr>
<tr>
<td>Mental</td>
<td>1.023</td>
<td>0.795</td>
<td>1.308</td>
<td>0.8712</td>
<td></td>
</tr>
<tr>
<td>Psychosocial</td>
<td>1.112</td>
<td>0.882</td>
<td>1.373</td>
<td>0.6762</td>
<td></td>
</tr>
<tr>
<td>Total (FLIC)</td>
<td>1.023</td>
<td>0.734</td>
<td>1.434</td>
<td>0.2512</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Odds Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (EORTC)</td>
<td>Face</td>
<td>2.257</td>
<td>1.051</td>
<td>4.862</td>
<td>0.0164</td>
</tr>
<tr>
<td>Total (EORTC)</td>
<td>1.073</td>
<td>0.583</td>
<td>1.127</td>
<td>0.9462</td>
<td></td>
</tr>
</tbody>
</table>

Table 7. Effect of Pre-CRT Score on Response Rate (Multivariate Analysis)

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Odds Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (FLIC)</td>
<td>Functional</td>
<td>0.951</td>
<td>0.802</td>
<td>1.135</td>
<td>0.2847</td>
</tr>
<tr>
<td>Physical</td>
<td>1.004</td>
<td>0.893</td>
<td>1.121</td>
<td>0.9419</td>
<td></td>
</tr>
<tr>
<td>Mental</td>
<td>1.059</td>
<td>0.825</td>
<td>1.361</td>
<td>0.4745</td>
<td></td>
</tr>
<tr>
<td>Psychosocial</td>
<td>0.973</td>
<td>0.854</td>
<td>1.046</td>
<td>0.8010</td>
<td></td>
</tr>
<tr>
<td>Total (FLIC)</td>
<td>1.044</td>
<td>0.823</td>
<td>1.300</td>
<td>0.4213</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>% Confidence Interval</th>
<th>Odds Ratio</th>
<th>Lower</th>
<th>Upper</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL (EORTC)</td>
<td>Face</td>
<td>2.257</td>
<td>1.051</td>
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<td>0.0164</td>
</tr>
<tr>
<td>Total (EORTC)</td>
<td>1.250</td>
<td>0.802</td>
<td>1.504</td>
<td>0.2847</td>
<td></td>
</tr>
</tbody>
</table>
Japanese cancer patients was developed in 1993 and has since been used widely in Japan.\textsuperscript{31}

To evaluate the impact of treatment on the QOL, the patients were asked to answer QOL-ACD before and after therapy.

Moreover, patients no. 3, 5, 8 have been excluded from our evaluation for these cases, we forgot to collect the QOL-ACD from them. Among these patients, 2 achieved CR and the remaining 1 patient showed PD.

It was suggested that the patients with improved global, functional, or mental score after CRT tended to have a better prognosis, indicating that the changes of these domain scores may be of prognostic value. Compared with the pre-CRT scores, the changes of scores during CRT seemed to have greater prognostic significance. This might be due to personality-dependent, inter-individual variations in interpretation of the questionnaire used to obtain pre-CRT QOL scores. Concerning the relationship between QOL and tumor response, the patients with a higher psychosocial QOL score before CRT tended to show a better local response to treatment. This is consistent with the result obtained in the patients with non-small-cell lung cancer by Morita \textit{et al.}\textsuperscript{31} documenting that cancer patients had the greatest interest in the psychosocial aspects of their life. Further studies will be necessary to clarify why the psychosocial QOL of cancer patients has a relationship with the local response to treatment.

Among the clinical parameters assessed, only the clinical stage at the start of CRT was a significant predictor of survival. No other parameter, such as the nutritional status or tumor markers, had a significant relationship with survival time, indicating that neither the pre-CRT clinical status nor the changes after short-term treatment were of prognostic significance.

Age was the only potential predictor of the tumor response to CRT, and older patients tended to respond better. However, this might be explained by the fact that more of the elderly patients had early disease.

A retrospective comparison with historical controls who received 5-FU/CDGP-based CRT showed that our patients treated with TS-1/CDGP-based CRT had significantly more leave time during inpatient treatment. And more than half of the patients treated with this CRT regimen (53.3% \textsuperscript{[8/15]}) had an unchanged or improved global QOL score after treatment. This finding also supports the idea that esophageal cancer patients treated with TS-1/CDGP-based CRT may have more chance of maintaining their QOL than those treated with the standard 5-FU/CDDP-based CRT.

\textbf{Acknowledgments}

The authors appreciate the help of Yoshihide Tsuchiya of Biostatistics Department, Shionogi & Co., Ltd., and acknowledge the cooperation and support given by the members of the division of Gastroenterology and Hepatology, St. Marianna University School of Medicine.

\textbf{References}

7) Tatsumi K, Fukushima M, Shirasaka T and Fujii S. Inhibitory Effects of Pyrimidine, Barburiac Acid and Pyridine Derivatives on 5-Fluorouracil Degradation in Rat Liver Ex-
Quality of Life for Esophageal Cancer

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Quality Of Life を中心とした食道癌に対する
TS-1/CDGP 放射線併用療法の
臨床的検討

宮崎 彩
稲葉 博之
津田 享志
伊東 文生

抄 録

現在、食道癌に対する放射線化学療法（CRT）は患者の局所効果と生存効果が得られることで注目されている。

今回我々は、患者の QOL を維持する目的で食道癌に対する TS-1/CDGP 放射線併用療法の臨床試験を施行した。

2001年6月から2002年9月まで、TS-1/CDGP 放射線併用療法の臨床試験を開始し、計18例の臨床的検討をおこなった。
総合評価で奏効率は66.7%、著効率（CR 率）は50.0%であった。
QOL に関しては CRT 前、後に QOL-ACD を使用し検討した。
総合、活動性、精神性的QOLスコアが上昇した症例は有意に（significance）、もしくは marginal significance で予後が良かった。以前当科で行われた 5-FU を使用した放射線併用療法群と比較し TS-1/CDGP 放射線併用療法群は外出・外泊日数が有意に多かった。
食道癌に対する TS-1/CDGP 放射線併用療法は標準的治療である 5-FU/CDDP 放射線化学療法と比較し過色のない成績をおさめ重篤な副作用も認めず、また QOL が比較的維持できる治療と考えられた。

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